60 YEARS

SBFTE

PROGRAM & ABSTRACTS

58th Brazilian Congress of Pharmacology and Experimental Therapeutics

20th–23rd October 2026

João Pessoa Convention Center

XX FeSBE Regional Meeting

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Welcome Letter

Dear Colleagues,

On behalf of the Organising Committee, it is our great pleasure to welcome you to João Pessoa for the 60th Annual Congress of the Brazilian Society of Pharmacology and Experimental Therapeutics (SBFTE), held jointly this year with the 20th Regional Meeting of the Federation of Societies for Experimental Biology (FESBE), from 20–23 October 2026.

This year's meeting holds particular significance as we celebrate the Diamond Jubilee of SBFTE, marking 60 years of commitment to scientific excellence and contributions to the advancement of pharmacology and experimental therapeutics in Brazil. This landmark edition is further enriched by the 20th Regional Meeting of FESBE, bringing together the SBFTE and FESBE scientific communities and broadening opportunities for scientific exchange, interdisciplinary dialogue and collaboration. Hosting this special joint meeting in João Pessoa also highlights the growing scientific strength of Brazil's Northeast, a region renowned for its rich culture, biodiversity and expanding academic community.

The meeting brings together students and early-career researchers, established scientists, Brazilian and international guests, exhibitors and institutional partners, creating a diverse and stimulating environment for sharing knowledge, establishing new collaborations and strengthening connections across pharmacology and related fields of experimental biology.

The scientific programme will comprise symposia, keynote lectures, oral and poster presentations by distinguished Brazilian and international researchers, alongside the active participation of students and young investigators. Among its traditional highlights are the Rocha e Silva Memorial Lecture by Professor Clive Page (King's College London), the 3rd Brazilian Women in Pharmacology Award and the José Ribeiro do Valle Young Investigator Award. The programme will also feature the Second Science and Art Exhibition, celebrating the dialogue between scientific discovery, creativity and artistic expression within our community.

Together, these activities will provide a vibrant, inclusive and inspiring forum in which to exchange ideas, strengthen collaborations, celebrate scientific achievements and encourage the next generation of scientists.

As we celebrate 60 years of SBFTE, we honour the generations of scientists who have shaped our history while looking towards the future of pharmacology and experimental science with renewed enthusiasm and a shared commitment to advancing science and innovation in health.

We hope you enjoy an inspiring scientific programme, fruitful discussions and the warm hospitality of João Pessoa.

Welcome to the 60th Annual Congress of SBFTE and the 20th Regional Meeting of FESBE.

Warm regards,

Soraia K. P. Costa



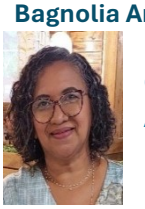
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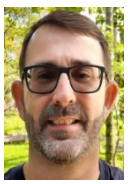
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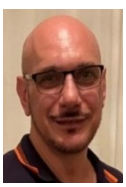
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About SBFTE Jovem

SBFTE Jovem is a committee composed of young pharmacologists within the Brazilian Society of Pharmacology and Experimental Therapeutics (SBFTE), founded in 2013. We work closely with the SBFTE Board of Directors in order to create a permanent political-scientific forum dedicated to undergraduate and graduate students, postdoctoral fellows, early-career researchers, and junior faculty. Our goal is to foster the discussion of Pharmacology-related scientific topics, support the development of early-career researchers, and encourage th e participation, integration, and collaboration of young members in SBFTE activities. This year, during the 58th Brazilian Congress of Pharmacology and Experimental Therapeutics in João Pessoa, we are organizing the following activities: **Promoting Pharmacology in Public Schools** – A science outreach initiative held on October 20th, 2026. In the morning, we will visit the *EEEFM Padre Roma* and in the afternoon, the students will visit the congress venue. With this project, we bring science education to high-school students through accessible language and interactive activities. At the congress, students are also invited to visit our stand and poster sessions to experience the scientific environment and witness knowledge exchange first-hand. **Meet the Expert**: A welcoming space for undergraduate and graduate students to interact with established professors, share experiences, and exchange ideas on career challenges, scientific projects, and academic development. This event will take place on October 21st, 2026, from 4:00 pm to 5:30 pm. **Beyond Academia Roundtable**: An open discussion on innovation, emerging scientific challenges, and opportunities beyond academic careers, including engagement with the pharmaceutical industry and other professional pathways. This session is scheduled for October 22nd, 2026, from 08:00 to 9:30 am. In addition, we are pleased to announce the **6th edition of the SBFTE Jovem Cultural Contest for Scientific Dissemination**, an initiative that promotes the popularization of science. This year, students are encouraged to produce creative and informative videos on the history of Pharmacology in Brazil using audiovisual resources, lay terms, and metaphors. Submissions are first evaluated by pharmacology professors and experts, and the finalists are then selected by public vote on social media. The winners will be announced during the Closing Session of the 2026 Congress. Finally, we warmly invite young pharmacologists to participate in our annual Assembly, to be held October 21st, 2026, from 12:00pm to 2:00 pm, to share your expectations, questions, plans, and prospects for the future. Can't make it? Visit our stand, open during the entire event with activities, charades, prize draws and more. Let's build the future of Pharmacology together.

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Useful Information

Congress Secretariat

The Congress Secretariat will be open daily from 7:30 am to 6:00 pm.
Please note that the scientific program starts at 8:00 am, so we recommend arriving early to allow enough time for registration and any necessary assistance.

Congress App – Makadu

Download the Makadu app to access the congress program and stay up to date with the latest information.
Through the app, you will be able to check the scientific program, session times and other congress information directly from your mobile device.
We recommend downloading the app before the beginning of the congress.

iOS - https://apps.apple.com/br/app/makadu-app-para-eventos/id923457992
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E-Posters

All e-posters will be available on the digital totems and will be presented according to the schedule below:

- ✓ **Session 1: October 20th,** 3:00 pm to 4:30 pm; **Session 2: October 21st**, 5:40 pm to 7:10 pm; **Session 3: October 23rd**, 9:30 am to 11:00 am

Certificates

Certificates will be made available online through each participant's individual login on the registration website (https://web.eventogyn.com.br/event/sbfte2026/site/content/participant-area) up to 10 days after the end of the Congress. You can download the PDF file in the Certificates area.

Course Certificates

Course certificates will be issued to participants who attend at least two classes.

Presentations – Speakers

All speakers are kindly requested to send their presentation, preferably by email by the day before their presentation.
Presentations should be sent in PDF or PowerPoint (PPT/PPTX) format to:

adm@criandoelo.com.br
gabriela@criandoelo.com.brgabriela@criandoelo.com.br

If it is not possible to send the presentation in advance, the file must be delivered in person at the Speakers' Desk, located at the Congress Secretariat, at least 2 hours before the scheduled presentation. All presentation rooms are equipped with a data projector. If you require additional equipment or technical support, please inform the Congress Secretariat in advance. The organizing committee will check the feasibility of your request.

Badges

The use of the congress badge is mandatory for all congress activities and for access to the event areas.
Please wear your badge visibly throughout the congress.

Food & Beverage

For the convenience of participants, the congress has arranged for **a cafeteria and a restaurant to operate at the Convention Center during the event**. The restaurant will offer **buffet lunch service**. Please note that **lunch is not included in the congress registration fee**, and all purchases at the restaurant and cafeteria are at the participant's own expense.

Abstracts

Abstracts presented during the Poster Sessions will be made available on the SBFTE website: https://sbfte.org.br/congressos-anteriores

Rocha e Silva Memorial Lecture



1984 *The role of endothelial cells and relaxation of vascular smooth muscle by acetilcoline and bradikinin*. Robert Furchgott (04/07)
1987 *Caracterização do fator de relaxamento arterial*. Salvador Moncada
1989 *Asma: uma doença inflamatória*. Boris Vargaftig
1991 *A morada Perigosa: morte e a vida da Leishmania nos fagolisossomas*. Michel Rabinovich
1993 *Structure, dinamics and functions of atrial natriuretic factor receptor*. Tomas Maack
1995 *Receptores para Bradicinina*. Domenico Regoli
1997 *Disfunções na produção de fatores vasoativos em doenças cardiovasculares* Paul Vanhoutte
1999 *Purinergic signalling*-Geoffrey Burnstock
2001 *Mecanismos celulares da Asma Brônquica*. Bernardo Boris Vargaftig
2003 *Pharmacology adventures down a long and winding Road*. John Wallace (University of Calgary)
2005 *Inflammation: my wanderings along Mauricio Rocha e Silva's trail*. Roderick John Flower (University of London, Inglaterra)
2007 *Can we develop anti-inflammatory drugs for infectious diseases*? Mauro Martins Teixeira (UFMG)
2009 *Understanding peripheral analgesics*. Sérgio Henrique Ferreira (USP)
2011 *Bradykinin revisited 62 years after its discovery*. João Batista Calixto (UFSC)
2012 *Discovery of nitric oxide and cyclic GMP in cell signaling and their role in drug development*. Ferid Murad (Nobel Prize Laureate, George Washington University, USA)
2014 *Resolution pharmacology: A new approach to anti-inflammatory therapy*. Mauro Perretti (The William Harvey Research Institute, UK)
2016 *The joy of discovery: My life in Pharmacology*, Salvador Moncada (University of Manchester, UK)
2018 *Functional selectivity and spatio-temporal propagation of GPCR signaling; from structural determinants to better drugs*. Michel Bouvier (University of Montreal, Canada)
2021 *6-NitroDopamine, the New kidDo in town*. Gilberto de Nucci (Unicamp)
2022 *Neuroprotective Mechanisms of Angiotensin II Receptor Blockers*. Juan M. Saavedra (Georgetown University, USA)
2024 *Calcitonin Gene-Related Peptide (CGRP) Agonists Protects against Remodeling in Heart Failure* .Susan D. Brain (King´s College London, UK)

Keynote Speaker - 2026 Mauricio Rocha e Silva Memorial Lecture

Six Decades of Pharmacology: Emerging Drug Targets and Therapies for Asthma and Chronic Obstructive Pulmonary Disease (COPD) Clive Page (Kings College, UK



Clive Page is Emeritus Professor of Pharmacology, King's College London and Director of The Pulmonary Pharmacology Unit, King's College London. Clive's main research interests are in the pharmacology of inflammation and respiratory disease, and he has published over 250 scientific papers. Clive was the co-founder and previous Chairman of the Board of Verona Pharma plc, an AIM listed Company developing new drugs for the treatment of respiratory diseases. He is a Non-Executive Director of Babraham Biotechnology Ltd, as well as being a Trustee of the Babraham Institute in Cambridge and a Non-Executive Director of the Board of ImmunoRegulation Ltd, PreP Biopharma and EpiEndo. Clive started his early career in the Pharmaceutical Industry at Sandoz Ltd, Basel, Switzerland and regularly consults to both the Pharmaceutical and Biotech Industry. Clive has previously held Non-Executive Board positions at Cardiome in Canada and Stirling Products Ltd in Perth, Australia. Clive is a recent former Chairman of the Animal Science Group of the Society of Biology and has contributed widely to the public debate about the use of animals in Research. He was awarded the Society of Biology President's Medal in 2012 for an outstanding contribution to the life sciences over the previous year. He is a Fellow of the Royal Society of Biology and an Honorary Fellow and President Elect of the British Pharmacological Society. In 2017, Clive was awarded an OBE for Services to Pharmacology

José Ribeiro do Valle Award (Sponsored by Biolab)

First Place Winner History



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1999: José Eduardo da Silva Santos (UFSC; Adviser: Jamil Assreuy)
2000: Ana Paula V. Dantas (USP-SP; Adviser: Maria Helena Catelli de Carvalho)
2001: Liliam Fernandes (USP-SP; Adviser: Maria Helena Catelli de Carvalho)
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2004: João Alfredo de Moraes (UERJ; Adviser: Thereza Christina Barja-Fidalgo)
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2007: Maria Fernanda de Paula Werner (UFSC; Adviser: Giles A. Rae)
2008: Ana Luiza Andrade de Paula Lopes (Unifesp-EPM; Adviser: Rosely O. Godinho)
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2025 Julia Sapienza Passos (USP-SP) Adviser: Luciana Biagini Lopes

José Ribeiro do Valle Award – 2025 Finalists



Natália Pressuto Pennachioni
BSc in Nursery (UFSCar) (2017 – 2021)
MsC in Biotecnology (USP-SP)
Adviser: Vanessa Olzon Zambelli

05.019 **Mitochondrial Aldehyde Dehydrogenase-2 and 4-Hydroxynonenal Mediates Morphine Analgesic Tolerance and Hyperalgesia via TRPA1 Activation**. Pennachioni NP[1,2], Hosch NG[1], Martins BB[1], Silva GSA[1], Troitiño VC[1,2], Dallazen JL[1,3], Kiataki LGS[1,3], Andersson D[4], Bevan S[4], Zambelli VO[1,3]. [1]IBu. Pain and Signaling Lab, IBu, São Paulo. [2]University of Sao Paulo, Interunits Biotechnology Postgraduate Program. [3]Kings College London, Wolfson Sensory, Pain and Regeneration Centre, [4]IBu, Centre of Excellence in New Target Discovery, São Paulo



Isaac Alef Barbosa Gomes
BSc in Biotechnology
MSc (2019 – 2025) (UFDPar)
Adviser: Lucas Antonio Duarte Nicolau

08.020 **Refluxate Components Drive NETosis and Promote Experimental Reflux Esophagitis Trough PAD4-Dependente Mechanisms**. Gomes IAB[1]; da Silva GCP[2]; Ramos AS[3]; Pérez MM[3]; Sales TMAL[3]; Costa VF[3]; Araújo AVV[1]; da Silva KS[1]; Medeiros JVR[1]; Saraiva EM[2]; Cunha FQ[3]; Nicolau LAD[1]. [1]UFDPar, PPG in Biotechnology, Brazil; [2]UFRJ, Dept Immunology, Brazil; [3]CRID-FMRP-USP, Brazil.



Samuel Duarte Maia
BSc in Biotechnology (UFPB) (2018-2023)
PhD in Pharmacology (Unicamp)
Adviser: Renato Simões Gaspar

06.040 **Glycated collagen drives vascular remodeling and smooth-muscle dysfunction in hyperglycemia**. Duarte-Maia S, Silva-Oliveira N, Simões Gaspar R. FCM-Unicamp, Depto Farmacologia, Lab Matriz Extracelular, PPG em Farmacologia



Stella Jasmine Arruda Coelho
BSc in Biomedicine (2021-2025) (UFPA)
PhD in Pharmacology (USP-RP)
Adviser: Felipe Villela Gomes

03.040 **Meningeal Inflammatory Responses and Long-Term Behavioral Alterations Induced by Adolescent Stress**. Coelho S, Pigatto G, Meschick CG Verza FA, Freitas IS, Grigório-de-Sant'Ana M, Guimaraes FS, Cunha TM, Gomes FV. FMRP-USP, PPG em Farmacologia , Brasil



José Yuri Gomes da Silva
BsC in Biological Sciences (2017-2022) (UFC)
MSc in Pharmacology (2022-2024) (UFC)
PhD in Pharmacology (UFC)
Adviser: Diego Veras Wilke

10.049 **Systems Biology Identifies a Chaperone-Mediated Network Associated with Doxorubicin Response and Poor Survival in Triple-Negative Breast Cancer**. Silva JYG[1], Azevedo GM[2], Dalmolin RJS[2], Wilke DV[1] [1]UFC, PPG Pharmacology, Brazil [2]UFRN, Bioinformatics Multidisciplinary Environment - BioME, IMD, Rio Grande do Norte, Natal, Brazil

Women in Pharmacology in Brazil Award (Sponsored by Eurofarma)

MULHERES NA FARMACOLOGIA NO BRASIL

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Category Emerging Leader: Prof. Dr Regina di Sordi (UFSC)

2024 Second Women in Pharmacology in Brazil Award
Category Leader: Leticia Veras Costa-Lotufo (USP-SP)
Category Emerging Leader: Cristina Aparecida Jark Stern (UFPR)

2026 Third Women in Pharmacology in Brazil Award
Category Leader: Rita C. A. Tostes (USP-RP)
Category Emerging Leader: Francislaine Aparecida dos Reis Lívero (UFPR)

II Mostra de Ciência & Arte – SBFTE

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✓ Maria Christina W. Avellar (Unifesp-EPM)
✓ Norberto Garcia-Cairasco (USP-RP)

Apresentação

A Sociedade Brasileira de Farmacologia e Terapêutica Experimental (SBFTE), pelo Grupo Especial de Iniciativas Educacionais SBFTE - IE/SBFTE, tem o prazer de apresentar as obras selecionadas para a II MOSTRA DE CIÊNCIA & ARTE SBFTE. Esta iniciativa, objetiva estimular a produção e a divulgação de obras digitais que unem ciência e arte, em temáticas de ciência, tecnologia e inovação na área de Farmacologia e Terapêutica Experimental e áreas afins, para contribuir com a divulgação e a popularização da ciência e tecnologia e contribuir para o acervo de materiais educacionais SBFTE. CIÊNCIA E ARTE é tendência global para incentivar a integração de tecnologias tradicionais e inovações eletrônico-digitais na produção de imagens artísticas associadas à pesquisa científica.

Aberta aos sócios da SBFTE, esta iniciativa visa: (i) revelar e divulgar trabalhos e obras digitais de qualidade, categorizados como "originais" ou "originais/inéditos", concebidos por "Cientistas-Artistas" ou resultantes da "Colaboração entre Cientistas e Artistas", originados em instituições de Ensino Superior e de Pesquisa no país ou no exterior, que intersectam as fronteiras dos conceitos e teorias da ciência incluindo o olhar e despertar de percepções da arte no campo da Farmacologia e Terapêutica Experimental e áreas afins e (ii) estimular estudantes e pesquisadores a incorporar conceitos e recursos de arte para expressar suas pesquisas e iniciativas educacionais que tenham adesão a temáticas de ciência, tecnologia e inovação em Farmacologia e Terapêutica Experimental.

A meta de estabelecer a Mostra Ciência & Arte SBFTE como evento permanente bianual no calendário da sociedade, está mostrando o sucesso da iniciativa, pelo maior interesse entre seus associados para participarem de um espaço para promoção e divulgação dos seus trabalhos/obras. Esperamos que as obras de nossos cientistas-artistas motivem a todos para participarem das próximas edições.

Atenciosamente,

Grupo Especial de Iniciativas Educacionais - IE/SBFTE

I Prêmio SBFTE de Excelência em Educação em Farmacologia

Grupo Especial de Iniciativas Educacionais - SBFTE (IE/SBFTE)

Comissão Julgadora das Obras:

- ✓ François Germain Noël (UFRJ, Coordenador)
- ✓ Jamille Nunes de Souza Ferro (UFAL,AL)
- ✓ Felipe B. Almeida (SBFTE jovem)
- ✓ Pablo Augusto Silva (USP)
- ✓ Giselle Zenker Justo (UNIFESP/EPM)

Apresentação

A Sociedade Brasileira de Farmacologia e Terapêutica Experimental (SBFTE), pelo Grupo Especial de Iniciativas Educacionais SBFTE - IE/SBFTE, tem o prazer de apresentar o **I PRÊMIO SBFTE DE EXCELÊNCIA EM EDUCAÇÃO EM FARMACOLOGIA**, uma iniciativa destinada a valorizar e divulgar experiências educacionais inovadoras relacionadas ao ensino de Farmacologia. Esta iniciativa busca fortalecer a educação em Farmacologia como eixo estratégico para uma formação científica crítica, ética, inovadora e socialmente comprometida, estimulando novas formas de ensinar e aprender e promovendo a integração entre diferentes metodologias, recursos e estratégias educacionais.

Aberto a toda comunidade de docentes, pesquisadores, pós-graduandos, graduandos e profissionais envolvidos com atividades educacionais em Farmacologia, o Prêmio visa: (i) dar visibilidade a experiências inovadoras no ensino de Farmacologia, Terapêutica e Toxicologia; (ii) promover a troca de experiências entre docentes, pesquisadores e estudantes; (iii) incentivar a disseminação de metodologias, recursos e estratégias educacionais inovadoras; (iv) reconhecer iniciativas que contribuam para a melhoria da formação em Farmacologia; e (v) fortalecer a atuação da IE/SBFTE como espaço permanente de compartilhamento de práticas educacionais.

As experiências educacionais foram apresentadas nas modalidades **Relato de Experiência Educacional** ou **Produto Educacional**, contemplando estratégias, atividades, projetos, disciplinas, ações extensionistas, intervenções educacionais e recursos destinados a apoiar os processos de ensino e aprendizagem. Entre as temáticas de interesse estavam a gamificação e aprendizagem baseada em jogos, tecnologias educacionais, inteligência artificial aplicada ao ensino, estratégias inovadoras de avaliação, desenvolvimento de materiais didáticos, simulações e estudos de caso, integração ensino-pesquisa-extensão, formação docente e discente, ensino lúdico e artes no ensino, entre outras experiências inovadoras voltadas ao ensino de Farmacologia.

Convidamos a todos participantes do congresso a visitarem a **Mostra de Experiências Educacionais da IE/SBFTE**, realizada durante o 58º Congresso da SBFTE, para conhecerem as diversas experiências educacionais sobre Farmacologia que estão ocorrendo no Brasil. Convidamos a todos para assistirem as apresentações das 5 experiências selecionadas para comporem o **Laboratório de Ideias da IE/SBFTE**, em uma sessão de Experiências Inspiradoras, promovendo o compartilhamento, a reflexão crítica e a construção coletiva de caminhos para o fortalecimento da educação em Farmacologia.

A meta é estabelecer o **Prêmio SBFTE de Excelência em Educação em Farmacologia** como uma iniciativa permanente de reconhecimento e valorização da excelência educacional, permitindo à sociedade promover, compartilhar e disseminar experiências capazes de transformar os processos de ensino e aprendizagem em Farmacologia. Esperamos que as experiências apresentadas inspirem docentes, pesquisadores e estudantes e estimulem a todos a participar das próximas edições.

Atenciosamente,

Grupo Especial de Iniciativas Educacionais - IE/SBFTE

Produtos Educacionais

1) **Título:** Ensino da Farmacologia Baseado em Mapas Mentais
Autores: Vitor Mateus Machado Schneider; Regina Azevedo Costa; Ana Paula da Silva Borges; Thaís Alencar de Souza; Darciane Favero Baggio; Aleksander Roberto Zampronio
Instituição: Universidade Federal do Paraná

2) **Título:** Entre sintoma e prognóstico: um Escape Room para o ensino da Farmacologia da Insuficiência Cardíaca
Autores: Mariana Santos de Paula; Rayssa Rafaella Moura Ribeiro; Arisa Namie Higashijima; Camila Silva Bezerra; Leticia Ribeiro Ferreira; Nattaly Viana Lowen; Rafaela Caroline Santa Clara de Amorim; Francislaine Aparecida dos Reis Lívero
Instituição: Universidade Federal do Paraná

3) **Título:** Farmagol: uma estratégia de gamificação baseada no futebol de botão para a aprendizagem ativa em farmacologia
Autores: Railson Pereira Souza; Milena Monteiro de Freitas; Kauan Ferreira da Rocha; Aldeídia Pereira de Oliveira
Instituição: Universidade Federal do Piauí

4) **Título:** Glossário Ilustrado e Interativo de Farmacologia: desenvolvimento de uma tecnologia educacional para o ensino e a aprendizagem significativa nas Ciências da Saúde
Autores: Railson Pereira Souza; Aldeídia Pereira de Oliveira
Instituição: Universidade Federal do Piauí

5) **Título:** Integração de Metodologias Ativas e Tecnologias Inovadoras na Aprendizagem em Farmacologia – Construção de Produtos Educacionais
Autores: Gabriela Soares da Silva; Alice Reis do Nascimento; Yhorrana Silva Gonçalves; Giovanna Lemes Dorneles; Patrícia Ferreira da Silva Castro
Instituição: Universidade Estadual de Goiás

6) **Título:** Mapeando a Hemostasia: produto educacional para desenvolver o raciocínio farmacológico em cenários de decisão clínica
Autores: Nattaly Viana Lowen; Rafaela Caroline Santa Clara de Amorim; Arisa Namie Higashijima; Camila Silva Bezerra; Leticia Ribeiro Ferreira; Mariana Santos de Paula; Rayssa Rafaella Moura Ribeiro; Francislaine Aparecida dos Reis Lívero
Instituição: Universidade Federal do Paraná

7) **Título:** Mapear o alvo, compreender o fármaco: aprendizagem por estações no ensino da farmacologia cardiometabólica
Autores: Arisa Namie Higashijima; Camila Silva Bezerra; Leticia Ribeiro Ferreira; Mariana Santos de Paula; Nattaly Viana Lowen; Rayssa Rafaella Moura Ribeiro; Rafaela Caroline Santa Clara de Amorim; Francislaine Aparecida dos Reis Lívero
Instituição: Universidade Federal do Paraná

8) **Título:** Metaboly: um jogo de tabuleiro para integrar fisiopatologia, farmacologia e tomada de decisão terapêutica na obesidade
Autores: Leticia Ribeiro Ferreira; Camila Silva Bezerra; Arisa Namie Higashijima; Mariana Santos de Paula; Nattaly Viana Lowen; Rayssa Rafaella Moura Ribeiro; Rafaela Caroline Santa Clara de Amorim; Francislaine Aparecida dos Reis Lívero
Instituição: Universidade Federal do Paraná

9) **Título:** Operação anabolizante: um micromundo lúdico e gamificado no Minecraft® para o ensino de farmacologia na educação física
Autores: Márcia Regina Holanda da Cunha; Sâmela da Silva Santos; Fabiana de Andrade Cavalcante Oliveira; Maria Tereza Martins de Araújo; João Vitor Santana Torres
Instituição: Universidade Federal do Espírito Santo e Universidade Federal da Paraíba

10) **Título:** PharmaMind Learning Framework (PLF): um ecossistema inteligente de aprendizagem adaptativa para o desenvolvimento do raciocínio clínico-farmacológico
Autores: Eduardo Mariano de Andrade; Alana Martins Gonçalves; Péterson Alves Santos
Instituição: UNINTER – Centro Universitário Internacional; Universidade Federal do Rio Grande do Sul; Instituto Federal do Rio Grande do Sul

11) **Título:** Planejar, imprimir e aplicar: 13 recursos didáticos para o ensino da Farmacologia Cardiometabólica com metodologias ativas
Autores: Rafaela Caroline Santa Clara de Amorim; Arisa Namie Higashijima; Camila Silva Bezerra; Leticia Ribeiro Ferreira; Mariana Santos de Paula; Nattaly Viana Lowen; Rayssa Rafaella Moura Ribeiro; Francislaine Aparecida dos Reis Lívero
Instituição: Universidade Federal do Paraná

12) **Título:** Que Ligante Farmacológico Sou Eu? - Um jogo educacional para o ensino de farmacodinâmica
Autores: César Augusto Manduca e Silva; Marla de Oliveira Calazans; Izadora Rodrigues Dias Martins; Júlia Fonseca Pereira; Marina Gomes Miranda e Castor; Stefany Bruno de Assis Cau
Instituição: Universidade Federal de Minas Gerais

13) **Título:** Quem Sou Eu? Farmacologia em Pistas: uma metodologia ativa e gamificada para transformar a revisão em investigação farmacológica
Autores: Thaís Alencar de Souza; Darciane Favero Baggio; Ana Paula da Silva Borges; Regina Azevedo Costa; Vitor Mateus Machado Schneider; João Henrique da Silva Filho; Thayna Fujisawa Lima; Aleksander Roberto Zampronio
Instituição: Universidade Federal do Paraná

Relatos de experiência educacional

1) **Título:** "Drug Challenge": gamificação na educação sobre substâncias psicoativas lícitas em uma ação de Extensão Universitária com estudantes do Ensino Médio
Autores: Ana Olívia Martins Laurentino; Gabriella Duarte de Oliveira; Ashley Isabelle de Medeiros; Rosane Gomez; Mirna Bainy Leal
Instituição: Universidade Federal do Rio Grande do Sul

2) **Título:** Bora Falar de Farmacologia? Gamificação e Metodologias Ativas na Popularização da Ciência para o Ensino Médio
Autores: Caio Henrique Willrich; Bruna Longo; Luana Nunes Mariot; Livia Melo Arruda Cunha; Isabella Mazuco de Oliveira; Marcos Rizzon Santos; Fernanda de Souza Guterres; Gabriel Estevam Santos Amorin; Luisa Mota da Silva
Instituição: Universidade Federal de Santa Catarina

3) **Título:** Canastra farmacológica: um jogo educacional para o ensino ativo da farmacocinética
Autores: Mariana Correia de Oliveira Alves; André Luiz Costa de Souza
Instituição: Universidade de São Paulo; Universidade São Judas; Universidade Cruzeiro do Sul

4) **Título:** Discutindo a potência de antagonistas usando aorta de rato: proposta de uma abordagem educacional para a pós-graduação em Farmacologia
Autores: Maisa Sousa Sampaio; Kalinne Kelly Lima Gadelha; Karine Lima Silva; Abdourahmane Dairou; Maria

Eduarda Damasceno Veríssimo de Araújo; Nicole Castro Brasil; Armênio Aguiar dos Santos; Pedro Jorge Caldas Magalhães
Instituição: Universidade Federal do Ceará

5) **Título:** Ensinar Farmacologia por meio de controvérsias científicas: uma experiência de aprendizagem ativa na pós-graduação
Autores: Camila Silva Bezerra; Rayssa Rafaella Moura Ribeiro; Mariana Santos de Paula; Arisa Namie Higashijima; Leticia Ribeiro Ferreira; Nattaly Viana Lowen; Rafaela Caroline Santa Clara de Amorim; Francislaine Aparecida dos Reis Lívero
Instituição: Universidade Federal do Paraná

6) **Título:** Estratégias Gamificadas Inspiradas em Programas de Auditório para Revisão de Conteúdos em Farmacologia
Autores: Mauricio Schüler Nin
Instituição: Universidade Federal de Ciências da Saúde de Porto Alegre

7) **Título:** Explorando o conceito de atividade constitutiva de receptores em abordagem didática com aorta isolada de rato
Autores: Abdourahmane Dairou; Maria Eduarda Damasceno Veríssimo de Araújo; Nicole Castro Brasil; Maisa Sousa Sampaio; Kalinne Kelly Lima Gadelha; Armênio Aguiar dos Santos; Pedro Jorge Caldas Magalhães
Instituição: Universidade Federal do Ceará

8) **Título:** O método de rotação por estações no ensino de farmacologia
Autores: Ana Paula Herrmann; Angelo Piato
Instituição: Universidade Federal do Rio Grande do Sul

9) **Título:** Farmacologia: integrando a teoria e a prática da prescrição racional de medicamentos
Autores: Luiz Antonio Ranzeiro de Bragança; Lucas Vazquez Barreira Ranzeiro de Bragança
Instituição: Universidade Federal Fluminense

Trabalhos premiados

1º Lugar – Produto Educacional

Título: Operação anabolizante: um micromundo lúdico e gamificado no Minecraft® para o ensino de farmacologia na educação física
Autores: Márcia Regina Holanda da Cunha; Sâmela da Silva Santos; Fabiana de Andrade Cavalcante Oliveira; Maria Tereza Martins de Araújo; João Vitor Santana Torres
Instituição: Universidade Federal do Espírito Santo e Universidade Federal da Paraíba

2º Lugar – Relato de Experiência Educacional

Título: "Drug Challenge": gamificação na educação sobre substâncias psicoativas lícitas em uma ação de Extensão Universitária com estudantes do Ensino Médio
Autores: Ana Olívia Martins Laurentino; Gabriella Duarte de Oliveira; Ashley Isabelle de Medeiros; Rosane Gomez; Mirna Bainy Leal
Instituição: Universidade Federal do Rio Grande do Sul

3º Lugar – Relato de Experiência Educacional

6) **Título:** Estratégias Gamificadas Inspiradas em Programas de Auditório para Revisão de Conteúdos em Farmacologia
Autores: Mauricio Schüler Nin
Instituição: Universidade Federal de Ciências da Saúde de Porto Alegre

4º Lugar – Produto Educacional

Título: Entre sintoma e prognóstico: um Escape Room para o ensino da Farmacologia da Insuficiência Cardíaca
Autores: Mariana Santos de Paula; Rayssa Rafaella Moura Ribeiro; Arisa Namie Higashijima; Camila Silva Bezerra; Leticia Ribeiro Ferreira; Nattaly Viana Lowen; Rafaela Caroline Santa Clara de Amorim; Francislaine Aparecida dos Reis Lívero
Instituição: Universidade Federal do Paraná

5º Lugar – Relato de Experiência Educacional

Título: O método de rotação por estações no ensino de farmacologia
Autores: Ana Paula Herrmann; Angelo Piato
Instituição: Universidade Federal do Rio Grande do Sul

Comissão Julgadora Prêmio SBFTE de Excelência em Educação em Farmacologia
François Germain Noël (UFRJ, Coordenador)
Jamille Nunes de Souza Ferro (UFAL, AL)
Felipe B. Almeida (SBFTE jovem)
Pablo Augusto Silva (USP)
Giselle Zenker Justo (Unifesp-EPM)

Scientific Program at a Glance

Oct 20th, 2026 (Tuesday)

8:00 am	SBFTE e Divulgação de Farmacologia na Escola Pública (Promoting Pharmacology in Primary Public Schools in João Pessoa, PB)							
8:00 am	Venue Secretariat							
	Mauricio Rocha e Silva Auditorium	**Jose Ribeiro do Valle Auditorium**	**Alexandre P. Corrado Auditorium**	**Hanna A. Rothschild Auditorium**	**Elisaldo Carlini Auditorium**	**Eline S. Prado Room**	**João Garcia Leme Room**	**Oswaldo Vital Brasil Room**
8:30 am Pre-Congress Course				**Active Methodologies in Pharmacology Education: From Theory to Practice with PBL, Problem-Based Learning, and Playful Strategies** (Presented in Portuguese)				
9:00 am								**Meeting** Board of SBFTE Directors and Advisory Board Members
10:45 am	Interval							
11:00 am			**Meeting** SBFTE Permanent Forum of Graduate Courses in Pharmacology					
12:00 pm	Lunch							
1:30 pm			**Roundtable** RT1 – **Soberania Científica em Debate: Regulação, Biotérios, Importação e os**	**Pre-Congress Course:** **Active Methodologies in Pharmacology Education: From Theory to Practice**				

			Desafios da Pesquisa Brasileira (Presented in Portuguese)	**with PBL, Problem-Based Learning, and Playful Strategies** (Presented in Portuguese)				
3:00 pm **Foyer**	**Poster Session 1** (with Coffee break)							
4:40 pm	**Opening** II Mostra de Arte & Ciência SBFTE (I Science and Art Exhibit – SBFTE)							
5:40-pm	**Opening Session**							
06:10 pm **Opening Lecture** *Rocha e Silva Memorial Lecture*	L1 – **Six Decades of Pharmacology: Emerging Drug Targets and Therapies for Asthma and Chronic Obstructive Pulmonary Disease (COPD)**							

Oct 21st, 2026 (Wednesday)

8:00 am	II Mostra de Arte & Ciência SBFTE (I Science and Art Exhibit – SBFTE)						
8:00 am	Venue Secretariat and SBFTE Secretariat Opening						
	Mauricio Rocha e Silva Auditorium	**Jose Ribeiro do Valle Auditorium**	**Alexandre P. Corrado Auditorium**	**Hanna A. Rothschild Auditorium**	**Elisaldo Carlini Auditorium**	**Eline S. Prado Room**	**João Garcia Leme Room**
8:00 am Courses		Cr1 – **Pharmacology-Oriented Metabolomics: Biomarker Discovery and Therapeutic Targets** (Metabolômica Orientada à Farmacologia: Descoberta de Biomarcadores e Alvos Terapêuticos)	Cr2 – **Introduction to Atomistic Simulations of Biomolecular Systems for Drug Development** (Introdução a Simulações Atomísticas de Sistemas Biomoleculares para Desenvolvimento de Fármacos)	Cr3 – **Statistical Delusions and Questionable Research Practices** (Delírios Estatísticos e Práticas Questionáveis de Pesquisa)	Cr4 – **Pharmacogenetics, Toxicology, and Clinical Practice** (Farmacogenética, Toxicologia e Prática Clínica)		
09:15 am	**Coffee break**						
9:40 am Symposia / XX FeSBE Regional Meeting		S1 – **Molecular Pharmacology: How Fine can We Tune?**	S2 – **Molecular Mechanisms of Neuronal Signaling and Therapeutic Modulation in Brain Function and Disease**	S3 – **Vascular Signaling in the Gut–Lung Axis during Infectious Disease**	**SBFTE Educational Initiatives- Ideas Laboratory: Building the Future of Pharmacology Education** (Laboratório de Ideias da IE-SBFTE: Construindo o Futuro da Educação em Farmacologia)	SFR1– **Endocrine Disruptors Chemicals and DOHaD**	SFR2 – **Teaching in Basic Health Sciences: Successful Experiences**
11:15 am Lectures / XX FeSBE Regional Meeting		L2 – **Traveling Along the Neutrophil Recruitment Cascade**	L3 – **Potential Physiopathological Roles of the Novel Endogenous Catecholamines**	L4 – **Transfer of Chronic Primary Pain from Patients to Mice; Novel Insights and Opportunities**	L5 – **Human PMN-MDSCs: Novel Insights for Old Unanswered and Newly Emerging Questions**	LFR1 – **Update on DOHaD Concepts**	LFR2 – **Theranostic Radiopharmaceuticals: The New Frontier of Translational Pharmacology**
12:05 pm	**Lunch**						
12:05 pm						**SBFTE Young Assembly** (with Lunch Box)	
02:05 pm Symposia		S4 – **Cell Communication on Immune Response,**	S5 – **Biomarkers in Cancer: An Opportunity**	S6 – **Across Land, Water, and Air: Animal**	SFR3 – **Gut Microbiome and Cardiometabolic Health: Experimental**	SFR4 – **Impacts of the Perinatal Environment on Health and Disease**	SFR5 – **Biology of Nicotine and Respiratory Diseases**

XX FeSBE Regional Meeting		**Aldosteronism, and Hypertension: Old Questions, New Insights**	**for the Development of New Drugs**	**Models in Psychopharmacology**	**Basis for Nutraceutical Interventions**		
03:35 pm	**Coffee break**						
4:00 pm			**Meet the Expert**	**Meeting** N-NE and CW Region Pharmacology Network	TSFR1– **From Bench to Bedside in Pain Research: New Targets, Analgesics and Therapeutic Strategies**	TSFR2 – **Developmental Programming of Cardiometabolic Diseases: From Early-Life Insults to Adult Health**	TSFR3 - **Neuroimmunology: Basic and Translational Aspects**
5:40 pm	**Poster Session 2**						

Oct 22nd, 2026 (Thursday)

8:00 am	II Mostra de Arte & Ciência SBFTE (I Science and Art Exhibit – SBFTE)						
8:00 am	Venue Secretariat and SBFTE Secretariat Opening						
	Mauricio Rocha e Silva Auditorium	**Jose Ribeiro do Valle Auditorium**	**Alexandre P. Corrado Auditorium**	**Hanna A. Rothschild Auditorium**	**Elisaldo Carlini Auditorium**	**Eline S. Prado Room**	**João Garcia Leme Room**
8:00 am Symposia / Roundtable / XX FeSBE Regional Meeting		S7 – **Advances in Model-Informed Precision Dosing for Antimicrobials**	S8 – **Targeting Cellular Dysfunction in Complex Diseases: From Cancer to Parkinsonism**	RT2 – **Beyond Academia**	SFR6 – **Research in Ecophysiology and Comparative Physiology in the Northeast Region: Challenges and Perspectives**	SFR7 – **Pain, Inflammation and Emotion: Therapeutic Challenges and Opportunities**	TSFR4 – **From Model to Mechanism: The Role of Experimental Choice in Pharmacological Research**
9:30 am	**Coffee break**						
10:00 am	**José Ribeiro do Valle Award**						
11:40 am	**Lunch**						
11:40 am **Technical Lecture**				**Cortellis Drug Discovery Intelligence: A Platform for Transforming Knowledge into Pharmacological Innovation**			
12:40 pm	**SBFTE Assembly**						
2:00 pm	**RT3 – Celebrating 60 years** **SBFTE aos 60 anos: O Futuro da Farmacologia no Brasil – Formação, Identidade, Representação e Avaliação da Qualidade dos Programas de Pós-Graduação** (SBFTE at 60: The Future of Pharmacology in Brazil -						

	Training, Identity, Representation and Quality Assessment of Graduate Programmes)						

Oct 23rd, 2026 (Friday)

8:00 am	II Mostra de Arte & Ciência SBFTE (I Science and Art Exhibit – SBFTE)						
8:00 am	Venue Secretariat and SBFTE Secretariat Opening						
	Mauricio Rocha e Silva Auditorium	**Jose Ribeiro do Valle Auditorium**	**Alexandre P. Corrado Auditorium**	**Hanna A. Rothschild Auditorium**	**Elisaldo Carlini Auditorium**	**Eline S. Prado Room**	**João Garcia Leme Room**
8:00 am **Courses**		Cr1 – **Pharmacology-Oriented Metabolomics: Biomarker Discovery and Therapeutic Targets** (Metabolômica Orientada à Farmacologia: Descoberta de Biomarcadores e Alvos Terapêuticos)	Cr2 – **Introduction to Atomistic Simulations of Biomolecular Systems for Drug Development** (Introdução a Simulações Atomísticas de Sistemas Biomoleculares para Desenvolvimento de Fármacos)	Cr3 – **Statistical Delusions and Questionable Research Practices** (Delírios Estatísticos e Práticas	Cr4 – **Pharmacogenetics, Toxicology, and Clinical Practice** (*Farmacogenética, Toxicologia e Prática Clínica*)		
09:30 am	**E-Poster Session 3**						
11:00 am	**Coffee break (Brunch)**						
11:30 am **Lectures / XX FeSBE Regional Meeting**		L6 – **Translational Perspectives on Psychoactive Therapies for Cognitive and Substance Use Disorders**	L7 – **Regulation of Cardiovascular Functions during Extreme Conditions in Reptiles**	LFR3 – **Medicalization of Suffering and Use of Psychotropic Drugs: An Evidence-Based Analysis**	LFR4 – **The DOHaD Paradigm at the Crossroads of Nutritional Transition**		
12:30 pm **Closing Lecture**	Brazilian Women in Pharmacology Award– 2026 Edition **Closing Ceremony**						
1:50 pm							

Scientific Program

Oct 20th, 2026 (Tuesday)

8:00 am	Venue Secretariat
8:00 am	**SBFTE e Divulgação de Farmacologia na Escola Pública** (Promoting Pharmacology in Primary Public Schools in João Pessoa, PB) Escola Estadual de Ensino Fundamental e Médio Padre Roma (Estudantes dos 2º e 3º anos do Ensino Médio) Chairs: Soraia K. P. Costa (SBFTE President, USP-SP) / Isis Nem de Oliveira Souza (Coordinator SBFTE Jovem Committee, UFRJ)
8:30 am-12:00 pm	Pre-Congress Course
Hanna A. Rothschild Auditorium	**Active Methodologies in Pharmacology Education: From Theory to Practice with PBL, Problem-Based Learning, and Playful Strategies** (Metodologias Ativas no Ensino de Farmacologia: da Teoria à Prática com PBL, Problematização e Estratégias Lúdicas) (Presented in Portuguese) **Chair**: Francislaine Aparecida dos Reis Lívero (Educational Initiatives Coordinator, UFPR)
9:00 am-10:30 am Oswaldo Vital Brasil Room	**Meeting of the Board of SBFTE Directors and** Advisory Board Members (Advisory Board and Directory Board Members only)
10:45 am-11:00 am	Interval
11:00 am-12:30 pm Alexandre P. Corrado Auditorium	Meeting of SBFTE Permanent Forum of Graduate Courses in Pharmacology
1:30-16:30	Pre-Congress Course
Hanna A. Rothschild Auditorium	**Active Methodologies in Pharmacology Education: From Theory to Practice with PBL, Problem-Based Learning, and Playful Strategies** (Metodologias Ativas no Ensino de Farmacologia: da Teoria à Prática com PBL, Problematização e Estratégias Lúdicas) (Presented in Portuguese) **Chair**: Francislaine Aparecida dos Reis Lívero (SBFTE Educational Initiatives, UFPR)
12:00 pm-1:30 pm	Lunch
1:30 pm-3:00 pm	Roundtable
Alexandre P. Corrado Auditorium	RT1 – **Soberania Científica em Debate: Regulação, Biotérios, Importação e os Desafios da Pesquisa Brasileira** (Debating Scientific Sovereignty: Regulation, Animal Research Facilities, Imports, and the Challenges of Brazilian Research) (Presented in Portuguese) **Chairs**: Bibiana Verlindo Araújo (Coordinator Permanent Forum of Graduate Courses in Pharmacology, UFRGS) / Soraia K. P. Costa (SBFTE President, USP-SP) • Márcio Flávio Dutra de Moraes (Concea, UFMG) • Jose Luiz Jivago de Paula Rolo (UnB) • Ricardo Gattass (UFRJ)
3:00 pm-4:30 pm	**E-Poster Session 1** (with Coffee break)

	01. Cellular and Molecular Pharmacology
	Totem 01: 01.001-01.003
	02. Neuropharmacology
	Totem 02: 02.001-02.006
	Totem 03: 02.020-02.025, 02.038
	Totem 04: 02.026-02.031
	Totem 05: 02.042-02.045, 02.059
	Totem 06: 02.060-02.066
	03. Psychopharmacology
	Totem 07: 03.001-03.006
	Totem 08: 03.018-03.022
	04. Inflammation and Immunopharmacology
	Totem 01: 04.001-04003
	Totem 09: 04.020-04.024
	Totem 10: 04.036-04.042, 04.061, 04.062
	Totem 11: 04.043-04.049
	Totem 12: 04.064-04.068
	Totem 13: 04.069-04.073
	04. Biology and Cardiovascular Diseases
	Totem 20: 04.006FR, 04.007FR
	05. Pain and Nociception Pharmacology
	Totem 14: 05.001-05.007, 05.011
	Totem 15: 05.015-05.021, 05.027
	Totem 16: 05.029-05.033
	Totem 17: 05.041-05.043
	05. Biology and Gastrointestinal Diseases
	Totem 27: 05.001FR
	06. Cardiovascular and Renal Pharmacology
	Totem 18: 06.001-06.005
	Totem 19: 06.017-06.023
	Totem 20: 06.031-06.034
	Totem 21: 06.035-06.040
	Totem 22: 06.057-06.059
	06. Biology and Metabolic and Reproductive Diseases
	Totem 24: 06.001FR-06.006FR
	08. Respiratory and Gastrointestinal Pharmacology
	Totem 25: 08.001-08.006
	Totem 26: 08.019-08.023
	Totem 27: 08.024-08.027
	Totem 28: 08.039-08.045
	09. Natural Products and Toxinology
	Totem 22: 09.090-09.092
	Totem 29: 09.001, 09.003-09.005
	Totem 30: 09.052-09.057,
	Totem 31: 09.072-09.078
	Totem 32: 09.093-09.096

	10. Cancer Pharmacology **Totem 33:** 10.001-10.006 **Totem 34:** 10.037-10.041 **Totem 35:** 10.043, 10.044, 10.046-10.049 **Totem 36:** 10.063-10.066 **10. DOHaD and Developmental Biology** **Totem 41:** 10.002FR-10.005FR **Totem 42:** 10.006FR-10.009FR **Totem 43:** 10.010FR-10.012FR, 10.016FR **11. Clinical Pharmacology, Pharmacokinetics, Pharmacogenomics and Toxicology** **Totem 37:** 11.012-11.017 **12. Drug Discovery and Development** **Totem 38:** 12.001-12.006 **Totem 39:** 12.028-12.032 **13. Pharmacology Education** **Totem 40:** 13.001-13.008 **13. Immunology, Microbiology and Parasitology** **Totem 29:** 13.003FR **14. Pharmacology: Other** **Totem 44:** 14.011-14.015 **15. Neurobiology and Neuronal Diseases** **Totem 05:** 15.008FR, 15.009FR **Totem 06:** 15.010FR **Totem 23:** 15.001FR-15.005FR **16. Toxinology, Natural Products and Medicinal Chemistry** **Totem 29:** 16.001FR, 16.002FR **Totem 32:** 16.007FR
Mauricio Rocha e Silva Auditorium	
4:40 pm-5:35 pm	**Opening II Mostra de Arte & Ciência SBFTE** (I Science and Art Exhibit – SBFTE)
5:40 pm-6:10 pm	**Opening Session**
6:10 pm-7:00 pm	**Opening Lecture**
	Rocha e Silva Memorial Lecture L1 – **Six Decades of Pharmacology: Emerging Drug Targets and Therapies for Asthma and Chronic Obstructive Pulmonary Disease (COPD)** Clive Page (Kings College, UK) Presented by Soraia K P Costa (USP-SP)
	Cocktail

Oct 21st, 2026 (Wednesday)

08:00 am	II Mostra de Arte & Ciência SBFTE (I Science and Art Exhibit – SBFTE)
08:00 am	Venue Secretariat and SBFTE Secretariat Opening
08:00 am-09:15 am	**Courses**
Jose Ribeiro do Valle Auditorium	Cr1 – **Pharmacology-Oriented Metabolomics: Biomarker Discovery and Therapeutic Targets** (Metabolômica Orientada à Farmacologia: Descoberta de Biomarcadores e Alvos Terapêuticos) (Presented in Portuguese) **Chair**: Adriane Ribeiro Rosa (UFRGS) • Class 1: *Integrated metabolomics: concepts, workflow, and instrumental technologies* (*Metabolômica integrada: conceitos, fluxo de trabalho e tecnologia instrumental*) Adriane Ribeiro Rosa (UFRGS)
Alexandre P. Corrado Auditorium	Cr2 – **Introduction to Atomistic Simulations of Biomolecular Systems for Drug Development** (Introdução a Simulações Atomísticas de Sistemas Biomoleculares para Desenvolvimento de Fármacos) (Presented in Portuguese) **Chair**: Marcelo N. Muscará (USP-SP) • Class 1: *Theoretic and practical fundamentals of atomistic simulations and molecular dynamics in biomolecular systems*. (*Fundamentos teóricos e práticos de simulações atomísticas e de dinâmica molecular em sistemas biomoleculares*) Santiago Di Lella (University of Buenos Aires , Argentina)
Hanna A. Rothschild Auditorium	Cr3 – **Statistical Delusions and Questionable Research Practices** (Delírios Estatísticos e Práticas Questionáveis de Pesquisa) (Presented in Portuguese) **Chair**: Ana Paula Herrmann (UFRGS) • Class 1: *Mindless statistics and the illusion of p<005* (*Estatísticas sem sentido e a ilusão do p<0,05*) Ana Paula Herrmann (UFRGS)
Elisaldo Carlini Auditorium	**Pharmacogenetics, Toxicology, and Clinical Practice** (Farmacogenética, Toxicologia e Prática Clínica) (Presented in Portuguese) **Chair**: Paulo Caleb Júnior de Lima Santos (Unifesp-EPM) • Class 1: *Pharmacogenetics in clinical practice: integrating evidence and therapeutic decision-making* (*Farmacogenética na prática clínica: integrando evidências e tomada de decisões terapêuticas*) José Wilson do Nascimento Correa (UFAM) / Paulo Caleb J. L. Santos (Unifesp-EPM)
09:15 am-09:35 am	**Coffee break**
09:40 am-11:10 am	**Symposia / XX FeSBE Regional Meeting**
Jose Ribeiro do Valle Auditorium	S1 – **Molecular Pharmacology: How Fine can We Tune?** **Chair**: Marcelo Nicolás Muscará (USP-SP) • *Insights into* Mycobacterium tuberculosis *from computer simulations: can this knowledge help new treatments*? Luciana Capece (University of Buenos Aires, Argentina) • *Unravelling the catalytic mechanism of thiol-based redox enzymes* Ari Zeida (University of the Republic, Uruguay)

	• *Engineering antiviral biopharmaceuticals* Roberto Dias Lins Neto (Fiocruz)
Alexandre P. Corrado Auditorium	S2 – **Molecular Mechanisms of Neuronal Signaling and Therapeutic Modulation in Brain Function and Disease** **Chair**: Luciene Bruno Vieira (UFMG) • *Sex-Specific G protein-coupled receptor signaling in Alzheimer's disease mice* Stephen Ferguson (University of Ottawa, Canada) • *mGlur5 positive allosteric modulators to treat neurodegeneration* Fabíola Mara Ribeiro (UFMG) • *Oral Communication 1:* 02.019 *Effects of the lithium treatment on early stage of Sporadic Alzheimer's* (*sAD*) *Disease in male rats*. Lima, TF, Kanazawa LKS, Fernandes, SMA, Vital, MABF. UFPR, Pharmacology Dept, Brazil • *Oral Communication 2:* 02.024 *Integrated network pharmacology, molecular docking, and cellular analysis of beta-ciclodextrin complexed 1,8-cineole in Parkinson´s Disease*. Araújo-Monteiro L[1], Carvalhinho-Lopes PS[1], Soares-Silva B[1], Donzelli NIZ[1], Quintans-Junior LR[2], Rando DG[3], Ribeiro AM[1] [1]Unifesp-Baixada Santista, PPG in Bioproducts and Bioprocesses, Brazil; [2]UFS, PPG in Pharmaceutical Sciences, Brazil; [3]Unifesp-Diadema, PPG in Pharmaceutical Sciences; Brazil.
Hanna A. Rothschild Auditorium	S3 – **Vascular Signaling in the Gut–Lung Axis during Infectious Disease** **Chair**: Claudia Lucia Martins da Silva (UFRJ) • *Insights on the gut-lung axis in pulmonary arterial hypertension: a poorly investigated crossroad* Suellen D´Arc Santos Oliveira (University of Illinois Chicago, USA) • *Caveolin-1–dependent endothelial P2Y2–P2X7 receptors crosstalk in intestinal inflammation contrasts with P2Y6 receptor regulation* Claudia Lucia Martins da Silva (UFRJ) • *Oral Communication 1:* 04.024 *Evaluation of the effects of docosahexaenoic acid* (*dha*) *and dha-loaded nanocapsules on the endothelium in* in vitro *and* in vivo *models*. Gomes-Reis GLS[1], Moraes BPT[2], Saraiva JSG[2], Cunha CMC[1], Ferreira-Costa M[1], Santos FS[3], Ferreira AM[1], Bozza PT[1], Castro-Faria-Neto HC[1], Ferrarini SR[4], Silva AR[1], Gonçalves-de-Albuquerque CF[1,2]. [1]IOC-Fiocruz, Immunopharmacology Lab and PPG in Cellular and Molecular Biology, Rio de Janeiro, Brazil; [2]Unirio, Immunopharmacology Lab and PPG in Molecular and Cellular Biology, Rio de Janeiro, Brazil; [3]UFF, PPG, in Neuroscience, Niterói, Brazil; [4]UFMT-Sinop, PPG Health Sciences, Brazil • *Oral Communication 2:* 04.042 *Ouabain improves pulmonary function in a murine model of mixed asthma*. *Ribeiro*, MR[1], Souza-Lima T[1], Siena A[1], Francelino-Alves V[1], Melhado IV[1], Fernandes PH[1], de Sá Lima L[1], Andreotti DZ[1], Oliveira MA[1], Leite J[2], Moriya HT[3], Rodrigues-Mascarenhas S[4], Tavares-de-Lima W[1], Scavone C[1] [1]ICB-USP, Dept. of Pharmacology, SP, Brazil; [2]ICB-UFG, Dept. of Pharmacology, GO, Brazil; [3]EP-USP, Dept. of Telecommunication and Control Engineering, SP Brazil; [4]UFPB, Dept of Cell and Molecular Biology, João Pessoa, PB, Brazil
Elisaldo Carlini Auditorium	**SBFTE Educational Initiatives- Ideas Laboratory: Building the Future of Pharmacology Education** (Laboratório de Ideias da IE-SBFTE: Construindo o Futuro da Educação em Farmacologia) (Presented in Portuguese) **Chair**: Francislaine Aparecida dos Reis Lívero (SBFTE Educational Initiatives, UFPR)

Eline S. Prado Room	SFR1– **Endocrine Disruptors Chemicals and DOHaD** **Chair**: Egberto Gaspar de Moura (UERJ) • *Endocrine disruptors – does the exposure window matter?* Caroline Serrano do Nascimento (Unifesp-Diadema) • *Endocrine-disrupting drugs: developmental exposure and sex-specific cardiovascular effects* Graziela Scalianti Ceravolo (UEL) • *The danger of chemical substances in the environment, acting on the first thousand days of life, to increase the risk of diseases during development* • Egberto Gaspar de Moura (UERJ)
João Garcia Leme Room	SFR2 – **Teaching in Basic Health Sciences: Successful Experiences** **Chair**: Josiane de Campos Cruz (UFPB) • *@faciologia in action: reels, memes, visual maps in the teaching human physiology* Aline de Freitas Brito (UPE) • *Exploring physiology through art* Josiane de Campos Cruz (UFPB) • *Oral Communication 1:* 14.005FR *Three-dimensional cold porcelain modeling as a pedagogical tool for human physiology education*. Nóbrega VC, Cruz JC UFPB, Dept. of Biotechnology, PPG Physiological Sciences, Brazil • *Oral Communication 2:* 13.005 *Developing scientific literacy through neuropharmacology education and research training in middle grade students*. Fonseca RD[1], Costa SF[2], Machado LHR[2], Nin MS[3], Barros HMT[4] [1]UFCSPA, Lab. Neuropsychopharmacology, PPG Health Sciences: Pharmacology and Toxicology, Brazil. [2]UFCSPA, Lab. Neuropsychopharmacology, Brazil. [3]UFCSPA, Dept. of Pharmacosciences, Lab. Neuropsychopharmacology, Brazil. [4]UFCSPA, Dept. of Pharmacosciences, Lab. Neuropsychopharmacology, PPG Health Sciences: Pharmacology and Toxicology, Brazil.
11:15 am-12:05 pm	**Lectures / XX FeSBE Regional Meeting**
Jose Ribeiro do Valle Auditorium	L2 – **Traveling Along the Neutrophil Recruitment Cascade** Markus Sperandio (Ludwig-Maximilians-Universität, Germany) Presented by Cassiano Felippe Gonçalves de Albuquerque (Unirio)
Alexandre P. Corrado Auditorium	L3 – **Potential Physiopathological Roles of the Novel Endogenous Catecholamines** Gilberto De Nucci (Unicamp) Presented by Patricia M. R. Martins (Fiocruz)
Hanna A. Rothschild Auditorium	L4 – **Transfer of Chronic Primary Pain from Patients to Mice; Novel Insights and Opportunities** David Andersson (Kings College, UK) Presented by Soraia Katia Pereira Costa (USP-SP)
Elisaldo Carlini Auditorium	L5 – **Human PMN-MDSCs: Novel Insights for Old Unanswered and Newly Emerging Questions** Marco Antonio Cassatella (University of Verona, Italy) Presented by Thereza Christina Barja-Fidalgo (UERJ)
Eline S. Prado Room	LFR1 – **Update on DOHaD Concepts** Erika Vanesa Cadena Burbano (UFPE)
João Garcia Leme Room	LFR2– **The DOHaD Paradigm at the Crossroads of Nutritional Transition** Antônio Marcus de Andrade Paes (UFMA)

12:05 pm-2h05 pm	**Lunch**
12h05 pm-2:05 pm Eline S. Prado Room	**SBFTE Young Assembly** (with Lunch Box)
2:05 pm-3:35 pm	**Symposia / XX FeSBE Regional Meeting**
Jose Ribeiro do Valle Auditorium	S4 – **Cell Communication on Immune Response, Aldosteronism, and Hypertension: Old Questions, New Insights** **Chairs**: Rita C. A. Tostes (USP-RP) / Tiago J. Costa (USP-SP) • *A chemogenetic mouse model to uncover the pharmacological mechanisms behind primary aldosteronism* Sheerazed Boulkroun (Inserm, France) • *Endothelial cell–immune crosstalk: mechanisms and clinical implications* Gisele Facholi Bomfim (UFMT) • *Oral Communication 1:* 06.050 *Mineralocorticoid receptors promote Th17 polarization in lymph nodes while IL-17RA drives pro-inflammatory phenotypic changes in perivascular adipose tissue during obesity*. Dourado TMH[1], Pimenta GF[1], Elias-Oliveira J[2], Rodrigues VF[2], Fazan-Junior R[3], Sartori DC[2], Tirapelli CR[4] [1]FMRP-USP, Depto Farmacologia; [2]FMRP-USP, Depto Bioquímica e Imunologia, [3]FMRP-USP, Depto Fisiologia; [4]FCFRP-USP, Depto Ciências BioMoleculares • *Oral Communication 2:* 06.038 *Distinct glycation modifications of Type I collagen differentially regulate platelet reactivity*. Fróes RBL, Silva BS, Gaspar RS FCM-Unicamp, PPG Farmacologia, Lab Matriz Extracelular, Brasil.
Alexandre P. Corrado Auditorium	S5 – **Biomarkers in Cancer: An Opportunity for the Development of New Drugs** **Chair**: Roberto César Pereira Lima Junior (UFC) • *Preclinical models for functional precision medicine in cancer* Hellen Kuasne (McGill University, Canada) • *Marine natural products inducers of immunogenic cell death on melanoma: prospection and pre-clinical development of anticancer candidates* Diego Veras Wilke (UFC) • *Oral Communication:* 10.047 *Apoptosis induction by the angucycline saquayamycin B1 in melanoma cells: involvement of oxidative stress and MAPK signaling*. Silvestre GFG[1], Souza RRM[1], Marques KKG[1], Dantas MM[1], Duarte SS[1], Castro IO[1], Ramalho IGS[1], Queiroga LM[2], Araújo YKO[2], Cibulski S[3], Nascimento IJS[4], Moura RO[4], Tavares JF[5], Gonçalves JCR[1], Sobral MV[1]. [1]UFPB, ONCOFAR, PPG of Bioactive Natural and Synthetic Products, Brazil. [2]UFPB, ONCOFAR, Undergraduate in Pharmacy, Brazil. [3]UFRN, FACISA, Faculty of Health Sciences, Brazil. [4]UEPB, LDSF, PPG of Pharmaceutical Sciences, Brazil. [5]UFPB, LMCA, PPG of Bioactive Natural and Synthetic Products, Brazil. • *Oral Communication 2:* 10.035 *VLA-4 integrin and VEGFR blockade regulates B16F10 melanoma adhesion, migration and proliferation*. Cavalcante KDM[1], Cavalcante MLS[1], Paixão MS[2], Lima KFN[1], Monte SJH[3], Pereira EM[3], Guimarães PPG[4], Sousa JMC[5], Ferreira PMP[1,6,7], Dittz D[1,5] [1]UFPI, Graduate Program in Pharmacology, Brazil; [2]UFPI, School of Pharmacy, Brazil; [3]UFPI, Immunogenetics and Molecular Biology Lab (LIB), Brazil; [4]UFMG, Dept Biophysics and Physiology, Brazil; [5]UFPI, Dept Biochemistry and Pharmacology, Brazil; [6]UFPI, Experimental Cancerology Lab (LabCancer), Brazil;

	[7]UFC, Experimental Oncology Lab (LOE), Drug Development Research Center (NPDM), Brazil.
Hanna A. Rothschild Auditorium	S6 – **Across Land, Water, and Air: Animal Models in Psychopharmacology** **Chair**: Vanessa de Paula Soares Rachetti (UFRN) • *Fast-tracking platforms for screening the* in vitro *and* in vivo *pharmacological profile of cannabidiol in the context of autism spectrum disorder* Alline Cristina Campos (USP-RP) • *Towards vertebrates' replacement in antidepressant discovery* Cilene Lino de Oliveira (UFSC) • *Oral Communication 1: Oral Communication 1:* 03.*004* in silico *and* in vivo *evaluation of gabaergic neurotransmission in the anxiolytic-like effect of the thiophenic derivative 6CN07*. Mendes LM, Naves FB, Almeida JVM, Pereira CHL, Alves HAR , Alves ARS, Teixeira JL, Neri LCD, Barbosa NMMV, Martins AMO, Oliveira LN, Soares MFS, Silva PR, Monteiro AB, Felipe CFB • *Oral Communication 2:* 03.032 *Effects of antagonism of orexin receptors, administered during the acquisition phase, on alcohol preference in the two-bottle choice model in swiss male mice*. Silva VS[1], Costa RCA[1], Costa EF[1], Ferreira KR[1], Santos RS[2], Carneiro DM[2], Zhang Y[3],Marinho ELAM4, Marinho EAV[2], Lima AJO[2], Berro LF5. [1]UESC, PPG Health Sciences, Brazil, [2]UESC, Dept Health Sciences, Brazil, [3]Research Triangle Institute, USA, [4]UESC, Dept Biological Sciences, Brazil, 5University of Mississippi Medical Center, USA
Elisaldo Carlini Auditorium	SFR3 – **Gut Microbiome and Cardiometabolic Health: Experimental Basis for Nutraceutical Interventions** **Chair**: José Luiz de Brito Alves (UFPB) • *Gut microbiome and cardiometabolic disease: mechanisms and signatures* Paulo César Trindade da Costa (Afya-PB) • *Development and characterization of microbiome-targeted nutraceuticals* Fillipe de Oliveira Pereira (UFCG) • *From Microbiome modulation to cardiovascular outcomes: translational applications of nutraceuticals* José Luiz de Brito Alves (UFPB)
Eline S. Prado Room	SFR4 – **Impacts of the Perinatal Environment on Health and Disease** **Chair**: Carmen Cabanelas Pazos de Moura (UFRJ) • *Does exposure to vaccines, pesticides, and microplastics during pregnancy and lactation cause autism in offspring*? Maria Tereza Nunes (USP-SP) • *Anthropometric, metabolic, and hormonal profile of the mother-child dyad of overweight children* Vinicius José Baccin Martins (UFPB) • *Maternal obesity: metabolic and mitochondrial dysfunctions in offspring* Carmen Cabanelas Pazos de Moura (UFRJ)
João Garcia Leme Room	SFR5 – **Biology of Nicotine and Respiratory Diseases** **Chair**: Joelmir Lucena Veiga da Silva (FMO) • *Systemic biological effects of nicotine* Ingrid Dragan Taricano (SBRed) • *Pharmacological aspects of nicotine in the body* Joelmir Lucena Veiga da Silva (FMO)

	• *Nicotine and respiratory diseases* Rodolfo Fred Behrsin (Unirio)
3:35 pm-3:50 am	**Coffee break**
4:00 pm-5:30 pm	**Meet the Expert / Meeting / Thematic Symposia**
Alexandre P. Corrado Auditorium	**Meet the Expert** **Chair:** Isis Nem de Oliveira Souza (Coordinator SBFTE Jovem, UFRJ) ✓ Belén Pérez Solans (Pharmactuarials, LLC, Spain) ✓ David Andersson (Kings College, UK) ✓ Hellen Kuasne (McGill University, Canada) ✓ Marco Antonio Cassatella (University of Verona, Italy) ✓ Mohamad Aljofan (Nazarbayev University - Kazakhstan) ✓ Santiago Di Lella (University of Buenos Aires , Argentina) ✓ Sheerazed Boulkroun (Inserm, France) ✓ Suellen D´Arc Santos Oliveira (University of Illinois Chicago, USA)
Hanna A. Rothschild Auditorium	**Meeting of the N-NE and CW Region Pharmacology Network**
Thematic Symposia Elisaldo Carlini Auditorium	TSFR1 – **Developmental Programming of Cardiometabolic Diseases: From Early-Life Insults to Adult Health** **Chair**: João Henrique da Costa Silva (UFPE-Vitoria) • *Maternal protein restriction and cardiovascular risk: new insights into developmental programming mechanisms* João Henrique da Costa Silva (UFPE-Vitoria) • *Oral Communication 1:* 10.012FR *Maternal protein restriction reprograms placental proteomic networks and ultrastructure: insights into early developmental adaptation*. Barata LA[1], Fioretto MN[1], Magosso N[1], Ferreira MR[2], Maciel FA[1], Felipe VAA[1], Ribeiro IT[1], Dos Santos DC[1], Justulin LA[1] [1]IBB-Unesp-Botucatu, Dept Cellular and Molecular Biology, PPG in General and Applied Biology, Brazil. [2]Unesp-Botucatu, School of Medicine, Experimental Research Unit - Unipex, Molecular Genetics and Bioinformatics Lab, Brazil. • *Oral Communication 2:* 10.010FR *Effects of moderate-continuous training on cardiac mitochondrial bioenergetics and redox status in rats subjected to early-life overnutrition*. Silva JTA, Fernandes MSS, Correia-Filho RC, Melo TSM, Fernandes MP, Lagranha CJ UFPE, Graduate Program in Nutrition, Physical Activity, and Phenotypic Plasticity, Brazil; UEFS, Brazil • *Oral Communication 3:* 10.013FR *Early life protein restriction impairs glp-1-induced insulin secretion despite increased intra-islet GLP-1 Production*. Oliveira KM[1], Silva-Junior JA[2], Carvalho MS[1], Bem KCP[1], Barbosa HCL[1], Carneiro, EM[1] [1]Unicamp, Obesity and Comorbidities Research Center (OCRC), Brazil; [2]Universidad Miguel Hernández, Instituto de Investigación en Biotecnología y Salud
Thematic Symposia Eline S. Prado Room	TSFR2 - **Neuroimmunology: Basic and Translational Aspects** **Chair**: Alexandre A. Steiner (USP-SP) • *Sympathetic modulation of immunity: focus on neutrophil heterogeneity* Alexandre A. Steiner (USP-SP) • *Oral Communication 1:* 04.062 *SIRT2 Inhibition attenuates neuroinflammation induced by* Klebsiella pneumoniae *infection*. Ferreira-Costa M[1], Thiele E[2], Almeida MAP[2], Santos, FS[2], Gomes-Reis, GLS[1], Cunha, CMC[1], Ferreira, A[1], Bozza PT[1], Castro-

	Faria-Neto HC[1], Gonçalves-de Albuquerque CF[2,3], Silva AR[1] [1]IOC-Fiocruz, Immunopharmacology Lab, PPG in Cellular and Molecular Biology, Rio de Janeiro, Brazil, [2]UFF, PPG in Neuroscience, Rio de Janeiro, Brazil, [3]Unirio, Immunopharmacology Lab, PPG in Molecular and Cellular Biology, Rio de Janeiro, Brazil • *Oral Communication 2:* 04.060 *Graft-versus-host disease promotes central neuroinflammation and glutamatergic dysfunction associated with anxiety-like behavior in mice*. Linhares AFS[1], Lima ALD[1], Berg BB[1], Rocha ES[2], Ruggio GMF[1], Sales MA[2], Silva MCM[1], Oliveira NFM[3], Campos ZDT[1], Vieira LB[4], Machado FS[5], Pinho V6, Teixeira MM[5], Oliveira ACP[4], Romero MGMC[4]. [1]UFMG, Graduate Program in Pharmacology and Physiology, Brazil; [2]UFMG, Undergraduate student in Biomedical Sciences, Brazil; [3]UFMG Graduate Program in Biochemistry and Immunology, Brazil; [4]UFMG Dept Physiology and Pharmacology, Brazil; [5]UFMG, Dept Biochemistry and Immunology, Brazil; [6]UFMG, Dept Morphology, Brazil. • *Oral Communication 3:* 04.026 *Chronic kidney disease and cognitive impairment from the perspective of neuroinflammation: evaluation of the exposure of healthy astrocytes to uremic serum*. Custodio GT[1], Russo FB[2], Beltrão PCB[2], Kawamoto EM [1] [1]USP, Dept Pharmacology, Brazil, [2]USP Dept Microbiology, Brazil, PPG Functional and Molecular Biology, Brazil.
5:40 pm-7:10 pm	**E-Poster Session 2**
	01. Cellular and Molecular Pharmacology **Totem 01:** 01.004-01.010 **02. Neuropharmacology** **Totem 02:** 02.007-02.012 **Totem 03:** 02.032-02.034 **Totem 04:** 02.046-02.052, 02.054 **02. Environmental Biology, Evolution and Comparative Biology** **Totem 38:** 02.001FR **Totem 41:** 02.002FR **03. Psychopharmacology** **Totem 05:** 03.007-03.012 **Totem 06:** 03.023-03.027 **Totem 07:** 03.033-03.036 **04. Inflammation and Immunopharmacology** **Totem 08:** 04.004-04.008 **Totem 09:** 04.025-04.030 **Totem 10:** 04.050-04.056 **04. Biology and Cardiovascular Diseases** **Totem 13:** 04.001FR **05. Pain and Nociception Pharmacology** **Totem 11:** 05.034-05.037 **Totem 12:** 05.045-05.048 **06. Cardiovascular and Renal Pharmacology** **Totem 13:** 06.006-06.010 **Totem 14:** 06.041-06.045, 06.051 **Totem 15:** 06.060-06.065

	06. Biology and Metabolic and Reproductive Diseases
	Totem 17: 06.012FR
	Totem 18: 06.013FR, 06.014FR
	07. Endocrine, Reproductive and Urinary Pharmacology
	Totem 16: 07.001-07.007
	Totem 17: 07.008-07.013,
	Totem 18: 07.014-07.017
	08. Respiratory and Gastrointestinal Pharmacology
	Totem 19: 08.007-08.012
	Totem 20: 08.028-08.032, 08.034
	09. Natural Products and Toxinology
	Totem 21: 09.006-09.011
	Totem 22: 09.012-09.017
	Totem 23: 09.018-09.023
	Totem 24: 09.024-09.030
	Totem 25: 09.058-09.064
	Totem 26: 09.079-09.085
	Totem 27: 09.086-09.089,
	Totem 28: 09.097-09.101
	10. Cancer Pharmacology
	Totem 29: 10.007-10.012
	Totem 30: 10.013-10.019
	Totem 31: 10.027-10.031
	Totem 32: 10.050-10.056
	Totem 33: 10.067-10.070
	10. DOHaD and Developmental Biology
	Totem 42: 10.013FR-10.015FR, 10.017FR
	11. Clinical Pharmacology, Pharmacokinetics, Pharmacogenomics and Toxicology
	Totem 34: 11.025-11.028, 11.029
	Totem 35: 11.033,
	Totem 44: 11.001-11.005
	11. General Pharmacology
	Totem 38: 11.001FR
	Totem 40: 11.006FR
	Totem 41: 11.002FR-11.005FR
	12. Drug Discovery and Development
	Totem 35: 12.039-12.042
	Totem 36: 12.007-12.013
	Totem 37: 12.021-12.027
	14. Pharmacology: Other
	Totem 38: 14.001-14.004
	Totem 39: 14.016-14.019
	Totem 40: 14.020, 14.021
	14. Scientific Methodology and Experimental Design in Biology
	Totem 43: 14.002FR-14.007FR
	15. Neurobiology and Neuronal Diseases
	Totem 03: 15.006FR -15.007FR

	16. Toxinology, Natural Products and Medicinal Chemistry **Totem 27:** 16.004FR-16.006FR 17. Vision and Ophthalmology **Totem 40**: 17.001FR

Oct 22nd, 2026 (Thursday)

08:00 am	II Mostra de Arte & Ciência SBFTE (I Science and Art Exhibit – SBFTE)
08:00 am	Venue Secretariat and SBFTE Secretariat Opening
08h00 am-09h30	**Symposia / Roundtable / XX FeSBE Regional Meeting**
Jose Ribeiro do Valle Auditorium	S7 – **Advances in Model-Informed Precision Dosing for Antimicrobials** **Chair**: Bibiana Verlindo de Araujo (UFRGS) • *Preclinical to clinical translation of antimalarial combinations* Francine Johansson Azeredo (University of Florida, USA) • *Pharmacokinetic modeling applied to the prediction of antimicrobial exposure in children and neonates* Ronaldo Morales Junior (HSL) • *Integrating nonclinical evidence to select the next successful regimens in tuberculosis* Belén Pérez Solans (Pharmactuarials, LLC, Spain)
Alexandre P. Corrado Auditorium	S8 – **Targeting Cellular Dysfunction in Complex Diseases: From Cancer to Parkinsonism** **Chair**: Enilton A Camargo (UFS) • *ERO1α overexpression in triple-negative breast cancer links to EMT and mitochondria-dependent inhibition* Mohamad Aljofan (Nazarbayev University - Kazakhstan) • *Biochanin A, a natural isoflavone, as a potential therapeutic agent in experimental parkinsonism* Enilton A Camargo (UFS) • *Oral Communication 1:* 09.086 *The triterpene friedelin attenuates TGF-β-Induced EMT in NCI-H292 lung cancer cells and upregulates TIMP3 expression*. Almeida JH[1], Bodin A[2], Victoni T[23], Barreto EO[1], Lagente V[2], Ferro JNS[1] [1]UFAL, Lab Biologia Celular, Maceió, AL, Brasil. [2]Université de Rennes, Inserm, Inrae, NuMeCan (Nutrition, Métabolismes et Cancer), Rennes, France. [3]Université de Lyon, VetAgro Sup, Lyon, France. • *Oral Communication 2:* 09.059 *Caulerpin modulates the calcineurin-NFAT signaling AXIS and attenuates T-cell activation in human peripheral blood mononuclear cells*. Santos-Junior SS, Dos Santos JSP, Correia AGV, Oliveira VS, Silva DKC, Souza CVC, Santos-Filho OA, Martinez ST, Soares MBP, Meira CS Fiocruz-BA, Salvador, UNEB, Salvador, SENAI CIMATEC-BA, Salvador, UFRJ-RJ, Rio de Janeiro FURG-RS, Rio Grande do Sul.
Hanna A. Rothschild Auditorium	RT2 – **Beyond Academia** (Presented in Portuguese) **Chair**: Isis Nem de Oliveira Souza (Coordinator SBFTE Jovem, UFRJ) • *The PhD in pharmacology as a strategic differential in aesthetics: from academia to entrepreneurship in healthcare* (*O doutorado em farmacologia como diferencial estratégico na estética: da academia ao empreendedorismo em saúde*) Samara Rodrigues Bonfim Damasceno (Cespu Europa)

	• *Beyond research: Pharmacology as cross-disciplinary training for multiple careers in Veterinary medicine* (*Muito além da pesquisa: a farmacologia como formação transversal para múltiplas carreiras na medicina veterinária*) Humberto Barbosa da Costa Filho (UFC) • *Between bench and data: A journey in science* (*Entre a bancada e os dados: uma jornada na ciência*) Paula Fontes Asprino (Clarivate)
Elisaldo Carlini Auditorium	SFR6 – **Research in Ecophysiology and Comparative Physiology in the Northeast Region: Challenges and Perspectives** **Chair**: Paulo Fernando Guedes Pereira Montenegro (UFPB) • *Diversity and ecophysiology of terrestrial vertebrates in northeast Brazil* Washington Luiz da Silva Vieira (UFPB) • *Urban impacts on sandy beaches: insights from mole crabs ecophysiology in Paraíba, northeastern Brazil* Enelise Marcelle Amado (UEPB) • *Research activities at the Animal Ecophysiology Laboratory at Federal University of Paraíba* Paulo Fernando Guedes Pereira Montenegro (UFPB)
Eline S. Prado Room	SFR7 – **Pain, Inflammation and Emotion: Therapeutic Challenges and Opportunities** Chair Marucia Chacur (USP-SP) / Janaína Menezes Zanoveli (UFPR) • *Chronic pain and cognition: neurobiological mechanisms and sex difference* Marucia Chacur (USP-SP) • *Sex-based differences in the prevention of stress-induced anxiety: effects of the pro-resolving lipid mediator Resolvin D5* Janaína Menezes Zanoveli (UFPR) • *Oral Communication 1:* 05.030 *Advanced glycation end-products promote neuronal dysfunction and neurodegeneration in sensory-like neurons and sensorimotor organoids*. Silva GSA[1], Bufalo MC[3,4], Chudzinski-Tavassi AM[3,4], Pereira JD[2], Zambelli VO[1,3]. [1]IBu, Lab Pain and Signaling, Brazil. [2]University of Alabama at Birmingham, Dept Neurology, USA. [2]IBu, Center of Excellence in New Target Discovery, Brazil. [4]IBu, Innovation and Development Center, Brazil. • *Oral Communication 2:* 05.009 *Antinociceptive effects of MSCs and MSC-EVs are associated with CXCR2 pathway in neuropathic pain mice model*. Velozo ACL[1], Opretzka LC[2], Jesus MVAC[1], Cruz ABO[1], Santos MGS[3], Santos GC[3], Soares MBP[3], Villarreal CF[1]. [1]UFBA, School of Pharmacy, Salvador, Brazil; [2]SENAI-CIMATEC, Salvador, Brazil; [3]Fiocruz-BA, Salvador, Brazil
João Garcia Leme Room	TSFR4 – **From Model to Mechanism: The Role of Experimental Choice in Pharmacological Research** Chair: Maria Martha Campos (PUC-RS) • *Complement or replacement? Animal models and new alternatives in drug research* Maria Martha Campos (PUC-RS) • *Oral Communication 1:* 12.035 in silico *Evaluation of LOE2208 and Its derivatives reveals predicted interactions with tubulin protein and suitable ADMET profiles*. Lima JM[1,2], Da Costa RF[3,4], Bezerra EM[3,4], Viera-Neto JB[1,2], Falcão JS[5,6], Lapa DP[5,6], Costa PRR[5,6], Caleffi GS[5,6], Pessoa C[1,2]. [1]UFC, Lab. of Experimental Oncology, Drug Research and Development Center, Brazil; [2]UFC PPG Pharmacology, Brazil; [3]UFERSA, Lab. of Computational Physics, Brazil; [4]UFERSA, PPG Science and

	Engineering of Materials, Brazil; [5]UFRJ, Lab. of Bioorganic Chemistry, Research Institute of Natural Products Walter Mors, Brazil; [6]UFRJ, PPG Chemistry of Natural Products, Brazil. • *Oral Communication 2:* 04.054 *Role of estradiol/GPER signaling in the sickness response during systemic inflammation*. Costa RA, Schneider RC, Santos MO, Pereira V, Borges AP, Schneider VMM, Alencar ST, Baggio DF, Zampronio AR. UFPR, Inflammation and Fever Lab, Dept Pharmacology, Brazil. • *Oral Comunication 3:*
09:30 am-9:50 am	**Coffee break**
10:00 am-11:40 am	**Symposium**
Mauricio Rocha e Silva Auditorium	**José Ribeiro do Valle Award** Chair: Emiliano O Barreto (UFAL) *Natália Pressuto Pennachioni* • 05.019 **Mitochondrial Aldehyde Dehydrogenase-2 and 4-Hydroxynonenal Mediates Morphine Analgesic Tolerance and Hyperalgesia via TRPA1 Activation**. Pennachioni NP[1,2], Hosch NG[1], Martins BB[1], Silva GSA[1], Troitiño VC[1,2], Dallazen JL[1,3], Kiataki LGS[1,3], Andersson D[4], Bevan S[4], Zambelli VO[1,3]. [1]IBu. Pain and Signaling Lab, IBu, São Paulo. [2]University of Sao Paulo, Interunits Biotechnology Postgraduate Program. [3]Kings College London, Wolfson Sensory, Pain and Regeneration Centre, [4]IBu, Centre of Excellence in New Target Discovery, São Paulo *Isaac Alef Barbosa Gomes* • 08.020 **Refluxate Components Drive NETosis and Promote Experimental Reflux Esophagitis Trough PAD4-Dependente Mechanisms**. Gomes IAB[1]; da Silva GCP[2]; Ramos AS[3]; Pérez MM[3]; Sales TMAL[3]; Costa VF[3]; Araújo AVV[1]; da Silva KS[1]; Medeiros JVR[1]; Saraiva EM[2]; Cunha FQ[3]; Nicolau LAD[1]. [1]UFDPar, PPG in Biotechnology, Brazil; [2]UFRJ, Dept Immunology, Brazil; [3]CRID-FMRP-USP, Brazil. *Samuel Duarte Maia* • 06.040 **Glycated Collagen Drives Vascular Remodeling and Smooth-Muscle Dysfunction in Hyperglycemia**. Duarte-Maia S, Silva-Oliveira N, Simões Gaspar R. FCM-Unicamp, Depto Farmacologia, Lab Matriz Extracelular, PPG em Farmacologia *Stella Jasmine Arruda Coelho* • 03.040 **Meningeal Inflammatory Responses and Long-Term Behavioral Alterations Induced by Adolescent Stress**. Coelho S, Pigatto G, Meschick CG Verza FA, Freitas IS, Grigório-de-Sant'Ana M, Guimaraes FS, Cunha TM, Gomes FV. FMRP-USP, PPG em Farmacologia , Brasil *José Yuri Gomes da Silva* • 10.049 **Systems Biology Identifies a Chaperone-Mediated Network Associated with Doxorubicin Response and Poor Survival in Triple-Negative Breast Cancer**. Silva JYG[1], Azevedo GM[2], Dalmolin RJS[2], Wilke DV[1] [1]UFC, PPG Pharmacology, Brazil [2]UFRN, Bioinformatics Multidisciplinary Environment - BioME, IMD, Rio Grande do Norte, Natal, Brazil

11:40 am-12:40 pm	**Technical Lecture**
Hanna A. Rothschild Auditorium	**Cortellis Drug Discovery Intelligence: A Platform for Transforming Knowledge into Pharmacological Innovation** (*Cortellis Drug Discovery Intelligence*: Uma Plataforma para Transformar Conhecimento em Inovação Farmacológica) Paula Fontes Asprino (Clarivate)
Mauricio Rocha e Silva Auditorium	
12:40 pm-02:00 pm	**SBFTE Assembly**
02:00 pm-03:30 pm	**Roundtable**
Mauricio Rocha e Silva Auditorium	**RT3 – Celebrating 60 years** **SBFTE aos 60 anos: O Futuro da Farmacologia no Brasil – Formação, Identidade, Representação e Avaliação da Qualidade dos Programas de Pós-Graduação** (SBFTE at 60: The Future of Pharmacology in Brazil - Training, Identity, Representation and Quality Assessment of Graduate Programmes) Chair: Soraia K. P. Costa (USP-SP) (2024-2026) ✓ Antonio José Lapa (Unifesp-EPM) (2000-2001) ✓ Giles A. Rae (UFSC) (2002-2003; 2004-2005) ✓ Regina P. Markus (USP-SP) (2006-2008) ✓ Jamil Assreuy (UFSC) (2009-2011) ✓ Maria Christina Avellar (Unifesp-EPM) (2015-2017) ✓ André Sampaio Pupo (Unesp-Botucatu) (2018-2020) ✓ Marco Aurelio Martins (Fiocruz) (2021-2023)
06:00 pm-10:00 pm	**Get Together Party** Lovina Ponta de Campina | Bar | Restaurante R. Vitorino Cardoso, 908 Ponta de Campina Cabedelo – PB

Oct 23rd, 2026 (Friday)

08:00 am	II Mostra de Arte & Ciência SBFTE (I Science and Art Exhibit – SBFTE)
08:00 am	Venue Secretariat and SBFTE Secretariat Opening
08:00 am-09:15 am	**Courses**
Jose Ribeiro do Valle Auditorium	Cr1 – **Pharmacology-Oriented Metabolomics: Biomarker Discovery and Therapeutic Targets** (Metabolômica Orientada à Farmacologia: Descoberta de Biomarcadores e Alvos Terapêuticos) (Presented in Portuguese) **Chair**: Adriane Ribeiro Rosa (UFRGS) • Class 2: *Analytical strategies in metabolomics: integrating biostatistics and case studies in pharmacology* (*Estratégias analíticas em metabolômica: integrando a bioestatística e estudos de caso em Farmacologia*) Charles Francisco Ferreira (UFRGS)
Alexandre P. Corrado Auditorium	Cr2 – **Introduction to Atomistic Simulations of Biomolecular Systems for Drug Development** (Introdução a Simulações Atomísticas de Sistemas Biomoleculares para Desenvolvimento de Fármacos) (Presented in Portuguese) **Chair**: Marcelo N. Muscará (USP-SP) • Class 2: *Applications of computational simulations in drug development: molecular recognition, docking methodologies, complex stability and therapeutic targets.* (*Aplicações de simulações computacionais no desenvolvimento de fármacos: reconhecimento molecular, metodologias de docking, estabilidade de complexos e alvos terapêuticos*) Santiago Di Lella (University of Buenos Aires , Argentina)
Hanna A. Rothschild Auditorium	Cr3 – **Statistical Delusions and Questionable Research Practices** (Delírios Estatísticos e Práticas Questionáveis de Pesquisa) (Presented in Portuguese) **Chair**: Ana Paula Herrmann (UFRGS) • Class 2: *The four horsemen of the reproducibility apocalypse* (*Os quatro cavaleiros do apocalipse da reprodutibilidade*) Ana Paula Herrmann (UFRGS)
Elisaldo Carlini Auditorium	Cr4 – **Pharmacogenetics, Toxicology, and Clinical Practice** (*Farmacogenética, Toxicologia e Prática Clínica*) (Presented in Portuguese) **Chair**: Paulo Caleb Júnior de Lima Santos (Unifesp-EPM) • Class 2: *Toxicology: environmental exposure, progressive neurotoxicity, and insights from experimental models for cumulative human risk assessment* (*Toxicologia: exposição ambiental, neurotoxicidade progressiva e insights de modelos experimentais para avaliação do risco cumulativo em humanos*) Paulo C. Ghedini (UFG)
09:15 am-9:30 am	**Interval**
09:30 am-11:00 am	E-Poster Session 3
	01. Cellular and Molecular Pharmacology **Totem 01:** 01.011-01.017 **Totem 02:** 01.018-01.021

	02. Neuropharmacology **Totem 03:** 02.013-02.019 **Totem 04:** 02.036-02.037; 02.039-02.041 **Totem 05:** 02.053, 02.055-02.058 **Totem 06:** 02.067-02.069 **Totem 07:** 02.070-02.074 03. Psychopharmacology **Totem 08:** 03.013-03.017 **Totem 09:** 03.028-03.032 **Totem 10:** 03.037-03.040 **Totem 11:** 03.041-03.044 04. Inflammation and Immunopharmacology **Totem 12:** 04.009-04.013 **Totem 13:** 04.014-04.019 **Totem 14:** 04.031-04.035 **Totem 15:** 04.057-04.060, 04.063 04. Biology and Cardiovascular Diseases **Totem 22:** 04.002FR-04.005FR 05. Pain and Nociception Pharmacology **Totem 02:** 05.038-05.040 **Totem 16:** 05.008-05.010, 05.012-05.014 **Totem 17:** 05.022-05.026, 05.028 06. Cardiovascular and Renal Pharmacology **Totem 18:** 06.011-06.016 **Totem 19:** 06.024-06.030 **Totem 20:** 06.046-06.050 **Totem 21:** 06.052-06.056 06. Biology and Metabolic and Reproductive Diseases **Totem 23:** 06.015FR **Totem 44:** 06.007FR-06.011FR 07. Endocrine, Reproductive and Urinary Pharmacology **Totem 23:** 07.018-07.020 **Totem 24:** 07.021-07.026 08. Respiratory and Gastrointestinal Pharmacology **Totem 23:** 08.038 **Totem 25:** 08.013-08.018 **Totem 26:** 08.033, 05.035-08.037 09. Natural Products and Toxinology **Totem 27:** 09.031-09.037 **Totem 28:** 09.038-09.044 **Totem 29:** 09.045-09.048, 09.050, 09.051 **Totem 30:** 09.065-09.071 **Totem 31:** 09.102-09.106 10. Cancer Pharmacology **Totem 32:** 10.020-10.026

	Totem 33: 10.032-10.036 **Totem 34:** 10.047, 10.057-10.062, **Totem 35:** 10.071-10.074 **11. Clinical Pharmacology, Pharmacokinetics, Pharmacogenomics and Toxicology** **Totem 36:** 11.006-11.011 **Totem 37:** 11.019-11.024 **Totem 38:** 11.030-11.032 **Totem 39:** 11.034-11.036 **12. Drug Discovery and Development** **Totem 39:** 12.043-12.045 **Totem 40:** 12.014-12.020 **Totem 41:** 12.033-12.038 **13. Immunology, Microbiology and Parasitology** **Totem 42:** 13.001FR, 13.002FR, 13.004FR-13.006FR **14. Pharmacology: Other** **Totem 43:** 14.005-14.010 **15. Neurobiology and Neuronal Diseases** **Totem 06:** 15.011FR, 15.012FR **Totem 07:** 15.013FR **16. Toxinology, Natural Products and Medicinal Chemistry** **Totem 30**: 16.003FR
11:00 am-11:30 am	Coffee break (Brunch)
11:30 am-12:20 pm	Lectures / XX FeSBE Regional Meeting
Jose Ribeiro do Valle Auditorium	L6 – **Translational Perspectives on Psychoactive Therapies for Cognitive and Substance Use Disorders** Mohamed Kabbaj (Florida State University, USA) Presented by Silvana Chiavegatto (USP-SP)
Alexandre P. Corrado Auditorium	L7 – **Regulation of Cardiovascular Functions during Extreme Conditions in Reptiles** Tobias Wang (Aarhus University, Denmark) Presented by Gilberto De Nucci (Unicamp)
Hanna A. Rothschild Auditorium	LFR3 – **Medicalization of Suffering and Use of Psychotropic Drugs: An Evidence-Based Analysis** Marcos Rochedo Ferraz (UERJ)
Elisaldo Carlini Auditorium	LFR4 – **Theranostic Radiopharma-ceuticals: The New Frontier of Translational Pharmacology** Fabio Luiz Navarro Marques (USP-SP)
Mauricio Rocha e Silva Auditorium	
12:30 pm-1:50 pm **Closing Lecture**	Brazilian Women in Pharmacology Award– 2026 Edition Chair: Soraia K. P. Costa (SBFTE President, USP-SP) Leader: **Sex hormones in cardiovascular pharmacology: an exciting journey** Rita C. A. Tostes (USP-RP) Emerging Leader

	Beyond the Laboratory: A Journey Through Pharmacology, Research and Education Francislaine Aparecida dos Reis Lívero (Educational Initiatives Coordinator, UFPR)
1:50 pm-2:30 pm	**Closing Ceremony**

E-Poster Session 1 – Oct. 20th 2026

01. Cellular and Molecular Pharmacology

Totem 01

01.001 **Detection of bacterial DNA in the Plasma of Breast Cancer Patients by qPCR and the Influence of Obesity Phenotype on Bacterial Translocation**. Alves ROF[1], Freitas GL[1], Cajado AG[1], Florêncio KGD[1], Teixeira-Filho JIF[1], Ribeiro MVS[1], Maia DCBSC[2], Vale ML[1], Rocha-Filho DR[3], Arruda LM[4], Lima-Júnior RCP[1],Wong DVT[1] [1]UFC, Lab Inflammation and Cancer Pharmacology, Dept Physiology and Pharmacology [2]Dpt of Pathology and Forensic Medicine, Brazil; [3]HUWC-UFC, Walter Cantídio University Hospital. [4]ICC, Haroldo Juaçaba Hospital, Cancer Institute of Ceará. Fortaleza, Brazil

01.002 **Quinoxalinylhydrazone as a Potential HDAC Inhibitor in Acute Myeloid Leukemia (AML): Evaluation of Antileukemic Activity and Epigenetic Effects**. Macêdo SMN[1], Sales SLA[1,2], Mota JA[1,2], Gress LSB[1,2], Lima JM[1,2], Oliveira KAF[1], Bastos RS[1,2], Desiderio GA[1,2], Xavier EEP[1], Soares IF[1], Maranhão SS[1,3], Furtado CLM[4] and Pessoa C[1,2]. [1]UFC, Lab. of Experimental Oncology, Drug Research and Development Center, Brazil; [2]UFC, PPG Pharmacology, Brazil; [3]UFC, PPG Translational Medicine, Brazil; [4]UFMG, Dept Genetics, Ecology and Evolution, Institute of Biological Sciences, Brazil.

01.003 **6-Nitrodopamine Potentiates Noradrenaline-Induced Intracellular Calcium Signalling Via a Tetrodotoxin-Sensitive Mechanism in Human Aortic Endothelial Cells**. Ribeiro LC[1,2], Britto-Júnior J[1,2], La Scala T[1], Nawaci A[1], De Nucci G[2], Ferro A[1] [1]King's College London, Faculty of Life Sciences and Medicine, London, UK; [2]Unicamp, Dept Pharmacology, Faculty of Medical Sciences, Campinas, SP, Brazil.

02. Neuropharmacology

Totem 02

02.001 **Investigation of the Neuroprotective Potential of Purple Pitanga** (*Eugenia uniflora*) **Extract on Non-Motor Symptoms of Parkinson's Disease in Female Rats**. Streb BL, Fontoura EA Fidelis EM, Rodrigues ES, Gomes J, Comis-Neto, AA, Batista WT, Pinton S, Rosa SG Unipampa

02.002 **Prevalence of the APOE ε4 Allele and its Association with Lipid Markers in Cognitive Decline Profiles**. Canafístula LS[1], Barbosa ISA[1], Oliveira CA[2], Xavier JMC[1], Soares MVR[3], Gonçalves PVS[4], Santos LTR[5], Frota AF[3], Lôbo RR[5], Aires-Peixoto-Júnior A[5], Gaspar DM[3]. [1]UFC, Faculty of Pharmacy, Brazil; [2]UFC, Graduate Program in Pharmacology, Brazil; [3]UFC, Neuropsychopharmacology Lab, Graduate Program in Translational Medicine, Brazil; [4]UFC, Faculty of Medicine, Brazil; [5]UFC, Faculty of Medicine, Dept Clinical Medicine, Graduate Program in Translational Medicine, Brazil.

02.003 **Systematic Review and Meta-Analysis of Brain Na^+,K^+-ATPase Activity in Alzheimer's Disease and Epilepsy Preclinical Models**. Carneiro MA[1], Ribeiro LR[1,3], Bariviera JL[1,3], Da Rosa GK[1,3], Ramos RB[1], Freitas JW[2], Oliveira MS[1,3] [1]UFSM, Lab Experimental Neurology, [2]UFSM, Lab Exercise Biochemistry, [3]UFSM, PPG Pharmacology, Brazil

02.004 **Effects of the β-Carboline Alkaloids Harmine and Harmaline On Scopolamine-Induced Cognitive Impairment**. Rossi NRC, Morales-Lima G, Falconi-Souto A, Mendes FR UFABC Center for Natural and Human Sciences Brazil

02.005 **Evaluation of Subacute Co-Administration of Oxytocin and Cannabidiol in a Mouse Model of Post-Traumatic Stress Disorder**. Souza MA, Albuquerque EA, Silva RC, Arruda JM, Crispim JG, Lima JPF, Silva RL, Lima CAO, Rosa MM NUPIT-UFPE, PPG in Therapeutic Innovation, Brazil

02.006 **Evaluation of the Effect of the P1G10 Proteolytic Fraction of *Vasconcellea cudinamarcensis* on MHV-A59 Infection in a Murine Model of Type 1 Diabetes**. Baptista, ACS[1], Lima ALD[1], Morais ALB[1], Pimenta JC[3], Gonçalves JPCS[1], Queiroz Junior C[3], Litwinski VVC[3], Lopes MTP[2], Vieira, LB[1] [1]UFMG, Neuropharmacology Lab, Dept Pharmacology, PPG Physiology and Pharmacology, Brazil; [2]UFMG, Antitumor Substances Lab, Dept Pharmacology, PPG Physiology, and Pharmacology, Brazil; [3]UFMG, Immunopharmacology Lab, Dept Cell Biology, PPG Biochemistry, Brazil

Totem 03

02.020 **BD-8 has no Effect Under Oxidative Stress in the Cerebellum of LPS-Challenged Mice**. Neves EPFI[1], Fonseca MFR[1], Ghedini PC[1], Mazaro e Costa R[1], Villar JAP[2], Barbosa LA[2], Leite JA[1] [1]ICB-UFG, Dept Pharmacology, Goiânia, Brazil; [2]UFSJ, Cellular Biochemistry Lab, Brazil.

02.021 **Gamma-Decanolactone Recovers Reserpine-Induced Dopaminergic and Cholinergic Neuronal Damage in *Caenorhabditis elegans***. Farias MS, Souza VL, Andrade EM, Garofalo CB, Santos PA, Pereira P UFRGS, Institute of Basic Health Sciences, Dept Pharmacology, Lab Neuropharmacology and Clinical Toxicology, PPG in Pharmacology and Therapeutics, Brazil.

02.022 **Evaluation of the Toxicity and Neuroprotective Potential of an Isatin Derivative in a *Caenorhabditis elegans* Model for Alzheimer's Disease**. Vieira CFA[1], Marreiro VS[1,2], Sousa LVBS[1], Almeida Filho GP[1], Lima TCBS[1], Carneiro CA[1], Campos CENS[1], Galdino FS[1,2], Costa MESM[1], Diniz MFFM[1,2], Lima-Junior CG[3], Olegário TR[3], Janebro DI[1,2]. [1]UFPB, Toxicological Testing Lab, Brazil, [2]UFPB, PPG in Natural and Synthetic Bioactive Products, Brazil, [3]UFPB, Lab Medicinal Organic Synthesis of Paraíba, Brazil

02.023 **Cytoprotective and Redox-Modulating Effects of *Achyrocline satureioides* Infusion in BV-2 Microglial Cells Exposed to Hydrocortisone**. Pulcinelli DLF, Turra BO, Bonotto NCA, Santos É, Escher ALK, Musachio E, Barbisan F UFSM, Dept Pathology, Biogenomics Lab, Brazil

02.024 **Integrated Network Pharmacology, Molecular Docking, and Cellular Analysis of beta-Ciclodextrin Complexed 1,8-cineole in Parkinson´s Disease**. Araújo-Monteiro L[1], Carvalhinho-Lopes PS[1], Soares-Silva B[1], Donzelli NIZ[1], Quintans-Junior LR[2], Rando DG[3], Ribeiro AM[1] [1]Unifesp-Baixada Santista, PPG in Bioproducts and Bioprocesses, Brazil; [2]UFS, PPG in Pharmaceutical Sciences, Brazil; [3]Unifesp-Diadema, PPG in Pharmaceutical Sciences; Brazil.

02.025 **Comparison Between Preventive and Concomitant Treatment Effects of Potentially Psychobiotic Bacteria on Ethanol-Induced Conditioned Place Preference Associated with Sleep Deprivation**. Resende GR[1,2], Silva KSO[2], Fighera YCM[2], Souza CS[2], Marinho EAV[4], Berro LF[3], Tamura EK[2,4] [1]UESC PPG in Health Sciences, [2]UESC Chronobiology Research Group, [3]University of Mississipi Medical Center Dept Psychiatry and Human Behavior, [4]UESC Dept Health Sciences

02.038 **Acute Naltrexone Effects on Short-Term Memory of Wistar Rats**. Silva-Filho JH, Kanazawa LKS, Lima TF, Pagnussat AL, Vital MABF UFPR, PPG Pharmacology Dept, Brazil

Totem 04

02.026 **Purple Pitanga Extract Reduces Neuroinflammation and Motor Impairment in a Postmenopausal Parkinson's Disease Model**. Fontoura EA, Streb BL, Fidelis EM, Da Costa NHC, Rodrigues ES, Gomes J, Comis-Neto AA, Batista WT, Pinton S, Rosa SG Unipampa

02.027 **iNOS Deletion in Mice Alters CaMKII-alpha S-Nitrosylation and Phosphorylation Dynamics in the Prefrontal Cortex Across Contextual Fear Conditioning Phases**. Silva TA[1], Ferreira BF[2,3], Barbosa KE[1], Meyer E[1], Tella SC[2], dos

Santos JE[2], Fronza MG[2,4], Lisboa SF[1] [1]FCFRP-USP, [2]FMRP-USP, [3]University of Quebéc – Tróis-Riviére, Canada, [4]Universitat Autònoma de Barcelona, Spain

02.028 **The Role of mGluR5 and the PI3K/AKT/mTOR Pathway in Regulating Body Weight in Obese Mice**. Morais ALBM, Silva LP, Barahuna-Filho PFR, Avelar CDFL, Vieira, LB UFMG, Dept Pharmacology, PPG Physiology and Pharmacology, Brazil

02.029 **Liposomal Nanoencapsulation Potentiates the Anticonvulsant and Neuroprotective Effects of γ-Decanolactone Through GABAergic Pathway Modulation in** *Caenorhabditis elegans*. Souza VL, Andrade EM, Garofalo CB, Santos PA, Pereira P UFRGS – Institute of Basic Health Sciences, Dept Pharmacology, Lab Neuropharmacology and Clinical Toxicology, PPG in Pharmacology and Therapeutics. Brazil.

02.030 **Role of α1A-Adrenoceptors on Anxiety-Related Behavior in Mice**. Figueredo BS, Gomes LTC, Sena MO, Gavioli EC, Silva Junior ED. UFRN, Dept Biophysics and Pharmacology, Brazil.

02.031 **Genetic Mutations of Na+, K+-ATPase Involved in the Onset of Neurological Disorders – A Systematic Review**. Rosa GK[1,2], Ribeiro LR[1,2], Bariviera JL[1,2], Carneiro MA[2], Vargas, LS[2], Fonseca, CPW[2], Oliveira MS[1,2] [1]UFSM, PPG Pharmacology, Brazil, [2]UFSM, Lab Experimental Neurology

Totem 05

02.042 **Neuroprotective and Antioxidant Activity of Sweet Orange Essential Oil in** *Caenorhabditis elegans*. Lisboa JS[1], Sá MEB[2], De Jesus LFS[2], Barreto MS[1], De Souza JB, Silva AS[1], Araújo ZS[3], Pacheco PGS[1], Silva VGO[2], Guimarães AG[2] [1]UFS-São Cristóvão, Graduate Program in Pharmaceutical Sciences, [2]UFS-São Cristóvão, Dept Pharmacy, [3]UFS-Lagarto, Graduate Program in Health Sciences

02.043 **Behavioral Profile of Male Offspring from Sedentary Dams Exposed to Prenatal Valproic Acid**. Rodrigues BA, Santiago Prestes TC, Kawamoto EM ICB-USP, Pharmacology Dept. Lab Molecular and Functional Neurobiology.

02.044 **Cannabidiol Nanoemulsion Enhances Permeability Across a Biomimetic Blood-Brain Barrier Model**. Dias KM[1], Dias CMN[1], Montes GC[1], Maluf D 2, Ferreira FS[1], Mattos JA[1], Nascimento JMD-F[1], Soares LN[1], Caetano AC[1], Soares SCS[1], Ognibene DT[1], Costa CA[1], Resende AC[1], Matsuura C[1], Bem GF[1] [1]UERJ, Research Line in Neuropharmacology and Medicinal Plants (NFPM), PPG in Clinical and Experimental Pathophysiology (Fisclinex), Brazil, [2]UFPR, Dept Pharmacy, Graduate Program in Pharmaceutical Sciences, Brazil

02.045 **Biochanin A Attenuates Nigrostriatal Degeneration and Motor/Non-Motor Impairments in Progressive Reserpine-Induced Parkinsonism**. Nascimento ACS[1], Souza JLS[2], Mendonça MS[2], Tavares MM[2], França RJO[2], Brito SC[1], Santos GJ[1], Dantas IC[2], Oliveira MCS[2], Santos JR[2], Camargo EA[1]. [1]UFS-São Cristóvão, Dept Physiology, Lab Pharmacology of Inflammatory Process, SE, Brazil; [2]UFS-Itabaiana Behavioral and Evolutionary Neurobiology Lab, Dept Biosciences, SE, Brazil.

02.059 **Plumieride Attenuates Long-Term Behavioral, Oxidative, Neuronal, and Barrier Dysfunction Following Neonatal Carbonyl Iron Exposure in Rats**. Eisendecker HI[1], Harle M[1], Guimarães GM[1], Sievers J[1], Nilz ACS[1], Malheiros A[1], Dalmagro AP[1,2], Souza MM[1]. [1]Univali, Itajaí, Santa Catarina, Brazil. [2]FURB, Blumenau, Santa Catarina, Brazil.

Totem 06

02.060 **Efficacy and Safety of Cannabidiol plus Δ^9-Tetrahydrocannabinol in Parkinson's Disease: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial**. Ruver-Martins AC[1], Silva ES[1], Matheus FM[1], Recchia MB[1], Cassenotte ACV[1], Franchi C[1], Lopes SC[2], Silva MD[3], Prediger RD[1] [1]UFSC, Experimental Lab Neurodegenerative

Diseases, Dept Pharmacology, Center of Biological Sciences, Florianópolis, Santa Catarina, Brazil. [2]UNIDAVI, Research Center in Medical Sciences, Investigations in Health (NPCMed), Faculty of Medicine, Rio do Sul, Santa Catarina, Brazil. [3]UFSC, Lab Neurobiology of Pain and Inflammation, Dept Physiological Sciences, Center for Biological Sciences, Florianópolis, Santa Catarina, Brazil.

02.061 **Gene–Environment Interaction in Transgenic Rats Overexpressing Human DISC1: Effects of Early Social Isolation on Behavioral Domains**. Pedroso-Fidelis GS, Ávila FC, Cruz FC, Hayashi MAF. Unifesp-EPM, Depto Farmacologia, PPG em Farmacologia, Brasil.

02.062 **Effect of Ibogaine on Hippocampus and Striatum NMDAR and GABAAR Expression in Male and Female Rats after Cocaine-CPP Exposure**. Heidrich N[1], Almeida FB[1], Ávila MS[2], Rocha DP[2], Barth RA[2] Silva IAG[1], Freese L[3], Barros HMT[1,2] [1]UFCSPA, PPG Ciências da Saúde, Brazil, [2]UFCSPA, Neuropsychopharmacology Lab, Brazil, [3]Northwestern University, Feinberg School of Medicine, Augustin Lab, Chicago, USA

02.063 **SARS-CoV-2 Spike Protein Induces Gut–Brain Axis Disruption and Cognitive Decline in a sex-Dependent Manner in mice**. Willrich CH[1], Cazarin CA[1,2], Cury BJ[1], Longo B[1], de Amorim GES[1,2], Machado GM[1], de Oliveira IM[1], Queiroz LY[1], Casimiro LM[1], Santos MR[1], Mariot, LN[1], de Sordi, R[1] Cimarosti HI[1,2], Prediger RDS[1,2], da Silva LM[1,2] [1]UFSC, Dept Pharmacology, Brazil; [2]UFSC, Neuroscience Postgraduate Program, Brazil

02.065 **Topical Modulation of cortical Dopamine D2 Receptors Alters Cortical Spreading Depression Propagation and Neuronal Activation in Rats**. Prieto SG[1], Cabrera-Baez M[2], Guedes RC[1] [1]UFPE, Center of Health Sciences, Nutrition Dept, Brazil, [2]UFPE, Center for Exact and Natural Sciences, Physics Dept, Brazil

02.066 **Effects of Klotho on cognitive and motor function in a mouse model of LPS-induced neuroinflammation**. Silva JN, Tavares ALPF, Lima TAS, Scavone C, Kawamoto EM. ICB-USP, Dept Pharmacology, Brazil.

03. Psychopharmacology

Totem 07

03.001 **Neuroprotection-Associated Reduction of Anxiety-Like Behavior Induced by *Spondias tuberosa* Arruda in Aged Wistar Rats Assessed by the Light-Dark Box and Open Field Tests**. Lessa IN[1], Souza ETN[1], Costa LL[3], Araújo AB[1,2], Araújo IGA[1,2], Medeiros IA[1,2], Soares JKB[1] [1]UFPB, Cardiovascular Pharmacology Lab, Institute for Research in Drugs and Medicines (IPeFarM), Brazil, [2]UFPB, Professional Master's Program in Gerontology (PPPGERONTO), Brazil, [3]UFCG-Cuité, Graduate Program in Natural Sciences and Biotechnology, Brazil.

03.002 **Potential Neuroprotective Effect of Free and Nanoencapsulated THC-Rich *Cannabis sativa* extract against nitrosative stress *in vivo***. Cunha MVS[1,3], Gonçalves MCF[1,2], Silva-Netto LS[1,3], Serra GL[1,3], Almeida JVM[1,3], Teixeira JL[1,3], Neri LCD[1,3], Matos ALLS[1], Dias AL[1,4], Pires HFO[1,4], Cruz LS[2], Silva PR[1,2],4, Xavier-Junior FH[2,3], Santos SG[2,3], Golzio AMFO[1,4,5] [1]UFPB, Psychopharmacology Lab, Brazil, [2]UFPB, PPG Bioactive Natural and Synthetic Products, Institute of Research in Drugs and Medicines, Brazil, [3]UFPB, Health Sciences Center, Brazil, [4]UFPB, PPG Cognitive Neuroscience and Behavior, Brazil, [5]UFPB, Dept Food Technology, Center for Technology and Regional Development, Brazil

03.003 **Aminothiophene Derivative 7CN03 as a Potential Anti-Inflammatory Agent: *In vitro* Analysis of Nitrite and Cytokine Modulation in J774 Macrophage Culture**. Almeida JVM, Mendes LM, Naves FB, Pereira CHL, Alves HAR, Neri LCD, Teixeira JL, Cunha MVS, Barbosa NMMV, Martins AMO, Oliveira LN, Soares MFS, Monteiro AB, Felipe CFB, Silva PR. UFPB, Psychopharmacology Lab

03.004 *in silico* and *in vivo* Evaluation of GABAergic Neurotransmission in the Anxiolytic-Like Effect of the Thiophenic Derivative 6CN07. Mendes LM, Naves FB, Almeida JVM, Pereira CHL, Alves HAR , Alves ARS, Teixeira JL, Neri LCD, Barbosa NMMV, Martins AMO, Oliveira LN, Soares MFS, Silva PR, Monteiro AB, Felipe CFB UFPB, Psychopharmacology Lab, Brazil

03.005 Evaluation of the Potential Anxiolytic-Like Effect of the Compound (Z)-N'-(1-Benzyl-2-Oxoindolin-3-Ylidene)-2-Fluorobenzohydrazide (ISA) Through *in silico* and *In vivo* Studies. Naves FB[1], Mendes LM[1], Pereira CHL[1] Almeida JVM[1], Alves HAR[1], Teixeira JL[1], Barbosa NMMV[1], Martins AMO[1], Oliveira LN[1], Neri, LCD[1], Soares MFS[1], Silva PR[1], Monteiro AB[1], Lima-Junior CG[2], Felipe CFB[1]. [1]UFPB. Psychopharmacology Lab, Brazil. [2]UFPB. Medicinal Organic Synthesis Lab.

03.006 Paroxetine Dose-Dependently Attenuated the Impaired Fear Extinction in Female iNOS Knockout Mice. Barbosa KE, Meyer E, Da Silva TA, Lisboa SF FCFRP-USP, Dept Biomolecular Sciences, Brazil

Totem 08

03.018 Spermidine and Arcaine Modulate Defensive Behavior in Mice. Zambon AF, Timm A, Martins FC, Costa EF, Mello CF UFSM, Dept Physiology and Pharmacology, PPG in Pharmacology

03.019 Effects of Association Between Resveratrol and Ketamine on Behavioral and Biochemical Analysis in Mice. Juliani PZ[1], Silva MF[1], Rodrigues T[1], Bressan GN[2], Camponogara C[2], Oliveira SM[2], Brucker N, Fachinetto R[1,2]. [1]UFSM, PPG in Biological Sciences: Pharmacology, Brazil; [2]UFSM, PPG in Biological Sciences: Toxicological Biochemistry, Santa Maria, RS, Brazil

03.020 Investigation of the Antinociceptive Effect of the Monoterpene Hydroxycitronellal in mice. Dias AL[1], Remígio MCRB[2], Pires HFO[1], Gonçalves MCF[2], Neri LCD[1], Salvadori MGSS[1] [1]UFPB, PPG in Cognitive Neuroscience and Behavior, Brazil. [2]UFPB, Psychopharmacology Lab, Institute of Drugs and Medicines Research, Brazil.

03.021 Quantification of Neurotransmitters in the Striatum of Rats with Distinct Immobility Profiles in the Forced Swimming Test. Silva IAG[1], Almeida FB[1], Guasselli MD[2], Nin MS[1,2], Eller SCWS[3], Barros HMT[1,2] [1]UFCSPA, PPG Ciências da Saúde, Porto Alegre, RS; [2]UFCSPA, Lab Neuropsicofarmacologia, Dept. de Farmacociências, Porto Alegre - RS; [3]UFCSPA, Lab Toxicologia Analítica, Central Analítica, Porto Alegre - RS.

03.022 Potential Antioxidant Effect of Free and Nanoencapsulated *Cannabis sativa* L. Extract in a Dexamethasone-Induced Depression Model. Gonçalves MCF[1,2], Silva-Netto LS[1,3], Cunha MVS[1,3], Serra GL[1,4], Neri LCD [1,4], Matos ALLS1, Dias AL[1,5], Pires HFO[1,5], Cruz LS2, Xavier-Junior FH2,3, Santos SG2,3, Silva PR[1,2],5, Golzio AMFO[1,5,6] [1]UFPB, Psychopharmacology Lab, [2]UFPB, PPG Bioactive Natural and Synthetic Products, Institute of Research in Drugs and Medicines, Brazil, [3]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil, [4]UFPB, Dept Biomedical Sciences, Health Sciences Center, Brazil, [5]UFPB, PPG Cognitive Neuroscience and Behavior, Brazil, [6]UFPB, Dept Food Technology, Center for Technology and Regional Development, Brazil

04. Inflammation and Immunopharmacology

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04.001 Anti-Inflammatory Activity of Methyl 2-(3-hydroxy-1-methyl-2-oxoindolin-3-yl) acrylate (MISACM) in Murine Acute Lung Injury. Mota PRV, Pordeus GM, Silva TGd, Félix MJD, Rodrigues MRF, Laurentino MVS, Moura BVS, Oliveira JB, Gadelha FAAF, Vieira GC, Dejani NN. UFPB, Lab Immunopharmacology, Brazil.

04.002 Structural and Quantum Perspective on the Potential Anti-Inflammatory Mechanisms of Caulerpin as a TLR2 Modulator. Coringa WV[1], Assunção AS[1], Paiva EA[1], Santos BVO[5], Menezes GL[3], Sena CPS4, Vieira D S4, Fulco UL[3], Bezerra KS[2,3], Souto JT[1]. [1]UFRN, Lab Immunopharmacology, Brazil. [2]Unicamp, Gleb Wathing Institute of Physics,

Brazil. [3]UFRN, Dept Biophysics and Pharmacology, Brazil. [4]UFRN, Institute of Chemistry, Brazil. [5]UFCG, PPG in Development and Technological Innovation in Medicines, Brazil.

04.003 **Role of the Endogenous Hydrogen Sulfide (H_2S) in the Inflammatory Response Induced by Bacterial Membrane Lipopolysaccharide (LPS) in cultured THP-1 Macrophages**. Rodrigues JLG, Coavoy-Sánchez SA, Teixeira SA, Costa SKP, Muscará MN ICB-USP, Pharmacology Dept, Lab Free Radicals, Inflammation and Pain.

Totem 09

04.020 **Sexual Dimorphism in Viral Inflammatory Responses**. Schneider VMM, Alencar ST, Costa RA, Borges AP, Pereira V, Malheiros MB, Baggio FD, Zampronio RA UFPR

04.021 **Investigation of the Immunomodulatory Potential of the Alkaloid 6,6a-Dihydrodismethoxyguadiscine Isolated from** *Guatteria friesiana*. Neto AC[1], Cezar IS1,2, Ramos KS2,3, Silva DKC2,3, Gonçalves RS4, Soares MBP1,2, Costa EV5, Meira CS1,2,3. 1 Fiocruz-BA, Salvador, 2 SENAI CIMATEC-BA, Salvador, 3 UNEB-BA, Salvador, 4 UFPR-PR, Palotina, 5 UFAM-AM, Manaus.

04.022 **Hydroethanolic extract from** *Selaginella selowii* **(EHSS) reduces** *In vitro* **Neutrophil Chemotaxis without Inducing Cytotoxicity**. Diniz FS, Machado LL, Lossavaro PKMB, Fernandes, MML, Toffoli-Kadri MC, Silva-Filho, SE. UFMS, FACFAN

04.023 **A Role for Protease-Activated Receptor (PAR) 4 on the Impairment of LPS-Induced Nitric Oxide Production by P1G10 Proteolytic Fraction Obtained from** *Vasconcellea cundinamarcensis* **in Macrophages**. Silva CR[1], Torres MPB[1], Lopes MTP[2], Klein A[1] [1]ICB-UFMG, Lab Inflamação e Proteases, [2]ICB-UFMG, Lab Substâncias Antitumorais, Depto Farmacologia, Belo Horizonte, MG, Brasil.

04.024 **Evaluation of the Effects of Docosahexaenoic Acid (DHA) and DHA-Loaded Nanocapsules on the Endothelium in** *In vitro* **and** *in vivo* **models**. Gomes-Reis GLS[1], Moraes BPT[2], Saraiva JSG[2], Cunha CMC[1], Ferreira-Costa M[1], Santos FS[3], Ferreira AM[1], Bozza PT[1], Castro-Faria-Neto HC[1], Ferrarini SR[4], Silva AR[1], Gonçalves-de-Albuquerque CF[12]. [1]IOC-Fiocruz, Immunopharmacology Lab and PPG in Cellular and Molecular Biology, Rio de Janeiro, Brazil; [2]Unirio, Immunopharmacology Lab and PPG in Molecular and Cellular Biology, Rio de Janeiro, Brazil; [3]UFF, PPG, in Neuroscience, Niterói, Brazil; [4]UFMT-Sinop, PPG Health Sciences, Brazil

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04.036 **Novel Dual-Acting MAO/PDE4 Inhibitors: Pharmacological Characterization of a Potential Multitarget Approach for Inflammatory Lung Diseases**. Ota RSN[1,2], Bezerra LCA[3], Souza LM[1], Ferreira TPT[1], Chavarria DF[4], Borges MFM[4], Kümmerle AE[3], Martins MA[1], Silva PMR[1] [1]IOC-Fiocruz, Lab of Inflammation, Rio de Janeiro, Brazil; [2]UFRJ, PPG Pharmacology and Medicinal Chemistry, Rio de Janeiro, Brazil; [3]UFRRJ, LaDMol-QM, Rio de Janeiro, Brazil; [4]University of Porto, Porto, Portugal.

04.037 **Biomaterials from Sea-cucumber Body Wall Promote Bioactive Responses in RAW264. 7 Macrophages**. Penno SM[1], Cahú TB[1,2], Silva JCA[1], Motta JM[1], Todeschini AR[2], Vilela-Silva ACES[3], Mourão PAS.[1] [1]IBqM-UFRJ, Lab Tecido Conjuntivo-, [2]IBCCF-UFRJ, Lab Glicobiologia Estrutural e Funcional, [3]ICB-UFRJ, Lab Atividade Biológica de Glicoconjugados, Brasil.

04.038 **Anti-Inflammatory Potential and Toxicity of Sulcatone (6-Methyl-5-hepten-2-one) in a** *Zophobas morio* **Larval Model**. Ferreira CES[1], Acha BT[1], Cunha FCS[2], Soares T[1], Oliveira MP[3], Rêgo AF[4], Macedo JL[1], Alves MMM[3], Oliveira AP[6], Arcanjo DDR[6], Martins MCC[6,7] [1]UFPI, PPG em Biotecnologia (Renorbio), Teresina, PI, Brazil, [2]UFPI, PPG em Tecnologias Aplicadas a Animais de Interesse Regional, Teresina, PI, Brasil, [3]UFDPar, Parnaíba, PI, Brasil, [4]UFPI,

PPG em Farmacologia, Teresina, PI, Brasil, [5]UFPI, Depto Morfofisiologia Veterinária, Teresina, PI, Brasil, [6]UFPI, Depto Biofísica e Fisiologia, Teresina, PI, Brasil, [7]UNIFAESF, Centro Universitário

04.039 **Bosutinib Modulates Microglial Inflammation Induced by Bacterial Insult**. Cunha CMC[1,2,3], Patricio IM[1,2,3], Ferreira-Costa M[1,2,3], Santos FS35, Gomes-Reis GLS[1,2,3], Moraes BPT[3,4], Ferreira AMS[1,2,3], Sayão PGF[1,3,4], Alves-Nunes L[1,3], Ferreira LN[1,3], Bozza PT[1,2], Castro-Faria-Neto HC[1,2], Gonçalves-de-Albuquerque CF[1,2,3,4,5], Silva AR[1,2,5] 1IOC-Fiocruz, Immunopharmacology Lab, Rio de Janeiro, Brazil. [2]IOC-Fiocruz PPG in Cellular and Molecular Biology, Rio de Janeiro, Brazil. [3]Unirio, Immunopharmacology Lab, Rio de Janeiro, Brazil. [4]Unirio, PPG in Molecular and Cellular Biology, Rio de Janeiro, Brazil. [5]UFF, PPG in Neuroscience, Niteroi, Brazil.

04.040 **Gastroprotective Effects of Isoflavones in Experimental Models of Gastric Ulcer: A Systematic Review**. Santos GJ[1], Couto CM[2], Souza DA[1], Aragão JMDA[1], Ramos LS[1], Grespan R[1], Camargo EA[1] [1]UFS-São Cristóvão, Lab Pharmacology of the Inflammatory Process, Dept Physiology, SE, Brazil; [2]UFS, Dept Pharmacy, Brazil

04.041 **Anti-Inflammatory Effect of the Synthetic Alkaloid Tetrahydroisoquinoline 2-(7-Methoxy-1,2,3,4-Tetrahydroisoquinoline-1-YL)Phenol (MTF) In Murine Models of Acute Inflammation**. Oliveira JB[1], Vieira CID[1], Lima LM[1], Moura BVS[1], Laurentino MVS[1], Mota PRV[1], Pordeus GM[1], Ferreira LKDP[2], Silva TG[1], Ferreira LAMP[1], Bernardo LR[1], Gadelha FAAF[3], Dejani NN[1], Piuvezam MR[1] [1]UFPB, Immunopharmacology Lab, Brazil, [2]UFAL, Center for Medical and Nursing Sciences, Brazil, [3]UFPB, Institute for Drug and Medicine Research, Brazil

04.042 **Ouabain Improves Pulmonary Function in a Murine Model of Mixed Asthma**. Ribeiro, MR[1], Souza-Lima T[1], Siena A[1], Francelino-Alves V[1], Melhado IV[1], Fernandes PH[1], de Sá Lima L[1], Andreotti DZ[1], Oliveira MA[1], Leite J[2], Moriya HT[3], Rodrigues-Mascarenhas S[4], Tavares-de-Lima W[1], Scavone C[1] [1]ICB-USP, Dept. of Pharmacology, SP, Brazil; [2]ICB-UFG, Dept. of Pharmacology, GO, Brazil; [3]EP-USP, Dept. of Telecommunication and Control Engineering, SP Brazil; [4]UFPB, Dept of Cell and Molecular Biology, João Pessoa, PB, Brazil

04.061 **Curcumin Modulates Nitric Oxide Production in BV2 Microglial Cells Exposed to** *Escherichia coli*. Barbosa RS[1,2,3], Santos FS[1,2], Castro-Faria-Neto HC[1], Bozza PT[1], Silva AR[1,2], Gonçalves-de-Albuquerque CF[1,2,3] [1]Unirio, Lab Immunopharmacology, Dept Physiological Sciences, Federal, Rio de Janeiro, Brazil. [2]IOC-Fiocruz, Lab Immunopharmacology, Rio de Janeiro, Brazil. [3]Unirio, PPG in Molecular and Cellular Biology, Rio de Janeiro, Brazil.

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04.043 **Evaluation of the Anti-Inflammatory Activity Of Novel PPARγ Agonists**. Krepsky LM, Vaz CR, Mello M, Pereira MES, Buzzi FC, Corrêa R, Quintão NL, Benvenutti L, Santin JR Univali, PPG Ciências Farmacêuticas, Brasil

04.044 **PPAR-γ Participates in the Anti-Inflammatory and Immunomodulatory Action of Palmitoylethanolamide in Murine Graft-versus-Host Disease**. Tonidandel ZD[1], Linhares AFS[1], Ruggio GMF[1], Rocha ES[1], Sales MA[1], Galvão I[2], Rezende BM[3], Teixeira MM[2], Romero TRL[4], Pinho V[5], Castor MGM[4] [1]UFMG, PPG Pharmacology and Physiology, Brazil. [2]UFMG, Dept. of Biochemistry and Immunology, Brazil. [3]UFMG, Dept. of Pathology, Brazil. [4]UFMG, Dept. of Physiology and Pharmacology, Brazil. [5] UFMG, Dept. of Morphology, Brazil

04.045 **Thiazoquinoline Derivatives Modulate Cytokine Production in PBMCs from Patients with Systemic Sclerosis and in Mouse Splenocytes**. Gonçalves MEO, Ferreira JRS, Cunha EGC, Almei AR, Pereira MC, Pitta MGR. UFPE, Núcleo de Pesquisa em Inovação Terapêutica - Suely Galdino, PPG em Inovação Terapêutica, Brasil.

04.046 **Bioactivity-Guided Study of the Anti-Inflammatory Effects of Brazilian Brown Propolis from Mimosa tenuiflora in LPS-Stimulated RAW 264. 7 Macrophages**. Felício IM[1], Silva TMS[2], Baranger K[3], Picot L[3], Cavalcante FA[1] [1]CCS-UFPB, PPgPNSB, Brazil; [2]DQ-UFPE, Brazil; [3]La Rochelle Université, LIENSs, France

04.047 **Long-Term Impact of Hormone-Induced Premature Ovulation on Pulmonary Responses to Experimental Asthma: Role of Calcitonin Gene-Related Peptide** (**CGRP**). Alves VF[1], Frajblat M[3], Moriya HT[2], Serra CSM[1], Teixeira SA[1], Brain SD[4], Tavares-de-Lima W[1], Muscará NM[1], Costa SKP[1] [1]ICB-USP, Dept. of Pharmacology, São Paulo Brazil; [2]IBCCF-UFRJ, Health Sciences Center; [3]EP-USP, Dept. of Telecommunication and Control Engineering, São Paulo, Brazil; [4]King's College London, School of Cardiovascular Medicine & Sciences, Waterloo Campus.

04.048 **Effects of Inactivated** *Bifidobacterium animalis* **subsp. lactis CCT 7858 on Inflammatory Parameters Induced by Monosodium Glutamate in Wistar Rats**. Comis Neto AA, Arena RV, Batista WT, Luzardo BFS, Gomes, J, Fontoura, EA, Rodrigues, ES, Streb, BL, Rosa SG, Pinton S Unipampa-Uruguaiana, Brazil

04.049 **Modulation of Pro-inflammatory Cytokines and Oxidative Stress by Isoquercitrin Complexed with γ-Cyclodextrin in a CFA-Induced Arthritis Model**. Moreira FAS, Veloso VL, Oliveira FA UFPI, Center for Research on Medicinal Plants

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04.064 **Marine-Derived Collagen and Chondroitin Sulfate Biomaterial Associated With Natural Antioxidants for Experimental Osteoarthritis**. Cahú, TB[1,2,3], Xavier, CHO[1,2], Oliveira, JL[1,3], Penno, SM[1], Freire-de-Lima, CG[4], Todeschini, AR[3], Mourão, PAS[1]IBqM-UFRJ, Lab Tecido Conjuntivo, [2]BioMatrix Inova Simples, [3]IBCCF-UFRJ, Lab Glicobiologia Estrutural e Funcional, [4]IBCCF/UFRJ, Lab Imunomodulação, Rio de Janeiro, Brazil.

04.065 **Nanocoumarin as a Leishmanicidal** (*Leishmania braziliensis*) **Strategy: Apoptotic Effects, TNF-α Production, and Molecular Interaction with Matrix Metalloproteinase-9 and Trypanothione Reductase**. Araújo AB[1], Gonçalves IFS[1], Almeida TS[1], Colares NN[1], Lopes AJSB[1], Pereira PIO[1], Rodrigues NLC[2], Teixeira MJ[2], Leal LKAM[1] [1]UFC, Dept Pharmacy, PPG Pharmaceutical Sciences, Brazil [2]UFC, Lab. of Parasitology, Brazil.

04.066 **Nanostructured Lipid Carriers as Topical Delivery Systems for the Hydrogen Sulfide Donor GYY4137 and Psoriasis Treatment**. Passos JS, Lopes LB ICB-USP, Brazil

04.067 **Ouabain Mitigates the Damage of Zika Virus Infection in SH-SY5Y Cells**. Sales-Neto JM[1], Magalhães DWA[2], Carvalho DCM[3], Silva PG[4], Pena LJ[4], Moura MT[5], Rodrigues-Mascarenhas S[1] [1]UFPB, Biotechnology Center, Lab Immunopharmacology, PPG in Biotechnology, João Pessoa, PB. [2]UFPB, Biotechnology Center, Lab Immunopharmacology, Multicenter PPG in Physiological Sciences, João Pessoa, PB. [3]ICB-Unifal, Lab Vaccines, MG, [4]Fiocruz, Aggeu Magalhães Institute, Dept Virology and Experimental Therapy, PPG in Biosciences and Biotechnology in Health, Recife, PE. [5]UFPB, Biotechnology Center, Lab Cellular Reprogramming, Multicenter PPG in Physiological Sciences, João Pessoa, PB

04.068 **Extracellular Vesicles from N2-like Neutrophils Enhance Triple-Negative Breast Cancer Aggressiveness through a L-Selectin-Dependent Protumoral Signaling Axis**. Amorim CS[1], Amorim NS[1], Frony AC[2], Miranda BT[3], Pires GS[4], Pinheiro, PSM[4], De-Freitas-Junior JCM[2], Renovato-Martins M[5], Barja-Fidalgo C[2], Moraes JA[1] [1]UFRJ, Redox Biology Lab, Brazil; [2]UERJ, Cellular and Molecular Pharmacology Lab, Brazil; [3]UFRJ, Cellular and Molecular Cardiology Lab, Brazil,[4]UFRJ, Lab for the evaluation and synthesis of bioactive substances, Brazil, [5]UFF, Inflammation and Metabolism Lab, Brazil.

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04.069 **Modulation of Bacteria–Host Interactions during Experimental Intestinal Mucositis by a Resveratrol Analog**. Oliveira LG, Reis ACC, Eufrásio ALL, Souza ILL, Silva AD, Meinel RS, Macedo GC, Avila TV UFJF

04.070 **Circulating IL-13 Levels Correlate with Oxidative Imbalance and Impaired Innate Immune Function** *in silica*-**Exposed Workers**. Ferreira TPT[1,2], Ribeiro PC[3], Arantes ACS[1], Guimarães FV[1], Castro-Faria-Neto HC[4], Martins MA[1], Castro HA[3], Silva, PMR[1] [1]IOC-Fiocruz, Lab Inflammation, [2]UFRJ-Duque de Caxias; [3]ENSP-Fiocruz, Occupational Lung Diseases Outpatient Clinic of the Center for Studies on Workers' Health and Human Ecology, [4]IOC-Fiocruz, Lab Immunopharmacology, RJ, Brazil.

04.071 **Tirzepatide Differentially Modulates Reactive Oxygen Species Production in Brown and White Adipose Tissues During Systemic Inflammation**. Aguiar SCR[1], Vale KBL[1], Cruz EKM[1], Franco GHSP[1], Trindade KP[1], Silva LC[1], Gonçalves LJF[1], Souza PEN[2], Souza FHV[1]. [1]UnB, Lab. of Experimental Biomodels, PPG in Health Sciences and Technologies, Brazil, [2]UnB, Lab. of Electron Paramagnetic Resonance, Brazil.

04.073 **Hydroethanolic Extract of** *Calycophyllum spruceanum* **Barks Attenuates Acute Inflammation by Modulation of NO-, TNF-α- and PGE2-Dependent Pathways**. Assreuy AMS[1], Azevedo VGS[1], Silva APAB[2], Nascimento FGS[1], Amorim RMF[1], Peixoto ABS[1], Araujo DF[1], Cunha RM[2] [1]ISCB-UECE, Brazil, [2]UFAC, Lab Fisiofarmacologia, Brazil

04. Biology and Cardiovascular Diseases

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04.006FR **Effects of a Multi-Strain Probiotic on Blood Pressure and Cardiovascular Function in Rats with Renovascular Hypertension**. Freire MOL[1], Souza RMP[2], Andrade JT[2], Fernandes KFD[1], Cruz Neto JPR[1], Flôr AFL[2], França-Falcão MS[2], Souza EL[1], Alves JLB[1] [1]UFPB, Dept Nutrition, Health Sciences Center, PPG Nutrition Sciences, Brazil; [2]UFPB, Dept Biotechnology, Multicenter Graduate Program in Physiological Sciences, Brazil

04.007FR **Intake of NaCl and $NaHCO_3$ during the Development of 2-Kidney-1-Clip Hypertension in Rats**. Pereira MS, Lima RVS, Cavalcante ABL, Cunha SMP, Figueiredo EVS, Roncari CF, David RB. UFC (UFC), School of Medicine, Dept Physiology and Pharmacology, Fortaleza, CE, Brazil.

05. Pain and Nociception Pharmacology

Totem 14

05.001 **α-Terpineol-Loaded Nanosystems for the Treatment of Pain Induced by Sarcoma 180 Cells**. Poderoso VM[1], Amorim JCG[1], Araujo DS[1], Fagundes LS[1], Sá MEB[1], Silva VGO[1], Barreto MS[2], Gonçalves VSS[2], Lisboa JS[2], Pacheco PGS[2], Silva AS[2], Souza JB[2], Araújo ZS[3], Guimarães AG[4]. [1]LAFACE-UFS, Dept Pharmacy, Lab Clinical and Experimental Pharmacology, Brazil, [2]UFS, Graduate Program in Pharmaceutical Sciences, Brazil, [3]UFS-Lagarto, Graduate Program in Health Sciences, Brazil, [4]UFS, Dept Pharmacy, Brazil.

05.002 **Correlation Between Antinociceptive Effects Previously Observed** *in vivo* **and Opioid Receptor Interactions of α-Phellandrene: Insights From Molecular Docking And Dynamics**. Dias WA[1], Martins RYC[1], Sales SCS[1], Santos ALS[1],Gomes JGF[1], Barbosa BDS, Sousa DP[2], Almeida FRC[1] [1]UFPI, CCS, PPGFARM, Lab Pain Pharmacology, [2]UFPB, Dept Pharmacy, Federal University of Paraíba, Brazil.

05.004 **Study of the Cutaneous Safety and Antinociceptive Potential of Canabigerol-Based Creams**. Bazilio YS[1], Rezende B[1], Macario VSG[1], Guedes GN[1], Maia EP[1], Romana B[1], Oliveira L[2], Maluf D[2], Antunes F[3], Fontes FL[1], Montes GC[1] [1]IBRAG-UERJ, Roberto Alcântara Gomes Institute of Biology, Brazil, [2]UFPR, Dept Pharmacy, Brazil, [3]UENF-Darcy Ribeiro, Center for Agricultural Sciences and Technology, Brazil

05.005 **Synthetic Flavonoid Presents Antinociceptive Effects in a Diabetic Peripheral Neuropathy Model**. Dambros LV[1], Silva RD[1], Atuati SF[1,2], Oliveira SM[1,2] [1]UFSM-Santa Maria, Lab Neurobiology of Pain – Pain Research Group, Brazil; [2]USFM-Santa Maria, PPG Biological Sciences: Toxicological Biochemistry, Brazil

05.006 **Evaluation of the Antinociceptive Activity of *Cereus jamacaru* DC. (Cactaceae) Roots**. Deus GO[1], Santos EE[2], Costa WK[3], Correia MTS[3], Souza TA[4], Abreu LS[5], Oliveira AM[2], Cibulski SP[2], Alves HS[1],[2] [1]UEPB, CCBS, Dept. of Pharmacy, Brazil, [2]UEPB, PPG in Pharmaceutical Sciences (PPGCF), Brazil, [3]UFPE, CB, Dept. of Biochemistry, Lab Natural Products, Brazil, [4]IPeFarM-UFPB, Institute of Research in Drugs and Medicines, Brazil, [5]UFF, Institute of Chemistry, Brazil

05.007 **Cannabinoid Receptor 2 as a Potential Therapeutic Target in an Experimental Model of Nociplastic Pain**. Lopes JPV, Atuati SF, Assis ACP, Oliveira SM. UFSM, Pain Neurobiology Lab, Graduate Program in Biological Sciences: Toxicological Biochemistry, Brazil.

05.011 **Antinociceptive Potential and Skin Irritation Profile of Ointments Containing Cannabis Extract**. Guedes GN[1], Macario VSG[1], Rezende B[1], Bazilio YS[1], Maia EP[1], Cunha LG[1], Romana B[2], Montes GC[1] [1]IBRAG-UERJ Lab Pharmacology and Psychology; [2]UERJ Dept Histology and Embryology; [3]UFPR, Dept Pharmacy, Brazil.

Totem 15

05.015 **Effects of the PPARγ Agonist TZD-D3 on Joint Degeneration and Pain in a Monoiodoacetate (MIA)-Induced Osteoarthritis Model**. Goldoni RC[1], Goldoni FC[1], Eisendecker HI[1], Malburg CC[2], Antunes AT[2], Pereira MES[1], de Campos-Buzzi F[1], Santin JRS[1], da Costa R[3], Quintão NLM[1] [1]Univali, PPG in Pharmaceutical Sciences, [2]Univali, Dentist Course, Santa Catarina, Brazil, [3]UFRJ, School of Pharmacy, RJ, Brazil.

05.016 **Network Pharmacology: Potential Therapeutic Targets of Melittin in Chronic Neuropathic Pain**. Teixeira RMS[1], Boaventura de Oliveira AM[1], Almeida TC[1], Sant'Anna MB[1], De Franco M[2], Picolo G[1]. [1]IBu, Lab Pain and Signaling, São Paulo, Brazil; [2]Pasteur Institute, Diagnostic Section, São Paulo, Brazil

05.017 **Protease Activated Receptor 2 Mediates the Migraine-Like Pain in a Nociplastic Pain Model**. Mendes, TO[1], Perazzio, ACA[1], Becker, G[1], Fialho, MFP[2], Brum, ES[3], Lopes, JPV[1], Oliveira, SM[1] [1]UFSM, Pain Neurobiology Lab, Graduate Program in Biological Sciences: Toxicological Biochemistry, Centre of Natural and Exact Sciences, Brazil; [2]New York University, College of Dentistry, Dept Molecular Pathobiology, Pain Research Center, United States of America; [3]UFRGS, NeuPain, Dept Biochemistry, Institute of Basic Health Sciences, Brazil,

05.018 **Nanosystems Containing α-Terpineol in the Treatment of Tumor-Induced Cancer Pain**. Silva AS[1], Gonçalves VSS[1], Souza JB1, Pacheco PGS[1], Barreto MS[1], Lisboa JS[1], Araújo ZS[2], Poderoso VM[3], Silva VGO[3], Sá MEB[3], Fagundes LS[3], Araujo DS[3], Amorim JCG[3], Guimarães AG[4]. [1]UFS, Graduate Program in Pharmaceutical Sciences, Brazil, [2]UFS, Graduate Program in Health Sciences, Lagarto Campus, Brazil, [3]LAFACE-UFS, Dept Pharmacy, Lab Clinical and Experimental Pharmacology, Brazil, [4]UFS, Dept Pharmacy, Brazil.

05.019 **Mitochondrial Aldehyde Dehydrogenase-2 and 4-Hydroxynonenal Mediates Morphine Analgesic Tolerance and Hyperalgesia via TRPA1 Activation**. Pennachioni NP[1,2], Hosch NG[1], Martins BB[1], Silva GSA[1], Troitiño VC[1,2], Dallazen JL[1,3], Kiataki LGS[1,3], Andersson D[4], Bevan S[4], Zambelli VO[1,3]. [1]IBu. Pain and Signaling Lab, IBu, São Paulo. [2]University of Sao Paulo, Interunits Biotechnology Postgraduate Program. [3]Kings College London, Wolfson Sensory, Pain and Regeneration Centre, [4]IBu, Centre of Excellence in New Target Discovery, São Paulo.

05.020 **Targeting Drp1-Mediated Mitochondrial Fission to Mitigate Paclitaxel-Induced Neurotoxicity in Dorsal Root Ganglion Sensory Neurons**. Troitiño VC[1,2], Hosch NG[1], Behr BB[1], Schiess, MC[1], Pennachioni NP, Santos LGK[1], Silva GSA[1], de Ocesano CP[3], Buri MV[3], Chudzinski-Tavassi AM[3], Zambelli VO[1,3]. [1]IBu, Pain and Signaling Lab, São Paulo. [2]USP, Interunits Biotechnology Postgraduate Program, São Paulo. [3]IBu, Centre of Excellence in New Target Discovery, IBu, São Paulo.

05.021 **Involvement of Transient Receptor Potential Ankyrin 1 in Nociplastic Pain-Associated Behaviours in Mice**. Favarin A[1], Perazzio AC[1], Fialho PMF[1,2], Saldanha BA[3], Oliveira SM[1], Brum ES[1,3] [1]UFSM, Graduate Program in Biological Sciences: Toxicological Biochemistry, Centre of Natural and Exact Sciences, Brazil, [2]NYU, Dept Molecular Pathobiology, College of Dentistry, Pain Research Center, United State of America; [3]UFRGS, Graduate Program in Biological Sciences: Biochemistry, Dept Biochemistry, Institute of Basic Health Sciences, Brazil

05.027 **Antinociceptive Effects of *Oxandra martiana* Extract in Acute and Neuropathic Pain Models**. Macario V[1,2], Rezende B[1,2], Santos YB[1], Guedes GN[1], Maia EP[1], Antunes F4, Abreu L[5], Fontes-Dantas FL[2,3], Montes GC[1,2] [1]UERJ, Neurobiology Lab, Brazil, [2]FISCLINEX/UERJ – PPG in Clinical and Experimental Physiopathology, Brazil, [3]UERJ, Neuropharmacogenetics Lab, Brazil, 4UENF, Animal Clinical and Surgical Lab, Brazil, [5]UFF, Chemistry and Natural Products Lab, Brazil.

Totem 16

05.029 **Cannabidiol-Loaded Microemulsion Enhances Antinociceptive Efficacy and Modulates Neuroinflammatory and Oxidative Stress Pathways in Neuropathic Pain**. Santana TCM[1], Cruz ABO[2], Oliveira LGS[3], Lauria PSS[4], Nunes VLC[5], Brustolim, D[2], Egito EST[3], Viana MDM[2], Villarreal CF[1,2] [1]Fiocruz-BA, Gonçalo Moniz Institute, Brazil; [2]UFBA, School of Pharmacy, Brazil, [3]UFRN, Federal University of Rio Grande do Norte, Pharmacy Dept, Brazil; [4]Dept Cell Biology and Human Anatomy, University of California Davis, Sacramento, United States; 5UFBA, School of Medicine, Brazil

05.030 **Advanced Glycation End-Products Promote Neuronal Dysfunction and Neurodegeneration in Sensory-Like Neurons and Sensorimotor Organoids**. Silva GSA[1], Bufalo MC[3,4], Chudzinski-Tavassi AM[3,4], Pereira JD[2], Zambelli VO[1,3]. [1]IBu, Lab Pain and Signaling, Brazil. [2]University of ALABAMA at Birmingham, Dept Neurology, USA. [2]IBu, Center of Excellence in New Target Discovery, Brazil. [4]IBu, Innovation and Development Center, Brazil.

05.031 **Therapeutic Effects of Botulinum Neurotoxin-A Formulations in a Model of Temporomandibular Joint Dysfunction**. Couto ACG[1], Silva TM[1], Costa ARG[2], Santos DO[2], Faria PR[2], Crosara TA[3], Januzzi E[3], Silva CR[1] [1]UFU, GPANI, PPGGB, Brazil; [2]UFU, Dep. Oral and Maxillofacial Pathology, Brazil; [3]NEON, MG, Brazil.

05.032 **Anti-Inflammatory and Chondroprotective Potential of *Hibiscus sabdariffa* L. in Experimental Osteoarthritis: Phytochemical Analysis and Histopathological Evaluation**. Cruz ACSN[1], Mesquita MJTAM[1], Miranda AJA[2], Lima VAS[2], Xavier JKAM[2], Ataides GC[2], Rocha CQ[2], Teixeira JTAMMM[3], Sousa JCS[4], Carvalho RC[5], Fernandes SCSS[7], França CPC[8] Andrade MS[6], Cartagenes MSS[1]. [1]LEED-UFMA, Experimental Lab for Pain Studies, Brazil; [2]LQPN, UFMA, Natural Products Chemistry Lab, Brazil; [3]CEUMA, Medical School, Brazil; [4]UFMA, Dept Morphology, Brazil; [5]UFMA, Graduate Program in Health Sciences, Brazil; [6]UFMA, Graduate Program in Adult Health, Brazil; [7]CEUMA, Nursing, Brazil; [8]UniRV-Formosa, Brazil.

05.033 **CBD- and CBG-Loaded Nanoemulsions in Experimental Models of Acute and Neuropathic Pain**. Rezende B[1,2], Macario VMS[1,2], Santos YB[1], Nascimento GG[1], Audízio LR[4], Antunes F[4], Maluf DF[5], Oliveira L[5], Lopes BA[6], Döll-Boscardin PM[6], Nadal JM[6], Farago PV[6], Fontes-Dantas FL[2,3], Montes GC[1,2,3] [1]UERJ, Neurobiology Lab, Brazil, [2]FISCLINEX-UERJ, PPG in Clinical and Experimental Physiopathology, Brazil, [3]UERJ, Neuropharmacogenetics Lab, Brazil, [4]UENF PPG Veterinary Medicine, Brazil, [5]UFPR, Brazil, 6UEPG, Brazil

Totem 17

05.041 **Microcirculatory and Antinociceptive Effects of Photobiomodulation in Chronic Constriction Injury**. Baptista FBO[1], Bonifácio RP[1], Santos MER[1], Elias MLC[2], Santos TCS[2], Gonçalves LRC[2], Zychar BC[2],Chacur M[1] [1]ICB-USP, Dept Anatomy, Functional Neuroanatomy of Pain Lab, Sao Paulo, Brazil. [2]IBu, Pathophysiology Lab, Sao Paulo, Brazil.

05.042 **Ketamine Reduces Formalin-Induced Inflammatory Nociception in Male Mice: Preliminary Dose-Response Evidence**. Silva AJM, Mascarenhas DC UEM, Dept Pharmacology and Therapeutics, Brazil Graduate Program in Pharmaceutical Sciences, Brazil

05.043 **Antinociceptive and Anti-Inflammatory Effects of Different Full Spectrum Oils of Phytocannabinoids in Mice Models of Pain and CFA Induced Inflammation**. Junger MG, Matheus ME, Oliveira DR, Miranda ALP. UFRJ, Faculty of Pharmacy, PPG Pharmaceutical Sciences, Brazil

05. Biology and Gastrointestinal Diseases

Totem 27

05.001FR **Gut Microbiota Profiles Across Insulin Resistance Levels in Children**. Neves TAFV[1], Moraes RCS[1], Clementino LCRF[1], Silva JVG[1], Alves JLB[1], Martins VJB[2] [1]UFPB Dept Nutrition, Brazil; [2]UFPB Dept Biomedical Sciences, Brazil

06. Cardiovascular and Renal Pharmacology

Totem 18

06.001 **Effects of Long-Acting Testosterone (Nebido®) on the Renal Function of Isolated Kidneys from Hypertensive and Normotensive Rats**. Portacio LFS, Sousa BMS, Santiago RO, Paz IA, Santos CF, Nascimento NRF. UFC

06.002 **Positive Inotropic Effect of Iochroma arborescens Extract in an Isolated Organ Bath Model**. Sousa BMS[1], Portácio LFS[1], Martins RES[1], Silva ALM[1], Paz IA[1], Rocha KAD[2], Pessoa ODL[2] Santos CF[1] Nascimento NRF[1] [1]UECE, Instituto Superior de Ciências Biomédicas, Lab Fisiofarmacologia Cardiovascular e Renal. [2]ISCB-UFC, Lab Análise Fitoquímica de Plantas Medicinais II

06.003 **Testosterone Enhances Stress-Induced Tachycardia without Altering Autonomic Modulation in Female Rats**. Martins SCA[1], Belem IJA[1], Suzuki GMF[1], Lautherbach N[2], Kettelhut IC[2], Correa FMA[1], Tostes RC[1], Santos JD[1] [1]USP, Dept of Pharmacology, Brazil, [2]USP, Dept of Biochemistry and Immunology, Brazil

06.004 **Closantel Attenuates Arterial Hypertension and Improves Renal Redox Profile in Spontaneously Hypertensive Rats**. Silva JK, Silva JWA, Farias TSP, Santana DC, Carvalho JM, Santos VBS, Cerqueira ACL, Calzerra NTM, Vieira LD. UFPE, Lab Vascular and Renal Physiology and Pharmacology, Brazil.

06.005 **Long-Acting Testosterone (Nebido®) Increases Albumin Endocytosis in Renal Epithelial Cells**. Martins, RES; Portacio, LFS; Santiago, RO; Paz, IA; Neves, CC; Santos, CF; Nascimento, NRF. UECE, UFC

Totem 19

06.017 **SC1, an Improved-Solubility Oxadiazolinone, Displays AT1 Antagonist-Like Vascular and Renal Effects in 5/6 Nephrectomy-Induced Chronic Kidney Disease**. Aires RS[1], Santana DC[2], Barbosa FM[1], Barbosa AMM[1], Monteidro VHS[1], Ferrreira LFL[3], Vieira LD[2], Calzerra NTM[2], Anjos JV[3], Araujo AV[1] [1]UFPE Centro Acadêmico de Vitória, Brasil; [2]UFPE, Lab Fisiologia e Farmacologia Cardiorrenal, Brasil; [3]UFPE, Lab Síntese Orgânica Medicinal, Centro de Ciências Exatas e da Natureza, Brasil

06.018 **Resistance Exercise Restores Cardiac Mechanical Function and Reduces Arrhythmogenic Susceptibility in Experimental Hypothyroidism**. Matos LFS[1]; Durço AO[2]; Bazilio JES [1]; Santos Júnior SA[1]; Miranda CM[1]; Gomes JVS[1]; Santana MNS[1]; Almeida MMSF[1]; Santo D[1] [1]UFS-São Cristovao, Heart Biophysics Lab, Dept, Brasil; [2]Unifesp, Cardiobiology Lab, Dept Biophysics, São Paulo, Brasil

06.019 **Basal Release of 6-Cyanodopamine and 6-Nitrodopamine from Rat Isolated Aorta and Their Role in Vascular Relaxation**. Cisota FNX[1], Said G[1], Lima AT[1], Junior JB[1,2], Souza VB[1], Schenka AA[1], Peterson LW[3], Ferro A[2], Antunes E[1], Nucci G[1,4] [1]FCM-Unicamp, Dept Pharmacology, Campinas, SP, Brazil; [2]King's College London, Faculty of Life Sciences and Medicine, London, UK; [3]Dept Chemistry, Rhodes College, Memphis, TN, USA; [4]ICB-USP, São Paulo, SP, Brazil

06.020 **Gentisic Acid Induces Vasorelaxation in the Superior Mesenteric Artery of SHR Through Activation of the NO/cGMP Pathway and Modulation of Calcium Influx**. Costa LFO[1], Santana DC[1], Oliveira KA2, Santos KMO2, Cerqueira ACL2, Santos VBS1, Vieira LD[1], Calzerra NTM[1] [1]UFPE, Depto Fisiologia e Farmacologia, Recife, Brazil; [2]UFPE, Depto Ciências Farmacêuticas, Recife, Brazil

06.021 **SATICl as an α1-Adrenergic Antagonist and Possibly a Potassium-Channel Opener**. Silva MEF1, Silva MCC1, Alves SML1, Feitosa SG2, dos Anjos JV2, Araújo AV1 1UFPE, Centro Acadêmico de Vitória, Brasil; 2CCEN-UFPE, Depto Química Fundamental, Brasil

06.022 **(-)-Borneol Inclusion Complex in β-Cyclodextrin Attenuates Isoproterenol-Induced Myocardial Inflammation in Rats Through Regulation of Cytokine Expression**. Souza, FM[1], Albuquerque, BA[2,3,4], Rego, AF[2,3,4], Rocha, VA[2,3,4], Portela, EP[2,3,4], Silva, ND[2,3,4], Oliveira, AP[2,3,4,5]. [1]UFPI, Northeast Biotechnology Network; [2]UFPI, PPG in Pharmacology; [3]NPPM-UFPI, Cardiovascular Pharmacology Lab; [4]UFPI, Medicinal Plant Research Center; [5]UFPI, Dept Biophysics and Physiology

06.023 **Effect of Cisplatin on the Perivascular Adipose Tissue Function: The Cellular Senescence Role**. Jesus BR, Almeida ACR, Da Silva GH, Akamine EH. USP, PPG Functional and Molecular Biology, Brazil.

Totem 20

06.031 **Influence of Estrogen Deficiency on Platelet Aggregation and Vascular Response in Rats**. Meneses CES[2], Azevedo PSS[2], Rego AMF[1], Santos MJ[1], Rocha KF[2], Albuquerque BA[2], Rêgo AF[2], Sena EP[2], Rocha VA[2], Oliveira AP[2,3] [1]UFPI, Center for Natural Sciences, Undergraduate Program in Biological Sciences, Brazil. [2]LAFAC/NPPM, UFPI, Health Sciences Center, Graduate Program in Pharmacology, Cardiovascular and Renal Pharmacology Lab, Brazil. [3]UFPI, Health Sciences Center, Dept Biophysics and Physiology, Brazil.

06.032 **Enhanced Platelet Response Induced by ·OH-Oxidized Collagen**. Cantuária NM[1], Toledo TA[1], Gibbins JM[2], Gaspar RS[1]. [1]FCM-Unicamp, Dept Pharmacology, Brazil, [2]University of Reading School of Biological Sciences, Reading, UK.

06.033 **Cardiovascular and Metabolic Effects Induced by *Cannabis sativa*-Based Oils in Spontaneously Hypertensive Rats**. Silva MC, Aires RS, Queiroz TM UFPE, Academic Center of Vitória, Multicenter Graduate Program in Physiological Sciences, Brazil

06.034 **Effects of γ-Terpinene on Hematological Parameters and Platelet Aggregation in Spontaneously Hypertensive Rats (SHR)**. Rêgo AF[1,2], Rocha VA[1,2], Sena EP[1,2], Albuquerque BA[1,2], Silva ND[1,2], Acha BT[3], Soares HS[2], Silva FAHV[2], Costa MRS[2], Rêgo AMF[2], Nascimento BN[2], Barbosa SLM[4], Ferreira PMP[4,5], Oliveira AP[1,2,6]. [1]UFPI, Health Sciences Center, Graduate Program in Pharmacology, Brazil. [3]Renorbio-UFPI, Northeast Biotechnology Network, Brazil. [4]UFPI, Health Sciences Center, Graduate Program in Pharmaceutical Sciences, Brazil. [5]LOE-UFC, Lab Experimental Oncology, Dept Physiology and Pharmacology, Brazil. [6]UFPI, Health Sciences Center, Dept Biophysics and Physiology, Brazil.

Totem 21

06.035 **Sodium Nitrate Treatment Attenuates Cardiac Dysfunction in an Experimental Model of Preeclampsia**. Toghi CJ[1,2], da Silva A[3], Palei AC[2], Dias-Junior CA[1] [1]IBB-Unesp, Dept Biophysics and Pharmacology, Botucatu, SP, Brazil, PPG Biomolecular and Pharmacological Sciences, Brazil; [2]University of Mississippi Medical Center, Dept Surgery, School of Medicine (SOM), Jackson, Mississippi, United States of America (USA); [3]University of Mississippi Medical Center, Dept Physiology and Biophysics, Jackson, USA

06.036 **Cardioprotective Effects of Naringenin Against Doxorubicin- and Isoproterenol-Induced Cardiotoxicity in Hypertensive Rats**. Dada A, Silva RCMVAF, Zanovello M, Macarini AF, Moser JC, Panizzi EA, Brandão LG, Boeing T, Cechinel Filho V, Souza P Univali, PPG em Ciências Farmacêuticas, Itajaí, Santa Catarina, Brazil

06.037 **Propafenone Analogs Promote Vasorelaxant Effects Involving Potassium and L-Type Calcium Channels**. Lima NCB, Rocha DG. Silva FAO. Mesquita JLF. de Souza ARL, de Mattos MC, Lima GC, Lima RF, Jamacaru FVF, Monteiro HSA, Jorge RJB LAFAVET-UFC-Porangabuçu, Depto Fisiologia e Farmacologia, Lab Farmacologia de Venenos e Toxinas, PPG em Farmacologia, Brasil

06.038 **Distinct Glycation Modifications of Type I Collagen Differentially Regulate Platelet Reactivity**. Fróes RBL, Silva BS, Gaspar RS FCM-Unicamp, PPG Farmacologia, Lab Matriz Extracelular, Brasil.

06.039 **Effect of Thiazolidinedione Derivatives, Possible AT1 Antagonists, on Vascular Reactivity in Isolated Wistar Rat Aorta**. Ferreira JG[1], Silva KT[1], Arrospide TM[2], Alves SML[1], Santos RCA[1], Ferreira LFL[2], Aires RS[1], Silva MCC[1], Dos Anjos JV[2], Araújo AV[1] [1]UFPE, Centro Acadêmico da Vitória, Brasil, [2]UFPE, Lab Síntese Orgânica, CCEN, Brasil

06.040 **Glycated collagen drives vascular remodeling and smooth-muscle dysfunction in hyperglycemia**. Duarte-Maia S, Silva-Oliveira N, Simões Gaspar R. FCM-Unicamp, Depto Farmacologia, Lab Matriz Extracelular, PPG em Farmacologia.

Totem 22

06.057 **Angiotensin II/AT1R Signaling Promotes Vascular NETosis in Ethanol-Treated Mice**. Silva AO[1], Melo BMS[2], Costa VF[2], Marchetti BM[2], Pimenta GF[2], Alves-Filho JC[2], Cunha FQ [2], Tirapelli CR[1] [1]FCFRP-USP, PPG in Pharmaceutical Sciences,Brazil. [2]USP, PPG in Pharmacology, Brazil.

06.058 **Cilostazol Improves Endothelial Function Via PKA/eNOS/PKG and Nrf2 Signaling and Attenuates Platelet Hyperreactivity in Experimental Model of Metabolic Syndrome**. Brazão SC[1,2], Lima GF[1,2], Pereira NCA[1,2], Mendes ABA[1,2], Autran LJ[1,2], Bragança LAR[1,2], Stein AT[1,2], Alves DS[1,2], Rosa GA[1,2], Alexandre-Santos B[3,4], Motta NAV[1,4], Brito FCF[1,2,4] [1]UFF, Lab. of Experimental Pharmacology, Brazil, [2]UFF, PPG Biomedical Sciences (Physiology and Pharmacology), Brazil, [3]UFF, Research Center on Morphology and Metabolism, Brazil, 4UFF, PPG Cardiovascular Sciences, Brazil.

06.059 **Targeted Gi signaling activation exclusively in cardiomyocytes reverses cardiac damage induced by adrenergic overload**. Eliezeck M[1], Scalzo Júnior SRA[1], Costa MC[1], Moura V[1], Silva TM[2], Silva CAA[2], Martins FL[4], Resende CR[1], Fazan Jr R[2], Salgado HC[2], Prado VF[3], Girardi AC[4], Prado MAM[3], and Guatimosim S[1] [1]ICB-UFMG, Dept Physiology and Biophysics, Belo Horizonte, Minas Gerais, Brazil. [2]FMRP-USP, Dept Physiology, Ribeirão Preto, São Paulo, Brazil. [3]The University of Western Ontario, Dept Physiology and Pharmacology, Dept Anatomy & Cell Biology, Robarts Research Institute, London, Ontario, Canada. [4]FMUSP, Lab Fisiologia Renal e Cardiometabolismo, Depto Cardiopneumologia, Brazil.

06. Biology and Metabolic and Reproductive Diseases

Totem 24

06.001FR **Evaluation of Reproductive Parameters in Wistar Male and Female Rats Subjected to Acute Physical Exercise**. Santos-Júnior JCS[1], Morgado VCC[1], Salustiano IM[1], Lopes RA[1], Melo MTBV[1], Noronha GL[1], Brandão CFCCM[2], Lacerda LT[3], Andrade MJO[4], Campos HO[6], Leite LHR[7], Coimbra CC[8], Drummond LR[1,2] [1]UEMG, Experimental Exercise Physiology Lab, [2]UEMG, Research Lab in Metabolism, Physiology and Physical Exercise, [3]UEMG, Strength Training in Health and Physical Conditioning Lab, [4]UEMG, Neuroscience, Chronobiology and Sleep Psychology Lab, [5]UFOP Animal Science Center, [6]UEMG Ubá Unit, [7]UFJF, [8]UFMG Endocrinology and Metabolism Lab, [9]UEMG, Brazil.

06.002FR **Analysis of Thermoregulation During the Estrous Cycle of Female and Male Rats**. Salustiano IM[1], Melo MTBV[1], Morgado VCC[1], Noronha GL[1], Martins JA[1], Santos JCS[1], Brandão CFC[1,2], Lacerda LT[1,2], Andrade MJO[1,2], Campos HO[3], Leite LHR[4], Coimbra CC[5], Lopes RA[1,2], Drummond LR[1,2]. [1]UEMG-Divinópolis, [2]UEMG, PPG em Biociências e Saúde Humana, [3]UEMG-Ubá, [4]UFJF, [5]UFMG.

06.003FR **Maternal Resistance Training Differentially Affects Growth and Developmental Milestones in Male and Female Offspring of Obese Dams**. Silva MLB[1], Silva RAA[2], Nelo SRB[2], Barros MRM[3], Oliveira MCMC[4], Martins MVA[4], Lima RS[1], Pereira TKM[4], Oliveira TRP[5], Antonio-Santos J[5], Da Silva Aragão R[5]. [1]UFPE, Physical Education Undergraduation, Brazil, [2]UFPE, PPG Nutrition, Brazil, [3]UFPE, PPG Nutrition, Physical Activity and Phenotypic Plasticity, Brazil, [4]UFPE, Nutrition Undergraduation, Brazil [5]UFPE, Dept Physical Education, Brazil.

06.004FR **Evaluation of Metabolic Parameters During the Estrous Cycle in Rats**. Melo MTB[1], Salustiano IM[1], Morgado VCC[1], Noronha GL[1], Martins JA[1], Santos JCS[1], Brandão CFC[1,2], Lacerda LT[1,2], Andrade MJO[1,2], Campos HO[3], Leite LHR[4], Coimbra CC[5], Lopes RA[1,2], Drummond LR[1,2] [1]UEMG-Divinópolis, [2]UEMG, PPG em Biociências e Saúde Humana, [3]UEMG-Ubá, [4]UFJF, [5]UFMG.

06.005FR **Influence of Volume Reduction on Heart Rate Behavior after Strength Training**. Luiz CM, Pires KC, Vieira YLM, Rodrigues IJS, Flora JMG, Lacerda LT, Brandão CFCCM, Andrade MJO, Drummond LR UEMG-Universidade Divinópolis, Depto Educação Física, Brasil; UEMG-Universidade Divinópolis, Depto Psicologia, Brasil

06.006FR **Maternal Diet-Induced Obesity Increases Adiposity and Modifies Triglyceride Levels During Pregnancy**. Pereira TKM[1], Silva RAA[2], Lima RS[3], Silva MLB[3], Oliveira PGS[1], Oliveira DKS[4], Oliveira DPL[5], Nelo SRB[2], Barros MRM[4], Oliveira RRP[6], Antonio-Santos J[1,5], Da Silva Aragão R[5]. [1]UFPE, Nutrition; [2]UFPE, PPG Nutrition; [3]UFPE, Physical Education; [4]UFPE, PPG Nutrition, Physical Activity and Phenotypic Plasticity; [5]FPS, Physical Education.

08. Respiratory and Gastrointestinal Pharmacology

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08.001 **Characterization of the Herbal Drug Obtained from the Leaves of *Spondias purpurea* and Antiulcer Activity of its Infusion**. Morais FS, Barbosa YV, Rodrigues CVS, Andrade Junior MA, Sales AO, Santos VL UEPB, Lab Pharmacological Assays, Brazil

08.002 **Renin-Angiotensin System Modulators may alter the Monocytes Profile in COPD Patients**. Martins NRS, Freitas JVC, Paiva YMA, Medeiros VLD, Medeiros GB, Silva FS, Kennedy-Feitosa E. UFERSA-Mossoró, Morphophysiopharmacology Lab

08.003 *In vivo* **and** *In vitro* **Study of the Acute Toxicity and Mechanisms Involved in the Antiulcerogenic Activity of the Compound 1-(4-chlorophenyl)-3-(1,3,4-thiadiazol-2-yl)thiourea (MS06)**. Rodrigues CVS, Costa TB, Andrade Junior

MA, Fonseca MLP, Cavalcanti, MAT, De Moura RO, Dos Santos VL. UEPB, Lab Pharmacological Assays, Brazil, UEPB, Lab Drug Design and Synthesis, Brazil.

08.004 **N-Acylhydrazone Derivatives Promote Mild Relaxation of Rat Tracheal Smooth Muscle**. Santos VF[1], Lima FJB[2], De Moura RO[3], Ramos KRLP[1] [1]UEPB, Pharmacy Dept, Brazil, [2]UNIFACISA, Centro Universitário, Brazil, [3]UEPB, Lab Drug Design and Synthesis, Brazil.

08.005 **Acute Bronchodilator Administration during Spirometry can Influence the Response in COPD Patients Treated with Renin-Angiotensin System Modulators**. Paiva YMA, Freitas JVC, Medeiros VLD, Medeiros GB, Martins NRS, Silva FS, Kennedy-Feitosa E UFERSA, Mossoró, Morphophysiopharmacology Lab

08.006 **Preventive Effect of *Arthrospira platensis* on Oxidative and Inflammatory Changes in the Ileum of Rats Subjected to a Hypercaloric Diet**. Santos TJ[1,3], Claudino BFO[1],2, Silva JMA[1,2], Arruda RRA[1,2], Melo MB[1,3], Sousa Filho JEC[1,3], Barros BC[1,2], Barbosa YV[1,2], Costa BA[1,2,3], Diniz AFA[1,2] [1]UFPB, Lab Functional Pharmacology Prof. George Thomas, Institute of Research in Drugs and Medicines, Brazil. [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil. [3]UFPB. Dept Pharmaceutical Sciences, Health Sciences Center, Brazil.

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08.019 **The Role of IL-17 in Pulmonary Inflammation and pro-fibrotic Changes Induced by Experimental Gastroesophageal Reflux Disease**. Silva BVL[1]; Sales TMAL[2]; Ferreira ABA[1]; Silva TML[1]; Alicrim SAC[1]; Monteiro CES[1]; Franco AX[1]; Almeida VM[2]; Azevedo YG[2]; Melo BMS[2]; Daniel AML[1]; Alves JCF[2]; Riteau NDM[2]; Soares PMG[1]; Souza MHLP[1]. [1]UFC, Lab Gastrointestinal Physiopharmacology, Brasil; [2]USP, Immune Health Lab, Brasil.

08.020 **Refluxate Components Drive NETosis and Promote Experimental Reflux Esophagitis Trough PAD4-Dependent Mechanisms**. Gomes IAB[1]; da Silva GCP[2]; Ramos AS[3]; Pérez MM[3]; Sales TMAL[3]; Costa VF[3]; Araújo AVV[1]; Carvalho KS[1]; Medeiros JVR[1]; Saraiva EM[2]; Cunha FQ[3]; Nicolau LAD[1]. [1]UFDPar, PPG in Biotechnology, Brazil; [2]UFRJ, Dept Immunology, Brazil; [3]CRID-FMRP-USP, Brazil.

08.021 **Evaluation of the Subchronic Safety Profile and Anticolytic Activity of an N-acylhydrazone Derivative in an Animal Model**. Oliveira JEB[1], Araruna MEC[2], Santos VL[1], Moura RO[1] [1]UEPB, PPG in Pharmaceutical Sciences, Brazill, [2]UEPB, Pharmacological Testing Lab, Brazil

08.022 **Investigation of the Gastroprotective Effect of a Formulation Based on Isoquercitrin Complexed with Gamma-Cyclodextrin: Role of the Nitric Oxide Pathway, Cytokines and Redox Homeostasis**. Barbosa TVGB[1], Rocha NA[1], Oliveira RCM[1], Sousa DP[2], Oliveira FA[1] [1]UFPI, Health Sciences Center, PPG Pharmacology, Brazil, [2]UFPB, Dept Pharmaceutical Sciences, Brazil

08.023 **Gastroprotective Activity of β-Pinene in Animal Models**. Alves VP, Pessoa MMB, Pessôa MLS, Menezes PMF, Pessoa LF, Batista LM UFPB, Gastrointestinal Pharmacology Lab, PGPNSB, Brazil.

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08.024 **Fasudil, a Rho Kinase Inhibitor, Attenuates Intestinal Hypocontractility in an Experimental Model of Autism Spectrum Disorder: Preliminary Findings**. Longo B[1], Lima-Moura SA[1], Cury BJ[1], Santos MR[1], Cazarin CA[2], Willrich CH[1], Da Silva-Santos JE[1], Da Silva LM[1,2]. [1]UFSC, Dept Pharmacology, Brazil, [2]UFSC, Neuroscience Postgraduate Program, Brazil.

08.025 **Effect of Farnesol Complexed with β-Cyclodextrin in a Model of Bronchial Asthma Induced by Ovalbumin** ***In vitro*** **and** ***in vivo***. Souza ORB[1], Oliveira MM[1], Silva RLT[1], Filho-Reis AC[1], Martins HRS[1], Reis ML[1], Sousa RWR[1,2], Ferreira PMP[1,2,3], Quintans, JSS[4], Quitans-Júnior LA[4], Oliveira AP[1], Almeida FRC[1], Santos, RF[1], Oliveira RCM[1] [1]UFPI,

Health Sciences Center, PPG Pharmacology, Brazil. [2]UFPI, Lab Experimental Cancerology (LabCancer), Dept Biophysics and Physiology. [3]LOE-UFC, Lab Experimental Oncology, Dept Physiology and Pharmacology. [4]LANEF-UFS, Lab Neurosciences and Pharmacological Assays, Dept Physiology, PPG Health Sciences, Brazil.

08.026 **Pharmacological Inhibition of the S100B/RAGE/NF-KB Pathway Attenuates the Inflammatory Response IN TNBS-Induced Colitis**. Silva TML[1], Sousa JJS[3], Almeida VPA[2], Sousa AK[2], Prudêncio RS[2], Furtado MGS[2], Costa ACC[2], Rodrigues VO[2], Rocha DML[2], Ferreira ABA[1], Silva BVL[1], Vale VS[3], Magalhães DA[2], Barbosa ALR[2] [1]UFC, Lab Gastrointestinal Physio-Pharmacology Studies, Brazil; [2]UFDPar, Lab Experimental Physiopharmacology, Brazil; [3]IFPI, Campus Parnaíba, Brazil

08.027 **Evaluation of Bionutri AR-1®, a Biotechnological Nutraceutical Formulation Rich in α-and β-Glucans and Amino Acids, in Experimental Erosive Esophagitis**. Araujo AVV[1], Gomes IAB[1], Oliveira BC[1], Pimentel TFM[2], Monte MM[2], Santos BL[2], RodriguesFSM[3], Gois MB[4], Medeiros JVR[1], Nicolau LAD[1] [1]UFDPar, PPG in Biotechnology, Brazil; [2]UFDPar, Lab of Inflammation and Translational Gastroenterology, Brazil; [3]Unifesp, Brazil. [4]UFR, Brazil.

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08.040 *Arthrospira platensis* **Supplementation Attenuates Airway Remodeling in Asthmatic Rats**. Oliveira GNM[1,2], Vieira MM[2], Silva JMA[2], Cavalcante-Silva LHA[3], Alves AF[2,4], Vasconcelos LHC[1,2,4] [1]UFPB, Lab Farmacologia Funcional Prof. George Thomas, Instituto de Pesquisa em Fármacos e Medicamentos, Brazil; [2]UFPB, PPG em Produtos Naturais e Sintéticos Bioativos, Brazil; [3]UFAL, Complexo de Ciências Médicas e Enfermagem, Brazil; [4]UFPB, Depto Ciências Biomédicas, Brazil.

08.041 **Experimental Acute Respiratory Distress Syndrome Model Induced by *Escherichia coli* Lipopolysaccharide: Single and Repeated Dose in Wistar Kyoto and Spontaneously Hypertensive Rats**. Araújo LP, Ponce F, Rodrigues SF ICB-USP, Lab Vascular Nanopharmacology, Functional and Molecular Biology Graduate Program, Brazil

08.042 **Endogenous 6-Nitrodopamine Release from Guinea Pig Trachea: A Novel Regulator of Airway Smooth Muscle Function**. Campos R, Ali K, Fuguhara V, Lorenzon F, Riffo- Vasquez Y, De Nucci G, Page CP Unicamp, Brazil, King's College London, United Kingdon, Unichristus, Brazil, USP, Brazil

08.043 **Gastroprotective and Antispasmodic Effects of 1-(4-Chlorophenyl)-3-(1,3,4-thiadiazol-2-yl) thiourea (MS06) in Mice**. Lima FJB[1,2], Costa TB[1], Barbosa YV[1], Fonseca MLP[1], Silva LMQ[1], Cavalcanti, MAT[3], De Moura RO[3], Dos Santos VL[1]. [1]UEPB, Lab Pharmacological Assays, Brazil, [2]Centro Universitário UNIFACISA, Brazil, [3]UEPB, Lab Drug Design and Synthesis, Brazil.

08.044 **Myrtenyl Laurate reduces Inflammatory Markers in a Non-Surgical Model of Gastroesophageal Reflux Disease**. Viana, AFSC[1,2,3], Oliveira, GH[1], Fernandes, HB[1,2], Martins, SCA[1], Araujo, PBM[2], Gomes, EGS[3], Neto, ADC[3], Reis, ML[1] Guerra, SPL[4], Gonçalves, LMF[4], Kutyła, M[5], Stankevič, M[6], Trytek, M[5], Oliveira, RCM[1,2] [1]UFPI, Medicinal Plants Research Center (NPPM), Brazil, [2]UFPI, PPG Farmacology, Brazil, [3]UEMA, Campus Santa Inês, Brazil, [4]UFPI, Depto Morfologia, Brazil, [5]MCSU, Akademicka, Lublin, Poland, [6] MCSU, Gliniana, Lublin, Poland.

08.045 **Altered FEV1-FVC Coupling After Pharmacological Bronchodilation in COPD Patients Using Renin-Angiotensin System Modulators**. Silva FS, Paiva YMA, Medeiros VLD, Freitas JVC, Santos JRA, Medeiros GB, Kennedy-Feitosa E UFERSA-Mossoró, Morphophysiopharmacology Lab

08.039 **Modulation of the Heme/NADPH Oxidase Pathway During Ethanol- Induced Gastropathy in Mice**. Almeida ML[1], Oliveira AP[2], Moraes JA[3], Figueiredo-Junior AT[3], Góis MB[4], Oliveira ACP[2], Medeiros JVR[2], Nicolau LAD[1,2] [1]UFPI,

Lab Inflammation and Translational Gastroenterology, Brazil; [2]UFDPar, Lab Inflammation and Translational Gastroenterology, Brazil; [3]UFRJ, Lab Redox Biology, Brazil; [4]UFR, Lab Morphology, Brazil.

09. Natural Products and Toxinology

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09.090 **Antioxidant Effects of Annatto Compounds during Aging: Involvement of the Nrf2 and p38MAPK Pathways in Human Mononuclear Cells**. Pádua BC[1,2], Barros e Silva JC[1], Borsato DF[1], Franco FN[1], Chaves MM[1] [1]ICB-UFMG, Biochemistry Lab Aging and Correlated Diseases, Graduate Program in Biochemistry and Immunology, Brazil. [2]CEFET- Curvelo-MG, Dept General Education, Brazil.

09.091 **Chalcones Counteract Ketamine-Induced Behavioral, Cognitive, and Neurochemical Alterations in a Schizophrenia-Like Model**. Dalmagro AP[1,2], Reginatto ABCM[3], Riffel IM[3], Valachinski AW[1,4], Lehmkuhl RA[1,5], Buzzi FC[1], Souza MM[1]. [1]Univali, PPG in Pharmaceutical Sciences. [2]FURB, Dept Pharmaceutical Sciences. [3]Univali, BSc Biomedicine. [4]Univali, BSc Psychology. [5]Univali, BSc Biological Sciences.

09.092 **P1G10 Proteolytic Fraction of** *Vasconcellea Cundinamarcensis* **Latex Induces Analgesia through Activation of the PI3Kγ/NOS/NO/KATP Signaling Pathway in neuropathic mice**. Machado DPD Araújo BS Cota MES Freitas KM Romero TRL Lopes MTP. ICB-UFMG, Dept Pharmacology, PPG in Biological Sciences: Physiology and Pharmacology, Brazil

Totem 29

09.001 **Terpenes Enhance Antibiotic Activity Against Multidrug-Resistant** *Klebsiella pneumoniae*. Lourenço MS, Dantas IGP, da Silva AJA, Rodrigues EN, Bernardino PKC, Nascimento PHA, Bento AJM, Coutinho HDM, Oliveira-Tintino CDM, Araújo IM URCA, Brazil

09.003 **Antioxidant Activity of** *Commiphora leptophloeos*. Ferreira CES, Andrade IA, Fialho MLS, Gonçalo YA, Martins SO, Nóbrega VM, Oliveira MVM, Medeiros FD UFCG-Cuité, Center for Education and Health, Brazil.

09.004 **Chemical and Biological Study of the Extract of** *Cecropia pachystachya* **Trec Collected in the Interior of the State of Ceara**. Pereira, LK[1], Santiago, MLA.[1], Costa MEP[1]., Silva, JBS[2], Morais SM[3], Maciel MHC[1], Moreira RF[1], Magalhães LC[1], Souza, EP[4], Pinto CCC[5]. [1]UNINTA, Faculdade de Medicina, [2]UFC, [3]UECE, Lab Química de Produtos Naturais, [4]UECE, Medicina, Depto Morfologia, Pós Graduação em Ciências Morfofuncionais, [5]UNINTA, Faculdade de Medicina, Lab Microbiologia

09.005 **Pharmacology Bioprospecting of the Brazilian Peppertree** (*Schinus terebinthifolia* **Raddi): A Systematic Review**. Calado LP[1], Medeiros AD[2], Boeira LS[2], Alves MS[3], Oliveira Filho AA[1] [1]UFCG, Center for Health and Rural Technology, Brazil, [2]UEPB, Center for Applied Biological and Social Sciences, Brazil [3]UFCG, PPG of Health and Science Animal, Brazil

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09.052 **Bioprospecting of Hydroalcoholic Extract from the Bark of a Native Caatinga Plant: Evaluation of Toxicity and Antiangiogenic Activity**. Brito JM[1,2], Dantas MEA[1], Alves AKL[1], Silva KKF[1,3], Nascimento JRS[1,2], Andrade IA[4], Medeiros FD[4,5], Dantas BB[4,5] [1]UFCG, Curimataú Cancer Observatory (OCC), Brazil; [2]UFCG, PPGCNBiotec, Brazil; [3]UFPB, Renorbio, Brazil; [4]UFCG, Pharmacognosy and Planetary Health Research Group, Brazil; [5]UFCG, Academic Health Unit, Center for Education and Health, Brazil

09.053 **Attenuation of UVA-Induced Cellular Senescence Activity and Reactive Oxygen Species Production by the Hydroalcoholic Extract of** *Spondias tuberosa* **Leaves in Immortalized Human Keratinocytes (HaCaT)**. Souza CMO[1,2], Gomes MLC[1,2], Pereira MEM[2], Albuquerque MN[2], Farias LRT[3], Langassner SMZ[3], Oliveira GD[1,4], Nascimento YM[1,4],

Veras RC[1,2], Araujo IGA[1,2], Medeiros IA[1,2] [1]UFPB, PPG in Bioactive Natural and Synthetic Products (PgPNSB), Brazil, [2]UFPB, Cardiovascular Pharmacology Lab, Institute for Drug and Medicine Research, Brazil, [3]UFRN, Pharmacognosy Lab, Brazil, [4]UFPB, Multi-user Lab for Characterization and Analysis, Brazil.

09.054 *Spondias tuberosa* **Arruda Extract Attenuates Pulmonary Oxidative Stress and Modulates NF-κB/P-JNK Signaling in Streptozotocin-Induced Diabetic Mice**. Albuquerque ECS[1], Pires LAB[1], Sena VNF[1], Donato FF[1], Albuquerque IA[2], Vieira RR[3], Santos DD[3], Gil CD[3], Medeiros KCP[1]. [1]UFRN, PPG Structural and Functional Biology, Brazil, [2]UFPB, Dept Pharmaceutical Sciences, Brazil [3]Unifesp, PPG Structural and Functional Biology, Brazil.

09.055 **Efficacy of** *Cannabis sativa* **L. Associated with Phonophoresis on Oxidative Stress in Skeletal Muscle of Rats**. Santana RAN[1], Sousa DS[2], Lima MM[1], Nascimento VS[1], Azevedo IO[1], Santos LB[1], Oliveira ED[1], [1]UFS-PROBIO-Brasil, [2]UFS-Renorbio-Brasil

09.056 **Topical Anti-Inflammatory Potential of Cannabigerol in Experimental Models of Cutaneous Inflammation** *in vivo* **and** *in vitro*. Silva NAA, Michelisa A, Sampaio EDSR, Christo EB, Lopes RV, Cabrini DA, Otuki MF UFPR, Dept Pharmacology, Graduate Program in Pharmacology, Brazil

09.057 **Evaluation of the Anti-Inflammatory Potential of an Oxygenated Withanolide Isolated from** *Athenaea velutina* **in LPS-Stimulated Macrophage Cells: Role of NO and IL-1beta**. Ribeiro MS[1], Da Silva LR[1], Rocha LM[1], Rocha KAD[2], Silva JGP[1], Procopio GS[1], Pessoa ODL[2], Santos FA[1]. [1]UFC, Faculty of Medicine, Dept Physiology and Pharmacology. [2]UFC, Science Center, Dept Organic and Inorganic Chemistry.

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09.072 **Chemical Characterization by LC/MS and the Lipid-Lowering Potential of the Aqueous Extract of** *Helianthus annuus* **L. Seeds in** *Caenorhabditis elegans*. Barreto MS[1], Araújo ZS[2], Pacheco PGS[1], Souza JB[1], Lisboa JS[1], Silva AS[1], Sá MEB[3], Santos VR[1], Oliveira DP[1], Cavalcante MD[1], Borges LP[1], Guimarães AG[1] [1]UFS, Graduate Program in Pharmaceutical Sciences, São Cristovão, Brazil, [2]UFS, Graduate Program in Health Sciences, Lagarto, Brazil, [3]UFS, Dept Pharmacy, Lab Clinical and Experimental Pharmacology (LAFACE), Brazil

09.073 **Evaluation of the Effects of Lauric Acid on Senescence in Human Umbilical Vein Endothelial Cells (HUVECs)**. Assis TFM[1], Gonçalves TAF[2], Oliveira JCPL[2], Queiroz TM[1] [1]CAV/UFPE; [2]CCS/UFPB

09.074 **Cardiotoxicity of Snake Venoms and Toxins Assessed Using Cockroach** (*Nauphoeta cinerea*) **Semi-isolated Heart Preparations**. Oliveira IN[1], Silva AB[1], Oliveira RS[1], Dias DRC[2], Guimarães MP[3], Vinadé L[4], Dal Belo CA[1,3], Silva Júnior NJ[5], Hyslop S[1] [1]Unicamp, Faculty of Medical Sciences, Dept Pharmacology, Pharmacology Graduate Program, Brazil; [2]UFES, Dept Statistics, Brazil; [3]Unifesp-Osasco, Paulista School of Politics, Economics and Business, Multidisciplinary Dept, Campus, Brazil; [4]Unipampa, São Gabriel Campus, Brazil; [5]PUC-GO, Graduate Program in Environmental and Health Sciences, Brazil.

09.075 **Antiproliferative Activity and** *In vitro* **Mechanisms of Casearin J on a Triple-Negative Breast Cancer Model**. Almeida ML[1], Barbosa SLM[1], Sousa RCL[1], Sousa RWR[1], Negreiros HA[3], Silva LRA[3], Zalewski S[2], Camargo JGS[2], Carvalho FA[2], Santos AG[2], Castro JMC[3], Dittz D[3], Ferreira PMP[1,4] [1]UFPI, Lab Experimental Cancerology (LabCancer), Dept Biophysics and Physiology; [2]Unesp, Lab Pharmacognosy, Faculty of Pharmaceutical Sciences; [3]UFPI, Dept Biochemistry and Pharmacology; [4]UFC, Lab Experimental Oncology (Loe), Dept Physiology and Pharmacology, Brazil

09.076 **p-Coumaric Acid Suppresses IL-1β-Induced ICAM-1 and CXCL8 Expression in Human Alveolar Epithelial Cells** Fidelix MSP, Barros ABB, Ferreira EGA, Silva GRS, Silva JP, Barreto E. UFAL, Lab Biologia Celular

09.077 **Biological Evaluation of** *Borreria verticillata*, *Monteverdia rigida* **and** *Sarcomphalus joazeiro* **and their Potential for the Development of Phytocosmetics in** *Aloe vera* **Gel**. Silva GNB[1], Ferreira EF[2], Pereira JBM[2], Santos HLS[1], Nascimento GILA[1], Silva BM[1], Sobral R[1], Santos AF[3], Correia ACC[3], Falcão REA[3], Albuquerque PBSA[1],[31]UPE, PPG Biologia Celular e Molecular Aplicada, Brazil, [2]UPE, Curso de Licenciatura em Ciências Biológicas, Brazil, [3]UPE, PPG Saúde e Desenvolvimento Socioambiental, Brazil.

09.078 *Arthrospira platensis* **Prevents Hypercaloric Diet-Induced Hepatic Histological and Oxidative Damage in Wistar rats**. Claudino BFO[1,2], Diniz AFA[1,2], Arruda RRA[1,2], Silva JMA[1,2], Melo MB[1], Sousa-Filho JEC[1], Santos TJ[1], Barros BC[1,2], Alves AF[2,3], Silva BA[1,2,4]. [1]UFPB, Lab Functional Pharmacology Prof. George Thomas, Institute of Research in Drugs and Medicines, Brazil [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil [3]UFPB, Dept Biomedical Sciences, Health Sciences Center, Brazil [4]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil

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09.094 **Antimicrobial and Antibiofilm Activity of Polymeric Nanocapsules Loaded with Oregano** (*Origanum vulgare* **L.) Essential Oil against Gram-Negative Bacteria**. Alves ARS[1], Oliveira-Filho JMD[1], Pessoa JVA[1], Azevedo KMS[1], Formiga ALD[3], Lacerda AF[1,2], Santos LFA[3], Lima EO[3], Vasconcelos U[2,3], Júnior FHX[3], Travassos RA[1,2] [1]UFPB, Laboratório de FarmacoBiotecnologia (FarmaBio), Brazil; [2]UFPB, Graduate Program in Cellular and Molecular Biology (PPgBCM), Brazil; [3]UFPB, Graduate Program in Bioactive Natural and Synthetic Products (PPgPNSB), Brazil.

09.095 **Glucomannan from** *Acrocomia corumbaensis* **Attenuates Inflammation and Preserves the Mucus Barrier in DSS-Induced Colitis**. Brito MSC[1], Taporoski AK[2], Rech KS[1], Santos LBS[1], Martins FG[1], Gois MB[3], Cordeiro LMC[2], Werner MFP[1] [1]UFPR, Pharmacology and [2]Biochemistry and Molecular Biology, [3]UFR, Faculty of Health Sciences

09.096 **Decrease of the Postprandial Hyperglycemia in Patients with Type 2 Diabetes by Raw Cinnamon in the Form of Hard Gelatin Capsules or Powder Dissolved in Water**. Welker AF, Moreira FD, Gallassi AD, Moreira DC, Reis CEG, UnB

09.093 **Esophagoprotective Effect of** *Arthrospira platensis* **in Experimental Erosive Esophagitis: Contribution of Antioxidant Activity Following Simulated Gastrointestinal Digestion**. Ferreira JL[1], Lopes ALF[1], Silva KC[1], Fernandes TMP[1], Oliveira AP[1], Gomes IAB[1], Rodrigues FSM[2], Medeiros JVR[1], Nicolau LAD[1]. [1]UFDPar, Lab Inflammation and Translational Gastroenterology, Brazil, [2]Unifesp, Lab Autonomic and Cardiovascular Pharmacology.

10. Cancer Pharmacology

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10.001 **The lncRNA H19 in Lung Adenocarcinoma** (**LUAD**)**: an** *in silico* **Prognostic, EMT-Pathway and Driver-Mutation Profile**. Soares IF[1,2], Mota JA[1,3], Scandolara TB[1], Sales SLA1,3,Manso MP[4], Melo VB[5], Gress LSB[2],[3], Macêdo SMN[1], Oliveira KAF[1], Xavier EEP[1,6], Bastos RS[1],[3], Fernandes MCR[1,7], Maranhão SS[1], Pessoa C[1,3], Furtado CLM[5] [1]UFC, Experimental Oncology Lab, Drug Research and Development Center, Brazil, [2]UNIFOR, Center for Health Sciences – CCS, Brazil, [3]UFC,Dept Physiology and Pharmacology, Graduate Program in Pharmacology, Brazil, [4]INCa, Cellular and Gene Immunotherapy Lab, Brazil, [5] UFMG, Dept Genetics, Ecology and Evolution, Institute of Biological Sciences, Brazil, [6]UFC, Faculty of Pharmacy, Brazil, [7]UFC, Graduate Program in Translational Medicine, Brazil.

10.002 **Enantioselective Antiproliferative Activity of Homoisoflavonoids from** *Urginea depressa* **against Non-Small Cell Lung Cancer Cell Lines with High Selectivity over non-Tumorigenic Cells**. Feijó Neto JR[1]; Pereira JVM[1,3] ; Vieira Neto JdB[1,3]; Castro CM[1]; Desiderio GA[1,3]; Falcão JS[2]; Silva MVO[2]; Costa PRR[2]; Caleffi GS[2]; Pessoa CÓ[1,3]. [1]UFC, Lab. de Oncologia Experimental, Brazil; [2]UFRJ, Lab. de Química Bioorgânica (LQB), Brazil; [3]UFC, PPG Pharmacology, Brazil.

10.003 **Evaluation of Apoptotic Mechanisms Associated with *Solanum jabrense* Agra & M. Nee Extract in MCF-7 Cells**. Gomes KNC[1], Alexandre HMS[2], Abreu-Junior AR[2], Santana PVS[2], Marques KKG[2], Pereira ERM[2], Souza RRM[2], Ramalho IGS[2], Santos PBG[1], Araújo YKO[1], Silva AL[2], Agra MF[3], Tavares JF[2], Sobral MV[2],Gonçalves JCR[2]. [1]UFPB, Health Sciences Center, Pharmacy, Brazil. [2]UFPB, Health Sciences Center, PPG in Bioactive Natural and Synthetic Products, Brazil. [3]UFPB,Biotechnology Center, Brazil.

10.004 **AMTAC-06 Induces ROS-Associated Cytotoxicity in HCT-116 Colorectal Cancer Cells**. Santana JP[1], Duarte SS[2], Souza RRM[2], Januário VHS[1], Rodrigues JS[1], Queiroga LM[2], Farias APGM[2], Ramalho IGS[2], Lyra GB[2], Gouveia RG[2], Silva JM[3], Moura RO[4], Gonçalves JCR[2], Sobral MV[2] [1]UFPB, Health Sciences Center, Pharmacy, Brazil. [2]UFPB, Health Sciences Center, PPG in Bioactive Natural and Synthetic Products, Brazil. [3]UFPE, PPG in Pharmaceutical Sciences, Brazil. [4]UEPB, Dept Pharmacy, Drug Development and Synthesis Lab, Brazil.

10.005 **Antileukemic Activity of LOE227, a Novel N-Aryl Azacoumostan, and its Synergism with the Apoptosis Inducer Venetoclax**. Castro CM[1], Feijó JRN[1], Novas RCV[2], Vieira JBN[1,3], Desidério GA[1,3], Carvalho MT[2], Lima JM[1,3], Bastos RS [1], Paier CK[1], Carneiro LSA[4], Pessoa C[1,3], Buarque CD[2] [1]UFC, Lab. of Experimental Oncology, Drug Research and Development Center, Brazil; [2]PUC-Rio, Dept Chemistry, Brazil; [3]UFC, PPG Pharmacology, Brazil; [4]UFRRJ, Dept Organic Chemistry, Institute of Chemistry, Brazil

10.006 **Evaluation of the *in vitro* Antitumor Potential of Flavonoids from a Cytotoxic Extract of Wood Waste from *Andira parviflora* (Ducke) in the Amazon Region**. Mota JF[1], Desiderio GA[1,4], Guimarães CJ[2], Melo JV[1,4], Araújo IM[3], Costa PMS[1], Guimarães AC[3], Paier CRK[1], Pessoa C[1]. [1]UFC, Lab. Experimental Oncology, Brazil; [2]Fiocruz, Institute of Drug Technology (Farmanguinhos), Brazil; [3]UFAM, Brazil; [4]UFC, PPG Pharmacology, Brazil

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10.037 **Copper(II) Coordination of Schiff Base Ligands Modulates Anticancer Activity in Melophen-Type Complexes**. Silva KKF[1,2], Andrade ASA[2], Araújo DAM[2], Cavalcanti ETDN[3], Lemos SG[3], De Souza-Ferrari J[2,3], Dantas BB[1,2,4] [1]UFCG, Curimataú Cancer Observatory (OCC), Brazil. [2]UFPB, PPG in Biotechnology – Northeast Biotechnology Network (Renorbio), Brazil. [3]UFPB, Dept Chemistry, Brazil. [4]UFCG, PPG in Natural Sciences and Biotechnology, Brazil

10.038 **Decyl Butyrate-Loaded Cubosomes: A Nose-to-Brain Approach Against Glioblastoma in a Preclinical Model**. Pimentel RS[1,7], Souza LCS[1,7], Ribeiro IRS[2], Silva FFF[3], Santos ARC[4,7], Eberhardt MJ[5], Spingolon G[5], Castro NET[5], Silveira ER[6], Santos DYAC[6], Rocha HVA[3], Martins MA[1,7], Frozza RL[4,7], Poletto F[5], Bernardi A[1,7]. [1]Fiocruz, Lab. of Inflammation, Brazil. [2]CNPEM, Brazilian Synchrotron Light Lab., Brazil. [3]Fiocruz, Lab. of Micro and Nanotechnology, Brazil. [4]Fiocruz, Lab. on Thymus Research, Brazil. [5]UFRGS, PPG Química, Brazil. [6]USP, Lab. of Phytochemistry, Brazil. [7]Fiocruz, PPG Biologia Celular e Molecular, Brazil.

10.039 **Investigation of a Low-Anticoagulant Heparin with the Potential to Inhibit Cancer Dissemination by Blocking Tumor Cell–Endothelium Interactions**. Roberto-Fernandes C, Motta JM, Lima AGF, Morandi V, Mourão PAS, Pereira MS. UFRJ, HUCFF, Brazil; UERJ, Lab. of Endothelial Cell Biology and Angiogenesis, Brazil.

10.040 **Selective Antiproliferative Activity of *Ampelozizyphus amazonicus* Infusion in HeLa Cells**. Chelotti ME[1], Turra BO[2], Bonotto NCA[1], Silva ES[2], Escher ALK[2], Miranda J[2], Cruz IBM[3], Barbisan F[1] [1]UFSM, Biogenomics Lab, PPG in Pharmacology, Brazil; [2]UFSM, Biogenomics Lab, Brazil, [3]Funati, Open University Foundation for the Third Age, Manaus, Brazil.

10.041 **The Compartmentalized Expression Profile of T-Box Transcription Factor 15 in Inflammatory Breast Cancer: Differential Profiles and Association with Clinicopathological Features**. Alves BES[1], Barrozo AEO[1], Teixeira-Filho

JIF[1], Maia IFVC[1], Batista RER[1], Coimbra RLS[1], Cajado AG[1], Arruda LM[2], Cavalcante DIM[3], Lima V[4], Diaz LAC[5], Alves APNN[5], Lima-Júnior RCP[1], Rogatto SR[6], Wong DVT[1]. [1]UFC, Dpt of Physiology and Pharmacology, Lab Inflammation and Cancer Pharmacology, Drug Research and Development Center, Brazil; [2]Haroldo Juaçaba Hospital, Cancer Institute of Ceara, Brazil; [3]UFC, Dpt of Pathology and Forensic Medicine, Brazil; [4]UFC, Dpt of Physiology and Pharmacology, Osteoimmunopharmacology Lab, Drug Research and Development Center, Brazil; [5]UFC, Dpt of Dental Clinic, Stomatology and Oral Pathology Sector, Faculty of Pharmacy, Dentistry and Nursing, Brazil; [6]Unesp, Botucatu Medical School Hospital, Brazil.

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10.043 **Toxicogenetic Characterization of the Synthetic Hydroxylated Chalcone CH-A3**. Bahia GFM[1], Castro AJS[1], dos Reis MA[1], Pérez CN[2], Valeze AB[3], Ribeiro RMS[1], Souza JMT[1], Marinho-Filho JDB[1], Araújo AJ[1] [1]UFDPar, Lab Cultura Celular do Delta, Brazil, [2]UFG, Instituto de Química, Brazil, [3]IFMT, campus Cuiabá, Brazil

10.044 **Cytotoxic and Pro-Apoptotic Effects of *Annona vepretorum* Extract on Human Colorectal Adenocarcinoma Cells**. Abreu-Junior AR[1], Santos PBG[2], Gomes KNC[2], Araújo YKO[2], Pereira ERM[1], Alexandre, HMS[1], Queiroga LM[1], Farias APGM[1,2], Silva ICF[1], Amorim GMW[1], Dutra LM[3], Costa EV[4], Tavares JF[1,2], Sobral MV[1,2], Gonçalves JCR[1,2]. [1]UFPB, PG Program in Bioactive Natural and Synthetic Products, Brazil; [2]UFPB, Dept Pharmaceutical Sciences, Brazil; [3]UFPR, Dept Chemistry, Brazil; [4]UFAM, Dept Chemistry, Brazil.

10.045 **The Thiosemicarbazone Derivative (PR-14) Promoted Alterations in the Cell Cycle and Induced Apoptosis in Lung Cancer Cells**. Carvalho VM[1], Nascimento ACM[1], Costa VCM[1], Silva TD[1], Barbosa FHS[1], Mendonça MJLV[1], Silva JOR[1], Silva BO[1], Souza GA[1], Gomes JPA[1], Soares JR[1], Lima MCA[2], Pitta MGR[1], Rego MBM[1], Pereira MC[1] [1]UFPE, Center for Research in Therapeutic Innovation - Suely Galdino (NUPIT-SG), Graduate Program in Therapeutic Innovation (PPGIT), Brazil. [2]UFPE, Dept Antibiotics, Graduate Program in Therapeutic Innovation (PPGIT), Brazil.

10.046 **A New Indium(III) Sulfonyldithiocarbimate Complex Exhibits *in vitro* Anticancer Activity Against Colorectal Cancer Cells**. Souza RRM[1], Marques KKG[1], Dantas MM[1], Silvestre GFG[1], Rodrigues JS[2], Santos PBG[2], Santana JP[2], Lyra GB[1], Gomes KNC[2], Carvalho LR[3], Faria WMA[3], Tavares EC[3], Gonçalves JCR[1], Ferreira RC[1], Sobral MV[1] [1]UFPB, Health Sciences Center, ONCOFAR, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]UFPB, Health Sciences Center, ONCOFAR, Undergraduate in pharmacy, Brazil. [3]UNIFEI, Institute of Physics and Chemistry, LaCSin, Brazil.

10.048 **Extracellular Vesicle-Mediated Modulation of the Melanoma-Macrophage Axis: A New Pharmacological Approach Using Low-Anticoagulant Heparin**. Pacheco-Silva NV[1], Cahu TB[1,2], Thaumaturgo MAS[2], Santos RCM[2], Bagri KM[3], Mermelstein C[3], Rizzo J[4], Castelo-Branco MTL[1], Todeschini AR[2], Pereira MS[1]. [1]UFRJ, HUCCFF, Brazil, [2]UFRJ, Lab Gliocobiologia Estrutural e Funcional, Brazil, [3]UFRJ, Lab Diferenciação Muscular, Instituto de Ciências Biomédicas, Brazil, [4]UFRJ, Lab Físico-Química Biológica Aída Hassón Voloch, Brazil.

10.049 **Systems Biology Identifies a Chaperone-Mediated Network Associated with Doxorubicin Response and Poor Survival in Triple-Negative Breast Cancer**. Silva JYG[1], Azevedo GM[2], Dalmolin RJS[2], Wilke DV[1] [1]UFC, PPG Pharmacology, Brazil [2]UFRN, Bioinformatics Multidisciplinary Environment - BioME, IMD, Natal, Brazil

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10.063 **Targeting the Premetastatic Lung Niche with Heparin in a Colon Adenocarcinoma Murine Model**. Motta JM, Oliveira MR, Hermsdorff-Brandt M, Peres ACL, Pereira MS, Mourão PAS IBqM-UFRJ

10.064 **Target-Based Discovery of an NQO1 Inhibitor with Pro-Apoptotic Effects in Lung Cancer Cells**. Costa PMS, Pereira JVM, Brito TL, Paier CRK, Pessoa C UFC, Lab. of Experimental Oncology, Drug Research and Development Center, Brazil; PPG Pharmacology, Brazil, Northeast Biotechnology Network Program (Renorbio), Brazil

10.065 **Serigueleiro Gum Reduces Colorectal Tumor Growth Through Immunomodulatory Mechanisms**. Araújo DD[1], Alves GOM[1], Fortes MM[1], Machado FS[1], Araújo GS[1], Cajado AG[2], Lima Júnior RCP[2], Lopes ALF[3], Medeiros JVR[3], Souza LP[4], Silva FBF[4], Ribeiro FOS[5], Silva DA[5], Araújo AJ[1], Marinho-Filho JDB[1] [1]UFDPar, LCCDelta, Brazil, [2]UFC, LAFICA, Brazil, [3]UFDPar, LIGAT, Brazil, [4]UFDPar, LAPHIS, Brazil, [5]UFDPar, BIOTEC, Brazil

10.066 **A Phenylpropanoid from *Croton Velutinus* Modulates Redox Status and MAPK Signaling in MCF-7 Breast Cancer Cells**. Ferreira RC[1], Abrantes RA[1], Duarte SS[1], Sousa VM[1], Souza RRM[1], Queiroga LM[1], Silvestre GFG[1], Castro IO[1], Araújo YKO[2], Abreu LS[3], Velozo ES[4], Goncalves JCR[1], Silva MS[1], Tavares JF[1], Sobral MV[1] [1]UFPB, Health Sciences Center, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]Health Sciences Center, ONCOFAR, Undergraduate in pharmacy, Brazil. [3]UFF, Dept Organic Chemistry, Brazil. [4]UFBA, School of Pharmacy, Research Lab in Materia Medica, Brazil

10. DOHaD and Developmental Biology

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10.002FR **Maternal Protein Restriction Shapes Hepatic Metabolic Trajectories During Aging in a Sex-Specific Manner**. Vitali PM, Ribeiro IT, Maciel FA, Barata LA, Lemos LS, Fioretto MN, Justulin LA IBB-Unesp-Botucatu, Cellular and Molecular Biology Dept

10.003FR **Perinatal Metabolic Programming: Impact of Maternal Protein Restriction on the Rat Hypothalamic Proteome Across the Lifespan**. Basso CBP, Fioretto MN, Barata LA, Lemos LS, Ribeiro IT, Maciel FA, Justulin LA IBB-Unesp-Botucatu, Cellular and Molecular Biology Dept, Brazil

10.005FR **Maternal Protein Restriction Reprograms the Pituitary Gland in a Sex-Specific Manner from Early Life to Old Age**. Cordeiro GM, Fioretto MN, Barata LA, Lemos LS, Maciel FA, Ribeiro IT, Justulin LA IBB-Unesp- Botucatu, Cellular and Molecular Biology Dept, Brazil

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10.006FR **Effects of Maternal Resistance Training on Growth and Working Memory in Offspring Prenatally Exposed to Valproic Acid**. Barros MRM[1], Silva RAA[1], Nelo SRB[1], Oliveira MCMC[1], Martins MVA[1], Lima RS[2], Silva MLB[2], Pereira TKM[1], Antonio-Santos J[2], Da Silva Aragão R[2] [1]UFPE, PPG Nutrition, Brazil; [2]UFPE, Physical Education

10.007FR **Influence of Gestational Exposure to Valproic Acid on Growth, Physical Characteristics, and Motor Development in Rats**. Nelo SRB[1]; Silva RAA[1], Barros MRM[1], Oliveira MCMC[1], Martins MVA[1], Lima RS[2], Silva MLB[2], Pereira TKM[1], Antonio-Santos J[2], Da Silva Aragão R[2]. [1] UFPE, PPG Nutrition, Brazil; [2]UFPE, Physical Education, Brazil;

10.008FR **Maternal Protein Restriction Compromises Structural, Electrophysiological, and Molecular Cardiac Parameters in Female Rat Offspring During Early Life**. Lemos LS, Gomes LC, Fioretto MN, Barata LA, Ribeiro IT, Maciel FA, Justulin LA IBB-Unesp-Botucatu, Cellular and Molecular Biology Dept

10.009FR **Offspring Voluntary Physical Activity on Skeletal Muscle Weight in a Maternal Obesogenic**. Lopes IGT[1], Silva PHS[1], Vasconcelos BHA[2]; Silva AA[2]; Silva BA, Bandeira VCA[1]; Melo SM[2], Rocha EP[2], Casi EJ[1] [1]UFPE-Vitória Academic Center, Vitória de Santo Antão – PE, Brazil. [2]UFPE, Center of Health Sciences, Nutrition Dept, Recife – PE, Brazil.

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10.016FR **NADPH Oxidase Participates of Intrauterine Growth Retardation and Nephrogenesis Impairment Induced by Maternal Inflammation**. Constantino TS, Veras AC, Farias JS, Lima NKS, Aires RS, Silva-Filho LF, Sant'Helena BRM, de Queiroz DB, Paixão AD, Vieira LD UFPE, UFRPE, IELUSC, UPE

10.010FR **Effects of Moderate-Continuous Training on Cardiac Mitochondrial Bioenergetics and Redox Status in Rats Subjected to Early-Life Overnutrition**. Silva JTA, Fernandes MSS, Correia-Filho RC, Melo TSM, Fernandes MP, Lagranha CJ UFPE, Graduate Program in Nutrition, Physical Activity, and Phenotypic Plasticity, Brazil; UEFS, Brazil

10.011FR **Effects of a Low-Protein or Obesogenic Diet during Pregnancy and Lactation on Body Mass, Fasting Glycemia, Food Intake and Indirectly Assessed Offspring Milk Consumption**. Vasconcelos BHA[1], Silva BA[2], Silva PHE[2], Lopes IGT[2], Bandeira VCA[2], Araújo FWC[1], Prieto SG[1], Rocha EP[1], Mousinho EM[1], Carreteiro EJC[1], Santos JVM[1], Vasconcelos DAA[1,2] [1]UFPE, Center of Health Sciences, Nutrition Dept, Recife – PE, Brazil. [2]UFPE-CAV, Vitória de Santo Antão – PE, Brazil.

10.012FR **Maternal Protein Restriction Reprograms Placental Proteomic Networks and Ultrastructure: Insights into Early Developmental Adaptation**. Barata LA[1], Fioretto MN[1], Magosso N[1], Ferreira MR[2], Maciel FA[1], Felipe VAA[1], Ribeiro IT[1], Dos Santos DC[1], Justulin LA[1] [1]IBB-Unesp-Botucatu, Dept Cellular and Molecular Biology, PPG in General and Applied Biology, Brazil. [2]Unesp-Botucatu, School of Medicine, Experimental Research Unit - Unipex, Molecular Genetics and Bioinformatics Lab, Brazil.

11. Clinical Pharmacology, Pharmacokinetics, Pharmacogenomics and Toxicology

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11.012 **Racial and Ethnic Influences on Post-Transplant Complications in a 634-Recipient Allogeneic Hematopoietic Cell Transplant Cohort Using Cyclosporine and Tacrolimus**. Pessoni JG[1], Costa-Junior LC[2,3], Leão AM[4,5], Izu M[3], Tavares RC[3], Maradei SC[3], Moreira MC[3,6], Nogueira MC[3], Lerner D[3], Bino FG[7,5], Moriel P[8], Fernandez TS[4], Santos PC[1,2] [1]EPM-Unifesp, Department of Pharmacology, São Paulo, Brazil, [2]FMUSP, Postgraduate Program in Medical Sciences, São Paulo, Brazil, [3]INCa, Bone Marrow Transplant Center, Rio de Janeiro, Brazil, [4]INCa, Cytogenetic Laboratory, Cell and Gene Therapy Program, Rio de Janeiro, Brazil, [5]Unigranrio, Duque de Caxias, Brazil, [6]UFRJ, Bone Marrow TransplantProgram, Rio de Janeiro, Brazil, [7]UFRJ, Division of Nephrology, Rio de Janeiro, Brazil, [8]Unicamp, Faculty of Medical Sciences, Campinas, Brazil

11.013 *In vitro* **Metabolism of Violacein, a Molecule with Antimalarial Therapeutic Potential, Using Human, Rat, and Mouse Liver Microsomes**. Calemi DBA[1], Guldoni LF[1,2], Godoi AB[1,3], Minuti G[1], Carnevale Neto F[4], Hispagnol GF[5], Pilon AC[5], Costa JL[1,3,6], Hyslop S[1], Antunes NJ[1] [1]FCM-Unicamp, Depto Farmacologia, Campinas, SP, Brasil, [2]UNOESTE, Lab Toxinologia e Estudos Cardiovasculares, Programa de Graduação em Ciências da Saúde, Brasil, [3]Unicamp, Centro de Informação e Assistência Toxicológica, Brasil, [4]Washington University, Centro de Pesquisa Metabolômica do Noroeste, Depto Anestesiologia e Medicina da Dor, Seattle, EUA, [5]Unesp, Depto Bioquímica e Química Orgânica, Instituto de Química, Brasil, [6]Unicamp, Faculdade de Ciências Farmacêuticas, Brasil.

11.016 **Acute Toxicity Evaluation of Compound LOE2208 by Up-and-Down Method (OEC D425) in NOD-SCID Mice**. Gress LSB[1,2], Bastos RS[1,2], Mota JA[1,2], Sales SLA[1,2], Maranhão SS[2,3], Oliveira KAF[2], Desidério GA[1,2], Macêdo SMN[2], Soares IF[2], Farias KM[4], Duque BR[1], Maria DA[4], Sampaio TL[1], Furtado CLM[5] and Pessoa CO[2] [1]UFC, PPG Pharmacology, Brazil; [2]UFC, Lab Experimental Oncology, Brazil; [3]UFC, PPG Translational Medicine, Brazil; [4]Lab Biotechnology and Innovation, Butantã, Brazil and [5]UFMG, Dept Genetics, Ecology and Evolution, Brazil.

11.017 **Clinical Response to Cannabidiol in a Pediatric Cohort with Autism Spectrum Disorder: A Randomized Placebo-Controlled Trial**. Canquerino YK, Feliz MC, Cunha JM. UFPR, Curitiba, Sector of Biological Sciences, Dept. of Pharmacology, PPG Pharmacology, Brazil.

12. Drug Discovery and Development

Totem 38

12.001 **Therapeutic Potential of a Promising N-Phenylacrylamide Derivative in the Treatment of Colitis**. Silva JVV[1,3], Araruna MEC[2], Barbosa YV[3], Farias AGC[1,2,3], Cavalcanti MAT[1], Menezes KJS[1], Leandro PF[1,3], Lima MKS[1,3] Fernandes HQA[1,3], Moura WCS[1,2,3], Lima AMAF[1,3], Oliveira MLA[1,3], Albino SL[1,2,3], Moura RO[1,2,3]. [1]UEPB, Lab Drug Devopment and Synthesis, Brazil; [2]UEPB, PPG in Pharmaceutical Sciences, Brazil; [3]UEPB, Dept Pharmacy, Brazil

12.002 **Expression, Purification, and Validation of an in-House Recombinant Taq DNA Polymerase for PCR Applications**. Salviano RA[1,3]; Costa PMS[1,2]; Silva AS[1,3]; Desiderio GA[1,2]; Paier CRK[1,2]; Pessoa C[1,2] [1]UFC, Lab Experimental Oncology, Brazil, Drug Research and Development Center, Brazil; [2]UFC PPG Pharmacology, Brazil; [3]UFC Faculty of Pharmacy, Dentistry and Nursing, Brazil

12.003 **Comparative Quantum Evaluation of Serotonin, DMT, 8-OH-DPAT, and 5-MeO-DMT Interactions with the 5-HT1A Receptor**. Dantas BLR, Silva MS, Silva FKO, Gavioli EC, Fulco UL, Bezerra KS, Silva-Junior ED UFRN, Dept Biophysics and Pharmacology, Brazil.

12.004 **Computer-Aided Drug Design Applied to the Discovery of Potential Falcipain-2 Inhibitors Against Plasmodium falciparum**. Rios EO[1], Silva AVX[1], Silva KWL[2], Nascimento IJS[1] [1]CESMAC, Faculty of Pharmacy, Brazil, [2]Estácio, Faculty of Biological Sciences, Brazil

12.005 **Evaluation of the Antinociceptive Potential of Oxyethylariamides in Experimental Pain Model**. Valente AG, França PRC, Franco GRR, Silva IMF, Viegas-Junior C, Fernandes PD UFRJ, Institute of Biomedical Science, Lab Pharmacology of Pain and Inflammation, PPG Pharmacology and Medicinal Chemistry, Brazil, UFAL, Chemistry Institute, Medicinal Chemistry Research Lab, PPG Pharmaceutical Sciences, Brazil.

12.006 *In vitro* **Evaluation of the Anti-Leishmania Potential of Isatin-Derived Cyanohydrazones Against** *Leishmania infantum*. Albuquerque YS[1], Machado GR[1], Fernandes ALM[1], Ferreira RS[1], Cardoso LL[1], Santos ESFR[2], Lima-Junior CG[2], Keesen TSL[1] [1]UFPB, Immunology Lab Infectious Diseases, Brazil, [2]UFPB, Lab Medicinal Organic Synthesis, Brazil

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12.028 *In vivo* **and** *In vitro* **Anti-Inflammatory Activity of CBD-Derived Terpene-Cinnamoyl-Acyl-Hydrazone Molecules**. Paiva JPB[1], Lontra ACP[1], Souza, MK[2], Franco GRR[2], Gontijo VS[2], Viegas-Jr C[2], Fernandes PD[1] [1]ICB-UFRJ, Program of Reserch and Drug Discovery, Lab. of Pharmacology of Pain and Inflammation, Brazil; [2]UNIFAL, Lab. of Research in Medicinal Chemistry, Brazil.

12.029 **Liposomal Coencapsulation of Piplartine and Fenretinide Aiming the Treatment of Non-Invasive Breast Cancer**. Melo GB, Lopes LB ICB-USP, Dept Pharmacology, Graduate Program Functional and Molecular Biology

12.030 **Preparation, Characterization and** *in vitro* **Evaluation of Liposomes Containing an Antitumor Prototype from the Pterocarpan Class**. Sousa GC[1,2], Maranhão SS[1,3], Vieira Neto JB[1,3], Bastos RS[1,3], Desiderio GA[1,3], Falcão JS[4,5], Lapa DP[4,5], Costa PRR[4,5], Caleffi GS[4,5], Pessoa C[1,3]. [1]UFC, Lab. of Experimental Oncology, Brazil, [2]UFC, PPG Biotechnology, Brazil, [3]UFC, PPG Pharmacology, Brazil, [4]UFRJ, Lab. of Bioorganic Chemistry, Research Institute of Natural Products Walter Mors, Brazil, [5]UFRJ, PPG Chemistry of Natural Products, Brazil.

12.031 **New Synthetic Morita-Baylis-Hillman Compounds as Candidates for the Treatment of Visceral Leishmaniasis**. Ferreira RS[1], Fernandes ALM[1], Cardoso LL[1], Lamec DTF[1], Albuquerque YS[1], Machado GR[1], Almeida FS[1], Santos ESFR[2], Lima-Junior CG[2], Keesen TSL[1] [1]UFPB, Dept Cell and Molecular Biology, Lab Immunology of

Infectious Diseases, Multicenter Graduate Program in Physiological Sciences (PMPGCF), Brazil. [2]UFPB, Dept Chemistry, Lab Medicinal Organic Synthesis, Brazil.

12.032 **Trypanothione Reductase as a Target in Drug Repurposing Strategies** *against L*. (*L*.) *amazonensis*. Melchert SSL, Passero LFD, Souza FF, Honorio KM, Laurenti MD. [1]FMUSP, Lab of Pathology of Infectious Diseases, PPG Experimental Pathophysiology, Brazil, [2]IEAMAR-Unesp, Brazil, [3]EACH/USP, Brazil.

13. Pharmacology Education

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13.008 **Gamification Inspired by Television Game Shows for Pharmacology Teaching: An Experience Report with Four Educational Strategies**. Nin MS UFCSPA, Lab Neuropsicofarmacologia, Depto Farmacociências, Brazil.

13.005 **Developing Scientific Literacy Through Neuropharmacology Education and Research Training in Middle Grade Students**. Fonseca RD[1], Costa SF[2], Machado LHR[2], Nin MS[3], Barros HMT[4] [1]UFCSPA, Lab. Neuropsychopharmacology, PPG Health Sciences: Pharmacology and Toxicology, Brazil. [2]UFCSPA, Lab. Neuropsychopharmacology, Brazil. [3]UFCSPA, Dept. of Pharmacosciences, Lab. Neuropsychopharmacology, Brazil. [4]UFCSPA, Dept. of Pharmacosciences, Lab. Neuropsychopharmacology, PPG Health Sciences: Pharmacology and Toxicology, Brazil.

13.006 **“ConsCIÊNCIA DOS MEDICAMENTOS”: Educational Game for Health Education on the Use and Disposal of Medications**. Silva VS[1,4], Reis MDS[2,4], Lins MP[3,4], Ferro JNS[1,2] [1]UFAL, PPG Ciências Farmacêuticas, Brasil, [2]UFAL, PPG Ciências da Saúde, Brasil, [3]UFMT, PPG Ciências da Saúde, Brasil, [4]INCT Neuroimunomodulação, Brasil

13.007 **The "MicroMuseu Somos Mar": A Portable, Interactive, and Accessible Totem for Marine Pharmacology and Environmental Education**. Nogueira CN[1], Oliveira AGNA[2], Sahm BB[3], Silva JYG[1], Brito TL[1], Costa-Lotufo LV[3], Longo G[4], Lima MMX[2], Wilke DV[1] [1]UFC, Graduate Program in Pharmacology, Fortaleza, CE, Brazil. [2]UFC, Graduate Program in Architecture, Urbanism and Design, Fortaleza, CE, Brazil. [3]USP, Graduate Program in Pharmacology, São Paulo, SP, Brazil. [4]UFRN, Dept Oceanography and Limnology, Natal, RN, Brazil.

13.001 **Problem-Based Learning and the Flipped Classroom as Innovative Tools in Pharmacology Teaching in Biomedical Sciences**. Silva GS, Dorneles GL, Correa ILO, Nascimento AR, Gonçalves YS, Castro PFS UEG, UnU Goiânia – Eseffego, Goiânia, Brazil

13.002 **Innovative Pedagogical Tools for Gamification in Pharmacology Education: Construction, Evaluation and Student Perception**. Gonçalves YS, Moreira EM, Monteiro IPG, Fontes MLS, Silva GS, Pires ARL, Castro PFS UEG - UnU Goiânia – Eseffego

13.003 **Creation and Impact of the Academic League of Pharmacology of the State University of Goiás: An Experience Report**. Nascimento AR, Silva GS, Monteiro JCL, Silva MCB, Reis BC, Fontes MLS, Gonçalves YS, Jacobina KF, Lima OM, Matheus EM, Castro PFS. UEG, UnU Goiânia – Eseffego, Goiânia, Brazil

13.004 **Development and Acceptance Evaluation of a Didactic Board Game as an Active Learning Tool for G Protein-Coupled Receptor Pharmacology**. Almeida KBS[1], Souza JB[1], Barreto MS[1], Santana ALS[2], Louzada RN[2], Lima YRS[2], Gomes VS[2], Guimarães AG[1] [1]UFS, Dept. of Pharmacy, Lab. of Clinical and Experimental Pharmacology, Brazil; [2]UFS, CCBS, Brazil

13. Immunology, Microbiology and Parasitology

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13.003FR **Antimicrobial Activity of the Extract Obtained from *Zingiber officinale* Roscoe Residues Enriched with Gingerol Against *Staphylococcus aureus* and *Pseudomonas aeruginosa***. Guilherme ACS, Almeida JBC, Souza SO, Silva AP, Sousa JCR, Lima CM UFS, Brasil

14. Pharmacology: Other

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14.011 **Relationship Between APOE Gene Polymorphisms and Neuropsychiatric and Neurodegenerative Disorders: Evidence from a Cohort in Ceará, Brazil**. Ferreira DMA[1,2], Souza TF[1,2], Guimarães APDS[1,2], Rosa R[3], Lima DP[3,4,5], Lima AB[5], Miyajima F[1,2] [1]Fiocruz-CE, Brasil, [2]ACMELab, Lab Analítico de Competências Moleculares e Epidemiológicas, Brasil, [3]UFC, Brasil, [4]Hospital Universitário Walter Cantídio, Brasil, [5]Hospital de Saúde Mental de Messejana, Brasil

14.012 **Biochanin A Promotes Wound Healing by Reducing the Inflammatory Response in Ovariectomized Mice**. Santos DN[1], Neres WS[1], Aragão JMDA[1], Nascimento ACS[1], Sant'ana ROS[1], Santos GJS[1], Souza MTS[3], Albuquerque-Júnior LC[2], Camargo EA[1], Grespan R[1]. [1]UFS, Pharmacology Lab the Inflammatory Process, Brazil, [2]UFSC, Pathology Departament, Brazil, [3]UFS, Pharmacy Dept, Brazil.

14.013 **Comparative Development and Characterization of PCL and PLGA Nanoparticles Co-Loaded with Itraconazole and Terbinafine**. Samuel AB[1], Cavalcante SB[1], Miguel RA[2], Gomes MAM[2], Passos JS[2], Lopes LB[2], Ishida K[1] [1]USP, Institute of Biomedical Science, Dept Microbiology, Lab. of Antifungal Chemotherapy, PPG Microbiology, Brazil, [2]ICB-USP, Dept Pharmacology, Lab. of Nanomedicine and Drug Delivery, PPG Funcional & Molecular Biology, Brazil

14.014 **Use of the Chorioallantoic Membrane in the Screening of Compounds with Antiangiogenic Potential: An Alternative Model to the Use of Animals**. Silva AP[1,3], Alves AKL[1,2], Dantas MEA[1,2], Brito JM[1,3], Silva KKF[1,4], Dantas BB[1,5] [1]UFCG, Curimataú Cancer Observatory (OCC), Brazil; [2]PIBIC/UFCG; [3]UFCG, PPGCNBiotec, Brazil; [4]UFPB, Renorbio, Brazil; [5]UFCG, Academic Health Unit, Center for Education and Health, Brazil

14.015 **Antimicrobial Activity and Pharmacological Modulation of the Compound 3,4-BZM Against Resistant Strains of MRSA and *Candidozyma auris***. Jesus ICTR[1], Vieira MM[2], Emídio JJ[2], Souza DP[2], Castro RD[2] [1]UFPB, PPG in Dentistry, Brazil. [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Brazil.

15. Neurobiology and Neuronal Diseases

Totem 05

15.008FR **Ventral Hippocampus Differentially Modulates Recruitment of Brainstem Catecholaminergic Cells During Acute and Chronic Restraint Stress**. Giatti LO[1,2], Crestani CC[1,2], Dunn T[2], Moore C[2], Packard BA[2], Chambers JB[2], Oliveira LA[1,2], Busnardo C[1,2], Herman JP[2,3] [1]FCFAr-Unesp-Araraquara, Lab Pharmacology, Araraquara, São Paulo, Brazil; [2]University of Cincinnati Dept Pharmacology, Physiology and Neurobiology; School of Medicine, Cincinnati, OH, USA; [3]Cincinnati VA Medical Center, Cincinnati, OH, USA

15.009FR **Central Irisin Administration Modulates Hypothalamic Energy Balance Pathways in Mice**. Bem KCP, Talpo TC, Nogueira GAS, Oliveira KM, Silva-Junior JA,Velloso LA, Barbosa HCL Unicamp, Obesity and Comorbidities Research Center (OCRC), Brazil

Totem 06

15.010FR **Behavioral and Nociceptive Changes Induced by Persistent Neuropathic Pain in Male and Female Rats**. Tavares LRR, Silva LLR, Ferronato MVS, Silva KS, Marinho JAN, Santos LO, Crestani CC FCFAr-Unesp, Lab Pharmacology, Araraquara, SP, Brazil

Totem 23

15.001FR *in silico* **Evaluation of the Neuroprotective Potential of** *Alpinia zerumbet* **Extract Bioactive Compounds in Alzheimer's Disease**. Soares LN[1], Ferreira FS[1], Medeiros IV[2], Mattos JA[1], Nascimento JM[1], Dias KM[1], Lopes CFO[1], Caetano AC[1], Soares SCS[1], Dias CMN[1], Cunha MET[2], Ognibene DT[1], Costa CA[1], Resende AC[1] and Bem GF[1] [1]NFPM-UERJ, Research Line in Neuropharmacology and Medicinal Plants, PPG in Clinical and Experimental Pathophysiology (Fisclinex), Brazil, [2]UNINTA, Pharmacy Course, PPG in Health Sciences, Brazil

15.002FR **The Impact of Immersive Virtual Reality on Cortico-Muscular Coherence of Two Individuals with Parkinson's Disease, one with Essential Tremor and a Healthy Control – Case Study**. Flora JMG[1], Tourino FD[1], Rosa MVP[1], Silva GAB[1], Camargos MF[1], Brito FG[1], Fonseca LAS[1], Rodrigues IJS[1], Leite IHA[1], De Souza HLR[1], Brandão CFCCM[1], Andrade MJO[2], Drummond LR[1], Lacerda LT[1] [1]UEMG, Dept Physical Education, Brazil, [2]UEMG, Dept Psychology, Brazil

15.003FR **Impacts of an Enriched Environment on the Modulation of Oxidative Balance in the Hippocampus of Mice over 120 Days**. Santos KH[1,6,] Souza VL[1,2,3,] Ramos TL[3,4], Bezerra EFB[1,5], Fidelis DES[3,4], Fernandes MSS[3,4], Souto FO[3,4], Lagranha CJ[1] [1]CAV-UFPE, Lab General, Molecular and Exercise Biochemistry, [2]UFPE, Graduate Program in Neuropsychology and Behavioral Sciences, [3]UFPE, Keizo Asami Institute; [4]UFPE, Graduate Program in Biology Applied to Health, [5]UNIFACOL, Veterinary Medicine, [6]CAV-UFPE, Physical Education

15.004FR **Prevalence of symptoms of neuropsychiatric disorders in women exposed to domestic violence by an intimate partner**. Xavier MJS[3], Freitas GA[1,4], Silva GM[1,4], Souza BTBA[1,4], Azevedo ATF[1], Silva VFB[1], Cavalcante AM[1], Albuquerque SCSO[1], Santos MEB[1], Souto JJS[1,4], Abreu DFP[1], Oliveira ACGA[2], Santos NA[1,4] [1]UFPB, PPG Neurociência Cognitiva e Comportamento, [2]UNIPÊ, PPG Direito. Brasil, [3]UNINASSAU, Lab Percepção, Neurociências e Comportamento, [4]PPG Psicologia Social

15.005FR **Effects of Enriched Environment on the Hippocampal Oxidative Balance of Female Mice at 60 Days**. Mota IRFS[1,5], Souza VL[1,2,3], Ramos TL[3,4]; Bezerra EFB[1,5], Fidelis DES[3,4], Fernandes MSS[3,4], Souto FO[3,4], Lagranha [1]CAV-UFPE, Lab General, Molecular and Exercise Biochemistry, [2]UFPE, Graduate Program in Neuropsychology and Behavioral Sciences, [3]UFPE, Keizo Asami Institute; [4]UFPE, Graduate Program in Biology Applied to Health, [5]UNIFACOL, Veterinary Medicine, [6]CAV-UFPE, Physical Education

16. Toxinology, Natural Products and Medicinal Chemistry

Totem 29

16.001FR **Development and Characterization of Starch Films Containing Red Propolis**. Sousa JCR[1], Souza SM[2], Guilherme ACS[2], Almeida JBC[2], Silva AP[2], Cardoso JC[2], Souza SO[1], Lima CM[1] [1]UFS-Lagarto. 2Universidade Tiradentes, Aracaju/Sergipe.

16.002FR **Investigation of the Lipid Composition of** *Cucumis anguria* **L. by Gas Chromatography–Mass Spectrometry** (**GC–MS**). Jorge SAS, Lima SG, Brito LL, Sousa YRF, Silva Neta ER, Rocha MS. UFPI, Organic Geochemistry Lab, Brazil.

Totem 32

16.007FR **Embryotoxicity Assessment of Brazilian Cerrado Plants in the Zebrafish Model**. Andrade ICB[1 4], Lima AKS[2,4], Linhares KJS[3,4], Carneiro ERC[3,4], Lira-Júnior EP[3,4], Moraes IB[1,2,4] [1]UFOB, PPG Investigative Pathology, Brazil,

[2]UFOB, PPG in Biochemistry and Molecular Biology, Brazil, [3]UFOB, Undergraduate Medical Programme, Brazil, [4]UFOB, Centre for Biological and Health Sciences, Brazil

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01. Cellular and Molecular Pharmacology

Totem 01

01.004 **Exploring the Relationship Between PTEN and Klotho in Autophagy**. dos Santos, GRO[1], Berwick, D[2], Kawamoto, EM[1] [1]ICB-USP, Functional and Molecular Biology, Brazil, [2]University of London, City St. George's, School of Health & Medical Sciences, England.

01.005 **Effects of Endogenous and Exogenous H_2S on the Activity of Antioxidant Enzymes of Cultured Human Umbilical Vein Endothelial Cells** (**HUVECs**). Sebastião MA, da Costa Marques LA, Coavoy-Sánchez SA, Costa SKP, Teixeira SA, Muscará MN ICB-USP, Depto Farmacologia, Lab Farmacologia Bioquímica dos Radicais Livres, Inflamação e Dor São Paulo, SP, Brasil

01.006 **APT20TTMG Suppresses Clonogenic Growth and Induces S-Phase Accumulation in U-87 MG Glioblastoma Cells**. Lobo EB[1,2], Oliveira VS[1,2], Silva DKC[1], Nogueira ML[2], Soares ES[3], Sinatti VVC[3], Silva JC[3], Bottos RM[3], Leal CBQS[3], Meira CS[1,2] [1]Fiocruz-BA, Salvador, [2]SENAI CIMATEC-BA, Salvador, [3]Aptah Bio, San Carlos, CA, USA.

01.007 **Assessment of the Wound Healing Potential of Dermocosmetics in Fibroblasts** (**L929**). Bertoncelli ACZ[1], Oliveira Mendes TO[1], Livinalli IC[1], Pedrozo ER[1], Peroza LR[1], Augusto RA[2], Milani JA[2], Santoro F[2], Mello GH[3], Cadoná FC[4] [1]UFN, Biomedicine Course, Brazil, [2]Company Smart Gr Lab (Smart Gr Lab - Compounding Lab Ltd.), Brazil, [3]UFN, Graduate Program in Nanosciences, Brasil, [4]UFN, Graduate Program in Health and Life Sciences, Brazil.

01.008 **Siglec-10 as a Potential Prognostic Biomarker and Therapeutic Response Marker in Osteosarcoma**. Paz Neta DC[1,2], Santos VL[1,2], Gomes JPA[1,2], Silva BO[1,2], Pereira MC[1,2,3] [1]UFPE, PPG Therapeutic Innovation, Brazil; [2]UFPE, Suely Galdino Center for Research in Therapeutic Innovation, Brazil; [3]UFPE, Departamento of Physiology and Pharmacology, Brazil

01.009 *in silico* **and** *in vitro* **Analysis of Melittin's Effect on Membranes and Its Regenerative Potential in Muscle Cells**. de Souza e Silva S, Boaventura de Oliveira AM, Almeida TC, Sant'anna MBM, Picolo G IBu, Pain and Signalling Lab

01.010 **A BRET-Based Platform for the Study of the Angiotensin II Type 1 Receptor** (**AT1R**) **and the Bradykinin B2 Receptor** (**B2R**) **Non-Canonical Signaling**. Sousa AC[1], Santos AM[2], Rodrigues FC[3], Bouvier M[5], Parreiras-e-Silva LT[1,2,3,4] [1]FCFRP-USP, PPG Biosciences and Biotechnology, Brazil, [2]FMRP-USP, PPG Pharmacology, Brazil, [3]FMRP-USP, PPG Biochemistry, [4]FCFRP-USP, Brazil, [5]University of Montreal, Institute for Research in Immunology and Cancer, Canada.

02. Neuropharmacology

Totem 02

02.007 **Effects of Oral Titanium Dioxide Nanoparticle Exposure on Cortical Spreading Depression**. Mousinho EM[1], França BNS[2], Melo SM[1], Gouveia JCA[3], Romero LJZ[4], Baez MC[4], Prieto SCG[1], Guedes RCA[1]. [1]UFPE, Center of Health Sciences, Nutrition Dept, Brazil; [2]UFPE, Center for Biosciences, Dept Physiology and Pharmacology, Brazil; [3]UFPE, Academic Center of Vitória, Vitória de Santo Antão, PE, Brazil; [4]UFPE, Center for Exact and Natural Sciences, Physics Dept, Brazil

02.008 **Prenatal Sodium Valproate Exposure Impairs Developmental Milestones in Swiss Mice Offspring**. Araújo JR[1], Duarte ALS[1], Herculano-Júnior FS[1], Honório-Júnior JER[4], Lima CBTM[2], Lima LM[2], Lima PJS[2], Pereira JRG[2], Silva SC[2], Sousa FCF[3] [1]UFC, Faculty of Pharmacy, Dentistry and Nursing, Brazil; [2]UFC, Dept. of Pharmacology, PPG in Pharmacology, Brazil; [3]UFC, Center for Research and Development of Medicines, Brazil; [4]Christus University, Brazil.

02.009 **Guarana Extract Modulates Antioxidant Responses and Oxidative Stress Resilience in TDP-43 Depleted Astrocytes**. Piristrello BS[1,2], Dale A[2], Levi J[2], Mendes FR[1], Sattler R[2] [1]Universidade Federal do ABC, São Bernardo do Campo SP, [2]Barrow Neurological Institute, Phoenix AZ

02.010 **Toxicity and Hemolytic Assessment of Novel Peptides with Affinity for Amyloid-β**. Costa CM[1,2], Taveira RAA[2], Camargo LC[2], [1]UCB, 2UnB, PPG Patologia Molecular Brasil

02.011 **Effects of Lyophilized Hydroalcoholic Extract of *Spondias tuberosa* Arruda on Anxiety-Like Behavior and Brain Lipid Peroxidation in D-Galactose-Aged Wistar Rats**. Souza ETN[1], Araújo AB[1,2], Araújo IGA[1,2], Medeiros IA[1,2], Soares JKB[1] [1]UFPB, Lab Farmacologia Cardiovascular, Instituto de Pesquisa em Fármacos e Medicamentos, Brasil, [2] UFPB, PPG Profissional em Gerontologia, Brasil.

02.012 **Evaluation of the Neuroprotective Effects of Intranasal Octovespin in Alzheimer's Disease Mouse Model**. Aguiar GP, Santos VRM, Camargo LC UnB, Darcy Ribeiro, Biology Institute, Dept Physiological Sciences, Neuropharma Lab, Brazil; UnB, Darcy Ribeiro, Biology Institute, PPG Animal Biology, Brazil; UnB, Darcy Ribeiro, Psychology Institute, Psychobiology Lab, Brazil

Totem 03

02.032 **Effects of Cannabigerol on Sensorimotor Gating and Behavioral Alterations Induced by MK-801 in Mice**. Correa BS, Souza JC, Pereira GJS, Abílio VC Unifesp, Graduate Program in Pharmacology, Brazil.

02.033 **Formulation and Characterization of an Octovespin Peptide Nanoemulsion for Intranasal Application for Alzheimer's Disease Treatment**. Penha GS[1,2,3], Santos VRM[1,2,3] Mota IFL[1,3], Resende MCS[1], Taveira RAA[1,3], Rabelo GS[1], Gomes CHF[1], Mortari MR[1], Camargo LC[2,3] [1]UnB, Darcy Ribeiro, Biology Institute, Dept Physiological Sciences, Neuropharma Lab, Brazil, [2]UnB, Darcy Ribeiro, Biology Institute, PPG Animal Biology, Brazil [3]UnB, Darcy Ribeiro, Psychology Institute, Psychobiology Lab, Brazil.

02.034 **Evaluation of the Anticonvulsant and Neuroprotective Potential of *Scenedesmus ecornis* and *Limnospira platensis* in a Chronic Pentylenetetrazol-Induced Kindling Model**. Bentes ILG[1,2], Pantoja EKM[1], Souto TL[1], Nascimento AA[1], Faustino SMM[1], Oliveira EDC[4], Do Nascimento JLM[3], Oliveira FR[1,2] [1]Unifap, School of Pharmacy, Brazil. [2]Unifap, PPG Pharmaceutical Sciences, Brazil. [3]UFPA, PPG Pharmacology and Biochemistry. [4]IEPA, Lab Taxonomy and Ecology of Cyanobacteria and Microalgae, Brazil.

Totem 04

02.046 **Therapeutic Potential of NeuroVal, a Bioinspired Wasp Peptide, in an Animal Model of Autism Spectrum Disorder**. Veras LG, Ferreira JW, Campos GAA, Mortari MR [1]UnB, Biological Sciences Institute, Neuropharmacology Lab, Brazil, [2]UnB, Faculty of Health Sciences, PPG Health Sciences, Brazil.

02.047 *Alpinia zerumbet* **Reverses and Prevents Cognitive Deficits, Neuroinflammation, and Neurodegeneration induced by Scopolamine Administration**. Ferreira FS[1], Soares LN[1], Mattos JA[1], Nascimento JM[1], Dias KM[1], Lopes CFO[1], Trefilio LM[1], Fontes-Dantas FL[1], Fernandes GG[2], Filgueiras CC[1], Cavalheira MA[1], Ognibene DT[1], Costa CA[1], Resende AC[1] and Bem GF[1] [1]UERJ, Research Line in Neuropharmacology and Medicinal Plants (NFPM), PPG in Clinical and Experimental Pathophysiology (Fisclinex), Brazil, [2]UFJF, Dept Biophysics and Physiology, Brazil

02.048 **Can Cannabidiol Alter Feeding Behavior? A Study of Binge Eating Behavior in C57BL Mice and Cross-Sensitization with Nicotine**. Manduca CA, Marçal AP, Costa RB, Araújo SS, Silva LRO, Moreira FA, Aguiar DC ICB-UFMG, Pharmacology Dept, Lab Neuropsychopharmacology, PPG in Physiology and Pharmacology, Brazil

02.049 **Synergistic Effects of 3-O-Methylquercetin and Polyphenols on Longevity, Healthspan, and Neuroprotection Via FOXO/Nrf2 Pathways in** *Caenorhabditis elegans*. Garofalo CB, Andrade EM, Souza VL, Farias MS, Santos PA, Pereira P. UFRGS, Institute of Basic Health Sciences, Dept Pharmacology, Lab Neuropharmacology and Clinical Toxicology, PPG in Pharmacology and Therapeutics. Brazil

02.050 **Modulation of Neuroinflammation in BV2 Cells Exposed to** *Pseudomonas aeruginosa* **and Treated with Omega 3 (DHA)**. Santos FS[1,2,3], Ferreira AMS[2], Reis GLSG[2], Costa MF[2], Silva AR[1,2,3], Castro-Faria-Neto HC[2], Bozza PT[2], Gonçalves-de-Albuquerque CF[1,2,3] [1]Unirio, Immunopharmacology Lab, Dept Physiological Sciences, Rio de Janeiro, Brazil; [2]IOC-Fiocruz, Immunopharmacology Lab, Rio de Janeiro, Brazil; [3]UFF, PPG in Neuroscience), Niterói, Brazil

02.051 **Early Pharmacological Intervention with NAC or BBG Produces Persistent Behavioral Improvements with Sex-Dependent Effects in MAM Rats**. Toscano LF[1], Vargas L[1], Ribeiro DE[2], Ulrich H[2], Salum C[1] [1]UFABC, PPG in Neuroscience and Cognition, Brazil; [2]USP, Dept Biochemistry, Institute of Chemistry, Brazil

02.052 **Immunomodulatory Effect of Laminarin in an Animal Model of Corticosterone-Induced Depression**. Nascimento, EF[1]; Batista, PVC[1]; Cunha, CS[1]; Lacerda, LRA[1]; Moura, VC[1]; Sousa, CNS[1]; Honório-Júnior, JER[2]; Chaves-Filho, AJM[3]; Oliveira, TQ[1]; Vasconcelos, SMM[1] [1]UFC, Neuropsychopharmacology Lab, Brazil, [2]Unichristus, Center for Translational Neuroscience, Brazil, [3]HCOR, Brazil.

02.054 **Role of Microglia in Adolescent Stress-Induced Behavioral Impairments and Alterations in Parvalbumin Interneurons and their Perineuronal Nets in Adult Mice**. Hadera V[1], Bobotis B[2], Guimarães FS[1], Tremblay ME[2], Gomes FV[1] [1]FMRP-USP, Dept Pharmacology, Brazil; [2]University of Victoria, Medical Sciences Building, Canada

02. Environmental Biology, Evolution and Comparative Biology

Totem 38

02.001FR **Monitoring of Post-Consumer Medicine Disposal: A Strategy for Mitigating Environmental Risks in Cabedelo, Paraíba, Brazil**. Oliveira RVS[1], Lira JVR[1], De Aróla AB[1], Nunes LFC[2], Martins ERV[3], Vitorino LM[4], Souza CO[4], Honório VM[4], Matos ACL[4], Lima GAS[4], Miranda LRHMB[4], Pontes AS[4], Luckwu RLB[4], Campana EH[5], Jales STL[5]. [1]UFPB, Undergraduate Program in Pharmacy, Brazil; [2]UFPB, Undergraduate Program in Physical Education, Brazil; [3]UFPB, Undergraduate Program in Speech-Language Pathology and Audiology, Brazil; [4]Municipal Health Dept Cabedelo, Brazil; [5]UFPB, Dept Pharmaceutical Sciences, Brazil

Totem 41

02.002FR **Hypertrophy of the Rectus Femoris and Vastus Lateralis Following Resistance Training with Greater Torque at Lengthened Muscle Positions**. Leite IHA[1], Rodrigues IJS[1], Flora JMG[1], Silva GAB[1], Brandão CFCCM[1], Andrade MJO[2], Drummond LR[1], Lacerda LT[1] [1]UEMG, Dept Physical Education; [2]UEMG Dept Psychology, Brazil

03. Psychopharmacology

Totem 05

03.007 **Investigation of the Antidepressant-Like Profile of Tetrahydrolinalool in a Lipopolysaccharide-Induced Neuroinflammation Model: an** *in vivo* **Study**. Neri LCD[1], Gonçalves MCF[1], Cunha MVS[1], Almeida JV[1], Mendes LM[1], Teixeira JL[1], Naves FB[1], Pereira CHL[1], Alves HAR[1], Barbosa NMMV[1], Rêgo IA[1], Monteiro AB[1], Felipe CFB[1,2], Alves ARS[1], Silva PR[1,2]. [1]UFPB, Psychopharmacology Lab, Institute of Drugs and Medicines Research, Brazil, [2]UFPB, PPG in Cognitive Neuroscience and Behavior, Brazil

03.008 **Effect of Dietary Inulin Supplementation on the Kynurenine Pathway and the Behavior of Rats Submitted to Alcohol Withdrawal**. Torres CLF[1], Albino MC[1], Oliveira JTA[1], Santos LC[1], Silva MS[1], Silva RT[1], Gavioli EC[1], Ferreira FR[2], Soares VP[1]. [1]UFRN, Dept Biophysics and Pharmacology, [2]Fiocruz, Brazil

03.009 **Evaluation of the Molecular Mechanisms of the Neuroprotective Action of Cinnamic Alcohol in the Pentylenetetrazol-Induced Chemical Kindling Model**. Alves HAR, Mendes LM, Naves FB, Almeida JVM, Pereira CHL, Neri LCD, Alves ARS, Teixeira JL, Barbosa NMMV, Martins AMO, Oliveira LN, Soares MFS, Silva PR, Monteiro AB, Felipe CFB UFPB, Psychopharmacology Lab, Brazil.

03.010 **Psychotropic Medication Use Among Medical Students in Paraíba, Brazil**. De Aragão MSO, De Oliveira Neto RG, De Andrade MRD, Viana MS Barbosa JLM1, Barbosa YCM, Lima FJB UNIFACISA, Centro Universitário

03.011 *in silico* **Evaluation of the Anti-Inflammatory Potential of the Aminothiophene Derivative 7CN03 on COX-2, iNOS, and NF-κB Molecular Targets**. Teixeira JL, Mendes LM, Naves FB, Pereira CHL, Alves HAR, Neri LCD, Almeida JVM, Cunha MVS, Barbosa NMMV, Martins AMO, Oliveira LN, Soares MFS, Monteiro AB, Felipe CFB, Silva PR, UFPB, Psychopharmacology Lab, Brazil

03.012 **Effects of** *Artocarpus heterophyllus* **Seed Core Extract on Behavioral, Metabolic, and Reproductive Parameters**. Alves ALF[1], Oliveira HL[1], Veríssimo TB[2], Alexandre SVD[1], Silva MS[1], Fernandes SEA[1], Costa Pinto MFN[1], Sena MO[1], Carvalho YV[1], Costa ML[1], Silva ED[1], Pedrini MR[2], Matsui KN[2], Soares VP[1]. [1]UFRN, Dept Biophysics and Pharmacology, [2]UFRN, Dept Food Engineering, Brazil.

Totem 06

03.023 **Evaluation of the Antagonism of Orexin Receptors (Types 1 and 2) During the Discontinuation Phase on Alcohol Preference in the Two-Bottle Choice Model in Swiss mice**. Costa RCA[1], Silva VS[1], Costa EF[1], Silva HC[2], Costa MEB[2], Sena AF[3], Oliveira ICS[1], Zhang Y[4], Malppezi-Marinho E[3], Marinho EAV[2], Berro LF[5], Oliveira-Lima AJ[2] [1]UESC, PPG in Health Sciences, Brazil; [2]UESC, Dept Health Sciences, Brazil; [3]UESC, Dept Biological Sciences, Brazil; [4]Research Triangle Institute, USA; [5] University of Mississippi Medical Center, USA

03.024 **Minocycline as a Possible Treatment for Anxiety and Depression Symptoms Associated with Ethanol Withdrawal In Female Wistar Rats**. Costa Pinto MFN, Santos LC, Albino MC, Lima FMS, Moura NPS, Costa JAM, Gavioli EC, Soares VP. UFRN, Biosciences Center, Dept Biophysics and Pharmacology, Psychopharmacology Lab, Graduate Program in Biochemistry and Molecular Biology, Brazil.

03.025 **Acute Buspirone Exposure Increases Shoal Cohesion in Adult Zebrafish**. Müller DV, Gallas-Lopes M, Patelli-Alves A, Portela SM, Piato A, Herrmann AP UFRGS, Dept. of Pharmacology, Brazil

03.026 **Rapid-Acting Antidepressants in the Prophylaxis of Inescapable Stress-Induced Behaviors in Mice: A Comparative Study between Esketamine and Dimethyltryptamine (DMT)**. Marques VB[1], Silva ANS[1], Moura CA[1], Torres CIO[1], Silva JMNS[1], Da Silva Jr ED[2], Gavioli EC[1] [1]UFRN, Dept Biophysics and Pharmacology, PPG Psychobiology, Brazil. [2]UFRN, Dept Biophysics and Pharmacology, PPG Biochemistry and Molecular Biology, Brazil.

03.027 **Effects of Spermidine on Alcohol Consumption in a Two-Bottle Choice Model in Mice**. Costa EF[1], Zambon AF[2], Costa RCA[1]., Silva VS[1], Sena AF[3], Silva HC[4], Dias, ES[4], Schat LES[5], Macedo IK[6], Marinho ELM[5], Lima AJD[4], Marinho AVL[4], Mello CF[2] [1]UESC, PPG in Health Sciences; [2]UFSM, Dept Physyology and Pharmacology, PPG in Pharmacology; [3]UESC, PPG in Biology and Biotechnology of Microorganisms; [4]UESC, Dept Health Sciences; [5]UESC, Dept Biological Sciences; [6]UESC, Dept Agricultural and Environmental Sciences

Totem 07

03.033 **N,N-Dimethyltryptamine Did Not Affect Associative Memory and Footshock Responses in Mice**. De Macedo SPF, Sousa-Silva AN, Moura CA, Torres CIO, Lima VVF, Gavioli EC. UFRN, Dept Biophysics and Pharmacology, PPG in Psychobiology, Natal, RN, Brazil.

03.034 **Role of 5-HT7 Receptors in the Dorsal Periaqueductal Gray in the Modulation Of Anxiety-Like Behavior**. Souza AF[1,2], Silveira MA[1], Gavioli, EC[1], Soares VP[1,2] [1]UFRN, Center for Biosciences, Dept Biophysics and Pharmacology, Brazil. [2]UFRN, Center for Biosciences, Dept Morphology, PPG Structural and Functional Biology, Brazil.

03.035 **Anticonvulsant and Neuroprotective Effects of Hydroxycitronellal in Experimental Models of Epilepsy**. Pires HFO[1,2], Dias AL[1,2], Gonçalves MCF[1,3], Neri LCD[1], Silva PR[1,2], Salvadori MGSS[1,2,3] [1]UFPB, Psychopharmacology Lab, Institute of Drugs and Medicines Research, Brazil, [2]UFPB, PPG in Cognitive Neuroscience And Behavior, Brazil, [3]UFPB, PPG in Bioactive Natural and Synthetic Products, Brazil.

03.036 **Behavioral and Biochemical Effects Of N,N-Dimethyltryptamine (DMT) and S-Ketamine in a Mouse Model of Glucocorticoid-induced Depression**. Torres CIO[1], Marques VB[1], Silva ANS[1], Moura CA[1], Silva JMN[1], Lima VVF[1], De Macedo SPF, Da Silva Jr ED[2], Gavioli EC[1] [1]UFRN, Dept Biophysics and Pharmacology, PPG Psychobiology, Brazil. [2]UFRN, Dept Biophysics and Pharmacology, PPG Biochemistry and Molecular Biology, Brazil.

04. Inflammation and Immunopharmacology

Totem 08

04.004 **Therapeutic Modulation of NF-κB and p38 MAPK Signaling by ZIB Reduces IL-6 Expression in LPS-Stimulated RAW 264. 7 Macrophages**. Pordeus GM[2], Moura BVS[1], Laurentino MVS[1], Rodrigues MRF[1], Oliveira JB[1], Mota PRV[2], Lima-Júnior CG[3], Gadelha FAAF[2], Dejani NN[2]. [1]UFPB, Immunopharmacology Lab, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]IPeFarM-UFPB, Immunopharmacology Lab, Institute of Pharmaceutical and Medicinal Research-, Brazil. [3]UFPB, Medicinal Organic Synthesis Lab Paraíba, Brazil.

04.005 *in silico* **Analysis of** *Chlamydia trachomatis* **MOMP Protein for the Identification of Immunogenic Epitopes**. Pinheiro IC[1], Conceição LS[2], Costa LFA[3], Sousa LR[4], Cartagenes MSS[5], Andrade MS6[1]UFMA, PPG Adult Health, Brazil, [2]UFMA, Biological Sciences Course, Brazil, [3]UFMA, Pharmacy Course, Brazil, [4]UFMA, PPG Adult Health, Brazil, [5]UFMA, Dept Physiological Sciences, PPG Health Sciences, Brazil, 6UFMA, Center for Biological and Health Sciences, Dept Physiological Sciences, PPG Adult Health, Brazil.

04.006 **Effect of Silymarin** (*Silybum marianum* **L.**) **on Adipocytokines in High Fat Diet-Fed C57BL/6 Mice**. Carvalho JPAQ[1], Ferreira ALN[1], Sousa GA[1], Costa SGA[1], Canafístula LS[1], Oliveira KS[1], Barbosa ISA[1], Silva FRC[2], Silva ME[2], Bezerra VM[2], Martins BVB[2], Yaochite JUN[2], Martins AMC[2], Sampaio TL[2], Menezes RRPPB[2] [1]UFC, Faculty of Pharmacy, Dentistry and Nursing, Dept of Clinical and Toxicological Analysis, Brazil; [2]UFC, Faculty of Pharmacy, Dentistry and Nursing, Dept of Clinical Analysis and Toxicological, PPG of Pharmaceutical Sciences, Brazil

04.007 **Investigation of the Immunopathogenesis Mediated by NETs (Neutrophil Extracellular Traps) in Chikungunya**. Barbosa ISA[1], Leal ARSN[2], Cesário IBB[1],Carvalho JPAQ[1], Costa SGA[1], Canafístula LS[1], Oliveira KS[1], Rodrigues RO[1], Barreto FKA[3], Silva TN[3], Cavalcanti LPG[3], Siqueira AM[4], Yaochite JNU[1]. [1]UFC, Faculty of Pharmacy, Dentistry, and Nursing, Dept Clinical and Toxicological Analysis, Brazil; [2]UFC, Faculty of Pharmacy, Dentistry, and Nursing, Dept Clinical and Toxicological Analysis, Graduate Program in Medical Microbiology, Brazil; [3]UFC, Faculty of Medicine, Brazil; [4]Fiocruz, Brazil

04.008 **Evaluation of the *In vitro* Cytotoxicity and Pharmacokinetic Properties of a New Green Synthetic Acetanilide with Potential Application in Neuroinflammation**. Silva TG[1], Sousa M. [1], Luís LRCS[1], Falcão MEES[1], Gadelha FAA[1], Dejani NN[1], Fiss GF[2], Luís JAS[2], Vieira GC[1]. [1]UFPB, Research Institute of Drug and Medicines, Lab. of Immunopharmacology, Brazil. [2]UFPB, Lab. of Bioenergy and Organic Synthesis Research, Brazil.

Totem 09

04.025 **Anti-Inflammatory and Anti-Hyperalgesic Effect of the New Isoxazole Analogue Based in the Celecoxib and Neolignans in Experimental Models**. Machado LL, Costa PAN, Lossavaro PKMB, Diniz FS, Venancio GSO, Lencina JS,Toffoli, Kadri MC, Baroni ACM, Silva-Filho SEU FMS, FACFAN, Pharmaceuticals Science

04.026 **Chronic Kidney Disease and Cognitive Impairment from the Perspective of Neuroinflammation: Evaluation of the Exposure of Healthy Astrocytes to Uremic Serum**. Custodio GT[1], Russo FB[2], Beltrão PCB[2], Kawamoto EM [1] [1]USP, Dept Pharmacology, Brazil, [2]USP Dept Microbiology, Brazil, PPG Functional and Molecular Biology, Brazil.

04.027 **Sex-Dependent Effects of Tirzepatide on Fever and Inflammatory Mediators during Systemic Inflammation**. Aguiar SCR, Oliveira BCC, Cruz EKM, Sousa GLS, Londe ABR, Alves GS, Trindade KP, Gomes BRB, Souza FHV. UnB, Faculty of Health Sciences and Technologies, Lab. of Experimental Biomodels, Brazil, UnB, Institute of Biology, Lab. of Protein Chemistry and Biochemistry, Brazil, UnB, PPG Parmaceutical Sciences, Brazil.

04.028 **Integrated *In Silico*, *In vitro*, and *In vivo* Evaluation of the anti-inflammatory Potential of Magnolin Isolated from *Annona pickelii***. Ramos KS[1,2], Cabral Neto A[3], Lobo EB[2,3], Silva DKC[1,2,3], Cezar IS[2,3], Dutra LM[4], Barreto BC[1,3], Souza CVC[5], Santos-Filho OA[5], Gonçalves RS6, Soares MBP[2,3], Costa EV7, Meira CS[1,2,3]. [1]UNEB-BA, Salvador, [2]SENAI CIMATEC-BA, Salvador, [3]Fiocruz-BA, Salvador, [4]UFS-SE, São Cristóvão, [5]UFRJ-RJ, Rio de Janeiro, [6]UFPR-PR, Palotina, [7]UFAM-AM, Manaus.

04.029 **A Ni(II) Complex with a Schiff Base Derived from Meldrum's Acid Reduces Lipopolysaccharide-Induced Acute Lung Injury in Mice**. Cândido JPS[1], Ramalho ABF[3], Santos, ABR[1], Pessoa WFB[2], Ferrari JS[3], Alves AF[1] [1]UFPB, PPG Produtos Naturais e Sintéticos Bioativos, Brasil [2]UFPB, Depto Ciências Biomédicas, Brasil, [3]UFPB, Depto Química, Brasil.

04.030 **Evaluation of the Anti-Inflammatory Potential of Morita-Baylis-Hillman Adduct CISACN in Acute Lung Injury-an *in vitro*, *in vivo* and *in silico* study**. Rodrigues MRF[1], Oliveira JB[1], Lima LM[2], Vieira CID[2], Ferreira LKD[2], Moura BVS[1], Laurentino MVS[1], Pordeus GM[2], Mota PRV[2], Gadelha FAAF[2], Lima-Júnior CG[3], Dejani NN[2], Piuvezam MR[2] [1]UFPB, Immunopharmacology Lab, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]UFPB, Immunopharmacology Lab, Institute of Pharmaceutical and Medicinal Research, Brazil. [3]UFPB, Medicinal Organic Synthesis Lab Paraíba, Brazil.

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04.050 *In vitro* **Quercetin-Mediated Immunomodulation may act as an Adjuvant Therapy to Amphotericin B in Visceral Leishmaniasis**. Cardoso LL, Fernandes ALM, Thyares DFL, Ferreira RS, Albuquerque YS, Machado GR, Vanderley SER, Comberlang, FC, Almeida, FS, Keesen, TSL. UFPB, Lab Imunologia de Doenças Infecciosas, Depto Biologia Celular e Molecular, João Pessoa, PB, Brazil.

04.051 **Liraglutide Attenuates Fever and Differentially Modulates Oxidative Stress and Thermogenic Markers in Brown Adipose Tissue of Male and Female Rats During Systemic Inflammation**. Cruz EKM, Sousa GLS, Aguiar SCR, Cajado VJ, Amato AA, Souza PEN, Souza FHV. UnB, Faculty of Health Sciences and Technologies, Lab. of Experimental Biomodels, Brazil, UnB, Faculty of Health Sciences, Lab. of Molecular Pharmacology, Brazil, UnB, Institute of Physics, Lab. of Electron Paramagnetic Resonance, Brazil, UnB, PPG Pharmaceutical Sciences, Brazil.

04.052 *In vitro* **Cytotoxicity and Pharmacokinetic Evaluation of a Novel Green Semisynthetic Acetanilide-Theobromine Hybrid Compound**. Sousa M[1], Silva TG[1], Luis LRCS[1], Falcão Mees[1], Gadelha, FAA[1], Dejani NN[1], Fiss GF[2], Luis JAS[2], Vieira GC[1] [1]UFPB, Research Institute for Drugs and Medicines, Lab Immunopharmacology, Brazil, [2]UFPB, Lab Bioenergy and Organic Synthesis Research, Brazil

04.053 **Ambroxol Repurposing: Radiographic and Histological Analysis of Joint Degeneration in an Experimental Osteoarthritis Model**. Mesquita MJTA, Cruz ACSN, Teixeira, JTAMMM, Reis ATF, Frota GM, Carvalho TGPM, Carvalho RAF, Teixeira JAM, Andrade, MS, Carvalho RC, Sousa EM, Sousa JCS, Morias SV, Cartágenes MSS, Garcia JBS UFMA PPG in Health sciences, Brazil; CEUMA, Medical School, University, Brazil; UFMA Medical School, Brazil; UFMA College of Pharmacy, Brazil; UFMA, Graduate Program in Biotechnology—Renorbio, Brazil; UFMA, PPG in Adult Health, Brazil; Graduate Program in Applied Biosciences to Health, UFMA Graduate Program in Health sciences, Brazil.

04.054 **Role of Estradiol/GPER Signaling in the Sickness Response during Systemic Inflammation**. Costa RA, Schneider RC, Santos MO, Pereira V, Borges AP, Schneider VMM, Alencar ST, Baggio DF, Zampronio AR. UFPR, Inflammation and Fever Lab, Dept Pharmacology, Brazil.

04.055 **Differential Effects of Hypothalamic ETB Receptor Blockade in Fever, Hypolocomotion and Serotonin Release During Systemic Inflammation in Male and Female Rats**. Alencar ST, Santos MO, Schneider VMM, Fernandes SMA, Borges AP, Guita GO, Costa RA, Zampronio, AR. UFPR, Inflammation and Fever Lab, PPG Pharmacology, Brazil

04.056 **Effects of Monoterpenes Linalool, Carvacrol, Gamma-Terpinene and Beta-Myrcene on Cytokine Profile in an Experimental Sepsis Model**. Silva GHO, Previato CFA, Da Rocha EMT, Cuman RKN. Lab Inflammation, State University of Maringá (UEM), Maringá, Paraná, Brazil.

04.062 **SIRT2 Inhibition Attenuates Neuroinflammation Induced by *Klebsiella pneumoniae* Infection**. Ferreira-Costa M[1], Thiele E[2], Almeida MAP[2], Santos, FS[2], Gomes-Reis, GLS[1], Cunha, CMC[1], Ferreira, A[1], Bozza PT[1], Castro-Faria-Neto HC[1], Gonçalves-de Albuquerque CF[2,3], Silva AR[1] [1]IOC-Fiocruz, Immunopharmacology Lab, PPG in Cellular and Molecular Biology, Rio de Janeiro, Brazil, [2]UFF, PPG in Neuroscience, Rio de Janeiro, Brazil, [3]Unirio, Immunopharmacology Lab, PPG in Molecular and Cellular Biology, Rio de Janeiro, Brazil

04. Biology and Cardiovascular Diseases

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04.001FR **Acute Cardiovascular Response to Resistance Training to Muscular Failure and Progressive Reductions in Training Volume**. Martins AJFM[1], Pires KC[1], Vieira YLM[2], Leite IAH[3], Flora JMG[5] , Santos M[2], Campos AVLL [2], Rodrigues IJS [2], Lacerda LT[2], Brandão CFCCM [2], Andrade MJO[2], Drummond LR [1] [1]UEMG, Dept Physical Education, Brazil, [2]UEMG, Dept Psychology, Brazil

05. Pain and Nociception Pharmacology

Totem 11

05.034 **Flavones Modulate Nociception and Neuroinflammation in Preclinical Models of Neuropathic Pain: A Systematic Review and Meta-Analysis**. Batista TSC, Nascimento ACS, Palmeira DN, Mota CMD, Camargo EA [1]UFS, PPG Health Sciences, Brazil, [2]UFS, PPG Physiological Sciences, [3]UECE, Facisc

05.035 **Repeated Low-Dose Dual FAAH/MAGL Inhibition Produces Central Behavioral Effects without Antiallodynic Efficacy in Experimental Neuropathic Pain**. Morais ITS[2,3], Marçal MM1, Silva BP[1], Chagas MC[2], Stein DJ[2,3], Caumo

W, Torres ILS[1,2,3] [1]UFRGS, Institute of Basic Health Sciences, PPG in Biological Sciences: Pharmacology and Therapeutics, Brazil. [2]HCPA, Lab Pain Pharmacology and Neuromodulation: Preclinical Investigations, Brazil. [3]UFRGS, School of Medicine, PPG in Medicine: Medical Sciences, Brazil.

05.036 **Antinociceptive Activity of Antidepressant Drugs**. Oliveira MMF[1], Batista CB[1], Rodrigues DCN[1], Sousa RWR[1], Almeida ML[1], Freitas MM[1], Silva CLA[1], Feitoza LLS[1], Ferreira PMP[1,2] [1]UFPI, Lab Experimental Cancerology (LabCancer), Dept Biophysics and Physiology, PPG Pharmacology, Brazil; [2]UFC, Lab Experimental Oncology (LOE), Dept Physiology and Pharmacology, Brazil

05.037 **Transcranial Direct Current Stimulation Attenuates Mechanical Hypernociception in Collagen-Induced Arthritis Mice without Modifying Disease Severity**. Santos, NG[1,2,3], Leite, ADD[2], Freitas, VS[2], Gaia, R[2], Flor, B[2,3], Vieira, MLG[2], Chapacais, GF[2], Pilotti, S[1,2,3], Stein, DJ[1,3], Torres, ILS[1,3], Xavier, RM[1,2]1UFRGS, School of Medicine, PPG in Medical Sciences, Porto Alegre, Brazil; [2]Hospital de Clínicas de Porto Alegre (HCPA), Division of Rheumatology, Lab Autoimmune, Porto Alegre, Brazil; [3]Hospital de Clínicas de Porto Alegre (HCPA), Lab Pain Pharmacology and Neuromodulation: Preclinical Investigations, Porto Alegre, Brazil

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05.045 **Development of Murine Platform for Investigating Neuroinflammatory Targets in Post-COVID Pain Induced by the Spike Protein**. Trefilio LM[1,2], Guimenes BD[1,3], Fernandes GG[1,4], Mesquita IA[1], Rezende B[1,3], Gonçalves VMS[1,3], Montes GC[1,2,4], Fontes-Dantas FL[1,2,4] [1]UERJ, Roberto Alcantara Gomes Biology Institute, Dept Pharmacology and Psychobiology, NeuroPharmacoGenetics Lab, Brazil. [2]UERJ, Roberto Alcantara Gomes Biology Institute, Dept Pharmacology and Psychobiology, PPG Biosciences, Brazil. [3]UERJ, Roberto Alcantara Gomes Biology Institute, Dept Pharmacology and Psychobiology, PPG Clinical and Experimental Pathophysiology, Brazil. [4]UFJF, Dept Biophysics and Physiology, Brazil.

05.046 **Sex and Environmental Factors Influence FFA1 Receptor and BDNF Expression in a Mouse Model of Inflammatory Pain**. Estrázulas M[1,2], Neculqueo GW[1,2], Farias ABS[1,2], Campos MM[1,2] [1]PUCRS, PPG em Medicina e Ciências da Saúde, Porto Alegre, RS, Brazil, [2]FADIC, Escola de Ciências da Saúde e da Vida, Porto Alegre, RS, Brazil.

05.047 **Structure–Property Relationship of Alkyl 4-Phenylbenzoates: ADMET profiling and Antinociceptive Activity of Pentyl 4-Phenylbenzoate in Experimental Neuropathic Pain**. Oliveira JLS[1], Prado FM[1], Reis Filho AC[1], Gomes JGF[2], Barbosa BS[2], Santos ALS[3], Sousa DP[4], Almeida FRC[1]. [1]UFPI, LAFDOR, PPGFARM, Brazil; [2]UFPI, LPNNEX, PPGFARM, Brazil; [3]UFPI, LPNNEX, PPGQ, Brazil; [4]UFPB, Dept Pharmacy, Brazil

05.048 **Effect Level Dependent Antinociceptive Interaction between Cannabidiol and Cannabigerol in a Rat Model of Streptozotocin-Induced Diabetic Neuropathy: an Isobolographic Analysis**. Rauchbach L[1], Ferreira MV[1], Rampim LR[1], Wolaniu L[1], Castro-Junior CJ[2]; Crippa JA[3]; Zanoveli JM[1], Cunha JM[1]. [1]UFPR, Dept Pharmacology, Curitiba, PR, Brazil; [2] IEP SCBH, Núcleo de Pós-Graduação, Belo Horizonte, MG, Brazil; [3]FMRP-USP, National Institute for Translational Medicine (INCT-TM, CNPq); Dept Neuroscience and Behavior, University of São Paulo, Ribeirão Preto, SP, Brazil.

06. Cardiovascular and Renal Pharmacology

Totem 13

06.006 **Metabolic State-Dependent Catecholamine Release and Vascular Responses in Fasting and Digesting Snakes**. Dal Pozzo CFS[1,2], Oliveira MG[1], Vicentini NCS[1], Castro SA [1], de Nucci G[1], Wang T[2] [1]Unicamp, Dept Pharmacology, Brazil [2]Aarhus University, Section for Zoophysiology, Denmark

06.007 **Cardiovascular Effects of Nerolidol in Hypertensive Animals**. Reis GS, Santana IR, Santana AS, Silva EAP, Barreto AS. UFS, Graduate Program in Health Sciences, Brazil.

06.008 **Sodium Nitrite Attenuates Increased Circulating Asymmetric Dimethylarginine Induced by Reduced Uterine Perfusion Pressure in Preeclamptic Rats**. da Costa LC, Silva MLS, Toghi CJ, Doreto AH, Kushima H, Colenci FBC, Dias-Junior CA, da Costa LC IBB-Unesp, Dept Biophysics and Pharmacology, Brazil

06.009 **Therapeutic Potential of *Spondias tuberosa* Against Age-Related Vascular Dysfunction: Evidence from EPC Modulation and Vascular Reactivity**. Gonçalves TAF[1,2], Sousa JRO[2], Silva LLM[2], Silva VO[2], Lima VS[1], Soares EMC[1], Oliveira JCPL[1], Fernandes GFS[3], Silva CCN[3], Cavalcante RV[1], Medeiros IA[1] [1]UFPB, Dept Pharmaceutical Sciences, Brazil, [2]UFPB, Dept Biomedical Sciences, Brazil, [3]UFPB, Dept Biotechnology

06.010 **Perivascular Adipose Tissue Dysfunction Induced by Acute Exposure to Cisplatin in male and female rats**. Almeida ACR, Jesus BR, Akamine EH ICB-USP, Dept. Pharmacology, Brazil. USP, Graduate Program in Functional and Molecular Biology, Brazil.

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06.041 **SGLT2 Inhibition Mitigates Hyperpalatable Diet-Induced Kidney Dysfunction in Ovariectomized Female Mice**. Moraes MC[1,2], Oliveira LBF[2], Parreira LS[1], Avelar CDFL[1], Peruchetti DB[2], Vieira LB[1] [1]ICB-UFMG, Dept Pharmacology, Neuropharmacology Lab, PPG Physiology and Pharmacology, Brazil. [2]ICB-UFMG, Dept Physiology and Biophysics, Renal Physiology, Lab, PPG Physiology and Pharmacology, Brazil.

06.042 **Oxytocin Promotes Natriuretic Effects by Inhibiting NHE3-Mediated Sodium Reabsorption in the Renal Proximal Tubules of Rats**. Paulino FWV, Oliveira NO, Moura FLC, Pires GS, Lima TDS, Lessa LMA, Pinto EV, Fonteles MC, Girardi ACC, Nascimento NRF, Santos CF [1]ISCB-UECE, Lab Fisiologia Renal, PPG em Ciências Fisiológicas, Brasil, [2]InCor-HCFM-USP, Lab Genetics and Molecular Cardiology, Brasil.

06.043 **Cardiovascular Effect of Neryl Acetate in an Experimental ModeL of Hypertension and Hemostasis**. Portela, EP[1,2,3], Rêgo, A. F,[2,3], Silva, ND[1,2,3], Albuquerque, BA[1,2,3], Rocha, VA [1,2,3], Almeida, FRC[1], Oliveira, AP[1,2,3,4] [1]UFPI, PPG in Pharmacology, [2]UFPI-NPPM, Lab Cardiovascular Pharmacology-, [3]UFPI, Medicinal Plant Research Center, 4DUFPI, Dept Biophysics and Physiology-UFPI.

06.044 **Effects of Isolated (-)-Borneol and Phonophoresis on Resistance Artery Responses to Ischemia-Reperfusion in an Experimental Model**. Anjos MS[1], Sousa CFAJ[1], Martins HRS[2], Acha BT[3], Silva RLT[1], Souza RP[1], Ferreira PMP4, Oliveira AP[1]. [1]UFPI, Health Sciences Center, Medicinal Plants Research Center, Graduate Program in Pharmacology; [2]PIBIC-UFPI, Scientific Initiation Program, Medicinal Plants Research Center, [3]Northeast Biotechnology Network (Renorbio); [4]UFC

06.045 **Carvacrol Attenuates Cardiorenal Damage in Spontaneously Hypertensive Rats by Reducing Oxidative Stress and Fribrosis**. Lima VS[1,2,4], Gonçalves TAF[1,5], Almeida AJPO[1,3], Veras ACMF[2,4], Gomes MLC[1,2,4], Alves AF[2,5], Medeiros IA[1,2,4]. [1]UFPB, Cardiovascular Pharmacology Lab, Institute for Drug and Medicine Research, Brazil. [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil. [3]UFPB, PPG in Development and Technological Innovation in Medicines, Health Sciences Center, Brazil. [4]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil. [5]UFPB, Dept Physiology and Pathology, Health Sciences Center, Brazil.

06.051 **Effects of γ-Terpinene on Hemodynamic and Oxidative Parameters in Spontaneously Hypertensive Rats**. Rocha VA[1,2,3], Rego AF[1,2,3], Sena EP[1,2,3], Acha BT[4,5], Silva FAHV[2], Soares HS[2], Costa MRS[2], Nascimento BN[2], Silva ND[1,2,3], Albuquerque BA[1,2,3], Oliveira AP[1,2,3,6] [1]UFPI, Graduate Program in Pharmacology, Brazil. [2]UFPI, Health Sciences Center, Cardiovascular Pharmacology Lab, Brazil. [3]UFPI, Research Center on Medicinal Plants, Brazil.

[4]UFPI, Northeast Biotechnology Network (Renorbio), Brazil. [5]UFPI, Lab Functional and Molecular Studies in Physiopharmacology, Brazil. [6]UFPI, Health Sciences Center, Dept Biophysics and Physiology, Brazil.

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06.061 **Structural Features of a Marine Sulfated Galactan Drive its Potent Prothrombotic Activity in Venous and Arterial Thrombosis Models.** Fonseca RJC[1], Imilhão BM[1], Cinelli LP[2], Mourão PAS[3] [1]CCS-ICB-UFRJ. Lab Coagulação e Trombose, Hospital Universitário Clementino Fraga Filho, Rio de Janeiro, RJ, Brasil. [2]IBqM-UFRJS, Lab Prospecção em Produtos Bioativos, Grupo de Glicofármacos, Rio de Janeiro, Brasil. [3]Lab Tecido Conjuntivo, Rio de Janeiro, Brasil.

06.062 **Cytomegalovirus m33-Dependent Chemokine Signaling Drives Endothelial Inflammation and Oxidative Dysfunction: Evidence from Cell Culture and Human Hypertension**. Santos CV[1,2], Gonçalves ES[3], Velasco DS[2], Carneiro FS[1], Sinhorin VDG[3], Tostes RC[1], Priviero F[2], Webb RC[2], Bomfim GF[2,3] [1]USP-RP; [2]University of South Carolina, CTRC - Cardiovascular Translational Research Center, USA; [3]UFMT-Sinop, MT.

06.063 **Subchronic Exposure to a Glyphosate-Based Herbicide causes Changes in Perivascular Innervation Function in the Superior Mesenteric Artery of Rats**. Alves KSS[1], Polo-Norte ME[1], Alves OS[2], Duarte-Filho LD[3], Menezes PMN[4], Ribeiro LAA[5], Silva FS[5], de Queiroz DB[1] [1]UP, [2]UFAL, [3]UFPE, [4]FACAPE, [5]UFVSF

06.064 **Carvacrol Enhances Endothelial Repair by Modulating Oxidative Stress and eNOS/Nrf2 Pathways in Endothelial Progenitor Cells**. Gonçalves TAF[1], Lima VS[1], Almeida AJPO[1,2], Soares EMC[1], Santos AC[1], Pontes LVS[1,3], Almeida Feitosa MS[1], Veras RC[1], Almeida IA[1]. [1]UFPB, Dept Pharmaceutical Sciences, Brazil, [2]University of Utah, Nora Eccles Harrison Cardiovascular Research and Training Institute, USA, [3]University of Utah, Dept Nutrition and Integrative Physiology, USA

06.065 **The Role of Potassium Channels in the Vasodilation Induced by a Novel Nitrosyl–Ruthenium Nitric Oxide Donor Complex**. Monteiro HSM[1], Silva FAO[1], Sousa AS[2], Lima NCB[1], Simonato SG[1], Franco VMF[1], Souza ARL[1], Viana LC[1], Souza RM[1], Jamacaru FVF[1], Lopes LGF[2], Jorge RJB[1] [1]UFC-Porangabuçu, Dept Physiology and Pharmacology, Graduate Program in Pharmacology – Brazil; [2]UFC-Pici, Dept Organic and Inorganic Chemistry, Lab Bioinorganic Chemistry - Brazil

06.060 **Dual α1-Adrenergic Receptor Antagonism and Voltage-Gated Calcium Channel Blockade Underlie the Vascular Effects of the Pyrimidinone Derivative STI4T-Et in Rat Aorta**. Silva MCC[1], Silva SB[1], Silva MEF[1], Barbosa FM[1], Souza MEVV[1], Feitosa SGD[2], Dos Anjos JV[2], Araújo AV[1] [1]UFPE, Centro Acadêmico da Vitória, Brazil; [2]CCEN-UFPE, Lab Síntese Orgânica, Brazil

06. Biology and Metabolic and Reproductive Diseases

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06.012FR **Effects of Combined Physical Exercise and Symbiotic Supplementation on Gut Microbiome and Inflammasome-Related Genes in the Gut-Kidney Axis of Obese Rats**. Coutinho DO[1], Costa PCT[1], Freire MOL[1], Cruz Neto JPR[1], Magnani M[2], Vidal H[3], Alves JLB[1] [1]UFPB, Dept Nutrition, Health Sciences Center, PPG Nutrition Sciences, Brazil; [2]UFPB, Dept Food Engineering, Lab Microbial Processes in Foods, Brazil; [3]Claude Bernard Lyon 1 Université, CarMeN Lab, France

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06.013FR **Maternal Obesity Induced by an Obesogenic Diet Reduces Exercise Capacity and Increases Adiposity in Rats**. Silva RAA[1], Silva RL[2], Silva MLB[2], Oliveira PGS[3], Oliveira DKS[4], Lima DPO[6], Oliveira TRP[6], Antonio-Santos J[6], Da Silva Aragão R[6] [1]UFPE, PPG Nutrition, Brazil; [2]UFPE, Physical Education Undergraduation, Brazil; [3]UFPE, Nutrition

Undergraduation, Brazil; [4]UFPE, PPG Nutrition, Physical Activity and Phenotypic Plasticity, Brazil; [5]FPS, Dept Physical Education, Brazil. [6]UFPE, Dept Physical Education, Brazil.

06.014FR **Metabolic Benefits of Tauroursodeoxycholic Acid, Alone or Combined with Resistance Exercise, in Aging Mice**. Carvalho MS, Zangerolamo L, Barrios NMF, Oliveira KM, Carneiro EM, Barbosa HCL. Unicamp, Obesity and Comorbidities Research Center, PPG Molecular and Morphofunctional Biology, Brazil. Université de Montréal, Dept Pharmacology and Physiology, Faculty of Medicine, Canada. Unicamp, Lab Nutrition and Cancer, PPG Molecular and Morphofunctional Biology, Brazil.

07. Endocrine, Reproductive and Urinary Pharmacology

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07.001 **Effect of Systemic Matrix Metalloproteinases Blocking in A Pre-Clinical Model of Menopause**. Baltazar RS[1], Pozes AB[1], Mendes, L. [1], Gonçalves, F. [1], Santos CED[1], Filho FLS[1], Maranhão, M[1], Santos, MLF[1], Belfort MFA[1], Palhano NBM[1], Moreno AVP[1], Borges, MOR[12], Borges, ACR[12],Oliveira RMGC[1], Brito HO[1] [1]UFMA, Research Center For Experimental and Clinical Physiopathology and Pharmacology (NEC), Bioanalyses Lab (LabIO), Brazil; [2]UFMA, Pharmacology Lab, Federal University of Maranhão, Brazil

07.002 **Evaluation of the Effects of *Morus nigra* L. (Black Mulberry) in Animal Models of Menopausal-Hot Flashes**. Cavalcante DCS, Rodrigues TAR, Santos CED, Bezerra HRR, Lima LAS, Bastos HAC, Belfort MFA, Palhano NBM, Baltazar RS, Moreno AVP, Borges, MOR, Borges, ACR, Oliveira RMGC, Brito HO UFMA, Research Center for Experimental and Clinical Physiology and Pharmacology, Bioanalyses Lab, Pharmacology Lab, Brazil

07.003 **Low-Dose Cannabidiol plus β-Estradiol Improve Symptoms Compared with Estrogen Replacement Therapy in a Rat Model of Menopause**. Santos CED[1], Moreno AVP[1], Bezerra HRR[1], Belfort MFA[1], Palhano NBM[1], Baltazar RS[1], Borges, MOR[1,2], Faria, M[1], Teixeira, CVP[1], Crippa, A[3], Hallak, JEC[3], Borges, ACR[1,2], Brito HO[1]. [1]NEC-UFMA, Research Center for Experimental and Clinical Physiopathology and Pharmacology, Brazil; [2]UFMA, Pharmacology Lab, Brazil; [3]FMRP-USP, Brazil

07.004 **COX-Derived Prostanoid Signaling Mediates the Anticontractile Effect of MRPs Inhibition in Human Prostatic Tissue**. Cardoso JS[1], Passos GR[1], Moretti, MB[1], D'Ancona CA2, Fregonesi A2, Antunes E[1], Monica FZ[1] [1]FCM-Unicamp, Dept Pharmacology, Brazil; [2]Dept Surgery (Urology), Brazil

07.005 **Full-Spectrum Cannabis Oil Combined with Insulin Promotes Glycemic and Antioxidant Benefits in an Experimental Model of Type 1 Diabetes Mellitus**. Barboza, ACS[1], Martins, JRN2, Silva ALM[1], Carmo DMQ[1], Lima GGS[1], Oliveira CC[2], Silva JGG[2], Cruz JC[1] [1]UFPB, [2]APEPI – Associação de Apoio à Pesquisa e Pacientes de Cannabis Medicinal, Rio de Janeiro, Brasil

07.006 *Arthrospira platensis* **Prevents Oxidative Stress and Testicular Alterations in Wistar Rats Subjected to a Hypercaloric Diet**. Melo MB[1], Sousa-Filho JEC[1], Barros BC[1,2], Arruda RRA[1,2], Silva JMA[1,2], Santos TJ[1], Claudino BFO[1,2], Barbosa YV[1,2], Diniz AFA[1,2], Alves AF[2,3], Silva BA[1,2,3] [1]UFPB, Lab Functional Pharmacology Prof. George Thomas, Institute of Research in Drugs and Medicines, Brazil; [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil; [3]UFPB, Dept Biomedical Sciences, Health Sciences Center, Brazil; [4]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil

07.007 **Effects of Topiramate on Rat Sperm Parameters**. Chaves HJC, Sena MO, Carvalho YV, Costa ML, Gavioli EC, Silva-Junior ED UFRN, Dept. of Biophysics and Pharmacology, Brazil.

Totem 17

07.008 **Evaluation of the Effects of an Incretin Mimetic on Depressive-Like and Compulsive-Like Behaviors in a Murine Model of Early Diet-Induced Obesity**. Lemos IL[12], Silva JGM[12], Weber IH[2], Moraes GR, Silva ABC[1], Miranda KKB[1], Bellozi PMQ[1] [1]UnB, Faculty of Health Sciences, Brazil, [2]UnB, Institute of Biological Sciences, PPG Animal Biology, Brazil

07.009 **Assessing Temporal Effects of Bladder Dysfunction in C57BL/6JUnib Mice Using Multiple-Low Dose of Streptozotocin-Induced Diabetes**. Barbalho TM, Horioka CP, Leutz MC, Medeiros ML, Oliveira AL, Antunes E. Unicamp, PPG Farmacologia, Brasil.

07.010 **Effect of Taurine on Time in Range in Individuals with Type 2 Diabetes Mellitus: A Secondary Analysis of a Randomized Clinical Trial**. Bispo ACC, Vidal BA, Cavalheiro LS, Selau B, Laurentino AOM, Leal MB, Bock PM, Gomez R. UFRGS, ICBS, PPG em Farmacologia e Terapêutica, Brasil.

07.011 **Effects of Lycopene on the Morphometry of Seminiferous Tubules in Diabetic Rats**. Gomes PD, Medeiros BC, Mota LSF, Silva JL, Leite TCR, Lima WG, Paula-Gomes S, Morais DB. UFRN, UFOP.

07.012 **Impact of Chronic Administration of Methylglyoxal in Diabetic Bladder Dysfunction in Obese Model** (**ob/ob**). Horioka CP, Barbalho TM, Oliveira AL, Medeiros ML, Antunes E. FCM-LABEA Unicamp, PGP Pharmacology area, Brazil

07.013 **Effects of Tirzepatide on Neurobehavioral Alterations in Mice Exposed to a High-Fat Diet Early in Life**. Melo Silva JG[1,2], Lemos IL[1,2], Weber IH[1], Moraes GR[1], Silva ABC[1,2], Miranda KKB[1,2], Bellozi PMQ[1,2] [1]UnB, Faculty of Health Sciences, Brazil, [2]UnB, Institute of Biological Sciences, PPG Animal Biology, Brazil

Totem 18

07.014 *Arthrospira platensis* **Prevents Macroscopic Inflammatory Alterations in Uterus and Ovaries in a Wistar Rat Model of Primary Dysmenorrhea**. Barbosa YV[1,2], Silva JMA[1,2], Claudino, BFO[1,2], Barros BC[1,2], Diniz AFA[1,2], Arruda RRA[1,2], Santos ABR[2], Melo MB[1], Sousa-Filho JEC[1], Santos TJ[1], Sousa TR[1], Soares MFS[2], Alves, AF[3], Silva BA[1,2,4] [1]UFPB, Lab Functional Pharmacology Prof. George Thomas, Institute of Research in Drugs and Medicines, Brazil. [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil. [3]UFPB, Dept Biomedical Sciences, Health Sciences Center, Brazil. [4]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil.

07.015 **Probenecid Reduces Phenylephrine-Induced Contractions in Human Prostate Tissue**. Moretti MB, Passos GR, Barros JVC, Lima JM, Antunes E, Monica FZ Unicamp, Lab of Lower Urinary Tract and Erectile Disfunction, Dept Pharmacology

07.016 *Arthrospira platensis* **Prevents Alterations in Histology and Increase of Eosinophilic Infiltrate Homogeneously along the Uterine Topography of Female Wistar Rats with Primary Dysmenorrhea**. Silva JMA[1,2], Barborsa YV[1,2], Claudino, BFO[1,2], Diniz AFA[1,2], Arruda RRA[1,2], Barros BC[1,2], Santos ABR[2], Santos TR[1], Santos TJ[1], Melo MB[1], Sousa-Filho JEC[1], Soares MFS[2], Alves AF[2,3], Silva BA[1,2,4] [1]UFPB, Lab Functional Pharmacology Prof. George Thomas, Institute of Research in Drugs and Medicines, Brazil; [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil; [3]UFPB, Dept Biomedical Sciences, Health Sciences Center, Brazil; [4]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil

07.017 **Sexually Dimorphic Responses to Oral Sodium Nitrite Treatment on Metabolic Parameters and Glucose Tolerance in an Experimental Model of Type 2 Diabetes Mellitus**. Silva-Cunha MS, Sanches-Lopes JM, Conde-Tella

SO, Medeiros CFA, Rebelo MA, Tostes RC, Tanus-Santos JE FMRP-USP, Dept Pharmacology, PPG Pharmacology, Brazil; Unicamp, Faculty of Medical Sciences, Dept Translational Medicine, PPG Pharmacology, Brazil

08. Respiratory and Gastrointestinal Pharmacology

Totem 19

08.007 *in silico* **Evaluation of the Pharmacokinetic and Toxicological Profile and Relaxant Effect of Free and β-Cyclodextrin-Complexed Farnesol** *in vitro*. Martins HRS[2], Souza ORB[1], Oliveira, MM[1], Silva PHS[2], Reis ML[1], Quintans JSS[3], Quintans-Júnor LJ[3], Oliveira AP[1], Santos RF[1], Oliveira RCM[1]. [1]UFPI, Center for Health Sciences, PPG Pharmacology, Brazil. [2]UFPI, Center for Research on Medicinal Plants, Brazil. [3]UFS, Lab Neurosciences and Pharmacological Assays (LANEF), Dept Physiology, PPG Health Sciences, Brazil.

08.008 *In vivo* **and** *in silico* **Antiulcerogenic Activity of Myrtenyl Ester Derived from (-)-Myrtenol Obtained by Biotransformation**. Oliveira, GH[1], Viana, AFSC[1,2,3], Fernandes, HB[1,2], Martins, SCA[1], Pinheiro, CS[4], Reis, ML[1], Araújo, PBM[1,2], Silva, SA[3], Brito, MES[3], Kutyła, M[5], Stankevič, M[6], Trytek, M[5], Oliveira, RCM[1,2] [1]UFPI, Medicinal Plants Research Center (NPPM), Brazil, [2]UFPI, PPG Pharmacology, [3]UEMA, Brazil, [4]UFPI, PPG Renorbio, Brazil, [5]Maria Curie-Skłodowska, Lublin, Poland, [6]Maria Curie-Skłodowska University, Gliniana, Lublin, Poland.

08.009 **Relaxant Effect of Ethanolic Extracts from Branches and Leaves of** *Machaerium acutifolium* **Vogel on Isolated Rat Trachea**. Moraes RR, Silva PHS, Souza ORB, Oliveira MM, Chaves MH, Santos RF, Oliveira RCM UFPI, Center for Research on Medicinal Plants, PPG Pharmacology, Lab. of Natural Products, Brazil.

08.010 **Terpinolene as a Potential Antidiarrheal Agent: Evaluation of Acute Toxicity, Gastrointestinal Motility, and Mechanisms of Action in Mice**. Menezes PMF, Pessoa LF, Alves VP, Pessoa MMB, Pessôa MLS, Batista LM, UFPB, Brazil. UFPB, Gastrointestinal Pharmacology Lab, PGPNSB, Brazil

08.011 **Brown Propolis from** *Mimosa tenuiflora* **Prevents Airway Hyperreactivity through Multitarget Mechanisms in Ovalbumin-Induced Asthmatic Rats**. Lima CCM[1], Felício IM[2], Alves BFL[3], Souza MLB[1], Figueiredo IAD[2], Silva TMS[4], Picot, L[5]; Cavalcante FA[2,6] [1]UFPB, Pivic/UFPB, Brazil; [2]UFPB, CCS, PPgPNSB, Brazil; [3]Pibic/CNPq/UFPB; [4]UFPE, DQ, Brazil; [5]La Rochelle Université, LIENSs, France; [6]UFPB, CCS, DCB, Brazil

08.012 **Association Between Catalase Activity and Pulmonary Function in Smokers and Former Smokers: The Modulatory Effect of the Renin-Angiotensin-System**. Medeiros GB, Freitas JLC, Paiva YMA, Medeiros VLD, Martins NRS, Amorim-Carmo B, Kennedy-Feitosa E, Silva FS UFERSA,Morphophysiopharmacology Lab. Brazil

Totem 20

08.028 **Hesperetin Ameliorate TNBS-Induced Intestinal Inflammation: Role of Antioxidant System and Immunomodulation**. Pessoa MMB[1], Pessôa MLS[1], Alves VP1, Menezes PMF[1], Pessoa LV1, Araújo AA[2], Batista LM[1] [1]UFPB, [2]UFRN

08.029 **Obesity Alters the Esophageal Mucosal Barrier in Diet-Induced Obese Mice**. Silva LMG[1], Sousa MKA[1], Alves ODC[5], Ribeiro TA[1], Freire PRP[1], Souza MFF[1], Silva FGO[1], Guimarães MB[1], Lopes BP[2], Vieira MESR[2], Mateus JS[3], Nascimento, JM[4], Fonsêca SGC[4], Soares PMG[2], Souza MHLP[2] [1]UFC, Lab Gastrointestinal Physiopharmacology, Graduate Program in Pharmacology, Brazil, [2]UFC, Lab Gastrointestinal Physiopharmacology, Brazil. [3]Estácio, Brazil. [4]UFC, Lab pharmaceutical technology, Brazil. [5]UFC, Lab Gastrointestinal Physiopharmacology, Graduate program in medical sciences, Brazil.

08.030 **Involvement of Prostaglandins in the Gastroprotective Effect of PHYTOL-βCD on Ethanol-Induced Gastric Lesions in Mice**. Sousa CFAJ[1], Amorim IF[2], Freitas FVS[2], Reis ML[2], Quintans-Junior LJ[3], Quintans JSS[3], Oliveira RCM[1,2]. [1]UFPI, PPG in Pharmacology; [2]UFPI, Research Center on Medicinal Plants; [3]UFS, Dept Physiology.

08.031 **Farnesol Attenuates Duodenal Lesions and Intestinal Inflammation in Experimental Models**. Pessôa MLS, Pessoa MM, Alves VP, Pessoa LF, Menezes PMF, Batista, LM. UFPB, Graduate Program in Natural and Synthetic Bioactive Products, Brazil.

08.032 **Effect of** *Akkermansia muciniphila* **Supplementation on Intestinal Environment and Glucose Homeostasis in Male and Female Mice**. Ribeiro TA[2], Newman PP[1], Allen-Gregory E[1], Mims TS[3], Pierre JF3, Soares PMG[2], van der Merwe M[1] [1]University of Memphis, College of Health Sciences, United States, [2]UFC, Lab. of Gastrointestinal Physiopharmacology Studies, PPG Pharmacology, Brazil, [3]University of Wisconsin–Madison, Dept Food and Nutritional Sciences, USA

08.034 **The Gut After Sepsis: Persistent Intestinal Dysmotility and Sex-Related Differences**. Lima-Moura SA, da Silva-Santos JE UFSC, Lab Cardiovascular and Smooth Muscle Biology, Dept Pharmacology, SC, Brazil.

09. Natural Products and Toxinology

Totem 21

09.006 **Evaluation of the Effects of Hydralazine Derivatives on Vas Deferens Contractility**. Avelino CTS, Portácio LFS, Sousa BMS, Ferreira Santos C, Lima PSC, Wanderley MV, Uchôa RPM, Nascimento NRF UECE, Brasil

09.007 **Effects of Dietary Flavonoids on Human Cognition: A Systematic Review**. Feitosa LFS[1], Azevedo ATF[1], Abreu DFP[2], Monteiro IO[1], Sousa PBC[1], Souza ADB[1], Silva JEB[1], Correia LCF[1], Silva VFB[123], Cruz YSES[123], Dantas DN[123], Vasconcelos KT1, Freitas GA[134], Sousa JMN[1,2], Santos NA[12345] [1]UFPB, Psychology Dpt, PGP Social Psychology Lab Perception, Neurosciencies, and Behavior, [2]UFPB, Psychology Dpt, PGP Cognitive Neuroscience and Behavior. Brazil.

09.008 **Evaluation of the Antifungal Potential of 10 Essential Oils Obtained from Different Hop Cultivars** (*Humulus lupulus*) **against** *Candida albicans*. Silva-Filho AM[1], Silva VA[1], TAVARES IGS[1], Freire KRL[2], Abílio GMF[3] [1]UFPB, Centro de Ciências da Saúde, Brasil [2]UFPB, Centro de Biotecnologia - Depto Biologia Celular e Molecular, Brasil [3]UFPB, Centro de Ciências da Saúde - Depto Ciências Biomédicas, Brasil

09.009 **Evaluation of the Antifungal Activity of** *Commiphora leptophloeos* **Extract**. Martins SO, Andrade IA, Ferreira CES, Fialho MLS, Gonçalo YA, Oliveira MVM, Nobrega VM, Pereira FO, Medeiros FD. UFCG, Cuité Campus, Center for Education and Health, Brazil.

09.010 **Potential Quorum Sensing Modulation by Ethyl Esters Derived from** *Pentaclethra macroloba* **Through Interaction with the LasR Receptor of** *Pseudomonas aeruginosa*. Lima AB[1], Castro MSM[2], Rodrigues ABL[3], Ramos RS[3], Oliveira FR[2], Nascimento AA[1,21]Unifap, PPG Ciências da Saúde, Brasil, [2]Unifap, Lab Experimentação Animal, Brasil, [3]Unifap, LMQC, Brasil.

09.011 **Prospection of the Gastroprotective Activity of the Crude Ethanolic Extract from** *Sideroxylon Obtusifolium*. Sales AO, Lopes FG, Rodrigues CVS, Santos ELS, Farias AGC, Santos BRP, Morais FS, Lima FJB, Santos VL. UEPB, Lab Pharmacological Assays, Brazil. Centro Universitário Unifacisa, Brazil.

Totem 22

09.012 **Evaluation of the Impact of N-Tosylindole Exposure on the Progeny of Caenorhabditis elegans**. Jesus LFS[1], Oliveira LMS[2], Cavalcanti SCH[2], Guimarães AD[2] [1]UFS-São Cristóvão, Dept Pharmacy, Brazil, [2]UFS-São Cristóvão, PPG in Pharmaceutical Sciences, Brazil

09.013 **Evaluation of the Antioxidant Activity of the Extract of** *Croton blanchetianus* **Baill**. Oliveira MVM, Ferreira CES, Fialho MLS, Martins SO, Nóbrega VM, Andrade IA, Gonçalo YA, Medeiros FD UFC-Cuité, Center for Education and Health, Brazil.

09.014 **Chemical Characterization and** *in vitro* **Antifungal Activity of Galaxy Essential Oil against Candida spp**. Silva VA[1], Tavares IGS[1], Gonçalves GS[2], Bastos SJV[2], Freire KRL[3], Abílio, GMF[4] [1]UFPB, Centro de Ciências da Saúde, Brasil [2]UFPB, Centro de Biotecnologia, Brasil [3]UFPB, Centro de Biotecnologia, Depto Biologia Celular e Molecular, Brasil, [4]UFPB, Centro de Ciências da Saúde - Depto Ciências Biomédicas, Brasil

09.015 **Glycosylated withanolide from** *Athenaea velutina* **Suppresses the Inflammatory Response in Macrophages via Inhibition of NF-κB, JNK, and iNOS**. Da Silva LR[1], de Araújo KGR[1], Ribeiro MS[1], Rocha LM[1], Mendonça LS[2], Silva JGP[1], Procopio GS[1], Ferreira AGG[1], Pessoa ODL[2], Santos FA[1]. [1]UFC, Dept Physiology and Pharmacology, Natural Products Lab, Brazil. [2]UFC, Science Center, Dept Organic and Inorganic Chemistry, Brazil.

09.016 **Extract from the Fruit of** *Sechium edule* **Induces Negative Inotropism, Vasorelaxation and Reduction of Blood Pressure in Rats**. Kistner MC[1], Peres VCA[1], Silva LKC[1], Soares JA[1], Brito DS[1,2], Rodrigues GA[1], Machado GI[1], Almeida JRGS[3], Silva DF[1,2] [1]UFBA, Brazi, [2]IGM-Fiocruz, PGBSMI, Brazil, [3]UNIVASF, Brazil

09.017 **Natural Product-Based Protection Against Diabetic Lung Injury: Effects of** *Spondias tuberosa* **Arruda Extract**. Montenegro, MCA[1], Morais, YCS[1], Donato FF[1], Pires LAB[1], Sena VNF[1], Silva CPC[1], Araújo, IGA[2], Medeiros KCP[1] [1]UFRN, Lab. of Experimental Morphology, Brazil. [2]UFPB, PPG Bioactive Natural and Synthetic Products, Brazil.

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09.018 **Evaluation of the Anti-Inflammatory Activity of** *Cereus jamacaru* **DC**. (**Cactaceae**) **Roots**. Araújo PHL[1], Santos EE[2],Deus GO[1], Costa WK[3], Correia MTS[3], Souza TA[4], Abreu LS[5], Oliveira AM[2], Cibulski SP[2], Alves HS[1,2] [1]UEPB, CCBS, Dept. of Pharmacy, Brazil, [2]UEPB, PPG in Pharmaceutical Sciences (PPGCF), Brazil, [3]UFPE, CB, Dept. of Biochemistry, Lab Natural Products, Brazil, [4]UFPB, Institute of Research in Drugs and Medicines (IPeFarM), Brazil, [5]UFF, Institute of Chemistry, Brazil

09.019 *Arthrospira platensis* **Prevents Uterine Hypercontractility Via Inhibition of Prostanoid and Nitric Oxide Pathways and Calcium Sensitization in a Wistar Female Rat Model of Primary Dysmenorrhea**. Sousa-Filho JEC[1], Silva JMA[1,2], Melo MB[1], Barbosa, YV[1,2], Santos TJ[1], Diniz AFA[1,2], Arruda RRA[1,2], Claudino BFO[1,2], Soares MFS2, Barros BC[1,2], Silva BA[1,2,3] [1]UFPB, Lab Functional Pharmacology Prof. George Thomas, Institute of Research in Drugs and Medicines, Brazil; [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil; [3]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil

09.020 **Evaluation of the Antifungal Activity of** *Ximenia americana* **Gel Against Dermatophytes**. Andrade IA, Ferreira CES, Fialho MLS, Gonçalo YA, Oliveira MVM, Martins SO, Nobrega VM, Pereira FO, Medeiros FD. UFCG-Cuité Campus, Center for Education and Health, Brazil.

09.021 **Pharmacological Evaluation of El Dorado Hop Oil: Chemical Characterization and Antifungal Activity Against Candida Species**. Tavares IGS[1], Silva VA[1], Gonçalves GS[2], Bastos SJV[2], Freire KRL[3], Abílio[1]UFPB, Health Sciences Center, Brazil [2]UFPB, Biotechnology Center, Brazil [3]UFPB, Biotechnology Center, Dept Cell and Molecular Biology, Brazil [4]UFPB, Health Sciences Center, Dept Biomedical Sciences, Brazil

09.022 **Development of an Antioxidant Serum Containing Leaf Extract of** *Eugenia uniflora* **L**. Almeida, JBC, Silva, AP, Souza, SO, Guilherme, ACS, Sousa, JCR, Lima, CM UFS-Lagarto, Brasil.

09.023 *In vivo* and *in silico* Toxicological Evaluation of Brazilian Brown Propolis from *Mimosa tenuiflora*. Alves BFL[1], Felício IM[2], Souza MLB[1], Silva TMS[3], Silva JLV[4], Picot L[5], Cavalcante FA[2],[61]UFPB, PIBIC, Brazil; [2]UFPB, CCS, PPgPNSB, Brazil; [3]UFPE, DQ, Brazil; [4]FMO, Lab. of Functional Practice, Brazil; [5]La Rochelle Université, LIENSs, France; [6]UFPB, CCS, DCB, Brazil

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09.024 Analysis of the Toxicity of a Series of Acylhydrazone Derivatives of Isatin in the *Caenorhabditis elegans* Model. Sousa LVBS[1], Almeida Filho GP[1], Lima TCBS[1], Carneiro CA[1], Campos CENS[1], Marreiro VS[1,3], Galdino FS[1,3], Costa MESM[1], Diniz MFFM[1,3], Janebro DI[1,3], Lima-Junior CG[3], Sousa FB[3] [1]UFPB, Lab Ensaios Toxicológicos, Brazil [3]UFPB, PPG Produtos Naturais, Brazil [3]UFPB, PPG Produtos Naturais, Brazil [3]UFPB, Lab Síntese Orgânica Medicinal da Paraíba, Brazil

09.025 Evaluation of the Antifungal Activity of the Extract of *Combretum leprosum* Mart. Against Dermatophytes. Nobrega VM, Andrade IA, Ferreira CES, Fialho MLS, Martins SO, Oliveira MVM, Almeida YA, Pereira FO, Medeiros FD UFCG-Cuité, Center for Education and Health, Brazil.

09.026 Dermal Safety of Curcumin Hydrogel in Mice: Evaluation of Toxicity Following OECD 402 Guidelines. Morais, MF[1], Falcão, ES[1], Oliveira, MX[2], Feitosa, JPA[2], Assreuy, AMS[1]. [1]UECE, Lab. of Physiopharmacology of Inflammation, PPG Physiological Science Brazil, [2]UFC, Lab. of Polymers Lab, PPG in Chemistry, Brazil.

09.027 Nanoencapsulation of *Lippia microphylla* Essential Oil in Nanostructured Lipid Carriers (NLCs): Antifungal Activity and Cytotoxicity. Moura DEG[1], Piancó MESV[2], Barreto JO[3], Silva LA[2], Lima LO[2], Nogueira PL[3], Alexandre HMS[2], Silva AL[2], Gonçalves JCR[2] [1]UFPB, Health Sciences Center, Dept Pharmaceutical Sciences, Undergraduate Program in Pharmacy, Brazil. [2]UFPB, Health Sciences Center, PPG in Bioactive Natural and Synthetic Products (PPgPNSB), Brazil. [3]UFPB, Health Sciences Center, PPG in Dentistry (PPGO), Brazil.

09.028 Evaluation of the Interaction Between Varespladib and Bothropstoxin-II Isolated from *Bothrops jararacussu* Venom on the Mouse Neuromuscular Junction. Silva HF[1], Pereira ES[1], Ortolani PL[2], Fortes CL[2], Cavalcante WLG[1] [1]UFMG, ICB, Dept. Pharmacology, Brazil; [2]FUNED, CPD, Brazil

09.029 Evaluation of the Embryotoxic Effect of *Bothrops lutzi* (Miranda-Ribeiro, 1915) Venom. Senna ESL, Novaes R, Braga JRM UFRB, Lab Reptiles and Amphibians, Cruz das Almas, Bahia, Brazil.

09.030 Biological Activity and Selectivity Profile of Balsam of Peru (*Myroxylon balsamum*) Oleoresin Against Clinically Relevant Microorganisms. Lacerda AF[1,2], Oliveira-Filho JMD[1], Alves ARS[1,3], Souza PHO[2], Cunha DBL[2], Alves RV[2], Gadelha TS[2], Faheina-Martins GV[2], Vasconcelos U[23], Travassos RA[1,2,3]. [1]UFPB, Lab FarmacoBiotecnologia (FarmaBio), Brazil; [2]UFPB, Graduate Program in Cellular and Molecular Biology (PPgBCM), Brazil; [3]UFPB, Centro de Biotecnologia (CBiotec), Brazil.

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09.058 Multisystemic Effects of *Hovenia dulcis* in a Complex Animal Model of Metabolic Syndrome: A Multitarget Perspective. Higashijima AN[1], Bezerra CS[1], Santa Clara-Amorim RC[1], Ribeiro RRM[1], Silva GR[1], Marcon MV[2], Barboza LN[3], Souza P[4], Sari MHM[5], Farago PV[2], Lívero FADR[1] [1]UFPR, Graduate Program in Pharmacology, Curitiba, Brazil; [2]UEPG, Graduate Program in Pharmaceutical Sciences, Ponta Grossa, Brazil; [3]UNIVEL, Biochemistry Lab, Cascavel, Brazil; [4]Univali, Graduate Program in Pharmaceutical Sciences, Itajaí, Brazil; [5]UFPR, Graduate Program in Pharmaceutical Sciences, Curitiba, Brazil

09.059 Caulerpin Modulates the Calcineurin-NFAT Signaling AXIS and Attenuates T-Cell Activation in Human Peripheral Blood Mononuclear Cells. Santos-Junior SS, Dos Santos JSP, Correia AGV, Oliveira VS, Silva DKC, Souza

CVC, Santos-Filho OA, Martinez ST, Soares MBP, Meira CS Fiocruz-BA, Salvador, UNEB, Salvador, SENAI CIMATEC-BA, Salvador, UFRJ-RJ, Rio de Janeiro FURG-RS, Rio Grande do Sul.

09.060 **Protective Effects of *Agaricus blazei* Polysaccharides on Cell Viability and Mitochondrial Membrane Potential in Human Renal Tubular Cells Subjected to Hypoxia-Reoxygenation**. Lima EQ[1], Ribeiro MENP[2], Menezes RRPPB[3], Queiroz MGR[3], Aragão DA[3], Magalhães EP[3], Sousa VQ[4], Sampaio TL[3], Martins AMC[1] [1]PPG in Pharmacology, UFC, Brazil. [2]PPG in Chemistry, UFC, Brazil. [3]PPG in Pharmaceutical Sciences, UFC, Brazil. [4]Undergraduate Program in Pharmacy, UFC, Brazil.

09.061 **Molecular Docking of Crotamine with the LDL Receptor: an Investigation of Animal Metabolism Regulation**. Soares JV[1], Cândido PA[2], Oliveira RJ[2], Hayashi MAF[1] [1]Unifesp-EPM, Dept Pharmacology, SP, Brazil, [2]UFTM, Dept Physics, Brazil

09.062 **Investigation by MTT Assay and Raman Spectroscopy of the Effects of *Caryocar brasiliense* Oil on the Viability of L929 Fibroblasts**. Lima RF[1], Reis ATF[2], Lima GMSF[3], de Lima RF[2], Carvalho TGPM[4], Barreto FS[5], Diniz Filho JFS[7], Dos Santos CC[7], Dittz Junior D[8], Garcia JBS[1], Carvalho RC[6], Andrade MS[5], Cartagenes MSS[1] [1]UFMA, LEED, PPGSAD, Brazil; [2]UFMA, LEED, PPGCS, Brazil; [3]UFMA, LEED, Pharmacy Course, Brazil; [4]UFMA, LEED, Renorbio, Brazil; [5]UFMA, PPGSAD, Brazil; [6]UFMA, Animal Facility, Brazil; [7]UFMA, Vibrational and Impedance Spectroscopy Lab, Brazil; [8]UFPI, Dept Biochemistry and Pharmacology, Brazil

09.063 **Effect of Hydroalcoholic Extract of *Piper klotzschianum* (Kunth) C. DC. on the Evaluation of Anti-Inflammatory Activity in Mice**. Silva MT[1], Silva JM[2], Nunes ERS[3], Sales MR[3], Lima JVJS[3], Jesus RA[2], Nascimento ACS[3], Aragão JMD[3], Ramos LS[3], Santos GJ[3], Fabricante JR[1] Gois AM[1], Camargo EA[3], Moraes VRS[2], Santos JR[3] [1]UFS, PPG Ciências Naturais, Brasil, [2]UFS, PPG Química, Brasil, [3]UFS, PPG Ciências Fisiológicas, Brasil.

09.064 **Gel Containing Naringin Combined with Phonophoresis Reduces Inflammatory and Oxidative Biomarkers After Musculoskeletal Injury**. Nascimento VS[1], Santana CBL[1], Sousa DS[2], Oliveira ED[1]. [1]UFS, Programa de Pós-Graduação em Biotecnologia (PROBIO), Brasil. [2]UFS, Rede Nordeste de Biotecnologia (Renorbio), Brasil.

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09.079 **Varespladib Reverses Neuromuscular Blockade induced by Crotoxin in Mouse Phrenic Nerve-Diaphragm Preparations**. Pereira ES[1], Silva HF[1], Ortolani PL[2], Fortes CL[2], Cavalcante WLG[1] ICB-UFMG, Dept. Pharmacology, Brazil. [2]FUNED, CPD, Brazil.

09.080 **Green Synthesis and Characterization of Silver Nanoparticles from *Tocoyena bullata*: antioxidant, cytotoxic, and wound-healing activities**. Santos HLS[1], Santos AF[2], Araújo AAB[2], Almeida, ERM[2], Silva GNB[1], Silva BM[1], Sobral R[1], Costa CACB[3], Sette-de-Souza PH[2], Freitas JD[3], Correia ACC[2], Albuquerque PBSA[1,2]. [1]UPE, PPG Biologia Celular e Molecular aplicada, Brazil, [2]UPE, PPG Saúde e Desenvolvimento Socioambiental, Brazil, [3]IFAL, Lab Síntese, Análise Química e Caracterização de Materiais, Brazil.

09.081 **Validation of Leaf Infusions of *Moringa oleifera* Lamarck in the Prevention of Hypertension and Platelet Aggregation**. Portela JVF[1,3,5] ; Silva ND[1,2,3]; Portela EP[1,2,3]; Rêgo AF[2,3]; Albuquerque BA[1,2,3]; Rocha VA[1,2,3]; Oliveira AP[1,2,3,4]. [1]UFPI, Graduate Program in Pharmacology, Brazil; [2]UFPI, Lab Cardiovascular Pharmacology, Brazil; [3]UFPI, Center for Research on Medicinal Plants, Brazil; [4]UFPI, Dept Biophysics and Physiology, Brazil; [5] UFPI, Graduate Program in Biotechnology – Renorbio, Brazil.

09.082 **Anti-Aging Effect of *Spondias tuberosa* Arruda Fruit Peel Extract in a Model of Cellular Photoaging in Immortalized Human Keratinocyte Cells**. Gomes MLC[1,2,3], Pereira MEM[1,3], Albuquerque MN[1,3], Oliveira JCPL[1,2,3],

Souza CMO[1,2,3], Fernandes GFS[1], Lima VS[1,2,3], Farias LRT[4], Langassner SMZ[4], Oliveira GD[2,5], Nascimento YM[2,5], Medeiros KCP[6], Veras RC[1,3], Araújo IGA[1,2,3], Medeiros IA[1,2,3]. [1]UFPB, Cardiovascular Pharmacology Lab, Institute for Drug and Medicine Research, Brazil. [2]UFPB, PPG in Bioactive Natural and Synthetic Products (PgPNSB), Health Sciences Center, Brazil. [3]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil. [4]UFRN, PharmacognosyLab, Brazil. [5]UFPB, Multi-User Lab for Characterization and Analysis, Brazil. [6]UFRN, Dept Morphology, Brazil.

09.083 **Does Cannabidiol Associated with Pulsed Therapeutic Ultrasound Potentiate Antioxidant Responses in Skeletal Muscle Injury?** Sousa DS, Dos Santos LB, Santana RAN, Lima MM, Azevedo IO, Nascimento VS, Oliveira ED UFS

09.084 **Evaluation of the Effects of Mentha x villosa Ethanolic Extract on the Vascular Reactivity of Rat Aorta**. Alves SML[1], Silva KT[1], Oliveira SKM[1], Ferreira JG[1], Silva MEF[1], Silva MCC[1], Tavares, JF, Araújo AV[1] [1] UFPE-Centro Acadêmico de Vitória (CAV), Brazil [2]UFPB, Brazil

09.085 **Evaluation of the Genotoxicity and/or Antigenotoxicity of Natural and Amination-Modified Cashew Gum, through the Somatic Mutation and Recombination Test in** *Drosophila melanogaster* **Wings**. Castro AJS[1], Machado FS[1], Ribeiro IS[2,3], Paula RCM[3], Araújo AJ[1], Marinho-Filho JDB[1]. [1]UFDpar, Lab Cultura de Células do Delta-PPGBIOTEC- Brasil; [2]IFPI-Brasil; [3]UFC- Brasil

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09.086 **The Triterpene Friedelin Attenuates TGF-β-Induced EMT in NCI-H292 Lung Cancer Cells and Upregulates TIMP3 Expression**. Almeida JH[1], Bodin A[2], Victoni T[23], Barreto EO[1], Lagente V[2], Ferro JNS[1] [1]UFAL, Lab Biologia Celular, Maceió, AL, Brasil. [2]Université de Rennes, Inserm, Inrae, NuMeCan (Nutrition, Métabolismes et Cancer), Rennes, France. [3]Université de Lyon, VetAgro Sup, Lyon, France.

09.087 *in silico* **Characterization of Babassu Oil Constituents as Cyclooxygenase Ligands**. Marques MA, da Silveira Cruz-Machado S, Quilenda JC, Nascimento Neto DE, Soares WRA UESB, Dept Health II, Lab Biomedical Sciences and Innovation, Graduate Program in Nursing and Health, Brazil

09.088 **Antioxidant Effect of Extract of** *Spondias tuberosa* **Arruda in Experimental Diabetic Nephropathy**. Sena VNF[1], Pires LAB[1], Donato FF[2], Albuquerque ECS[1], Araújo IGA[5], Vilar NF[4], Araújo RF[3], Medeiros KCP[3] [1]UFRN, Center for Biosciences, PPG in Biology Structure and Function, Brazil. [2]UFRN, Center for Biosciences, Brazil. [3]UFRN, Center for Biosciences, Morphology Dept, Brazil. [4]UFRN, Center for Biosciences, PPG in Health Sciences, Brazil. [5]UFPB, Health Sciences Center, PPG in Bioactive Natural and Synthetic Products, Brazil.

09.089 **Hepatoprotective Effect of** *Spondias tuberosa* **Arruda Extract in Experimental Diabetes and Isolated Hepatocyte Cell Line: Involvement of Oxidative Stress and the PI3K/AKT Pathway**. Pires, LAB[1], Sena, VNF[1], Felipe, FD[2], Vilar, NF[2], Araújo Júnior, RF[2], Vieira, RR[3], Gil, CD[3], Santos, DD[3], Medeiros, IA4, Gonçalves, IGA4, Medeiros, KCP[2] [1]UFRN, Biosciences Center, Graduate Program in Structural and Functional Biology, Brazil, [2]UFRN, Biosciences Center, Dept Morphology, Brazil; [3]Unifesp-EPM, Lab Morphological Sciences and Inflammation, Brazil; [4]UFPB, PPG in Bioactive Natural and Synthetic Products, Brazil

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09.097 *In vitro* **and** *in vivo* **Neuropharmacological Evaluation of Guarana and Mate Aqueous Extracts**. Falconi-Souto A, Piristrello BS, Marques AA, Chaves VSOG, Lago JHG, Mendes FR. UFABC

09.098 **Oral Supplementation with** *Pennisetum glaucum* **(L.) Mitigates Multi-Organic Dysfunction in HPV16-Transgenic Mice**. Lima LAS, Oliveira PA, Hajri L, Bastos MMSM, Medeiros R, Ghodbane S, Ammari M, Faustino-

Rocha AI, Gil da Costa RM [1]UFMA, PPG in Adult Health, Brazil. [2]University of Trás-os-Montes and Alto Douro, Centre for the Research and Technology of Agro-Environmental and Biological Sciences, Portugal. [3]University of Tunis El Manar, Higher Institute of Applied Biological Sciences of Tunis, Tunisia. [4]University of Porto, Lab for Process Engineering, Environment, Biotechnology and Energy, Portugal. [5]Research Center of IPO-Porto, Molecular Oncology and Viral Pathology Group, Portugal.

09.099 **Preliminary Evaluation of Cytotoxicity and Survival Rate After Beta-Myrcene and Gamma Terpinene Treatment in Experimental Sepsis**. Silva GHO, Previato CFA, Rocha EMT, Cuman RKN UEM

09. 100 **Cytotoxic Activity of Sediment-Associated Bacteria Isolated from the Parnaíba Delta EPA, Northeastern Brazil**. Garcia IAA[1], Dias LFS[1], Trindade MAC[1], Lacerda JC[1], Silva JYG[2], Florêncio KGD[2], Wilke DV[2], Guimarães LA[1] [1]UFPI, Senador Helvídio Nunes de Barros Campus, School of Medicine, Picos, Piaui, Brazil; [2]UFC, School of Medicine, Dept Physiology and Pharmacology, Drug Research and Development Center, Fortaleza, Ceara, Brazil.

09. 101 **Exploring the Analgesic and Anti-Inflammatory Potential of** *Oxyuranus scutellatus* **Snake Venom**. Giorgi R[1], Corrêa RCD[1], Camilo MEP[1], Spencer P[2], Gonçalves LRC[1], Zychar BC[1], Chacur M4 [1]IBu, Lab Pathophysiology, PPG in Toxinology, Brazil; [2]Nuclear and Energy Research Institute, Brazil; [3]ICB-USP, Dept Anatomy, Brazil.

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10.007 **Evaluation of BPO-DPPV as a Cytotoxic Agent Against** *in vitro*-**Induced Chemoresistant Osteosarcoma Cells**. Strauss LC, Pereira THR, Zamariolli LS, Moura TR, Netto AVG, Bincoletto C Unifesp-EPM, Depto Farmacologia, Unesp-Araraquara, Instituto de Química

10.008 **Antileukemic Activity of Synthetic Naphthoquinones in HL-60 Cells: Antiproliferative Effects and Morphological Alterations**. Pinheiro KS[1], Oliveira DA[2], Lima AB[3], Oliveira FL[4], Zelaya EAE[4], Silva EL[4], Moraes LGC[5], Rocha DR[5], Montenegro RC[4]. [1]UFC, Faculty of Pharmacy, Lab Pharmacogenetics, Brazil. [2]UFC, Faculty of, Biotechnology, Lab Pharmacogenetics, Brazil. [3]UFC, PPG in Medical Sciences, Lab Pharmacogenetics, Brazil. [4]UFC, Lab Pharmacogenetics, PPG in Pharmacology, Brazil. [5]UFF, Lab Synthesis of Molecules of Biological Interest, PPG in Chemistry, Brazil.

10.009 **Melittin as a Potential Therapeutic Agent Against Bladder Cancer: Effects on Cell Viability, Migration, and Cell Cycle Regulation**. Brayn GA1; Poiato GEH1; Oliveira AMB1; Porto RM2; Silva GN3; Almeida TC1; Picolo G1. 1 Lab Pain and Signaling, IBu, São Paulo, Brazil; 2 Lab Development and Innovation, IBu, São Paulo, Brazil; 3 Toxicogenetic, Epidemiological and Clinical Study and Research Group, Federal University of Ouro Preto, Ouro Preto, Brazil.

10.010 **A Role for Female Sex Hormone Receptors and Stromal Remodeling in the Differential Incidence of Tongue Base Cancer in Male and Female HPV16-Transgenic Mice**. Rodrigues TAR[1], Neto CPO[1], Medeiros-Fonseca B[2], Andrade FE[3], Oliveira PA[2], Bastos MMSM[4], Medeiros R[5], Gil da Costa RM[1,2,3,4,5]. [1]UFMA, PPG in Adult Health, Brazil. [2]University of Trás-os-Montes and Alto Douro, Centre for the Research and Technology of Agro-Environmental and Biological Sciences, Portugal. [3]UEMA, Dept Pathology, Brazil. [4]University of Porto, Lab for Process Engineering, Environment, Biotechnology and Energy, Portugal. [5]Portuguese Institute of Oncology in Porto Research Centre, Molecular Oncology and Viral Pathology Group, Portugal.

10.011 **Oxidative Stress-Associated Cytotoxicity of a Selenium Compound in the HeLa Cervical Cancer Cell Line**. Januario VHS[1], Rodrigues JS[1], Santana PS[1], Silvestre GFG[2], Ferreira RC[2], Sousa NF[3], Athayde-Filho PF[4], Souza HDS[4], Scotti MT[3], Scotti L[3], Amorim GMW[2], Loureiro PBA[2], Goncalves JCR[2], Sobral MV[2] [1]UFPB, Health Sciences Center,

ONCOFAR, Undergraduate in Pharmacy, Brazil, [2]UFPB, Health Sciences Center, ONCOFAR, PPG in Bioactives Natural and Synthetic Products, Brazil, [3]UFPB, Health Sciences Center, PPG in Bioactives Natural and Synthetic Products, Brazil, [4]UFPB, PPG in Chemistry, Brazil

10.012 **Prospecting Marine Bacteria Associated with *Zoanthus sociatus* from the Piauí Coastline with Anticancer Potential**. Pena JMP[1], Almeida RC[1], Silva JYG[1], Pessoa ODL, Guimarães LA[3], Florêncio KGD[1], Wilke DV[1] [1]UFC, Drug Research and Development Center, Dept Physiology and Pharmacology, School of Medicine, Ceara, Brazil. [2]UFC, Dept Organic and Inorganic Chemistry, Sciences Center, Ceara, Brazil. [3]UFPI-Senador Helvidio Nunes de Barros, Piaui, Brazil.

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10.013 **WIN55,212-2 Reduces Cell Migration in a Murine Colorectal Adenocarcinoma Cell Line (CT26. WT) Through Alterations in Oncogenic Pathways**. Bezerra BS[1], França JC[2], Pereira AF[2], Nascimento RR[2], Moura MNS[2], Moraes MEA[3], Wong DVT[2], Brito DMS[4], Zelaya EAE[4], Oliveira LLB[3], Paier CRK[3], Montenegro RC[4], Souza PFN[4], Vale ML[2] [1]UFC, Faculty of Medicine, Lab Inflammation and Cancer Pharmacology, Brazil; [2]UFC, Faculty of Medicine, Lab Inflammation and Cancer Pharmacology, PPG Pharmacology, Brazil; [3]UFC, Faculty of Medicine, Lab Experimental Oncology, PPG Pharmacology, Brazil; [4]UFC, Faculty of Medicine, Lab Pharmacogenetics, PPG Pharmacology, Brazil

10.014 **Effects of a *Fucus vesiculosus* Extract on the Progression of Epithelial Carcinogenesis in HPV16-Transgenic Mice**. Bastos HAC[1], Belfort MFA[1], Santos CED[1],Bezerra HRR[1], Lima LAS[1], Palhano NBM[1], Moreno AVP[1], Medeiros-Fonseca[2], Faustino-Rocha AI[2], Oliveira PA[2], Medeiros R[3], Bastos MMSM[4], Gil da Costa RM[1,2,3,4], Brito HO[1] [1]UFMA, Research Center For Experimental and Clinical Physiology and Pharmacology (NEC), Bioanalyses Lab (LabIO), Brazil; [2]University of Trás-os-Montes and Alto Douro (UTAD) Centre for the Research and Technology of Agroenvironmental and Biological Sciences (CITAB), Portugal; [3]Research Center of IPO Porto, Molecular Oncology and Viral Pathology Group, Portugal; [4]University of Porto, Lab for Process Engineering, Environment, Biotechnology and Energy (LEPABE), Portugal

10.015 **Evaluation of the Resistance-Modulating Effect of the Alkaloids EB-PA and EB-PB in Cisplatin-Resistant Lung Cancer Cells**. Silveira TSN[1], Madrid MFM[2], Moraes-Filho MO[3], Pessoa CÓ[4], Rocha DDR[5] . [1]UFC, Dept Pharmacy, Brazil [2]USP, Faculty of Medicine, Brazil. [3]UFC, PPG in Pharmacology, Brazil. [4]UFC, PPG in Pharmacology, Brazil. [5] UFC, Lab. of Experimental Oncology, Drug Research and Development Center, Brazil.

10.016 **PI3K Gamma and PI3K Delta Expression in Breast Cancer Before and After Neoadjuvant Chemotherapy: Association with Pathological Response**. Paulo CKF[1], Cavalcante DIM[2], Alves BES[1], Sampaio MJS[1], Maia IFVC[1], Wong DVT[1], Lima-Júnior RCP[1] [1]UFC, Dpt of Physiology and Pharmacology, Lab Inflammation and Cancer Pharmacology, Drug Research and Development Center, Brazil; [2]UFC, Dpt Pathology and Forensic Medicine, Brazil.

10.017 **The Role of Kinin Receptors in a Mouse Model of Chemically-Induced Oral Cancer**. Neculqueo GW[1,2], Farias ABS[2], LG[2], Estrázulas M[1,2], Campos MM[1,2] [1]PUCRS, PPG Medicina e Ciências da Saúde, Brazil. [2]FADIC-PUCRS, Escola de Ciências da Saúde e da Vida, Brazil.

10.018 **KCNQ1OT1 Overexpression Marks a High-Risk Subset of Intermediate-Risk AML with FLT3-ITD Enrichment and Poor Survival**. Oliveira KAF[1,2]; Scandolara TB[1,3]; Sales SLA[1,4]; Maranhão SS[1]; Farias IR[3]; Mota JA[1,4]; Gress LSB[1,4]; Macêdo SMN[1]; Melo VB[5] ; Soares IF[1,6]; Ramos IA[7]; Xavier EEP[1,8]; Pessoa C[1,4]; Bezerra LRPS [3] [1]UFC, Experimental Oncology Lab, Center for Research and Drug Development, Brazil; [2]UFC, Dept Biology, Brazil; [3]UFC, Graduate Program in Translational Medicine, Brazil; [4]UFC, Dept Physiology and Pharmacology, Graduate Program in Pharmacology, Brazil; [5]UFMG, Dept Genetics, Ecology and Evolution, Institute of Biological Sciences, Brazil;

[6]UNIFOR, Center for Health Sciences (CCS), Brazil; [7]UFC, Faculty of Medicine, Brazil; [8]UFC, Faculty of Pharmacy, Brazil; [9]UFC, Dept Child and Adolescent Health, Brazil.

10.019 **Evaluation of the Therapeutic Potential of Cirsimarina in the Topical Treatment of Urogenital Lesions in Experimental Penile Cancer**. Moreno AVP[1], Santos CED, Bezerra HRR[1,2], Bastos HAC[1,2], Belfort MFA[1,2], Palhano NBM[1,2], Baltazar RS[1,2], Pozes AB[1,2], Borges, ACR [1,2], Borges, MOR [1,2],Rocha CQ[1], Brito HO [1,2 1]UFMA, Research Center for Experimental and Clinical Physiopathology and Pharmacology, Brazil; [2]UFMA, Pharmacology Lab, Brazil; [3]UFMA, Dept Chemistry, Federal University of Maranhão

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10.027 **Docetaxel-Loaded Alginate Nanoparticles Increase Selectivity and Apoptotic Cell Death in Triple-Negative Breast Cancer Cells**. Pereira ERM[1], Alexandre HMS[1], Abreu-Junior AR[1], Santos PBG[2], Gomes KNC[2], Araujo YKO[2], Queiroga LM[1], Januario VHS[2], Farias APGM[1], Silva ICF[1], Marques KKG[1], Mendes AN[3], Filgueiras LA[3], Sobral MV[1], Gonçalves JCR[11]UFPB, Lab Oncopharmacology (ONCOFAR), PPG in Natural and Synthetic Bioactive Products, Brazil; [2]UFPB, Lab Oncopharmacology (ONCOFAR), Pharmacy undergraduate student, Brazil; [3]UFPI, Dept Biophysics and Physiology, Lab Innovation in Science and Technology (LACITEC), Brazil

10.028 **Cytotoxicity of the Selenium Compound NC36 in Human Cervical Cancer Cells**. Lyra GB[1], Silva ICF[1], Amorim GMW[1], Dantas MM[1], Castro IO[1], Farias APGM[1], Pereira ERM[1], Loureiro PBA[1], Sousa NF[2], Souza HDS[3], Athayde-Filho PF[3], Scotti L[2], Scotti MT[2], Gonçalves JCR[1], Sobral MV[1] [1]UFPB, Health Sciences Center, ONCOFAR, PPG in Natural and Synthetic Bioactive Products, Brazil. [2]UFPB, PPG in Natural and Synthetic Bioactive Products, Brazil. [3]UFPB, PPG in Chemistry, Brazil.

10.029 **Evaluation of the Genotoxic and Tumorigenic Potential of Chromomycin A3 in** *Drosophila Melanogaster*. Reis MA, Ribeiro RMS, Araújo DD, Bahia GFM, Castro AJS, Marinho Filho JDB, Araújo AJ LCCDelta-UFDPar, Lab Cultura de Células, Brazil.

10.030 **Harpalicinone Induces Programmed Cell Death by Mitochondrial Depolarization In HCT-116 Cells**. Ribeiro, RMS[1], Machado, FS[1], Pereira, FIA[1], Oliveira, MP[1], de Sá, RE[1], Araujo, RM[2], Silva, SANM[1], Marinho-Filho, JDB[1], Araújo, AJ[1]. [1]UFDPar, Lab Cultura de Células do Delta, Brazil, [2]UFRN, Instituto de Química, Brazil.

10.031 **Evaluation of the Compound LOE2208 as a potential epigenetic modulator in the Treatment of Acute Myeloid Leukemia** (**AML**). Mota JA[1,2], Sales SLA[1,2], Manso MP[3], Bastos RS[1,2], Gress LSB[1,2], Desiderio GA[1,2], Oliveria KAF[1], Macêdo SMN [1], Vieira-Neto JB[1,2], Scandolara TB[1], Maranhão SS[1,2], Pessoa CÓ[1,2], Furtado CLM[4]. [1]UFC, Lab. of Experimental Oncology, Drug Discovery and Development Center, Brazil; [2]UFC, PPG in Pharmacology. [3]INCa, Research Center, Brazil. [4]UFMG, Dept Genetics, Ecology and Evolution, Institute of Biological Sciences, Brazil.

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10.050 **Selective Cytotoxicity of the Selenium Compound NC41 in HeLa Cervical Cancer Cells: Evidence of Intrinsic Apoptosis**. Amorim GMW[1], Lyra GB[1], Loureiro PBA[1], Dantas MM[1], Marques KKG[1], Castro IO[1], Abreu-Junior AR[1], Silva ICF[1], Sousa NF[3], Souza HD[2], Athayde-Filho PF[2], Scotti MT[3], Scotti L[3], Gonçalves JCR[1], Sobral MV[1] [1]UFPB, Lab. of Oncopharmacology, PPG in Natural and Synthetic Bioactive Products, Brazil. [2]UFPB, PPG in Chemistry, Brazil. [3]UFPB, PPG in Natural and Synthetic Bioactive Products, Brazil.

10.051 **Oviedomycin Triggers Cytotoxicity in Human Colorectal Carcinoma Cells via Oxidative Stress and Mitochondrial Apoptosis**. Dantas MM[1], Alexandre HMS[1], Castro IO[1], Silvestre GFG[1], Souza RRM[1], Marques KKG[1], Lyra GB[1], Abreu-Júnior AR[1], Ramalho, IGS[1], Duarte SS[1], Oliveira GD[2], Tavares JF[2], Cibulski SP[3], Gonçalves JCR[1], Sobral MV[1] [1]UFPB, Health Sciences Center, ONCOFAR, PPG in Bioactive Natural and Synthetic Products, Brazil.

[2]UFPB, Multiuser Lab for Characterization and Analysis, PPG in Bioactive Natural and Synthetic Products, Brazil. [3]UFRN, Faculty of Health Sciences of Trairi (FACISA), Brazil

10.052 **Organoselenium Compounds and Sulfur Analogues Exhibit Cytotoxicity in Human Glioma Tumor Cell Lines**. Ramalho IGS[1], Souza RRM[1], Marques KKG[1], Januário VHS[2], Rodrigues JS[2], Queiroga LM[1], Farias APGM[1], Firmino-Silva IC[1], Lyra GB[1], Mendonça-Júnior FJB[1], Sobral MV[1], Ferreira RC[1], Gonçalves JCR[1]. [1]UFPB, Health Sciences Center, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]UFPB, Health Sciences Center, ONCOFAR, Undergraduate in pharmacy, Brazil

10.053 **Increased Resistin Expression Predicts Poor Neoadjuvant Chemotherapy Response in Breast Cancer Patients**. Freitas GL[1], Cajado AG[1], Quispe CC[1], Capistrano-Junior VL[2], Caetano ML[1], Saraiva LC[1], Sauda MR[3], Rocha-Filho DR[4], Arruda LM5, Rogatto SR[2], Lima-Junior RCP[1], Wong DVT[1] [1]UFC, Lab Inflammation and Cancer Pharmacology, Brazil. [2]Health Institute, Fortaleza, Brazil. [3]Unesp-Botucatu, Brazil. [4]UFC-Walter Cantídio University Hospital, 5Haroldo Juaçaba Hospital, Cancer Institute of Ceará, Brazil.

10.054 *In vitro* **Evaluation of the Cytotoxic Potential of the Hydroalcoholic Extract and Alkaloid Fraction from the Aerial Parts of** *Solanum jabrense* **Agra & M. Nee**. Alexandre HMS[1], Dantas MM[1], Pereira ERM[1], Castro IO[1], Santos PBG[1], Ramalho IGS[1], Santana PVS[1], Gomes KNC[1], Abreu-Junior AR[1], Araújo YKO[1], Silva AL[1], Tavares JF[1], Agra MF[2], Sobral MV[1], Gonçalves JCR[1] [1]UFPB, Dept Pharmaceutical Sciences, [2]UFPB, Biotechnology Center, João Pessoa, Brazil

10.055 **Low-Anticoagulant Bovine Heparin and Its Low Molecular Weight Derivative as Antimetastatic Agents**. Micheli KVA, Motta JM, Oliveira SNM, Hermsdorff-Brandt M, Peres ACL, Mourão PAS, Pereira MS IBqM-UFRJ, Rio de Janeiro, RJ, Brazil

10.056 **APT20TTMG Suppresses Tumor Cell Growth and Induces Apoptosis Across Multiple Human Cancer Cell Lines**. Oliveira VS[1,2], Lobo EB[1,2], Silva DKC1, Nogueira ML1, Soares ES3, Sinatti VVC3, Silva JC3, Bottos RM3, Leal CBQS3, Meira CS[1,2]. [1]Fiocruz-BA, Salvador, [2]SENAI CIMATEC-BA, Salvador, [3]Aptah Bio Inc., San Carlos, CA, USA.

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10.067 **LOE2208 Induces G2/M Cell Cycle Arrest and Apoptosis in Non-Small Cell Lung Cancer Cells**. Brito TL[1,2], Vieira-Neto JB[1,2], Pereira JVM[1,2], Feijó-Neto JR[1], Pessoa C[1,2,3]. [1]UFC, Lab. of Experimental Oncology, Drug Research and Development Center, Brazil; [2]UFC, PPG Pharmacology, Brazil; [3]UFC, Northeast Biotechnology Network Program (Renorbio), Brazil.

10.068 **Antitumoral Effects of Melittin on Tridimensional Models of Bladder Cancer**. Gonçalves CFL, Almeida TC, Picolo G. IBu, Pain and Signaling Lab, Brazil.

10.069 **Effects of classical antidepressants in a novel protocol of sarcoma-related depressive-like behavior**. Sousa RWR[1], Santos IL[1], Rodrigues DCN[1], Conceição MLP[1], Freitas MM[1], Nascimento MLLB[2], Almeida ML[1], Sousa RCL[1], Souza RP[3], Batista CL[1], Pereira IC[4], Torres-Leal FL[4], Lopes LS[5], Ferreira PMP[1,6] [1]UFPI, Lab Experimental Cancerology (LabCancer), Dept Biophysics and Physiology; [2]UFPI, Lab Toxicological Genetics Research (Lapgenic), Dept Biochemistry and Pharmacology; [3]UFPI, Lab Cardiovascular Pharmacology (Lafac), Dept Biophysics and Physiology; [4]UFPI, Metabolic Diseases, Exercise and Nutrition Research Group (Domen), Dept Biophysics and Physiology; [5]UFPI, Lab for Research in Experimental Neurochemistry (Lapnex), Dept Biophysics and Physiology, [6]UFC, Lab Experimental Oncology (Loe), Dept Physiology and Pharmacology, Brazil

10.070 **Phenotypic Changes of Immunogenic Cell Death Induced by Marine Natural Product Chromomycin A5 in BRAF-Mutant Melanoma**. Florêncio KGD[1], Soeiro JEM[1], Brito TL[1], Teixeira PR[3], Lotufo LVC[3], Pinto FCL[2], Pessoa ODL[2], Wilke DV[1] [1]UFC, Drug Research and Development Center, Dept Physiology and Pharmacology, School of Medicine, Brazil. [2]UFC, Dept Organic and Inorganic Chemistry, Sciences Center, Ceara, Brazil. [3]ICB-USP, Dept Pharmacology, Sao Paulo, Brazil.

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10.017FR **Preconception and Gestational High-Fat Diet Differentially Affect Reflex Ontogeny and Somatic Maturation in Male and Female Rat Offspring: A Sex-Specific Developmental Study**. Chagas MAC, Dutra MLV, Souza DM, Aquino JS UFPB, Experimental Nutrition Lab João Pessoa, Paraíba, Brazil. [2]UFPB, , João Pessoa, Paraíba, Brazil.

10.013FR **Early life Protein Restriction Impairs GLP-1-Induced Insulin Secretion Despite Increased Intra-Islet GLP-1 Production**. Oliveira KM[1], Silva-Junior JA[2], Carvalho MS[1], Bem KCP[1], Barbosa HCL[1], Carneiro, EM[1] [1]Unicamp, Obesity and Comorbidities Research Center (OCRC), Brazil; [2]Universidad Miguel Hernández, Instituto de Investigación en Biotecnología y Salud

10.014FR **Developmental Exposure to Phthalates and Nanoplastics Disrupts Hypothalamic Neuroplasticity, Metabolic Homeostasis, and Glial Remodeling in Aging Male Rats**. Fioretto MN, Magosso N, Souza PV, Moreira MF, Rocha VA, Pinha VC, da Silva Maria VLR, Justulin LA, Scarano WR. IBB-Unesp, Dept Cellular and Molecular Biology, Institute of Biosciences, Sao Paulo State University, Botucatu, SP, Brazil.

10.015FR **Saturated Fat-Rich Diet Enhances Histone H3-lysine9 Acetylation and Lipid Metabolism in the Liver Following Perinatal Protein Undernutrition**. Simões-Alves AC, de Mello APFAC, Nogueira VO, Leandro CVG, Fernandes MP, Pirola L, Morio B, Costa-Silva JH. UFPE, Academic Center of Vitória Lab Nutrition, Physical Activity and Phenotypic Plasticity, Vitória de Santo Antão – PE, Brazil. UFPE, Lab General Biochemistry, Academic Center of Vitória, Molecular Biology and Exercise, Universidade Federal de Pernambuco-, Vitória de Santo Antão – PE, Brazil. Université Claude Bernard Lyon1, Laboratoire de Recherche en Cardiovasculaire, Métabolisme, Diabétologie et Nutrition, INSERM, Oullins, Lyon, France

11. Clinical Pharmacology, Pharmacokinetics, Pharmacogenomics and Toxicology

Totem 34

11.025 **Pharmacokinetic and Pharmacodynamic Evaluation of Nanoencapsulated Artemether**. Pereira LC[1], Silva MB[2], Miranda ALL[2] da Silva, RISde D[2], Pica K[3], Fialho MCP[4], Mosqueira VCF[4], Magalhães DRM[2], Azeredo FJ[3] [1]UFBA, Faculty of Pharmacy, Lab Pharmacokinetics and Pharmacometrics, PPG in Pharmacy, Brazil. [2]Fiocruz, Postgraduate Course in Biotechnology in Health and Investigative Medicine, Brazil. [3]University of Florida, College of Pharmacy, Center for Pharmacometrics and Systems Pharmacology, United States. [4]UFOP, School of Pharmacy, Galenic Development and Nanotechnology Lab, Brazil.

11.026 **Endothelial Biomarkers in Haff Disease-Related Acute Kidney Injury**. Santos PBS[1], Almeida IM[1], Araújo LM[1], Lopes NC[1], Aquino VHN[2], Costa MDR[3], Correia MN[4], Petruccelli KCS[5], Daher EDF[6], Silva-Júnior GB[7], Sampaio TL[3], Meneses GC[3], Martins AMC[1,3] [1]UFC, Faculty of Medicine, PPG in Pharmacology, Brazil; [2]UFC, Faculty of Pharmacy, Dept. of Pharmacy, Brazil; [3]UFC, Faculty of Pharmacy, PPG in Pharmaceutical Sciences, Brazil; [4]José Mendes Regional Hospital, Brazil; [5]UFAM, Faculty of Medicine, Brazil; [6]UFC, Faculty of Medicine, Dept. of Clinical Medicine, Brazil; [7]UNIFOR, Faculty of Medicine, Brazil.

11.027 **Investigating the Effectiveness of Subcutaneous Administration of Unfractionated Heparin: A Detailed Analysis of Absorption and Therapeutic Response**. Lopes JRM; Oliveira SNMCG; Gorinstein IVL; Mourão PAS UFRJ

Universidade Federal do Rio de Janeiro Lab Tecido Conjuntivo Instituto de Bioquímica Médica Leopoldo de Meis, Brasil

11.028 **CYP2D6 Intermediate Metabolizer Status, Fluoxetine Phenoconversion, and Serotonin Toxicity at Therapeutic Doses: A Mechanistic Clinical Neuropharmacology Case Series**. Poian L. R., Chiavegatto S. ICB-USP, Dept Pharmacology, Brazil

11.029 **A Starch-Based Bioabsorbable Dexamethasone-Loaded Implant Reduces Postoperative Pain and Inflammation in Mice**. Souza FMSR, Velozo ACL, Lemos PVF, Mäder[2] K, Villarreal CF. Gonçalo Moniz Institute, Fiocruz, Brazil, School of Pharmacy, UFBA, Brazil, Martin Luther University Halle-Wittenberg, Institute of Pharmacy, Germany.

Totem 35

11.033 **Validated LC-MS/MS Method for Quantifying Nicotine and Cotinine in Mouse Tissues: Application to Assess Nicotine Kinetics After Cigarette or e-Cigarette Exposure**. Santos, GCM, Rocha, BM, Oliveira, MEC, Santos, GRA, Carballo, LPF, Silva, PMR, Martins, MA. IOC-Fiocruz, Lab Inflammation, Brazil.

Totem 44

11.001 **Toxicological Evaluation of the Ruthenium Complex FOR0777G Using the HET-CAM Assay**. Costa SGA[1], Soares JJF[2], Silva FAO[2], Oliveira ACX[3], Andrade FRS[2], Lima NCB[2], Alves RS[3], Marinho AD[4], Jorge RJB[2], Manigat W[2], Júnior FSG[2], Pereira WG[2], Sousa EHS[2], Lopes LGF[2], Monteiro HSA[2]. [1]UFC, Dept Pharmacy, Dentistry and Nursing, Brazil. [2]UFC, Dept Pharmacology and Physiology, Brazil Graduate Program in Pharmacology, Brazil. [3]UFC, Graduate Program in Morphofunctional Sciences, Dept Clinical and Toxicological Analysis, Brazil. [5]UFC, Center for Research and Development of Medicines (NPDM), Brazil.

11.002 **Bothrops Venoms Induce a Bell-Shaped Effect on Platelet Aggregation**. Catela B[1], Pagliarani J[1], Zani KM[2], Gaspar RS[1] [1]Unicamp, Extracellular Matrix Lab, Brazil. [2]IBu, São Paulo, Brazil.

11.003 **Optimization of Meropenem Pharmacokinetic/Pharmacodynamic Targets in Critically Ill Pediatric Patients: An Integrative Review**. Santos AKFS, Carvalho RMC, Macedo CL, Landim ECS, Santos YKA, Ramos PS, Marreiro VS, Praxedes MRS ESP-PB, Residência Multiprofissional em Saúde da Criança

11.004 **Clinical Monitoring of Cardiovascular Risk in Patients Receiving Antipsychotic Therapy: A Narrative Review**. Oliveira KS[1], Araújo JR[1], Araújo MLF[1], Alves ROF[1], Costa SGA[1], Carvalho JPAQ[1], Barbosa ISA[1], Canafístula LS[1], Pinheiro KS[1], Andrade FGA[1], Sampaio TL[2] [1]UFC, Faculty of Pharmacy, Dentistry and Nursing, Dept Clinical and Toxicological Analysis, Brazil; [2]UFC, Faculty of Pharmacy, Dentistry and Nursing, Dept of Clinical Analysis and Toxicological, PPG of Pharmaceutical Sciences, Brazil

11.005 **Toxicological Assessment of Pharmaceutical Surfactants in *Caenorhabditis elegans* Using Physiological and Behavioral Endpoints**. Silva VGO[1], Fagundes LS[1], Sá MEB[1], Poderoso VM[1], Araujo DS[1], Lisboa JS[2], Pacheco PGS[2], Trancoso CT[2], Araujo ZS[3], Cândido-Santos JH[4], Guimarães AG[5], Lira AAM[5] [1]UFS-São Cristóvão, Dept Pharmacy, Lab. of Clinical and Experimental Pharmacology, Brazil, [2]UFS-São Cristóvão, PPG in Pharmaceutical Sciences, Brazil, [3]UFS, Campus Lagarto, PPG in Applied Health Sciences, Brazil, [4]UFS-São Cristóvão, PPG in Health Sciences, Brazil, [5] UFS, Dept Pharmacy, Brazil.

11. General Pharmacology

Totem 38

11.001FR **Structure-Activity Relationship of Thymol and Carvacrol Isomers in Human Umbilical Arteries from Healthy Parturients**. Silva PEO, Pereira LRS, Cruz JF, Duarte MRS, Batista PR, Calixto GL, Morais LP, Sales VS, Sales

EPN, Gonçalves SA, Cavalcante JMC, Silva FDS, Silva JA, Barbosa R URCA - Lab Physiopharmacology of Excitable Cells, Brazil

Totem 40

11.006FR **Polysaccharide-Rich Ointment of *Caesalpinia ferrea* Barks Inhibits Clinical Signs and Accelerates Skin Wounds Healing in Hyperglycemic Rats**. Lopes MR[1], Santos GA[1], Falcão ES[1], Leite LMP[2], Pereira MG[2], Mota MRL[3], Assreuy AMS[1] [1]ISCB-UECE, Lab Physiopharmacology of Inflammation, Brazil; [2]ISCB-UECE, Lab Polysaccharides Bioactives, Brazil; [3] UFC, Lab Oral Pathology, Brazil

Totem 41

11.002FR **Açaí Seed Extract Shows Antipsychotic-Like Effects in a Ketamine-Induced Schizophrenia Model**. Mattos JA, Caetano AC, Ferreira FS, Dias KM,1 Nascimento JM1, Soares LN, Lopes CFO, Trefilio LM, Fontes-Dantas FL, Tavares ACD, Villaça YA, Ognibene DT, Costa CA, Resende AC, Bem GF UERJ, Research Line in Neuropharmacology and Medicinal Plants (NFPM), PPG in Clinical and Experimental Pathophysiology (Fisclinex), Brazil

11.003FR **Anti-Inflammatory, Antioxidant and Antinociceptive Effects of the Hydroethanolic Extract from Piper sp. Leaves in Carrageenan-Induced Acute Inflammation in Mice**. Oliveira, SLMK[1], Azevedo VGS[1], Peixoto ABS[1], da Silva FGN[1], Lopes RF[2], Frota LS[3], de Morais SM[4], Assereuy AMS[1] [1]UECE, Instituto Superior de Ciências Biomédicas, PPG em Ciências Fisiológicas, Brazil; [2]UFAC, Lab Pesquisa em Fisiofarmacologia, Programa de Pós-Graduação em Biodiversidade e Biotecnologia da Rede BIONORTE, Brazil; [3]UECE, Lab Química de Produtos Naturais, PPG em Ciências Naturais, Brazil.

11.004FR **Polysaccharides from *Genipa americana* Leaves: An Evaluation in the Rat Model of Arthritis Induced by Zymosan**. Azevedo VGS[1], Peixoto ABS[1], Araujo DFA[1], Da Silva Nascimento FG[1], Leite LMP[2], Pereira MG[2], Assreuy AMS[1] [1]UECE, Institute of Biomedical Sciences, PPG Physiological, Brazil; [2]FECLESC/UECE, Faculty of Education, Sciences and Letters of the Central Hinterland, Brazil

11.005FR **Synergic Healing Effect of *Delonix regia* Galactomanans and Platelet Rich Plasma in Mice Cutaneous Wounds**. Alves PGM[1], Lima IC[3], Oliveira SLMK[1], Falcão ES1, Mota MRL[2], Assreuy AMS[1] [1]UECE, Lab. of Physio-Pharmacology of Inflammation, PPG Physiological Sciences, Brazil, [2]UFC, Dept. of Clinical Odontology of UFC, Lab. of Oral Pathology, Brazil, [3]Universidade Christus, Brazil.

12. Drug Discovery and Development

Totem 35

12.039 **Lipid Nanoparticle Containing Simvastatin and Adenosine-Loaded Hydrogel Improves Wound Healing: Evaluation of Skin Penetration, Biocompatibility, and Therapeutic Efficacy in HaCat Cells and Mice**. Daré RG, Rocco VM, Marques B, Akamine EH, Lopes LB ICB-USP, Dept Pharmacology, Brazil

12.040 **Drug Discovery: PAD4 Inhibitors as a Novel Pharmacological Approach for the Treatment of NET-mediated Inflammatory Diseases**. Augusto PSA, Costa VF, Miguel PEG, Lavorini LS, Melo IFS, Leandro MO, Cunha TM, Cunha FQ [1]FMRP-USP, Depto Farmacologia, Lab Inflamação e Dor, PPG em Farmacologia, Brasil, [2]FMRP-USP, Depto Bioquímica e Imunologia, Lab Inflamação e Dor, PPG em Imunologia Básica e Aplicada, Brasil

12.041 **Nanocarrier-Based Delivery of the Semi-Synthetic Digoxin Derivative BD-15: A Safer Therapeutic Strategy for Alternating Hemiplegia of Childhood**. de Andrade MM[1], Passos JS[1], Fernandes, PH[1] Barbosa LA[2], Lopes LB[1], Scavone C[1] [1]ICB-USP, Dept, of Pharmacology, Brazil. [2]UFSJ-Dona Lindu Central-West Campus, Brazil

12.042 **Scalable Liposomal Platform for Efficient Encapsulation and Oral Delivery of Angiotensin-(1–7): Proof of Concept in Acute Gouty Arthritis**. Mendes S[1], Matosinhos RC[2], Saúde-Guimarães DA[2], Santos RAS[1], Frézard F[1]

[1]FISFAR-ICB-UFMG, Dept Physiology and Biophysics, Graduate Program in Physiology and Pharmacology, Brazil; [2]UFOP, School of Pharmacy, Graduate, Program in Pharmaceutical Sciences (CiPharma), Brazil

Totem 36

12.007 **Synthesis, Characterization, and** *in silico* **Evaluation of Cyanoacrylate Derivatives for Treatment of Inflammatory Diseases**. Lima MKS[1], Silva JVV[1], Leandro PF[1], Farias AGC[1,2], Lima AMAF[1], Oliveira MLA[1], Fernandes HQA[1], Menezes KJS[1], Cavalcanti MAT[1], Albino SL[1,2], Silva JM[3], Moura RO[1,2] [1]UEPB, Lab Drug Development and Synthesis, Brazil [2]UEPB, PPG Pharmaceutical Sciences, Brazil [3]UFPE, PPG Pharmaceutical Sciences, Brazil

12.008 **Preliminary** *in silico* **Evaluation of the Pharmacodynamic Profile of Isatin Derivatives as Potential N-Myristoyltransferase Inhibitors against Neglected Tropical Diseases**. Leandro PF1, Lima MKS1, Oliveira MLA1, Albino SL1, Moura WCS[1,2], Fernandes HQA1, Menezes KJS1, Silva JVV1, Cavalcanti MAT1, Farias AGC[1,2], Lima AMAF1, Moura RO[1,2], Nascimento IJS[1,2]. [1]UEPB, Lab Drug Development and Synthesis, Brazil; [2]UEPB, PPG in Pharmaceutical Sciences, Brazil.

12.009 **Synthesis and Antimicrobial Activity of N-acyl-Hydrazones Derived from β-Lapachone**. Lima RRCF[1], Silva RF,[1] Pinheiro SM[1], Santos Filho J[2], Lima Júnior CG[3], Santos JRD[4], Lima EO[4] [1]UFPB, Center for Exact and Natural Sciences, Dept Chemistry, Lab Organic Synthesis and Biocatalysis, Brazil [2]UFPE, Technology and Geoscience Center, Chemical Engineering Dept, Lab Design and Synthesis Applied to Medicinal Chemistry, Brazil [3]UFPB, Center for Exact and Natural Sciences, Dept Chemistry, Lab Medicinal Organic Synthesis, Brazil [4]UFPB, Health Sciences Center, Dept Pharmaceutical Sciences, Lab Mycology, Brazil

12.010 **Synthesis, Structural Characterization, and** *in silico* **Evaluation of the Leishmanicidal Activity of an Indole-Spiroacridine Derivative**. Oliveira MLA[1,3], Lima AMAF[1,3], Silva JVV[1,3], Leandro PF[1,3], Lima MKSL[1,3], Farias AGC[1,2], Fernandes HQA[1,3], Albino SL[1,2,3], Moura RO[1,2,3] [1]UEPB, Lab Drug Development and Synthesis, Brazil, [2]UEPB, Graduate Program in Pharmaceutical Sciences, Brazil, [3]UEPB, Dept Pharmacy, Brazil

12.011 **Physicochemical Stability Evaluation of Polymeric Nanocapsules Containing Copaiba Oil under Forced Stress Conditions**. Santos IB, Souza PHO, Formiga ALD, Xavier-Junior FH UFPB, Lab Biotecnologia Farmacêutica (BioTecFarm), Brazil

12.012 **Virtual Screening of FDA-Approved Drugs as Potential N-Myristoyltransferase Inhibitors Useful Against Malaria**. Silva KWL[1], Rios EO[2], Silva AVX[2], Nascimento IJS[2] [1]Estácio, Faculty of Biological Sciences, Brazil, [2]CESMAC, Faculty of Pharmacy, Brazil

12.013 **Molecular Interaction Between Silymarin Flavolignans and Pancreatic Lipase: An** *in silico* **Study**. Ferreira ALN[1], Silva FRC[2], Bezerra VM[2], Magalhães EP[2], Aragão DA[2], Silva ME[2], Ribeiro LR[2], Carvalho JPAQ[1], Marinho ES[3], Marinho MM[3], Martins AMC[1], Menezes RRPPB[11]UFC, Clinical and Toxicological Analysis Dept, Brazil. [2]UFC, PPG of Pharmaceutical Sciences, Brazil, Brazil. [3]UECE, Bioprospecting and Natural Resource Monitoring Lab, Brazil

Totem 37

12.021 **Development of a Functional Screening Platform Targeting the Mitotic Kinesin Eg5 for Anticancer Drug Discovery**. Desiderio GA[1,2], Salviano RA[1], Silva AS[1], Mota JF[1], Macêdo SMN[1], Castro CM[1], Mota JA[1,2], Gress LSB[1,2], Feijó-Neto JRF[1], Sousa GC[1,3], Sales SLA[1,2], Almeida MCM[1,4] Costa PMS[1], Pessoa C[1,2,3], Paier CRK[1,2,4] [1]UFC, Lab. Experimental Oncology, Brazil [2]UFC, PPG Pharmacology, Brazil [3]UFC, Northeast Biotechnology Network, Brazil [4]UFC, PPG Translational Medicine, Brazil

12.022 **Pradimicin-IRD-Loaded PLGA Nanoparticles: A Novel Approach to Colorectal Cancer Treatment**. Gomes MAM, Miguel RA, Passos JS, Lotufo LVC, Lopes LB ICB-USP, Dept Pharmacology, Graduate Program in Functional and Molecular Biology, Brazil

12.024 **Antifungal Potential, Cytotoxicity, and *in silico* Analysis of (-)-Carveol Against *Sporothrix brasiliensis* Strains**. Piancó MESV[1], Moura DEG[2], Lima LO[3], Silva LA[3], Medeiros CIS[3], Alexandre HMS[3], Silva EVA[4], Souza LDG[4], Gonçalves JCR[3], Sobral MV[3], Barbosa-Filho JM[3], Lima EO[3], Guerra FQS[3] [1]UFPB, Graduate Program in Natural and Synthetic Bioactive Products (PPgPNSB), Brazil [2]UFPB, Undergraduate Program in Pharmacy, Brazil [3]UFPB, Graduate Program in Natural and Synthetic Bioactive Products (PPgPNSB), Brazil [4]UFPB, Graduate Program in Dentistry (PPGO), Brazil

12.025 **Subchronic Toxicity Assessment of Docetaxel-Loaded Lipid Nanoparticles: A Comparative Study Focusing on the Male Reproductive System of Rats**. Inácio, JM[1]; Carvalho, FV[1]; Geronimo, G[1], Paula, E[1], Rodrigues da Silva, GH[2] [1]Unicamp, Dept Biochemistry, Institute of Biology, Brazil. [2]CNPEM, Brazilian Biosciences National Lab, Brazil.

12.026 **Sedative and Anesthetic Activity of the Essential Oil of *Cymbopogon winterianus* in *Penaeus vannamei***. Meira-Graziela M[1], Schmidt D[1], Wasielesky Junior W[2], Cardozo AP[2] Giesta LB[2], Menossi O[3], Pedrosa VF[2], Toigo YL[4], Baldisserotto B[1] Heinzmann BM[1] [1]UFSM, Fish Physiology Lab, Brazil. [2]FURG, Shrimp Farming Lab. [3]FURG, Lab Immunology and Pathology of Aquatic Organisms. [4]UFRGS.

12.027 **Evaluation of the Tripanocidal Effect of the Combination Between Benznidazole and Antimicrobial Peptides Analogs Derived from the M-PONTx-Dq4e Fragment [1-10]**. Martins BVB[1], Magalhães EP[1], Martins BMS[1], R LR[1], da Silva Júnior PN[1], Sampaio BCC[1], Silva BP[2], Adelino SM[2], Ferreira ALN[2], Carvalho JPAQ[2], Lima AKP[2], Marques BMC[2], Amorim AC[2], de Menezes RRPPB[1], Martins AMC[1] [1]UFC, Faculty of Pharmacy, Dept Clinical and Toxicological Analysis, PPG Pharmacological Sciences, Brazil. [2]UFC, Faculty of Pharmacy, Dept Clinical and Toxicological Analysis, Brazil.

14. Pharmacology: Other

Totem 38

14.001 **Evaluation of the *In vitro* Antifungal Activity of 2-Benzyl-5-Methylbenz(d)oxazole against *Nakaseomyces glabratus* (*Candida glabrata*) isolates**. Dos Santos AC[1,2], Da Silva RBP[2], De Souza LDG[2,3], Da Silva EVA[2,3], Emídio JJ[1], De Sousa DP[1,4], Rocha WPS[2,3,4], Guerra FQS[1,2,3,4] [1]UFPB, Center for Health Sciences, PPG in Bioactive Natural and Synthetic Products, Brazil, [2]UFPB, Center for Health Sciences, Clinical Mycology Lab, Brazil, [3]UFPB, Center for Health Sciences, PPG in Dentistry, Brazil, [4]UFPB, Health Sciences Center, Dept Pharmaceutical Sciences, Brazil

14.002 **Evaluation of the Wound-Healing Potential of Polymeric Films Containing an N-Acylhydrazone Derivative in a Wistar Rat Model of Excisional Skin Wounds**. Dantas VG[1], Nascimento BKL[1,2], Sousa BG[1,2], Silva JF[1], Chaves MJRS[1], Medeiros KA[1,3], Guedes GG[1,3], Oliveira TKB[4], Nonaka CFW[5], Araújo PHL[1], Damasceno BPGL[1,2,3], Cavalcanti ALM[1]. [1]UEPB, Lab for the Development and Characterization of Pharmaceutical Products, Brazil. [2]UEPB, PPG Pharmaceutical Sciences, Brazil. [3]UFPB, PPG Development and Technological Innovation in Medicines, Brazil. [4]UNIFACISA University Center, Brazil. [5]UEPB, PPG Dentistry, Brazil.

14.003 **Effect of Eucalyptol (1,8-CINEOL) on Human Umbilical Artery Dysfunction Associated with Gestational Diabetes Mellitus: An *ex vivo* Study**. Silva JA, Machado STS, Bastos CMS, Sousa MJS, Araújo ERL, Oliveira PES, Duarte MRS, Silva DFS, Pereira LRS, Silva AA, Sales EPN, Lacerda JML, Sales VS, Barbosa R URCA, Lab Physiopharmacology of Excitable Cells, Brazil

14.004 **Cortico-Hippocampal Network Involvement in Time-Dependent Fear Generalization**. Castro JC[1], Corrêa MS[2], Lopes LV[1], dos Santos ACQ[1], Lourenço WTB[1], Ferreira TL[1], Fornari RV[1] [1]UFABC, Lab. of Neurobiology of Memory, PG Neuroscience, Brazil. [2]Leibniz Institute for Neurobiology, Germany.

Totem 39

14.016 **Anthocyanin Profile and Antioxidant Capacity of Syrah Winery By-Products from the Brazilian Cerrado**. Costa KCM[1], Pertuzatti PB[2], Giachini FR[1],[3]. [1]ICB-UFG, Goiania, Brazil; [2]UFMT-Barra do Garças, Brazil; [3]UFMT-Barra do Garças, Institute of Biological Sciences and Health, Federal University of Mato Grosso, Barra do Garças, Brazil

14.017 **Performance of Large Language Models in Title and Abstract Screening of Preclinical Systematic Reviews**. Gallas-Lopes M[1,2], Silva Neto FM[1,3], Herrmann AP[1,2], Amaral OB[1,4]. [1]BRISA ColLaboration, Brazil, [2]UFRGS, Dept. of Pharmacology, Brazil, [3]UEMA, Dept. of Medicine, Brazil, [4]UFRJ, Institute of Medical Biochemistry Leopoldo de Meis, Brazil.

14.018 **Potential Hepatoprotective Effects of *Helianthus tuberosus* Polysaccharides in Acute Liver Damage**. Leal LE[1], Pilger BI[1], Cordeiro LMC[2], Acco A[1] [1]UFPR, PPG Pharmacology, Brazil, [2]UFPR, Dept Biochemistry and Molecular Biology, Brazil

14.019 **The Polysaccharides in Passion Fruit Peel Attenuate Acute Hepatotoxicity Through Redox and Metabolic Modulation**. Pilger BI[1], Leal LE[1], Cordeiro LMC[2], Brownlee I[3], Acco A[1] [1]UFPR, Dept Pharmacology, Brazil, [2]UFPR, Dept Biochemistry and Molecular Biology, Brazil, [3]Northumbria University, Dept Applied Sciences, England

Totem 40

14.020 **Effect of D-Limonene on the Attenuation of *Staphylococcus aureus* Virulence and Wound Healing in a *Tenebrio molitor* Model**. Pessoa DLR[1,2], Lima KKS[2], Torres LRD[2], Soares MS[2], Sousa MF[2], Arruda CS[2], Silva, EDM[2], Ferro TAF[2], Lima Neto LD[2], Mendes SJF[2]. [1]UFMA, Research and Graduate Lab in Pharmacology, Brazil. [2]CEUMA, Graduate Program in Applied Biosciences to Health, Brazil.

14.021 **Establishment of a MASLD Mouse Model: Ultrasonographic, Biochemical, and Morphological Analysis**. Acco A[1], Leal LE[1], Longo-Filho A[2], Bejes HOC[1], Vilani JM[2], Ribeiro LS[1,3] [1]UFPR, Dept Pharmacology, Brazil; [2]UFPR, Veterinary Science Post Graduation Program, Brazil; [3]Unibrasil, Biomedicine course, Brazil

14. Scientific Methodology and Experimental Design in Biology

Totem 43

14.005FR **Three-Dimensional Cold Porcelain Modeling as a Pedagogical Tool for Human Physiology Education**. Nóbrega VC, Cruz JC UFPB, Dept. of Biotechnology, PPG Physiological Sciences, Brazil

14.006FR **Evaluating Artificial Intelligence Tools for Bibliographic Surveys on Natural Product-Induced Immunogenic Cell Death**. Carneiro, IBS[1], Codellos, LL[2], Ladeia, LGF[3], Rodrigues, SIA[4], Wilke, DV[1] [1]UFC, PPG Pharmacology, Brazil. [2]UFC, Institute of Culture and Art, Brazil. [3]UNEB, Campus VI, Dept Human Sciences, Brazil. [4]UFC, Dept Biochemistry and Molecular Biology, Brazil.

14.002FR **Involvement of Central Nitric Oxide in the Thermal Control of Rats During Physical Exercise**. Rocha LJ[1], Lopes RA[1], Noronha GL[1], Martins JA[1], Campos OC[2], Rodrigues QT[3], Silva KSC[3], Prímola-Gomes TN[4], Lacerda LT[1], Brandão CFCCM[1], Andrade MJO[5], Natali AJ[4], Szawka RE[3], Coimbra CC[3], Drummond LR[1] [1]UEMG, Dept Physical Education, Brazil; [2]UEMG, Dept Biological Sciences, Brazil; [3]UFMG, Dept Physiology and Biophysics, Brazil; [4]UFV, Dept Physical Education, Brazil; [5] UEMG, Dept Psychology, Brazil

14.003FR **Discrimination of EMT-Associated Phenotypes in A549 Cells Using Raman Spectroscopy and Supervised Machine Learning**. Silva EC[1], Oliveira J[2], Figueiredo CG[1], Ferreira EGA[1], Souza ST[2], Ferro JNS[1] [1]ICBS-UFAL, Maceió, Alagoas, Brazil; [2]UFAL, Group of Optics and Nanoscopy (GON), Institute of Physics, Maceió, AL, Brazil

14.004FR **Behavioral Characterization of Female Wistar Rats Subjected to D-Galactose-Induced Accelerated Aging**. Silva KRG[1], Pontual MMV[2], Lima RR[3], Aquino JS[4], Carvalho LRRA[4] [1]UFPB Course of Pharmacy, Health Sciences Center, João Pessoa, Brazil; [2]UNIPÊ, Course of Veterinary Medicine, Paraíba, Brazil; [3]UFPB, PPG in Gerontology, João Pessoa, Brazil; [4]UFPB, Experimental Nutrition Lab, João Pessoa, Brazil

14.007FR **Validation of Experimental Streptozotocin-Induced Diabetes Mellitus Models in Rodents: Clinical, Biochemical, and Morphological Aspects**. Donato FF[1], Pires LAB[1], Sena VNF[1], Silva CPC[1], Vieira RR[2], Gil CD[2], Medeiros KCP[1] [1]UFRN, Lab. of Experimental Morphology, [2]Unifesp, PPG Structural and Functional Biology, Brazil

15. Neurobiology and Neuronal Diseases

Totem 03

15.006FR **Association Between Screen Time and Sleep Quality in Children with Autism Spectrum Disorder: A Cross-Sectional Study**. Veloso CE, Drummond LR, Lopes RA, Augusto VG, Lima VVAF, Perina KCB UEMG-Divinópolis, Lab. of Experimental Exercise Physiology, PPG in Biosciences and Human Health, Brazil.

15.007FR **Functional Lateralization in the Posterior Insular Cortex Control of Conditioned Fear Responses in Rats**. Ferronato, MVS, Gomes-de-Souza, L, Reis-Silva, LL, Tavares, LRR, Crestani, CC FCFAr-Unesp, Lab Pharmacology, School of Pharmaceutical Sciences, São, Araraquara, Brazil.

16. Toxinology, Natural Products and Medicinal Chemistry

Totem 27

16.004FR **Cashew Nut Oil** (*Anacardium occidentale* **L.**) **as a Potential Anxiolytic-Like and GABAergic Neuromodulador in Zebrafish** (*Danio rerio*). Freire GA[1], Freitas YJS[2], Menezes JESA[2], Maciel JB[2], Santos HS[2], Martins CBR[1], Xavier Filho RRB[2], Canuto MJSF[1] [1]UFC, Lab Biochemistry and Pharmacology, Graduate Program in Pharmacology, Fortaleza, Ceará, Brazil; [2]UECE, Lab Chemical-Pharmacological and Environmental Bioassays, PPG in Natural Sciences, Fortaleza, Ceará, Brazil.

16.005FR **Bioassay-Guided Screening of Plant Species from the Gurupi Biological Reserve Reveals Promising Sources of Anti-Inflammatory Compounds**. Costa FF[1], Rocha CQ[2], Reis AS[1] [1]UFMA, Lab Pathophysiology and Therapeutic Research, Brazil; [2]UFMA, PPG Chemistry, Brazil

16.006FR **Ethanolic extract of** *Trema micrantha* (**Cannabaceae**) **Leaves Reduces Mechanical Hyperalgesia in a Murine Model of Musculoskeletal Hyperalgesia**. Souza JA[1], Quintans-Júnior LJ[1], Passos FRS[1], Quintans JSS[1], Duarte MC[2], Santos LDS[2], Santos KVB[3], Reis WS[3], Lima YRS[3]. [1]UFS, PPG em Ciências da Saúde, 2PPG em Ciências Farmacêuticas, [3]UFS-LANEF.

17. Vision and Ophthalmology

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17.001FR **Effect of Intimate Partner Violence on Women's Attentional Bias: An Eye-Tracking Study**. Souza BTBA[1,4], Freitas GA[1,4], Silva GM[1,4], Cavalcante AM[1,5], Albuquerque SCSO[1,5], Santos MEB[1,5], Xavier MJS[3], Souto JJS[1,4], Abreu DFP[1,5], Oliveira ACGA[2,6], Azevedo ATF[1], Silva VFB[1], Santos NA[1,4,5]. [1]UFPB, [2]UNIPÊ, [3]UNINASSAU, Lab Perception, Neurosciences, and Behavior, [4]PGP Social Psychology, [5]PGP Cognitive Neuroscience and Behavior, [6]PPG Law. Brazil.

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01. Cellular and Molecular Pharmacology

Totem 01

01.011 *In vitro* **Cellular Aging Determines Susceptibility to Cardiotonic Steroid-Induced Epithelial–Mesenchymal Transition in Renal Cells**. Barros GMO, Bagri KM, Mermelstein CS, Quintas LEM ICB-UFRJ, PPG in Pharmacology and Medicinal Chemistry, Lab Biochemical and Molecular Pharmacology, Rio de Janeiro, Brazil.

01.012 **Gestational Diabetes Mellitus (GDM) Promotes Plasmatic Matrix Metalloproteinase (MMP)-2 Activation and Suggests IR/IGF1R as a Potential Proteolytic Target in Murine Model**. Cantão MBS[1], Nakama RP[2], Sartori DC[2], Castro MM[1] [1]FMRP-USP, Dept Pharmacology, Brazil; [2]FMRP-USP, Dept Biochemistry and Immunology, Brazil

01.013 **Role of Dopamine (DA) and 6-Nitrodopamine (6ND) on *ex vivo* α-amylase Secretion by Murine Salivary Glands**. Alves MCO[1], Teixeira SA[1], Costa SKP[1], de Nucci G[1,2], Muscará MN[1] [1]ICB-USP, Lab Farmacologia Bioquímica da Inflamação e Dor, São Paulo, Brasil, PPG Biologia Funcional e Molecular; [2]Unicamp

01.015 **Extracellular cAMP–Adenosine Pathway Regulates β2-Adrenoceptor Agonist Anti-Proteolytic Effects in Skeletal Muscle Cells**. Satori NA, Godinho RO. Unifesp-EPM, Dept. of Pharmacology, Div. of Cellular Pharmacology; PPG Pharmacology, São Paulo, Brazil.

01.016 **Investigation of Non-Canonical Signaling Triggered by the G Protein-Coupled Receptor HCAR2 (GPR109A)**. Santos AM[1,2], Sousa AC[1,3], Rodrigues FC[1,4], Cunha TM2, Bouvier M[5], Parreiras-e-Silva LT[1,2,3,4] [1]USP, Ribeirão Preto School of Pharmaceutical Sciences, Lab Molecular Pharmacology of GPCRs, Brazil, [2]USP, PPG Pharmacology, Brazil, [3]USP, PPG Biosciences and Biotechnology, Brazil, [4]USP, PPG Biochemistry, Brazil, [5]University of Montreal, Institute for Research in Immunology and Cancer, Canada

01.017 **Functional Evaluation of miR-181a-5p in the Cisplatin Response in Lung Cancer Cell Lines**. Gomes JPA[1,4]; Pegado CBS[1,4]; Silva MGM[2]; Silva Junior MA[3,4]; Silva JRS[1,4]; Paz Neta DC[1,4]; Silva BO[1,4]; Pereira MC[1,4,5]. [1]UFPE, PPG Therapeutic Innovation, Brazil. [2]UFPE, PPG Genetics and Molecular Biology, Brazil. [3]Unisãomiguel, Brazil, [4]UFPE, Suely Galdino Center for Research in Therapeutic Innovation, Brazil [5]UFPE, Dept Physiology and Pharmacology, Brazil.

Totem 02

01.021 **Impact of Adipose Tissue Secretome on Endothelial Cells in Obesity**. Nascimento-Silva V[1], Souza MJ[1], Rodrigues-Silva G[1], Andrade-da-Costa J[1], Andrade-Santos C[1], Moraes JA[2], Barja-Fidalgo C[1] [1]UERJ, Lab Farmacologia Celular e Molecular, Brasil. [2]UFRJ, Lab de Biologia Redox, Brasil.

01.018 **Time-Dependent Modulation of Cardiomyocyte Contractility by Alamandine Involves Different Signaling Pathways**. Monteiro ALL[1], Eliezeck M[1], Scalzo SRA[1], Poletini MO[1], Cau SBA[2], Santos RAS[1], Guatimosim S[1]. [1]ICB-UFMG, ICB, Dept Physiology and Biophysics, Graduate Program in Biological Sciences: Physiology and Pharmacology Brazil. [2]UFMG, ICB, Dept Pharmacology, Graduate Program in Biological Sciences: Physiology and Pharmacology, Brazil.

01.019 **Endothelial P2Y2 and P2X7 Receptors Colocalization with Caveolin-1 Enhances Monocyte Adhesion in Intestinal Schistosomiasis**. Oliveira NF, Mainieri NS, Flores CO, Ribeiro DAS, Silva CLM. ICB-UFRJ, Lab Biochemical and Molecular Pharmacology, Brazil

01.020 **Increased hsa-miR-30e-3p Expression is Associated with Cisplatin Response in Lung Cancer**. Silva BO[1,3]; Gomes JPA[1,3]; Silva MGM[2]; Barbosa FHS[1,3]; Souza GA[1,3]; Silva TD[1,3]; Pegado CBS[1,3]; Paz Neta DC[1,3]; Silva JOR[3]; Pereira MC[1,3,4] [1]UFPE, PPG Therapeutic Innovation, Brazil; [2]UFPE, PPG Genetics and Molecular Biology, Brazil; [3]UFPE, Suely Galdino Center for Research in Therapeutic Innovation, Brazil; [4]UFPE, Dept Physiology and Pharmacology, Brazil

02. Neuropharmacology

Totem 03

02.013 **Multi-omics Analysis of Molecular Docking and Dynamics of Natural Compounds Targeting Tau Protein Aggregation in Tauopathies**. Farias NR, Souza VL, Andrade EM, Garofalo CB, Farias MS, Pereira P, Santos PA. UFRGS, Institute of Basic Health Sciences, Dept Pharmacology, Lab Neuropharmacology and Clinical Toxicology, PPG in Pharmacology and Therapeutics. Brazil.

02.014 **Toxicological Evaluation of the Peptide Fraternin-10 Administered Intranasally in Mice** (**Mus musculus**). Costa MOG[1], Azevedo CVIB[2], Mortari MR[1] [1]UnB, Institute of Biological Sciences, Neuropharmacology Lab., Brazil [2]UnB, Faculty of Health Sciences, PPG in Health Sciences, Brazil

02.015 **Cannabigerol Modulates Cocaine-Induced Reward in Mice in the Open Field Test**. Souza SS, Manduca CA, Moreira FA and Aguiar DC UFMG, Pharmacology Dept, Lab Neuropsychopharmacology, Brazil

02.016 **Neurovespina Reduces Hippocampal Neuronal Death and Microglial Proliferation in a Pilocarpine-Induced Temporal Lobe Epilepsy Model**. Fraga CH, Lima LS, Mortari MR. UnB, Darcy Ribeiro, Biology Institute, Neuropharma Lab, Brazil.

02.017 **Mulungu** (*Erythrina velutina*) **Infusion Prevents Cholinergic Dysfunction and Oxidative Stress in an Alzheimer's Disease Model in** *Drosophila melanogaster*. Razzera GA[1], Escher ALK[1], Rehbein CP[1], Schmidt JM[1], Silva ES[1], Thom SL[1], Kemmerich C[1], Medeiros CSS[1], Cruz IBM[4], Ribeiro EE[4], Schimith MD[3], Barbisan F[1,2], Musachio E[1,3] [1]UFSM, Biogenomics Lab, Brazil, [2]UFSM, Graduate Program in Biological Sciences: Pharmacology, Brazil, [3]UFSM, Graduate Program in Nursing, Brazil, [4]Open University for the Third Age Foundation, Brazil

02.018 **Behavioral and Metabolic Effects of** *Lacticaseibacillus rhamnosus* **64 in a Murine Model of Binge Eating**. Avelar CDFL[1], Malta GFA[1], Parreira, LS[1], Ribeiro, FM[2], Martins, FS[3], Vieira, LB[1] [1]ICB-UFMG, Dept Pharmacology, Neuropharmacology Lab, PPG Physiology and Pharmacology, Brazil; [2]ICB-UFMG, Dept Biochemistry, Neurobiochemistry Lab, PPG Biochemistry and Immunology, Brazil. [3]ICB-UFMG, Dept Microbiology, Biotherapeutic Agents Lab, PPG Microbiology, Brazil.

02.019 **Effects of the Lithium Treatment on Early Stage of Sporadic Alzheimer's** (**sAD**) **Disease in Male Rats**. Lima, TF, Kanazawa LKS, Fernandes, SMA, Vital, MABF. UFPR, Pharmacology Dept, Brazil.

Totem 04

02.036 *Alpinia zerumbet* **Modulates Intestinal Dysbiosis and Cognitive Impairment Induced by Chronic Scopolamine Exposure**. Nascimento JM[1], Ferreira FS[1], Soares SCS[1], Mattos JA[1], Dias KM[1], Lopes CFO[1], Trefilio LM[1], Guimenes BD[1], Fontes-Dantas FL[1], Filgueiras CC[1], Ognibene DT[1], Costa CA[1], Resende AC[1] and Vieira AKG[2], Bem GF[1] [1]UERJ, Roberto Alcantara Gomes Institute of Biology, Research Line in Neuropharmacology and Medicinal Plants, Graduate Program in Clinical and Experimental Pathophysiology, Brazil. [2]UERJ, Professional PPG Biology Teaching, Brazil.

02.037 **Systemic Metoclopramide Modulates Cortical Spreading Depression Parameters in Rats**. Melo SM, Prieto SG, Guedes RA UFPE, Center of Health Sciences, Nutrition Dept, Brazil

02.039 **Impact of Acute and Repeated inhalation of *Lavandula dentata* Essential Oil on the Anxiolytic and Antidepressant-Like Behavior of Mice: A Comparative Study with *Lavandula angustifolia***. Marco MR, Flores VG, Blauth T, Silva GC, Barcellos ES, Prestes RNB, Mattos CB, Betti AH Feevale University, Institute of Health Sciences, Brazil

02.040 **Standardized Functional Radioligand Assays for Investigating NeuroVAL Peptide Activity at Dopaminergic Receptors**. Ferreira JW, Mortari MR, Campos GAA, Veras LG UnB, Institute of Biological Sciences, Dept Physiological Sciences, Lab Neuropharmacology, Brazil

02.041 ***In vivo* and *in vitro* Effects of Na+/K+-ATPase Activating Monoclonal Antibodies**. Bariviera JL[1,2], Ribeiro LR[1,2], Da Rosa GK[1,2], Santos VT[2], Carneiro MA[2], Angelo, IJ[2], Bassoaldo, R[2], Oliveira MS[1,2] [1]UFSM, PPG Pharmacology, Brazil; [2]UFSM, Lab Experimental Neurology

Totem 05

02.053 **Clinical, Cognitive, and Sociodemographic Characterization of Patients with Mild Cognitive Impairment and Dementia Attended at Walter Cantídio University Hospital**. Souza TF[1,2], Ferreira DMA[1,2], Guimarães APDS[1,2], Rosa R[3], Lima DP[3,4,5] Lima AB[5], Miyajima F[1,2] [1]Fiocruz-Ceará, Brasil, [2]ACMELab Lab Analítico de Competências Moleculares e Epidemiológicas, Brasil, [3]UFC, Brasil, [4]Hospital Universitário Walter Cantídio, Brasil, [5]HSM-Messejana, Brasil

02.055 **Negative Correlation Between Cortical Acetylcholinesterase Activity and Spatial Working Memory in STZ-Induced Rats Treated with Probiotic and Postbiotic *Lactobacillus casei***. Rodrigues ES, Gomes J, Meus SS, Comis-Neto AA, Fontoura, EA, Batista, WT, Streb, BL, Fidelis, EM, Rosa, SG, Pinton S Unipampa-Uruguaiana, RS, Brazil

02.056 ***in silico* and Behavioral Evaluation of Geraniol and Geranyl Acetate Pharmacological Profile in Zebrafish**. Bastos LM[1,2], Fuentealba-Villarroel F[1,3], Gallas-Lopes M[1,2], Paulo M[1,2], Patelli-Alves A[1], Cardoso IP[1], Borges GO[1], Portela SM[1], Rosa GO[1], Costa PM[1,5], Herrmann AP[2], Rigo MM[4], Piato A[1,2,3] [1]UFRGS, Porto Alegre, Lab Psicofarmacologia e Comportamento, Brazil; [2]UFRGS, Porto Alegre, PPG Farmacologia e Terapêutica, Brazil; [3]UFRGS, Porto Alegre, PPG Neurociências, Brazil; [4]UFRGS, Porto Alegre, PPG Genética e Biologia Molecular, Brazil; [5]UFCSPA, Porto Alegre, Brazil.

02.057 **Sodium Valproate and Gabapentin Reduce the Seizure-Like Behavior Induced by Pentylenetetrazol and Mechanical Stress in *Drosophila melanogaster*: Sex Influence on Behavioral Responses**. Santos G, Goes AAD, Oliveira MS, Bressan GN, Fachinetto R UFSM, Centro de Ciências da Saúde, PPG em Ciências Biológicas: Farmacologia, Brasil.

02.058 **Paraprobiotic Treatment Preserves Striatal TH-Positive Neurons and Modulates Gut Microbiota Following Intranasal MPTP Administration**. Gomes J[1], Rodrigues ES[1], Comis-Neto AA[1], Fontura, EA[1], Evangelista, HC[1], Batista, WT[1], Streb, BL[1], Rosa, SG[1], Ribeiro, AM[2], Pinton, S[1] [1]Unipampa-Uruguaiana, RS, Brazil, [2]Unifesp, São Paulo, SP, Brazil

Totem 06

02.067 **Antimanic-Like Effect of Dipyridamole in the Methylphenidate-Induced Hyperlocomotion Model**. Kanazawa LKS, Santos AG, Kühl CE, Higashijima AN, de Souza STF, Andreatini R UFPR, PPG Pharmacology, Brazil

02.068 **Early Post-Treatment with Beta-Caryophyllene Prevents Motor Deficits and Hippocampal Neuronal Loss after Pilocarpine-Induced Status Epilepticus**. Ribeiro LR[1,2], Bariviera JL[1,2], Da Rosa GK[1,2], Santos VT[2], Carneiro MA[2], Prates DN[2], Furian AF[1,2], Oliveira MS[1,2] [1]UFSM, PPG Pharmacology, Brazil; [2]UFSM, Lab Experimental Neurology

02.069 **Serum-Induced TLR3/TLR4 Signaling and Neurotoxicity in Unipolar Depression, Bipolar Disorder, and Attention-Deficit/Hyperactivity Disorder Patients**. de Farias IS[1], Ximenes AX[1], Soares JV[1], Pereira VA[2], Fidalgo T[3], Lima GMA[4], Hayashi MAF[1] [1]Unifesp-EPM, Dept Pharmacology; [2]Institute of Science and Technology; [3]Unifesp-EPM, Dept Psychiatry; [4]Unifesp-EPM, Dept Neurology; São Paulo, Brazil.

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02.072 **Neuroprotective and Anticonvulsant Effects of *Limnospira platensis* Aqueous Extract in Acute Pentylenetetrazol-Induced Seizures in Mice**. Souto TL[1], Almeida LS[1], Bentes ILG[1,2] Nascimento AA[1], Do Nascimento JLM[3], Oliveira EDC[4], Faustino SMM[1], Oliveira FR[1,2] [1]Unifap, School of Pharmacy, Brazil. [2]Unifap, PPG Pharmaceutical Sciences, Brazil. [3]UFPA, PPG Pharmacology and Biochemistry. [4]IEPA, Lab Taxonomy and Ecology of Cyanobacteria and Microalgae, Brazil.

02.073 **Anti-Inflammatory and Antiapoptotic Effects of the Bioinspired Peptide Neurovespina in an Experimental Model of Temporal Lobe Epilepsy**. Mortari MR, Oliveira BCC, Camargo LC, Lima LS UnB, Lab Neurofarmacologia, Instituto de Ciências Biológicas, Brasília, DF, Brazil.

02.071 **Distinct Behavioral Effects of Short-Term Voluntary Running in Phosphatase and Tensin Homolog Deleted on Chromosome 10 Neuronal Haploinsufficient Mice**. Andreotti DZ[1], Mello NP[1], Paixão AG[1], Scavone C[2], Orellana AMM[2], Kawamoto E[1]. [1]ICB-USP, Lab Molecular and Functional Neurobiology; [2]ICB-USP, Lab Molecular Neuropharmacology

02.070 **Impact of Prolonged Sweetener Consumption in an Animal Model of Alzheimer's Disease**. Guaita GO[1], Kanazawa LKS[1], Pagnussat AL[1], Hortega JVM[2], Souza RLR[2], Tureck LV[2], Vital MABF[1] [1]UFPR, PPG Pharmacology, Brazil; [2]UFPR, PPG Genetics, Brazil

03. Psychopharmacology

Totem 08

03.013 **Involvement of Serotonergic Neurotransmission without Anxiolytic-Like Effect of the Thiophene Derivative 6CN07: *in silico* and *in vivo* Studies**. Pereira CHL, Mendes LM, Naves FB, Almeida JVM, Alves HAR, Alves ARS, Teixeira JL, Barbosa NMMV, Martins AMO, Oliveira LN, Neri, LCD, Soares MFS, Silva PR, Monteiro AB, Felipe CFB. UFPB. Psychopharmacology Lab, Brazil.

03.014 **Distinct Behavioral Consequences of Ethanol Withdrawal in Male and Female Rats: a Focus on Anxiety and Depression**. Jardim ACG, Costa LSR, Silva AJA, Santos RO, Costa Pinto M, Gavioli EC, Soares VP. UFRN, Dept Biophysics and Pharmacology, Brazil.

03.015 **Evaluation of the Effects of *Artocarpus heterophyllus* Seed Core Extract On Anxiety- and Depression-Related Behaviors and Jejunal Activity in Female Rats**. Alexandre SVD[1], Miguel TBV[2], Alves ALF[1], Oliveira JCA[2], Silva CRL[1], Lima FMS[1], Costa Pinto MFN[1], Silva MS[1], Pedrini MRS[2], Matsui KN[2], Silva Junior ED[1], Soares VP[1]. [1]UFRN, Dept Biophysics and Pharmacology, Brazil, [2]UFRN, Dept Food Engineering, Brazil.

03.016 **Phenacetin as a Cocaine Adulterant: Acute Effects on Anxiety-Like Behavior, Locomotor Activity and Sleep in Mice**. Silva BPH[1], Silva SMC[1], Castro Neto AG[2], Lira VELC[3], Duarte FS[4], Gomes DA[1] [1]UFPE-Recife, Biosciences Center, Dept Physiology and Pharmacology, Lab. of Neuroendocrinology and Metabolism; Center for Medical

Sciences, Graduate Program in Neuropsychiatry and Behavioral Sciences, Brazil; [2]UFPE-Recife, Biosciences Center, Dept Biophysics and Radiobiology; [3]Federal Police Dept Pernambuco, Recife, PE, Brazil; [4]UFPE-Recife, Biosciences Center, Dept Physiology and Pharmacology, Lab. of Experimental Neuropharmacology, Graduate Program in Biochemistry and Physiology, Brazil

03.017 **Effects of Learned Helplessness, an Uncontrollable Stress-Based Model of Depression, on Gastric, Intestinal, and Bladder Smooth Muscle Activity in Mice**. Gomes LTC, Gavioli EC, Silva-Junior ED Federal University of Rio Grande do Norte (UFRN), Dept Biophysics and Pharmacology, Brazil.

Totem 09

03.028 **N,N-dimethyltryptamine Reduced Anxiety-Like Behaviors in Escapable Stressed Mice Later After Administration**. Lima VVF, Sousa-Silva AN, Moura CA, Torres CIO, Gavioli EC. UFRN, Dept Biophysics and Pharmacology, PPG in Psychobiology, Natal, RN, Brazil.

03.029 **Behavioral and Neuroinflammatory Effects Caused by Lipopolysaccharide Application in Mice Exposed to CO_2**. Corsi LAF, Nascimento-Silva JM, Cabral BC, Rocha-Gomes A, Zangrossi-Júnior H USP, Lab. of Behavioral Pharmacology, PPG in Biological Sciences (Pharmacology), Brazil

03.030 **Physiological and Behavioral Characterization of the Effects of the Chronic Social Defeat Stress Model: Preliminary Findings**. De Souza D, Poian LR, Chiavegatto S. ICB-USP, Dept Pharmacology, Functional and Molecular Biology Post Graduation Program, Brazil.

03.031 **Effects of Neonatal Immune Challenge with Lipopolysaccharide on Panic-Related Behaviors in Adult Sprague Dawley Rats**. Aguiar L, Rocha-Gomes A, Nascimento-Silva JM, Hernandes PM, Zangrossi-Júnior H FMRP-USP, Dept. of Pharmacology, Lab. of Behavioral Pharmacology, PPG in Biological Sciences (Pharmacology), Brazil.

03.032 **Effects of Antagonism of Orexin Receptors, Administered during the Acquisition Phase, on Alcohol Preference in the Two-Bottle Choice Model in Swiss Male Mice**. Silva VS[1], Costa RCA[1], Costa EF[1], Ferreira KR[1], Santos RS[2], Carneiro DM[2], Zhang Y[3],Marinho ELAM4, Marinho EAV[2], Lima AJO[2], Berro LF5. [1]UESC, PPG Health Sciences, Brazil, [2]UESC, Dept Health Sciences, Brazil, [3]Research Triangle Institute, USA, [4]UESC, Dept Biological Sciences, Brazil, [5]University of Mississippi Medical Center, USA

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03.037 **N,N-dimethyltryptamine Produces Sustained Antidepressant- and Anxiolytic-Like Effects in Helpless Mice: Comparison with S-Ketamine**. Sousa-Silva AN, Moura CA, Torres CIO, Marques VB, Silva JMN, Gavioli EC. UFRN, Dept Biophysics and Pharmacology, PPG in Psychobiology, Natal, RN, Brazil.

03.038 **Effects of Aromatherapy with *Citrus bergamia* Essential Oil on Stress, Anxiety, and Depression in Public School Teachers: a Randomized Crossover Clinical Trial**. Sobral R[1], Santos HLS[1], Santos AF[2], Silva GNB[1], Silva BM[1], Sette-de-Souza PH[2], Albuquerque PBSA[1,2]. [1]UPE, PPG Biologia Celular e Molecular Aplicada, Brazil, [2]UPE, PPG Saúde e Desenvolvimento Socioambiental, Brazil.

03.039 **Antinociceptive Effect of Cinnamaldehyde in Male Mice: an *in silico* and *In vivo* Mechanistic Investigation**. Rêgo RIA[1], Pires HFO[1], Dias AL[1], Remigio MCRB[1], Andrade HHN[2], Silva PR[1], Sousa NF[1], Scotti L[1], Scotti MT, Salvadori MGSS, Castro RD[1]. [1]UFPB, PPG in Natural and Synthetic Bioactive Products, João Pessoa, Paraíba, Brazil; [2]PeFarM-UFPB, Institute of Research in Drugs and Medicines, João Pessoa, Paraíba, Brazil

03.040 **Meningeal Inflammatory Responses and Long-Term Behavioral Alterations Induced by Adolescent Stress**. Coelho S, Pigatto G, Meschick CG Verza FA, Freitas IS, Grigório-de-Sant'Ana M, Guimaraes FS, Cunha TM, Gomes FV. FMRP-USP, PPG em Farmacologia , Brasil

Totem 11

03.041 **Sex-Independent Recruitment of the Dorsal Periaqueductal Gray in Fear Memory Expression, Consolidation, and Generalization**. Zanoveli JM, Cunha JM, Oliveira PHA, Silva AHBL UFPR, Dept Pharmacology, Brazil.

03.042 **Modulation of Social Behavior in Adult Zebrafish: A Systematic Review and Meta-Analysis**. Gallas-Lopes M[1,2], Müller DV[1,2], Abreu MB[1,3], Arbo BD[1,2], Bastos LM[1,2], Fröhlich NT[1,4], Marcon M[1,5], Moraes IB[1,6], da Silva LCCP[1,7], Zurchimitten GR[1,8], Herrmann AP[1,2] [1]BRISA ColLaboration, Brazil, [2]UFRGS, Dept. of Pharmacology, Brazil, [3]UFRJ, Institute of Biophysics Carlos Chagas Filho, Brazil, [4]UFRGS, Dept. of Biochemistry, Brazil, [5]UFTM, Dept. of Biochemistry, Pharmacology and Physiology, Brazil, [6]UFOB, Center of Biological and Health Sciences, Brazil, [7]Fiocruz, Institute of Science and Technology in Biomodels, Brazil, [8]UFSC, Dept. of Pharmacology, Brazil

03.043 **Dealing with the Enemy: Antidepressant-Like Effects of N-Acetylcysteine Treatment in Vulnerable Rats to Social Defeat Stress**. Morais-Silva G[1,2], Giatti LO[2], Martins LLS[2], Marin MT[2]. [1]UEM, Dept. of Pharmacology and Therapeutics, Graduate Program in Pharmaceutical Sciences, Brazil. [2]Unesp, School of Pharmaceutical Sciences of Araraquara, Lab Pharmacology, Interinstitutional Graduate Program in Physiological Sciences UFSCar/Unesp, Brazil.

03.044 **Octovespin Ameliorates Cognitive Impairment and Amyloid-β Aggregation in Experimental Alzheimer's Disease**. Camargo LC[1], Alves LG[2], Veras LG[2], dos Santos VRM[2], Só YAdO[3], Costa CVS[3], Gargano R[3], Mortari MR[2] [1]UnB, Psychology Institute, Psychobiology Lab, PPG Behavior Sciences, Brazil; [2]UnB, Biological Sciences Institute, Neurofarmacology Lab, Brazil; [3]UnB, Physics Institute, Brazil

04. Inflammation and Immunopharmacology

Totem 12

04.009 **Differential Effect of Fluoxetine in the Febrile Response Induced by Lipopolysaccharide in Male and Female Rats**. Pereira V, Alencar TS, Schneider RC Schneider VMM, Borges AP, Costa RA, Baggio D, Zampronio AR UFPR Inflammation and Fever Lab Dept Pharmacology Brazil

04.010 **Healing Effect of Alginate Biomembrane with Biochanin A in Mice**. Brito SC[1], Aragão JMDA[1], Biano LS[1], Nascimento ACS[1], Ramos LS[1], Sales MR[1], Santos GJ[1], Vasconcelos ABS[1], Albuquerque-Júnior, RLC[2], Grespan R[1], Camargo EA[1] [1]UFS-São Cristovão, PPG Physiological Sciences, Lab Pharmacology of the Inflammatory Process, Dept Physiology, SE, Brazil; [2]UFSC, Dept Pathology, Lab Oral Pathology

04.011 **Impact of Diabetes and Annexin A1 Deficiency on Intact Skin Architecture**. Oliveira SS[1], Oliveira SM2, Gil CD[1], Silva RA[1], Ferreira LPS[1], Santos DD[1], Mimura KKO[1] [1] Unifesp, São Paulo - SP, Brasil. [2] UFMT-Pontal do Araguaia – MT, Brasil.

04.012 **Effect of the Phenylacetamide Derivative JM-01 on Leukocyte Migration in a Zymosan-Induced Peritonitis Model**. Silva Netto LS[1], Serra GL[2], Ferreira Gonçalves MC[3], Neri LCD[2], Souza Cunha MV[1], Freire Macêdo ME[2], Stiebbe Salvadori MGS[3,4,5], Moura RO[6], Santos VL[6], Villarreal CF[7], Oliveira Golzio AMF[5,8], Silva PR[5] [1]UFPB, Pharmacy, Brazil; [2]UFPB, Biomedicine, Brazil; [3]UFPB, PPG Natural and Synthetic Bioactive Products, Brazil; [4]UFPB, CCHLA, Dept. Psychology, Brazil; [5]UFPB, PPG Cognitive Neuroscience and Behavior, Brazil; [6]UEPB, PPG Pharmaceutical Sciences, Brazil; [7]Fiocruz, Instituto Gonçalo Moniz, Brazil; [8]UFPB, Dept. Food Technology, Brazil

04.013 **Anti-Inflammatory and Antioxidant Effect of Glycitein in a Mouse Model of Ear Edema**. Sales MR, Nascimento ACS, Santos GJ, Souza DA, Nunes ERS, Brito SC, Grespan R, Aragão JMDA, Camargo EA. UFS, PPG Physiological Sciences, Brazil.

Totem 13

04.019 **Anti-Inflammatory and Antioxidant Effects of the Total Polysaccharides of *Caesalpinia ferrea* Bark and Pod in Intestinal Mucositis Induced by 5-Fluorouracil**. Costa MEP[1], Santiago MLA[1], Pereira LK[1], Pinto CCC[3], Souza, EP[2.], [1]UNINTA, Faculdade de Medicina, [2]UFC, Faculdade de Medicina, Depto Morfologia, PPG de Ciências Morfofuncionais, [3]UNINTA, Faculdade de Medicina, Lab Microbiologia.

04.014 **Functional Study of 7-Nitroindazole Derivative Compounds on Edema and Vascular Smooth Muscle**. Santiago MLA[1], Costa MEP[1], Pereira, LK[1], Pinto CCC[2], Souza E[3] [1]UNINTA, Faculdade de Medicina, [2]UNINTA, Faculdade de Medicina, Lab Microbiologia, [3]UFC, Faculdade de Medicina, Depto Morfologia, PPG de Ciências Morfofuncionais

04.015 **Evaluation of Cell Viability and Nitrite Production by the Phenylacetamide Derivative JM-01 in J774 Macrophages**. Serra GL[1], Silva Netto LS[2], Gonçalves MCF[3], Neri LCD[1], Cunha MVS[2], Macêdo MEF[1], Salvadori MGSS[3,4,5], Moura RO[6], Santos VL[6], Villarreal CF[7], Golzio AMFO[5,8], Silva PR[5] [1]UFPB, Curso de Graduação em Biomedicina, Brazil, [2]UFPB, Curso de Graduação em Farmácia, Brazil, [3]UFPB, PPG em Produtos Naturais e Sintéticos Bioativos, Brazil, [4]UFPB, Centro de Ciências Humanas Letras e Artes, Depto Psicologia, Brazil, [5] UFPB, PPG em Neurociência Cognitiva e Comportamento, Brazil, [6]UEPB, PPG em Ciências Farmacêuticas, Brazil, [7],Fundação Oswaldo Cruz, Instituto Gonçalo Moniz, Brazil, [8]UFPB, Depto Tecnologia de Alimentos, Brazil.

04.016 **Multitarget *in silico* Evaluation of Novel Green Synthetic Acetanilides and Acetanilide–Theobromine Hybrids Targeting COX, iNOS, PDE and TLR4 Pathways**. Luís LRCS[1], Sousa M[1], Silva TG[1], Falcão MEES[1], Gadelha FAA[1], Dejani NN[1], Fiss GF[2], Luís JAS[2], Vieira GC[1]. [1]UFPB, Research Institute for Drugs and Medicines, Lab. of Immunopharmacology, Brazil. [2]UFPB, Lab. of Bioenergy and Organic Synthesis Research, Brazil.

04.017 **Renin-Angiotensin System Modulators Alter the Neutrophil-to-Lymphocyte relationship in Smokers but not in COPD Patients**. Medeiros VLD, Freitas JLC,Paiva YMA, Bezerra GB, Martins NRS, Kennedy-Feitosa E, Silva FS. UFERSA, Mossoró, Morphophysiopharmacology Lab.

04.018 **Preliminary Study of the Cytotoxicity Profile and Pharmacokinetic Characteristics of a Green Synthetic Acetanilide with Potential Application in Neuroinflammation**. Falcão MEES[1], Sousa M[1], Silva TG[1], Luís LRCS[1], Gadelha FAA[1], Dejani NN[1], Fiss GF[2], Luís JAS[2], Vieira GC[1]. [1]UFPB, Research Institute for Drugs and Medicines, Lab. of Immunopharmacology, Brazil. [2]UFPB, Lab. of Bioenergy and Organic Synthesis Research, Brazil.

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04.031 **Type 1 Diabetes Negatively Modulates Th2-Driven Airway Inflammation in a Murine Asthma Model**. Leutz MC, Barbalho TM, Oliveira AL, Horioka CP, Medeiros ML, Antunes E Unicamp, School of Medical Sciences, Lab. of Pharmacology of the Urogenital Tract and Inflammation, PPG Pharmacology, Brazil

04.032 **Pulmonary Effects of Nicotine Exposure from Cigarette Smoke and E-Cigarette Vapor in Experimental Allergic Asthma**. Rocha BM[1,2], Santos GCM[2,3,4], Motta DSE[2], Oliveira MECL[2], Santos GRA[2], Santana ACC[2], Arantes ACS[2], Ferreira TPT[2], Silva PMR[2], Martins MA[2,3,4] [1]ICB-UFRJ, , PPG Pharmacology and Medicinal Chemistry, Brazil; [2]IOC-Fiocruz, Lab Inflammation, Brazil; [3]Fiocruz, Preclinical Pharmacokinetic Platform, Brazil; [4]IOC-Fiocruz, PPG Biologia Celular e Molecular, Brazil.

04.033 **Anti-Inflammatory and Antioxidant Effects of** *Solanum stipulaceum* **Willd. ex Roem. & Schult on Cutaneous Inflammation in Mice**. Nunes ERS[1], Biano LS[1], Ramos LS[1], Sales MS[1], Souza DA[1], Silva MT[2], Matos TRG[1], Lima JCJS[1], Matos SS[3], Cavalcante MD[3], Grespan R[1], Aragão JMDA[1], Camargo, EA[1] [1]UFS, Lab Pharmacology of the Inflammatory Process, Graduate Program in Physiological Sciences, Brazil [2]UFS, Graduate Program in Natural Sciences, Brazil; [3]UFS, Graduate Program in Pharmaceutical Sciences, Brazil

04.034 **Deciphering Calcitoningene-Related Peptide (CGRP)-H_2S Crosstalk in cutaneous wound healing and Nociception**. Jamba MF[1], Tavares YPST[1], Teixeira SA[1], Brain SD[2], Muscará MN[1], Costa SKP[1] [1]ICB-USP, Depto Farmacologia; [2]King's College London-Waterloo, School of Cardiovascular Medicine & Sciences

04.035 **Therapeutic Effects of Oral** *Lactiplantibacillus plantarum* **6. 2 Supplementation on Experimental Acute Lung Injury Progression**. Santos ABR[1], Candido JPS[1], Araújo RS[1], Pessoa WFB[2], Alves AF[1,2] [1]UFPB, Program in Natural and Synthetic Products Bioactive, Brazil. [2]UFPB, Biomedical Sciences Dept, Brazil.

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04.057 **Effects of Ispinesib on Parameters Associated with Inflammatory Dynamics in Experimental Cystitis**. Oliveira MM[1], Frota-Gomes TLS[1], Souza ORB[1], Reis-Filho AC[1], Cavalcante DIM[2], Santos RF[1,3], Freitas GBL[1,3]. [1]UFPI, PPG Pharmacology, Brazil. [2]UFC, Dept Pathology and Legal Medicine, Brazil. [3]UFPI, Biochemistry and Pharmacology, Brazil.

04.058 **Increased MMP-2 Proteolytic Activity on Cardiac Function During Experimental Sepsis**. Ramos LVR, Cantão MBS, Castro MM FMRP-USP, Pharmacology Dept.

04.059 **BD-8, A Novel Digoxin Derivative, Suppresses Inflammatory Responses** *in vitro* **and Ameliorates Acute Lung Injury** *in vivo*. Ferreira DA[1], Medeiros ABA[1], Soares MM[1], Lima EA[1], Cunha TEDH[1], Magalhães DWA[1], Figueiredo ES[1], Silva TG[1], Vieira GC[1], Machado MV[2], Villar JAFP[2], Barbosa LA[2], Carvalho DCM[1,3], Mascarenhas SR[1] [1]UFPB, Lab Immunopharmacology, Biotechnology Center, UFPB, João Pessoa, PB, Brazil-Centro-Oeste Dona Lindú. [2]UFSJ-Lab Organic Synthesis and Nanostructure, UFSJ-Divinópolis, MG, Brazil. [3]ICB-UNIFAL Lab Vaccines, Dept Microbiology and Immunology, Alfenas, MG, Brazil.

04.060 **Graft-Versus-Host Disease Promotes Central Neuroinflammation and Glutamatergic Dysfunction Associated with Anxiety-Like Behavior in Mice**. Linhares AFS[1], Lima ALD[1], Berg BB[1], Rocha ES[2], Ruggio GMF[1], Sales MA[2], Silva MCM[1], Oliveira NFM[3], Campos ZDT[1], Vieira LB[4], Machado FS[5], Pinho V6, Teixeira MM[5], Oliveira ACP[4], Romero MGMC[4]. [1]UFMG, Graduate Program in Pharmacology and Physiology, Brazil; [2]UFMG, Undergraduate student in Biomedical Sciences, Brazil; [3]UFMG Graduate Program in Biochemistry and Immunology, Brazil; [4]UFMG Dept Physiology and Pharmacology, Brazil; [5]UFMG, Dept Biochemistry and Immunology, Brazil; [6]UFMG, Dept Morphology, Brazil.

04.063 **Neutrophil Polarization as an Anti-Tumor Approach**. Amorim NS[1], Amorim CS[2], Valença LS[2], Santos RCM[3], Moraes JA[2]. [1]ICB-UFRJ, Lab Biologia Redox, PPG em Biociências, UERJ, Brazil. [2]ICB-UFRJ, Lab Biologia Redox, Brazil. [3]IBCCF-UFRJ, Instituto de Biofisica Carlos Chagas Filho, Lab Glicobiologia Estrutural e Funcional, Brazil.

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04.002FR **Cardiovascular Responses to Baro-and Chemoreflex Activation in Rat Offspring Exposed to Different Maternal Folic Acid Doses**. Amorim SCB[1], Silva EGS[1], Lima LS[2], Lira MRS[2], Souza JVF[1], Silva JHC[3] [1]UFPE, Centro Acadêmico de Vitória, PPG Multicêntrico em Ciências Fisiológicas, Brasil. [2]UFPE, Centro Acadêmico de Vitória, Brasil. [3]UFPE, Centro Acadêmico de Vitória, Educação Física, Lab Multiusuário de Avaliação Física e Processamento de Sinais, PPG Multicêntrico em Ciências Fisiológicas, Vitória de Santo Antão, PE, Brasil.

04.003FR **Association Between Low Heart Rate Variability and Obesity on Blood Pressure and Glucose Metabolism in Women**. Clementino LCRF, Neves TAFV, Moraes RCS, Pereira JKG, Silva JVG, Alves JLB, Martins, VJB. UFPB, PPG in Nutritional Sciences, Brazil.

04.004FR **Influence of Different Resistance Training Volumes on Heart Rate Variability**. Pires KC[1], Vieira YLM[1], Rodrigues IJS[1], Flora JMG[1], Lacerda LT[1], Brandão CFCCM[1], Andrade MJO[2], Drummond LR[1] [1]UEMG, Dept Physical Education, Brazil; [2]UEMG, Dept Psychology, Brazil

04.005FR **Gut Microbiota and Cardiometabolic, Nutritional, and Redox Markers in Schoolchildren: A Cross-Sectional Study**. Marinho ABGF[12], Pereira JG[12], Nascimento MBESPN[12], Chongo CM[12], Silva RCF[3], Cruz HLA[4], Falcão RM[4], Simões-Alves AC[12], Balbino VQ[4], Morio B[5], Costa-Silva JH[12] [1]Lab Multiusuário de Avaliação Física e Processamento de Sinais, Centro Acadêmico de Vitória, Universidade Federal de Pernambuco, Brasil; [2]NAFPF-CAV-UFPE Lab Multiusuário em Nutrição, Atividade Física e Plasticidade Fenotípica, Brasil; [3]LABMEX-CAV-UFPE Lab Multiusuário de Bioquímica Geral, Molecular e do Exercício, Brasil; [4]Lab Bioinformática e Biologia Evolutiva, Centro de Ciências da Saúde, Universidade Federal de Pernambuco, Brasil; [5]Université Claude Bernard Lyon, França.

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05.038 **Central Sensitization in a Viral Infection Model Facilitates Migraine-like Responses in Female Rats**. Baggio DF., Borges AP., Schneider VMM., Costa RA., Alencar TS., Malheiros MB., Pereira V., Zampronio ARUFPR – Inflammation and Fever Lab, PPG Pharmacology, Brazil

05.039 **L-Malic Acid in a Mouse Model of Neuropathy: Pharmacodynamic and Pharmacokinetic Aspects**. Calazans MO[1], Viana GB[1], Machado DPD[1], Pires LO[2], Reis ISFS[2], Fernandes SOA[2], Cardoso VN[2], Romero TRL[1], Duarte IDG[1], Perez AC[1] [1]UFMG, Lab Pain and Analgesia, Dept Pharmacology, Institute of Biological Sciences, [2]UFMG, Lab Radioisotopes, Dept Clinical and Toxicological Analysis, Faculty of Pharmacy

05.040 **Treatment with Repeated Low Doses of JZL195, a Dual Inhibitor of Endocannabinoid-Metabolizing Enzymes, Fails to Reverse Thermal Hyperalgesia in Rats Subjected to a Neuropathic Pain Model**. Stein DJ[1,2], Marçal MM[1,3], Moreira ERAS1, Chagas MC1, Caumo W[1,2], Torres ILS[1,2,3] 1HCPA, Lab Pain Pharmacology and Neuromodulation: Preclinical Investigations, Brazil; [2]UFRGS, School of Medicine, PPG in Medicine: Medical Sciences, Brazil; [3]UFRGS, Institute of Basic Health Sciences, PPG in Biological Sciences: Pharmacology and Therapeutics, Brazil

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05.008 **Evaluation of the Antinociceptive Effect of Hydroalcoholic Extracts from the Leaves and Fruits of** *Libidibia ferrea* **(Mart. ex Tul.) L. P. Queiroz 2009 in a Formalin-Induced Pain Model**. Oliveira, JLS[1]; Barros, AG[1], Menezes, DP[2]; Almeida, FRC[1], Dittz, D[2] [1]UFPI, Pain Pharmacology Lab, Brazil; [2]UFPI, Antineoplastic Pharmacology Lab, Brazil.

05.009 **Antinociceptive Effects of MSCs and MSC-EVs are Associated with CXCR2 Pathway in Neuropathic Pain Mice Model**. Velozo ACL[1], Opretzka LC[2], Jesus MVAC[1], Cruz ABO[1], Santos MGS[3], Santos GC[3], Soares MBP[3], Villarreal CF[1]. [1]UFBA, School of Pharmacy, Salvador, Brazil; [2]SENAI-CIMATEC, Salvador, Brazil; [3]Fiocruz-BA, Salvador, Brazil

05.010 **Antihyperalgesic and Antinociceptive Effects of Delta-3-carene on Persistent Inflammation Induced by Complete Freund's Adjuvant in Mice Models**. Venâncio GSO, Lossavaro PKMB, Machado LL, Diniz FS, Toffoli-Kadri MC, Silva-Filho SE. UFMS, Faculty of Pharmaceutical Sciences, Food and Nutrition, Lab Pharmacology and Inflammation, PPG in Pharmaceutical Sciences, Brazil.

05.012 **Reserpine-Induced Fibromyalgia Model in Swiss Mice: Behavioral Characterization and Sex-Related Difference**. Rech KS, Camargo KGA, Brito MSC, Werner MFP UFPR, Gastrointestinal and Pain Lab., Dept Pharmacology, Brazil

05.013 **Comparative Study of Monoterpenes in the Treatment of Fibromyalgia in Murine Models: A Literature Review**. Araújo RBC[1], Oliveira, JLS[1], Jorge SAS[2]. [1]UFPI, Pain Pharmacology Lab, Brazil. [2]UFPI, Organic Geochemistry Lab, Brazil.

05.014 **Synthetic Flavonoid as a Therapeutic Alternative for the Treatment of Chemotherapy-Induced Neuropathic Pain**. Dias R, Serafini PT, Atuati SF, Oliveira SM UFSM Pain Neurobiology Lab Graduate Program in Biological Sciences: Toxicological Biochemistry, Brazil.

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05.022 **Aldehyde Dehydrogenase-2 Modulates Ethanol-Induced Neuropathy and Neuroinflammation**. Souza, DF[1]; Hösch, NG[1]; Troitiño, VC[1]; Pennachioni, NP[1]; Dallazen, JL[2]; Santos, LG[2]; Martins DO[3]; Campos, ACP[3]; Pagano, RL[3]; Zambelli, VO[1] [1]IBu, Lab Pain and Signaling, São Paulo, Brazil; [2]IBu, Centre of Excellence in New Target Discovery (CENTD), , São Paulo, Brazil. [3]HSL, Lab Neuroscience, , São Paulo, Brazil.

05.023 **Repetitive Transcranial Magnetic Stimulation Prevents the pro-Oxidative Effect of a Very Low Dose of Naltrexone and Modulates Nociception in Rats Subjected to a Model of Fibromyalgia**. Roland S[1,2], Dal Bosco T[1,3], Steimetz LC[1], da Silva BP[1], Chagas MC[1], Caumo W[1,3], Stein DJ[1,3], Torres ILS[1,2,3] [1]HCPA, Lab Pain Pharmacology and Neuromodulation: Preclinical Investigations, Brazil; [2]UFRGS, Institute of Basic Health Sciences, PPG in Biological Sciences: Pharmacology and Therapeutics, Brazil; [3]UFRGS, School of Medicine, PPG in Medicine: Medical Sciences, Brazil

05.024 **Assessment of Cognitive Deficits and Emotional Symptoms in a Model of Complex Regional Pain Syndrome Type I and the Effect of Pregabalin in Mice**. Morais RIF[1], Antoniazzi CTD[1], Fim YV[2], Brito HA[2], Dalmolin L[3], Trevisan G[1]. [1]UFSM, PPG in Pharmacology, Brazil, [2]UFSM, Undergraduate Program in Pharmacy, Brazil, [3]UFSM, Undergraduate Program in Medicine, Brazil.

05.025 **Sexual Dimorphism in Musculoskeletal Orofacial Pain Induced by Sleep Deprivation and Emotional Stress in Rats**. Alves BWF[1,2], Moura MNS[1.3], Menezes KLS[1], Nascimento RR[1.3], Magalhães FJP[1.3], Pereira LS[1], Alves MP[1], Ribeiro MVS[1], Cajado AG[1.3], Pereira AF[1.3], Vale ML[1.3] [1]NPDM-UFC, Lab Inflammation and Cancer Pharmacology, Drug Research and Development Center, Brazil; [2]UFC, Dpt of Morphology. [3]UFC, Dpt of Physiology and Pharmacology.

05.026 **Evaluation of the Effects of the Monoterpene Isopulegol on Locomotor Activity and Nociception in a Murine Model of Fibromyalgia**. Oliveira, JLS[1], Reis Filho, AC[1], Martins, RYC[1], Barros, AG, Araujo, RBC[1], Sousa, RCL[2], Almeida, FRC[1] [1]UFPI, Pain Pharmacology Lab, PPG Pharmacology, Brazil [2]UFPI, Cancerology Lab, PPG Pharmacology, Brazil.

05.028 **Sex Differences in Thermal Analgesia Induced by Pharmacoacupuncture with Melittin in Male and Female Rats**. Leonor MGR[1], Boaventura de Oliveira AM[1], Teixeira RMS[1], Almeida TC[1], Sant'anna MB[1], Marques-Porto R[2], Picolo G[1]. [1]IBu, Lab Pain and Signaling, São Paulo, Brazil; [2]IBu, Lab Development and Innovation, São Paulo, Brazil.

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06.011 **Cardiovascular Effects of Sesquiterpenes in Animal Models: A Systematic Review**. Reis GS, Reis-Sobrinho G, Santana IR, Santana AS, Silva EAP, Barreto AS. LAFAC-UFS, Dept Physiology, Lab. of Cardiovascular Pharmacology, PPG in Health and Science, Brazil.

06.012 **Sympathetic Neurogenic and Protein Kinase-Dependent Vasoconstriction Induced by Cardiotonic Steroids in Isolated Human and Animal Vessels**. Paiva JGM[1], Vieira EP1, Silva ALM[1], Oliveira IMB[1], Paz IA[1], Paulino FWV[1], Rocha MRS[1], Campos R[1], Lima CC2, Santos CF[1], Nascimento NRF[1] [1]ISCB-UECE, Lab Fisiofarmacologia Cardiovascular e Renal, PPG em Ciências Fisiológicas, Brasil. [2]ISCB-UECE, Lab Fisiologia Pulmonar, PPG em Ciências Fisiológicas, Brasil.

06.013 **Topical Treatment with a Lyophilized Hydroalcoholic Extract of *Spondias tuberosa* Fruit Peel Improves Erectile Function and Endothelial Reactivity in D-Galactose-Induced Aged Rats**. Cordeiro AIF, Soares EC, Gonçalves IGA, Veras RC, Medeiros IA UFPB, Lab Cardiovascular Pharmacology, PPG in Bioactive Natural and Synthetic Products / CCS, Brazil

06.014 **Standardization of a Neointimal Hyperplasia Model in Rat Carotid Artery: Full Lumen Occlusion and Elevated Oxidative Stress Four Weeks After Partial Carotid Ligation**. Fernandes GFS[1], Oliveira JCPL[2], Evangelista IP[1], Medeiros IA[3], Veras RC[3]. [1]UFPB, Biotechnology Center, Lab Cardiovascular Pharmacology, Brazil. [2]UFPB, Lab Cardiovascular Pharmacology, PPG in Bioactive Natural and Synthetic Products, Brazil. [3]UFPB, Dept Pharmaceutic Sciences, Health Sciences Center, Lab Cardiovascular Pharmacology, PPG in Bioactive Natural and Synthetic Products, Brazil.

06.015 **Attenuation of Angiotensin II-Induced Vasoconstriction by Novel Thiazolidinedione Derivatives in Isolated Aorta from Wistar Rats**. Silva KT[1], Ferreira JG[1], Arrospide TM[2], Alves SML[1], Aires RS[1], Santos RCA[1], Ferreira LFL[2], Dos Anjos JV[2], Silva MCC[1], Araújo AV[1] [1]UFPE, Centro Acadêmico da Vitória, Brasil, [2]UFPE, Lab Síntese Orgânica, CCEN, Brasil

06.016 **Vascular Effects Induced by Supplementation with Fermented Mangaba** (*Hancornia Speciosa*) **Pulp in Animals with Renovascular Hypertension**. Duarte MOAS, Galvão AC, Gadelha DDA, Fernandes GFS, Costa WKA, Magnani M, Medeiros IA, Falcão MSFUFPB, CBiotec, Brasil; UFPB, CCS, Brasil; UFPB, CCS, Brasil; UFPB, CBiotec, Brasil; UFPB, CT, Brasil; UFPB, CT, Brasil; UFPB, CCS, Brasil; UFPB, CBiotec, Brasil

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06.024 **Grape Pomace Attenuates Arterial Hypertension and Cardiac Remodeling in Spontaneously Hypertensive Rats**. Guimarães CS, Schiavinato TA, Costa KCM, Giachini FR UFMT, Graduate Program in Basic and Applied Immunology and Parasitology, Brazil.

06.025 **Evaluation of the Molecular Mechanisms Involved in the Antiplatelet Effect of Inosine**. Alves DS, Brazão SC, Lima GF, Brito FCF UFF, Lab. of Experimental Pharmacology, PPG Biomedical Sciences (Physiology and Pharmacology), Brazil

06.026 **Investigation of the Vasorelaxant Effect of Octyl Gallate Microemulsion in Isolated Rat Aorta**. Alves HF, Oliveira JCPL, Fernandes GFS, Veras RC, Medeiros IA UFPB, Dept Pharmaceutical Sciences, Cardiovascular Pharmacology Lab, Institute of Drug and Medicine Research, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil.

06.027 **Vascular Effects Screening of Propafenone Analogs in Isolated Aortas in Wistar Rats**. Souza, RM, Lima NCB, Silva FAO, Rocha DG, Mesquita JLF, Soares JJF, Franco VMF, Lima GC, de Mattos MC, Lima RF, Jamacaru FVF, Jorge RJB, Monteiro HSA. UFC

06.028 **Effects of *Arthrospira platensis* Supplementation on Cardiovascular Parameters in Asthmatic Rats**. Oliveira, GNM, Vieira, MM, Gadelha, DDA, Oliveira TA, Cavalcanti CO, Cruz, JC, Vasconcelos, LHC UFPB, Lab Farmacologia Funcional Prof. George Thomas, Instituto de Pesquisa em Fármacos e Medicamentos, Brazil; UFPB, PPG em Produtos Naturais e Sintéticos Bioativos, Brazil; UFPB, Programa Multicêntrico de Pós-graduação em Ciências Fisiológicas, Brazil; UFPB, Depto Biotecnologia, Brazil, UFPB, Depto Ciências Biomédicas, Brazil.

06.029 **Resveratrol Attenuates Vascular Dysfunction in Rats in a High Sugar Diet by Reducing Oxidative Stress, Visfatin and MMP-2 Activity**. Manoel LB[1], Blascke de Melo MM[1], Dourado TMH[1], Assis VO[1], Bueno EKP[1], Fazan Jr R[2], Tirapelli CR[1], Castro MM[1] [1]FMRP-USP, Dept Pharmacology, Brazil; [2]FMRP-USP, Dept Physiology, Brazil

06.030 **Inosine-Induced Vasodilation Is Partially Mediated by Endothelial NMDA Receptor Activation**. Stein AT[1,2], Brazão SC[1,2], Autran LJ[1,2], Pereira NCA[1,2], Mendes ABA[1,2], Motta NAV[1,3], Lima GF[1,2], Brito FCF[1,2]. [1]UFF, Lab. of Experimental Pharmacology, Brazil, [2]UFF, PPG Biomedical Sciences (Physiology and Pharmacology), Brazil, [3]UFF, PPG Cardiovascular Sciences, Brazil.

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06.046 **Burst-Release NO-Donor-Eluting Coatings for Balloon Angioplasty: Endothelial Protection and Restenosis Prevention in Peripheral Arterial Disease**. Silva FAO[1], Chevallier P[2], Lombardo ME[2], Viana LC[2], Mantovani D[2], Gouveia Júnior FS[3], Lopes LGF[3], Jorge RJB[1], Monteiro HSA[1] [1]UFC-Porangabuçu, Dept Physiology and Pharmacology, Graduate Program in Pharmacology - Brazil [2]Laval University, CHU de Québec Research Center, Lab Biomaterials and Bioengineering (LBB), Quebec City, QC, Canada [3] UFC-Pici, Dept Organic and Inorganic Chemistry, Lab Bioinorganic Chemistry - Brazil

06.047 **Gut Microbiota in Hypertension: Functional Signatures Linked to Inflammatory Pathways**. Brito DS[1,2], Rodrigues GA[1], Silva LS[1], Cavalcante MAR[1], Peres VCA[1], Soares JA[1], Kistner MC[1], Sena CFS[1], Santana BS, Lopes IS[1], Queiroz ATL[1], [3] Medeiros JMB, [3]Conceição E, [4]Nascimento RJM, Silva DF[1,2] [1]UFBA, Bahia, Brazil, [2]IGM-Fiocruz, PGBSMI, Brazil; [3]UFBA, Dept Nutrition Science, Brazil; [4]UFBA, Dept Bio-Interaction, Brazil.

06.048 **Cardioprotective Effect of Trans-4-Methoxy-β-Nitrostyrene in Isolated Rat Hearts Subjected to Ischemia-Reperfusion**. Freitas-Nascimento SR[1], Franco ES[1], Borges RS[2], Silva OA[3], Lahlou S[4], Duarte GP[1] [1]UFPE, Dept Physiology and Pharmacology, Brazil, [2]UFPA, Faculty of Pharmacy, Brazil, [3]UFAL, Physiology Section, Brazil, [4]UFC, Dept Physiology and Pharmacology, Brazil

06.049 **Pharmacological and Immunohistochemical Characterization of Dopamine D_2-Like Receptors in *Chelonoidis carbonarius* Aorta**. Santos EX[1], Britto-Júnior J[1], Mathias Netto FC[1], Cisota FNX [1], Said G[1], Campos R[2], Gonzalez PG[1], Souza VB[1], Antunes E[1], Wang T[3], Leite CAC[4],[1]FCM-Unicamp, Dept Pharmacology, Campinas, SP, Brazil; [2]UFC, Clinical Pharmacology Unit, Drug Research and Development Center, Fortaleza, CE, Brazil; [3]Aarhus University, Section for Zoophysiology, Dept Biosciences, Aarhus, Denmark; [4]UFSCar, Dept Physiological Sciences, São Paulo, Brazil; [5]ICB-USP, Dept Pharmacology, São Paulo, SP, Brazil.

06.050 **Mineralocorticoid Receptors Promote Th17 Polarization in Lymph Nodes while IL-17RA Drives Pro-Inflammatory Phenotypic Changes in Perivascular Adipose Tissue During Obesity**. Dourado TMH[1], Pimenta GF[1], Elias-Oliveira J[2], Rodrigues VF[2], Fazan-Junior R[3], Sartori DC[2], Tirapelli CR[4] [1]FMRP-USP, Depto Farmacologia; [2]FMRP-USP, Depto Bioquímica e Imunologia, [3]FMRP-USP, Depto Fisiologia; [4]FCFRP-USP, Depto Ciências BioMoleculares

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06.052 **The Role of Fluoxetine on Vascular Functions in Endotoxemia**. Santos TM[1], Pedersoli CA[2], Tostes RC[2], Linder AE[1] [1]UFSC, PPG Pharmacology, Brazil; [2]FMRP-USP, Dept. of Pharmacology, Brazil

06.053 **Basal Release of 6-Cyanodopamine from Rabbit Isolated Aorta and its Modulation of Vascular Reactivity**. Ali K[1], Santos EX[1], Britto-Júnior J[1], Peterson L[2], Morris JJL[2], Miller A[1,3,4], Jacintho FF[1], Moraes ME[3], Santagada V[4], Caliendo G[4], Severino B[4], Antunes E[1], De Nucci G[1,3,5] [1]FCM-Unicamp, Dept Pharmacology, Campinas, SP, Brazil; [2]Rhodes College, Dept Chemistry, Memphis, TN, USA; [3]UFC, Clinical Pharmacology Unit, Drug Research and Development Center, Fortaleza, CE, Brazil; [4]University of Naples Federico II, Dept Pharmacy, School of Medicine, Naples, Italy; [5]ICB-USP, Dept Pharmacology, , São Paulo, SP, Brazil; [6]Dept Pharmacology, São Leopoldo Mandic School of Medicine, Campinas, SP, Brazil.

06.054 **Vascular and Endothelial Actions of Rosmarinic Acid: Mechanistic Insights into Nitric Oxide Signaling and Calcium Channel Modulation**. Moser JC[1], Silva RCVAF[1], Valerie SK[2], de Souza P[1]. [1]Univali, PPG Pharmaceutical Sciences, Brazil; [2]UNISTRA, Strasbourg of University, France.

06.055 **Impact of Cilostazol on Cardiac Function and Redox Signaling in Experimental Metabolic Syndrome**. Autran LJ[1,2], Brazão SC[1,2], Lima GF[1,2], Mendes ABA[1], Assis NC[1], Motta NAV[1], Brito FCF[1]. [1] UFF, Lab. of Experimental Pharmacology, Brazil. [2]UFF, PPG Biomedical Sciences (Physiology and Pharmacology), Brazil

06.056 **Carvacrol Attenuates TRPV4 Agonist-Induced Calcium Influx and Membrane Depolarization in Rat Pulmonary Artery Smooth Muscle Cells: Experimental and Computational Evidence**. Souza Júnior JF[1,2], Sousa NF[2,3,4], Scotti L[2,3,4], Scotti MT[2,4], Guibert C[5], Quignard J-F[5], Medeiros IA[1,2,3] [1]UFPB, Cardiovascular Pharmacology Lab, Brazil. [2]UFPB, Graduate Program in Bioactive Natural and Synthetic Products, Brazil. [3]UFPB, Dept Pharmaceutical Sciences, Brazil. [4]UFPB, Cheminformatics Lab, Brazil. [5]Université de Bordeaux, Centre de Recherche Cardio-Thoracique de Bordeaux, INSERM, France

06. Biology and Metabolic and Reproductive Diseases

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06.015FR **Sexual Dimorphism in Thermoregulatory and Metabolic Responses in Cycling Rats and male**. Lopes RA[1],2; Melo MTB[1], Salustiano IM[1], Morgado VCC[1], Noronha GL[1], Martins JA[1], Santos JCS[1], Brandão CF[1,2], Lacerda LT[1,2], Andrade MJO[1,2], Campos HO3, Leite LHR4, Coimbra CC5, Lopes RA[1],2, Drummond LR[1],2[1]UEMG-Divinópolis, Brazil, [2]PPG em Biociências e Saúde Humana; Brazil; 3UEMG-Ubá, Brazil; 4UFJF, Brazil; 5UFMG, Brazil

Totem 44

06.007FR **Effects of Physical Training on Physical Performance and Dopaminergic Activity in the Preoptic Area in Hypertensive Rats**. Noronha GL[1], Martins JA[1], Lopes RA[1], Campos HO[2], Rodrigues QT[3], Silva KSC[3], Prímola-Gomes TN[4], Lacerda LT[1]; Brandão CFCCM[1]; Andrade MJO[5], Natali AJ[4], Szawka RE[3], Coimbra CC[3], Drummond LR[1] [1]UEMG, Dept Physical Education, Brazil; [2]UEMG, Dept Biological Sciences, Brazil; [3]UFMG, Dept Physiology and Biophysics, Brazil; [4]UFV, Dept Physical Education, Brazil; [5]UEMG, Dept Psychology, Brazil.

06.008FR **Effect of Physical Training on Serotonergic Activity in the Preoptic Area of Hypertensive Rats**. Martins JA[1], Lopes RA[1], Noronha GL[1], Campos HO[2], Rodrigues QT[3], Silva KSC[3], Prímola-Gomes TN[4], Lacerda LT[1]; Brandão CFCCM[1]; Andrade MJO[5], Natali AJ[4], Szawka RE[3], Coimbra CC[3], Drummond LR[1] [1]UEMG, Dept Physical Education, Brazil; [2]UEMG, Dept Biological Sciences, Brazil; [3]UFMG, Dept Physiology and Biophysics, Brazil; [4]UFV, Dept Physical Education, Brazil; [5]UEMG, Dept Psychology, Brazil.

06.009FR **Influence of the Polar Fraction of *P. aculeata* on Glycemia and Food Intake in Female Wistar Rats**. Silva EKL[1], Silva JCF[1], Franco ES2, Maia MBS2, Souto VS[1], Feitoza LHS[1], Barros CFN[1], Francelino JO[1], Araújo FWC[1], Nascimento E[1]. [1]UFPE, Dept Nutrition, Brazil. [2]UFPE, Dept Physiology and Pharmacology, Brazil.

06.010FR **Effects of the Polar Fraction of *P. aculeata* on Acute Stress Responses in Young Female Wistar Rats Subjected to Rest-Phase Time-Restricted Feeding**. Feitoza LHS[1], Silva JCF[1], Franco ES[2], Maia MBS[2], Souto VF[1], Araújo FWC[1], Barros CFN[1], Silva EKL[1], Francelino JO[1], Nascimento E[1]. [1]UFPE, Dept Nutrition, Brazil. [2]UFPE, Dept Physiology and Pharmacology, Brazil.

06.011FR **Outcomes of Rest Phase Time-Restricted Feeding on Phenotypic and Metabolic Parameters of Young Female Wistar Rats**. Barros CFN[1], Silva JCF[1], Franco ES[2], Souto VF[1], Feitoza LHS[1], Silva EKL[1], Francelino JO[1], Araújo FWC[1], Nascimento E[1]. [1]UFPE, Dept Nutrition, Brazil. [2]UFPE, Dept Physiology and Pharmacology, Brazil.

07. Endocrine, Reproductive and Urinary Pharmacology

Totem 23

07.018 **Inactivated SARS-CoV-2 Exposure Induces Pulmonary Inflammation Associated with Male Reproductive Dysfunction in K18-hACE2 Mice**. França PRC[1], Paiva JPB[1], Valente AG[1], Minho AS[1], Carvalho RS[1], Carvalho RR[2], Berbert LR[3], Frajblat M[3], Figueiredo MM[4], Marques DPA[5], Coelho-dos-Reis JGA[5], Fernandes PD[1]. [1]ICB-UFRJ, Lab Pharmacology of Pain and Inflammation, PPG Pharmacology and Medicinal Chemistry, Brazil, [2]ENSP-Fiocruz, Dept Biological Sciences, Lab Environmental Toxicology, Brazil, [3]UFRJ, Coordination of Activities with Experimental Biological Models, Brazil, [4]UEMG, Dept Natural and Earth Sciences, Brazil, [5]ICB-UFMG, Dept Microbiology, Lab Basic and Applied Virology, Brazil.

07.019 **Association of Probenecid and Tadalafil Enhances Corpus Cavernosum Relaxation in Spontaneously Hypertensive Rats**. Leonardi GR, Moretti MB, De Barros JVC, De Lima JM, Passos GR, Antunes E, Mónica FZ. Unicamp, Lab. of Lower Urinary Tract Disorders & Erectile Dysfunction, PPG Pharmacology, Brazil.

07.020 **Taurine as a Potential Modulator of Metabolic Aging and AGE–RAGE-Associated Pathways: Integrated *in silico* and Antiglycation Analyses**. Andrade EM, Souza VL, Santos PA. UFRGS, Institute of Basic Health Sciences, Dept Pharmacology, Lab Neuropharmacology and Clinical Toxicology, PPG in Pharmacology and Therapeutics. Brazil

Totem 24

07.021 **Modulation of Prostatic Carcinogenesis by Raloxifene: Histopathological and Immunohistochemical Evidence in Rats**. Pinho CF[1], Chamelete JLG[1], Silva LB[1], Takehara BAD[1], Fonseca MCBS[1], Cózaro LC[1], Santana ACP[2], Pereira S[1]. [1]Unesp-Bauru, Brazil, [2]IBB-Unesp-Botucatu, Brazil.

07.022 **Effects of Oral Gestrinone Administration on Adiposity and Hepatic Lipids in Obese Female Rats**. Ribeiro RA, Moreira AC, Santos AS, Silva RN, Scomparin DX, Rosa EPCC UEPG, Ponta Grossa, PR, Brazil.

07.023 **Tirzepatide Induces Sex-Dependent Metabolic Rescue, Anxiolytic-Like Effects, and Adipose Tissue Bioenergetic Restoration in Obese Mice**. Arancibia, JMDV[1], Domingues, DM[2], Sousa, ABS[1], Moschen, HTS[2], Ribeiro, SGPS[1], Lopes, NMCP[2], Ferreira, LD[2], Barros, WM[2], Gontijo, FSN[3], Costa, MRD[3], Goulart, JT[2], de Bem, AF[2], Amato, AA[1], Bellozi, PMQ[1] [1]UnB, Faculty of Health Sciences, Brazil, [2]UnB, Institute of Biological Sciences, Brazil, [3]UnB, Faculty of Medicine, Brazil

07.024 **Trazodone Compromises Male Reproductive Function by Damaging Testicular Tissue and Sperm Quality in Rats**. Silva Junior ED, Silva MS, Gavioli EC UFRN, Depto Biofísica e Farmacologia

07.025 **Effects of Herbal Supplements Based on *Tribulus terrestris* and *Lepidium meyenii* on the Female Reproductive System of Wistar Rats**. Lorenzon DN[1,2], Dunga CEC[1,2], Moura MJN[1,2], Oliveira LGG[1,2], Ângelo ABS[1,2], Silva AGG[1,2], Neto FES[1,2], Gomes FTS[3], Borges CS[1,2] [1]UFERSA, Lab Tissue Biology and Developmental Toxicology, Brazil, [2]UERN, Multicenter Graduate Program in Biochemistry and Molecular Biology, Brazil and [3]UERN, Lab. of Experimental Neurology, Brazil.

07.026 *Citrus sinensis* (L.) **Osbeck var. Moro extract (MOROSIL®): A Potential Adjuvant in the Treatment of Male Infertility**. Rosa GA[1], Feres MP[1], Oliveira LV[1], Lima GF, Brazão SC[1], Bragança LAR[1], Ribas JAS[1], Santos CM[2], Martins MA[3], Brito FCF[1], Marostica E[1]. [1]UFF, Dep. Physiology and Pharmacology, Lab Experimental Pharmacology, PPG Biomedical Sciences, Niterói, RJ, Brazil. [2]LEPHEC-UFF, Dep. Morphology, Niterói, RJ, Brazil. [3]UERJ, Dep. Pharmacology and Psycology, RJ, Brazil.

08. Respiratory and Gastrointestinal Pharmacology

Totem 23

08.038 *Arthrospira platensis* **Improves Intestinal Redox Homeostasis by Reducing Ileal $O_2^{\bullet-}$ and Increasing NRF2 Immunoreactivity in Hypercaloric Diet-Fed Wistar Rats**. Diniz AFA[1,2]; Claudino BFO[1,2], Santos TJ[1,5], Oliveira JCPL[2,3]; Fernandes GFS[3,4], Barbosa YV[1,2] Silva JMA[1,2], Arruda RRA[1,2], Melo MB[1,5], Sousa-Filho JEC[1,5], Cavalcanti BC[1,2], Medeiros IA[2,3], Veras RC[2,3], Silva BA[1,2,5] [1]UFPB, Lab Functional Pharmacology Prof. George Thomas, Institute of Research in Drugs and Medicines, Brazil; [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil; [3]UFPB, Lab. of Cardiovascular Pharmacology, PPG Natural and Synthetic Bioactive Products, Brazil; [4]UFPB, Center of Biotechnology, Dept. of Biotechnology, Brazil; [5]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil

Totem 25

08.013 **Evaluation of Acute Toxicity AND Antidiarrheal Activity of β-Pinene in Mice**. Pessoa LF, Menezes PMF, Alves VP, Pessoa MMB, Pessôa MLS,Batista LMUFPB, Gastrointestinal Pharmacology Lab, Brazil.

08.014 **Losartan does not Reduce the Risk of Respiratory Exacerbations in Hypertensive Smokers**. Costa GG, Santos JRA, Vidal TIR, Silva FS, Kennedy-Feitosa E Morphophysiopharmacology Lab, Federal University of the Semiarid Region (UFERSA), Mossoró, Brazil.

08.015 **Effect of LASSBio-468 on 5-fluorouracil-Induced Intestinal Mucositis in Mice**. Ferreira ABA[1], Monteiro CES[1], Franco AX[1], Silva BVL[1], Silva TML[1], Sales TMAL[2], Alicrim SAC[1], Monte AVO[1], Lopes AS[1], Souza MHLP[1], Soares PMG[1] [1]UFC, Lab Gastrointestinal Physiopharmacology Studies, Brazil; [2]USP, Immune Health Lab, Brazil.

08.016 **Lemon Gum Reduces Esophageal Inflammation and Oxidative Stress in Experimental Reflux Esophagitis**. Pimentel TFM[1], Teixeira LFLS[2], Silva KC[2], Ribeiro FOS[3], Freitas RA[4], Palumbo-Júnior A[5], Medeiros JVR[2], Souza MHLP[6], Cordeiro LMC[4], Silva DA[1], Nicolau LAD[2]. [1]UFDPar, Lab Inflammation and Translational Gastroenterology, Parnaíba, PI, Brazil. [2]UFDPar, PPG in Biotechnology, Parnaíba, PI, Brazil. [3] UFPR Dept Chemistry, PR, Brazil. [4] UFPR, BioPol, Dept Biochemistry and Molecular Biology, Curitiba, PR, Brazil. [5]UFC, Dept Physiology and Pharmacology, Fortaleza, CE, Brazil. [6]UFC Faculty of Medicine, , Fortaleza, CE, Brazil.

08.017 **The Use of a Pressurized Metered Dose Inhaler with Spacer at the Pediatric Emergency Care Units**. Dorneles GL[1], Matos IF[2], Silva GS[1], Pires ARL[1], Castro PFS[1] [1]UEG, Biomedicine Program, Brazil; [2]UniEvangélica, Nursing Program, Brazil.

08.018 **Eugenol Attenuates Pulmonary Parenchymal Damage in a Cigarette Smoke-Induced COPD Mouse Model**. Santos JRA[1], Amorim-Carmo B[1], Costa GG[1], Oliveira MF[2], Silva FS[1], Kennedy-Feitosa E[1] [1]UFERSA, Morphophysiopharmacology Lab ; [2]UFERSA, Dept Animal Science

Totem 26

08.033 *In vitro* and *In vivo* Evaluation of the Gastric Healing Effects of a Standardized *Citrus sinensis* (L.) Osbeck (Morosil®) Extract. Paz APS[1,2], Souza EMC[1], Ferreira RCS[1], Cardoso LP[1,2], Araújo BS[1], Ferreira DS[1], Kurogi KS[1], Lima IKC[1], Madeira LDPS[1], Mello VJ[1] [1]UFPA, Instituto de Ciências Biológicas, Lab Pesquisa, Ensino e Extensão em Análises Clínicas (LACPEE), Brazil; [2]PPG Farmacologia e Bioquímica

08.035 Effects of Bile Acids on Tracheal and Aortic Smooth Muscle Contractility in Isolated Rat Preparations. Abdourahmane D, Sampaio MS, Magalhães PJC UFC, Lab Smooth Muscle Pharmacology, PPG Pharmacology, Brazil

08.036 Effects of Selective Agonists of Bile Acid Receptors TGR5 and FXR on the Contractility of Isolated Rat Esophagus. Sampaio MS, Dairou A, Magalhães PJC UFC, Lab Smooth Muscle Pharmacology, PPG Pharmacology, Brazil

08.037 Effect of Kefir in Experimental Models of Gastroesophageal Reflux Disease: Changes in Gastric Juice and Effects on the Esophageal Mucosa. Silva KC[1,3], Gomes IAB[1,3], Teixeira LFLS[1,3], Oliveira ACP[1,3], Souza HCA[1], Oliveira AP[3], Medeiros JVR[1,3], Rocha JA[1], Gois MB[2], Nicolau LAD[1,3]. [1]UFDPar, PPG in Biotechnology, Brazil. [2]UFR, PPG in Biosciences and Health, Brazil. [3]UFDPar, Lab Inflammation and Translational Gastroenterology, Brazil.

09. Natural Products and Toxinology

Totem 27

09.031 Evaluation of the Genotoxicity and Antigenotoxicity of Natural and Aminated Red Angico Gum (*Anadenanthera colubrina*) in an *In vivo* Model of *Drosophila melanogaster*. Sousa JS[1], Castro AJS[1], Araújo DD[1], Silva DA[2], Ribeiro FOS[2], Araújo AJ[1], Marinho-Filho JDB[1] [1]UFDPar, Lab Cultura de Células do Delta, Brasil; [2]UFDPar, Núcleo de Pesquisa em Biodiversidade e Biotecnologia, Brasil

09.032 The Esophagoprotective Effect of Spilanthol, an N-Alkylamide from *Acmella oleracea*, In Experimental Gastroesophageal Reflux Disease. Santos BL[1], Monte MM[1], Oliveira ASS[2], Rodrigues MVN[2], Rodrigues RAF[2], Silva LMG[3], Souza MHLP[3], Sales TMAL[4], Rocha JA[5], Alves SKS[5], Nicolau LAD[1,5] [1]UFDPar, Lab Inflammation and Translational Gastroenterology, Brazil. [2]Unicamp, Multidisciplinary Center for Chemical, Biological and Agricultural Research, Brazil. [3]UFC, Lab Gastrointestinal Physio-Pharmacology Studies, Brazil. [4]USP, Ribeirão Preto Medical School, Brazil. [5]UFDPar, PPG in Biotechnology, Brazil.

09.033 Bioprospecting of Aqueous Extracts from *Pleurotus* spp. Mushrooms Cultivated on Agricultural Residues: Evaluation of Irritant Potential. Dantas MEA[1,2], Alves AKL[1,2], Costa-Neto RC[5,2], Araújo ES[5,2], Brito JM[1,3], Nascimento JRS[1,3], Silva KKF[1,4], Barbora KMS[5,6], Araújo PL[5,6], Pereira FO[5,7], Dantas BB[1,7] [1]UFCG, Lab of the Curimataú Cancer Observatory (OCC), Brazil; [2]PIBIC/UFCG; [3]UFCG, PPGCNBiotec, Brazil; [4]UFPB, Renorbio, Brazil; [5]Lab of the Fungi Research Group, Brazil; [6]UFPB, PPGCN, Brazil; [7]UFCG, Education and Health Center, Brazil

09.034 Lyophilized Hydroalcoholic Extract of *Spondias tuberosa* Arruda Leaves Reduces D-Galactose-Induced Oxidative Stress and Cellular Senescence-Associated β-galactosidase Activity in Endothelial Cells. Pereira MEM[1], Gomes MLC[1,2], Albuquerque MN[1], Souza CMO[1,2], Fernandes GFS[1], Oliveira JCPL[1,2], Oliveira GD[5], Medeiros KCP6, Farias LRT[4], Langassner SMZ[4], Nascimento YM[2,5], Veras RC[1,2,3], Medeiros IA[1,2,3], Araújo IGA[1,2,3] [1]UFPB, Cardiovascular Pharmacology Lab, Institute for Drug and Medicine Research, Brazil. [2]UFPB, PPG in Bioactive Natural and Synthetic Products (PgPNSB), Health Sciences Center, Brazil. [3]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil. [4]UFRN, Pharmacognosy Lab, Brazil. [5]UFPB, Multi-User Lab for Characterization and Analysis, Brazil. 6UFRN, Dept Morphology, Brazil.

09.035 **Brown Propolis from** *Mimosa tenuiflora* **Attenuates Oxidative Stress in a Rat Model of Allergic Asthma**. Souza MLB, Felício IM, Alves BFL, Figueiredo IAD, Golzio, AMFO, Silva TMS, Picot L, Cavalcante FA PPgPNSB/CCS/UFPB/Brazil, DPOA/CTDR/UFPB/Brazil, DQ/UFRPE/Brazil, , DCB/CCS/UFPB/Brazil La Rochelle Université/France

09.036 **Bioactive Compounds from Cocoa Bean Shells Protect Human Keratinocytes against UVB-Induced Photodamage**. Santos LFS[1], Queiroz LL[1], Vidal DM[1], Lopes MTP[3], Lima MD[1], Freitas KM[4] [1]UESC, Dept of Chemistry, [3]UFMG, Pharmacology, Belo Horizonte/MG, [4]UESC, Health Science, PPGCS, Ilhéus, BA, Brasil.

09.037 **Biocompatibility and Molecular Changes in L929 Fibroblasts Induced by the Essential Oil of** *Pectis brevipedunculata* **(Gardner) Sch. Bip.** Lima GMSF[1], Lima RF[2], Reis ATF[3], Carvalho TGPM[4], Andrade LGS[5], Diniz Filho JFS[6], Barreto FS[7], Andrade MS[7], Rocha CQ[8], Carvalho RC[9], Dittz Junior D[10], Cartágenes MSS[2] [1]UFMA, LEED, Pharmacy Course, Brazil, [2]UFMA, LEED, PPGSAD, Brazil, [3]UFMA, LEED, PPGCS, Brazil, [4]UFMA, LEED, Renorbio, Brazil [5] UFMA, LQPN, Pharmacy Course, Brazil [6]UFMA, Bacabal Campus, Brazil [7],UFMA, PPGSAD, Brazil [8]UFMA, LQPN, PPGQUIM, Brazil [9]UFMA, Animal Facility, Brazil [10]UFPI, Dept Biochemistry and Pharmacology, Brazil

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09.038 **Evaluation of Antioxidant Activity of Endophytic Fungi Extracts Isolated from** *Lactuca Sativa* **by DPPH, FRAP and ABTS Assays**. Dantas A, Oliveira G, Fonseca YM UnB-Darcy Ribeiro, School of Health Sciences, Dept. of Pharmacy, Natural Products Lab, Brazil

09.039 **Evaluation of the Antioxidant Activity of the Plant Species** *Vitex gardneriana*. Gonçalo YA, Ferreira CES, Andrade IA, Fialho MLS, Martins SO, Nóbrega VM, Oliveira MVM, Medeiros FD. Gonçalo YA, Ferreira CES, Andrade IA, Fialho MLS, Martins SO, Nóbrega VM, Oliveira MVM, Medeiros FD. UFCG-Cuité, Center for Education and Health, Brazil.

09.040 **Protective Effects of** *Spondias tuberosa* **Arruda Fruit Peel Extract on Oxidative Stress and Senescence-Associated β-Galactosidase Activity in D-Galactose-Induced Endothelial Senescence Model**. Albuquerque MN[1], Gomes MLC[1,2], Pereira MEM[1], Souza CMO[1,2], Fernandes GFS[1], Oliveira JCPL[1,2], Oliveira GD[2,5], Medeiros KCP[6], Farias LRT[4], Langassner SMZ[4], Nascimento YM[2,5], Veras RC[1,2,3], Medeiros IA[1,2,3], Araújo IGA[1,2,3]. [1]UFPB, Cardiovascular Pharmacology Lab, Institute for Drug and Medicine Research, Brazil. [2]UFPB, PPG in Bioactive Natural and Synthetic Products (PgPNSB), Brazil. [3]UFPB, Dept Pharmaceutical Sciences, Brazil. [4]UFRN, Pharmacognosy Lab, Brazil. [5]UFPB, Multi-User Lab for Characterization and Analysis, Brazil. [6]UFRN, Dept Morphology, Brazil.

09.041 **Use of a Nanoencapsulated Formulation to Enhance the Antifungal Activity of Carvacrol Against Oral** Candida albicans **Isolates**. Silva PAE[1], Costa Neto RE[1], Bezerra JAF[2], Cardoso, ALMR[2], Xavier-Júnior FH[2], Guerra FQS[1], Chaves GM[3], Silva-Rocha WP[11]UFPB, Lab Micologia Clínica, Depto Ciências Farmacêuticas, Brasil, [2]UFPB, Lab Biotecnologia Farmacêutica, Depto Ciências Farmacêuticas, Brasil, [3]UFPE, Lab Micologia Médica, Depto Micologia, Brasil.

09.042 **Healing Effect of Bioactive Polymeric Films Incorporating Gallic Acid and Ellagic Acid in Experimental Cutaneous Wounds**. Veloso RP[1,2], Amorim IF[2,3], Freitas FVS[2,3], Freitas Neto CAF[2,3], Martins HRS[2,3], Silva PHS[2,3], Moraes RR2,3, Santos LJC[1,2], Silva GFA[1,2], Souza LVSC[1,2], Reis ML[2,3], Carvalho ALM[1,2], Oliveira RCM[2,3,4]. [1]UFPI, Dermopharmacy Lab, [2]UFPI, Lab Gastrointestinal Pharmacology, [3]UFPI, PPGCF Graduate Program in Pharmaceutical Sciences, Brazil, [4]UFPI-NPPM, Medicinal Plants Research Center, Brazil [5]UFPI-PPGFarm, PPG in Pharmacology.

09.043 **Evaluation of the Antimicrobial Potential, Antibiofilm Activity, and Cytotoxic Effects of Andiroba Fixed Oil** (*Carapa guianensis*) **Against Clinically Relevant Microorganisms**. Azevedo KMS[1,3], Lacerda AF[1,2] Alves ARS[1,3], Souza PHO[2], Cunha DBL[2], Alves RV[2], Gadelha TS[2], Faheina-Martins GV[2], Vasconcelos U[2,3], Travassos RA[1,2,3] [1]UFPB, Lab FarmacoBiotecnologia (FarmaBio), Brazil; [2]UFPB, Graduate Program in Cellular and Molecular Biology (PPgBCM), Brazil; [3]UFPB, Centro de Biotecnologia (CBiotec), Brazil.

09.044 **Evaluation of the Antioxidant Activity of the Extract of** *Dysphania ambrosioides* **(L.)**. Fialho MLS, Ferreira CES, Andrade IA, Oliveira MVM, Martins SO, Nóbrega VM, Gonçalo YA, Medeiros FD. UFCG-Cuité, Center for Education and Health, Brazil.

Totem 29

09.045 *Cissampelos sympodialis* **Extract Mitigates Oxidative Stress and Lung Remodeling in Cigarette Smoke-Induced Emphysema through Nrf2-Associated Mechanisms**. Barros-Moura MM[1,2], Queiroz-Neto RF[2], Silva FS[2], Oliveira MF[2], Kennedy-Feitosa E[2] [1]FMO - Olinda, PE, Brazil; [2]UFERSA, Morphophisiopharmacology Lab, Mossoro, Brazil

09.046 **Evaluation of the Oxidative, Antioxidant, and Antimicrobial Activities of Isatin Acylhydrazone Derivatives**. Almeida Filho GP[1], Rodrigues WDT[1], Sousa LVBS[1], Marreiro VS[1], Lima TCBS[1], Carneiro CA[1], Campos CENS[1], Galdino FS[1], Costa MESM[1], Sousa FB[2], Santos ESFR[3], Pessoa HLFP[1], Lima-Junior CG[2], Diniz MFFM[1], Janebro DI[1], [1]UFPB, Toxicological Testing Lab, PPG in Bioactive Natural and Synthetic Products, Brazil; UFPB, (PPgPNSB), Brazil [2]UFPB, Paraíba Lab Medicinal Organic Synthesis (LASOM), Brazil

09.047 **Preventive and Therapeutic Actions of** *Spondias tuberosa* **Arruda Extract on Diabetes-Associated Lung Injury**. Fernandes HEO[1], Albuquerque ECS[1], Pires LAB[1], Sena VNF[1], Felipe FD[1], Vieira RR2, Santos DD2, Araújo IGA3, Gil CD2, Medeiros KCP[1] [1]UFRN, PPG Structural and Functional Biology, Brazil, [2]Unifesp, Brazil, [3]UFPB, PPG in Bioactive Natural and Synthetic Products, Brazil

09.048 **Antimicrobial and Antibiofilm Potential of Jupati Oil** (*Raphia taedigera*)**: Cytotoxicity Profile and Selectivity Index Assessment**. Lacerda AF[1,3], Alves ARS[1,3], Souza PHO[2], Cunha DBL[2], Alves RV[2], Gadelha TS[2], Faheina-Martins GV[2], Vasconcelos U[2,3], Travassos RA[1,2,3]. [1]UFPB, Lab FarmacoBiotecnologia (FarmaBio), Brazil; [2]UFPB, Graduate Program in Cellular and Molecular Biology (PPgBCM), Brazil; [3]UFPB, Centro de Biotecnologia (CBiotec), Brazil.

09.050 **Antifungal and Antibiofilm Activity of Nanoencapsulated Oregano** (*Origanum vulgare* **L.**) **Essential Oil against Clinically Relevant Yeasts**. Alves ARS[1], Pessoa JVA[1], Oliveira-Filho JMD[1], Azevedo KMS[1], Lacerda AF[1,2], Formiga ALD[3]; Santos LFA[3], Lima EO[3], Vasconcelos U[2,3], Júnior FHX[3], Travassos RA[1,2]. [1]UFPB, Lab FarmacoBiotecnologia (FarmaBio), Brazil; [2]UFPB, Graduate Program in Cellular and Molecular Biology, Brazil; [3]UFPB, Graduate Program in Bioactive Natural and Synthetic Products, Brazil.

09.051 **Renoprotective Action of Extract of** *Spondias tuberosa* **Arruda: Morphological Analysis in Experimental Diabetic Nephropathy**. Melo MEG[2] Sena VNF[1] Pires LAB[1] Felipe FD[2] Albuquerque[1] ECS Ladd FWL[3] Medeiros KCP[3] [1]UFRN, Center for Biosciences, Graduate Program in Biology Structure and Function, Brazil. [2]UFRN, Center for Biosciences, Brazil. [3]UFRN, Center for Biosciences, morphology Dept, Brazil.

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09.065 **Investigation of the Toxicological Profile of Surfactants Used in Nanoformulations in an** *in vivo Caenorhabditis elegans* **Model**. Pacheco PGS[1], Silva VGO[2], Fagundes LS[2], Sá MEB[2], Poderoso VM[2], Araujo DS[2], Lisboa JS[1], Souza JB[1], Trancoso CT[1], Cândido-Santos JH[4], Araujo ZS[3], Barreto MS[2], Silva AS[1], Guimarães AG[5], Lira AAM[5]. [1]UFS-São Cristóvão, PPG in Pharmaceutical Sciences, Brazil, [2]UFS-São Cristóvão, Dept Pharmacy, Lab. of

Clinical and Experimental Pharmacology, Brazil, [3]UFS, Campus Lagarto, PPG in Applied Health Sciences, Brazil, [4]UFS-São Cristóvão, PPG in Health Sciences, Brazil, 5UFS, Dept Pharmacy, Brazil

09.066 **Methyl Cinnamate Attenuates Epithelial-to-Mesenchymal Transition via Endoplasmic Reticulum Stress in TGF-β1-activated Alveolar Epithelial Cells**. Ferreira EGA, Barros ABB, Fidelix MSP, Silva GRS, Santana JR, Silva JP, Barreto E UFAL, Lab Biologia Celular

09.067 **From Popular Use to Scientific Evidence: Safety and Bioactivity of** *Baccharis dracunculifolia* **DC**. Bezerra CS[1], De Paula MS[1], Lowen NV[2], Higashijima AN[1], Santa-Clara RC[1], Silva GR[3], Lívero FAR[1] [1]UFPR, Cardiometabolic Pharmacology Lab, PPG Pharmacology, Brazil, [2]UFPR, Cardiometabolic Pharmacology Lab, Pharmacy Course, Brazil. [3]Unipar, Lab Preclinical Research of Natural Products, PPG Animal Science with Emphasis on Bioactive Products, Brazil.

09.068 **Effect of Orange** (*Citrus sinensis*) **Free Oil on Stearic Acid-Induced Lipid Accumulation in** *Caenorhabditis elegans*. Araújo ZS[1], Pacheco PGS[2], Barreto MS[2], Santos AS[2], Lisboa JS[2], Silva VGO[3], Sá MEB[3], Guimarães AG[1,2,3] [1]UFS-Lagarto, Graduate Program in Applied Health Sciences (PPGCAS), Brazil, [2]UFS-São Cristóvão, Graduate Program in Pharmaceutical Sciences (PPGCF), Brazil, [3]UFS-São Cristóvão, Dept Pharmacy (DFA), Brazil.

09.069 **Uvaol Mitigates TGF-β1-Induced Activation of Human Hepatic Stellate Cells Through Anti-Inflammatory and Antioxidant Mechanisms**. Barros ABB[1], Ferreira EGA[1], Fidelix MSP[1], Pereira JP[1], Lagente V[2], Barreto E[1] [1]UFAL, Lab Cell Biology, Brazil. [2]UMR991-INSERM, Université de Rennes 1, Rennes, France.

09.070 **Antioxidant and Cytoprotective Action of** *Cenostigma pyramidale* (**TUL.**) **Gagnon & G. P. Lewis in HaCaT Cells Exposed to Lipopolysaccharide**. Santos AF[1], Albuquerque, MCS[1], Silva GNB[2], Silva BM[2], Sobral R[2], Sette-de-Souza PH[1], Santos HLS[2], Correia ACC[1,3]. [1]UPE, PPG Saúde e Desenvolvimento Socioambiental, Brazil, [2]UPE, PPG Biologia Celular e Molecular aplicada, Brazil. [3]UPE, Curso de Licenciatura em Ciências Biológicas, Brazil.

09.071 **Antidiabetic Potential of Cocoa Bean Shell Extract** (*Theobroma cacao* **L.**)**: Phytochemical Profile, α-Glucosidase Inhibition, and GLP-1 Modulation**. Martins CBR, Freire GA, Xavier Filho RR, Silveira MS, Canuto KM, Wurlitzer NJ, Frederico MJS UFC, Faculty of Medicine, Dept Physiology and Pharmacology, Center for Research and Development of Medicines, Lab Biochemistry and Pharmacology, Graduate Program in Pharmacology, Fortaleza, Ceará, Brazil; UFC, Center for Agricultural Sciences, Dept Food Engineering, Graduate Program in Food Science and Technology, Fortaleza, Ceará, Brazil; EMBRAPA, Brazilian Agricultural Research Corporation, Tropical Agroindustry, Fortaleza, Ceará, Brazil.

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09. 102 **Toxicity and Genotoxicity Evaluation of the Aqueous Extract of** *Mimosa tenuiflora* (**Willd.**) **Poir.** (**Fabaceae**) **in Mice**. Santana JI[1], Dorvigny BM[2], Carvalho MEO[1], Silva TG[2], Aguilar CN[3], Chagas CA[5], Martins RD[5], Ximenes RM[2] [1]UFPE, PPG in Biological Sciences, Brazil, [2]UFPE, Dept Antibiotics, Brazil, [3]Universidad Autónoma de Coahuila, School of Chemistry, Mexico, [5]UFPE, Academic Center of Vitoria, Brazil.

09. 103 **Low Molecular Weight Heparin Improves Mouse Muscle Regeneration after Damage Induced by Bothrops Venom**. Elias SC[3], Souza PDN[1], Machado MM[1], Strauch MA[1,2], Melo PA[1]. [1]ICB-UFRJ, Lab Farmacologia das Toxinas, PPG em Farmacologia e Química Medicinal, Rio de Janeiro, RJ, Brazil; [2]ICBS-UFRRJ, Depto Ciências Fisiológicas, Seropédica, Brazil; 3FF-UFF,-Depto Farmácia e Administração Farmacêutica, Niterói, RJ, Brazil

09. 104 **Gastroprotective Effect of** *Plectranthus gandris* **Decoction Against Ethanol-Induced Gastric Lesions in Mice: Involvement of Antioxidant Activity**. Santos FA[1], Rocha LM[1], Procopio GS[1], Silva JGP[1], Ribeiro MS[1], de Araújo

KGR[1], da Silva LR[1], Fontes GCCAB[1], de Souza GS[2], da Silva MEF[2], Pessoa ODL[2]. [1]UFC, Dept Physiology and Pharmacology, Natural Products Lab, Brazil, [2]UFC, Dept Organic and Inorganic Chemistry, Brazil

09. 105 **Octyl Gallate Exhibits Antiplatelet Activity and Promotes Synergic Antithrombotic Effects in Rats When Associated with Enoxiparin**. Oliveira JCPL[1], Ramalho, RC[1,4], Fernandes GFS[1,2], Medeiros IA[1,3,4], Veras RC[1,4], [1]UFPB, Lab Cardiovascular Pharmacology, Brazil. [2]UFPB, Biotechnology Center, Brazil. [3]UFPB, PPG in Bioactive Natural and Synthetic Products, Brazil. [4]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil.

09. 106 **Effect of the Volatile Fraction of** *Thymus vulgaris* **L. (thyme) Essential Oil and Thymol on Cell Viability of Fibroblasts and Lung Tumor Cells**. Kanunfre CC[1], Santos JG[2], Verde LL[1] [1]UEPG,Dept General Biology, Ponta Grossa, PR, Brazil; [2]Unicentro, Dept Biological Sciences, Guarapuava, PR, Brazil.

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10.020 *In vitro* **Evaluation of the Cytotoxic Potential of the Petroleum Ether Extract from the Stem Bark of** *Annona vepretorum* **Mart**. Santos PBG[1], Abreu-Junior AR[2], Gomes KNC[1], Alexandre HMS[2], Marques KKG[2], Pereira ERM[2], Santana PVS[2], Araújo YKOA[1], Januario VHS[1], Silva ICF[2], Tavares JF[2], Dutra LM[3], Costa EV[4], Sobral MV[2], Gonçalves JCR[2]. [1]UFPB, Health Sciences Center, ONCOFAR, Pharmacy, Brazil, [2]UFPB, Health Sciences Center, ONCOFAR, PPG in Bioactive Natural and Synthetic Products, Brazil, [3]UFPR, Dept Chemistry, Brazil, [4]UFAM, Dept Chemistry, Brazil

10.021 **Evaluation of the Cytotoxic Activity of** *Conyza bonariensis* **(L). Cronquist. in Breast Cancer Cells**. Araújo YKO[1], Abreu-Junior AR[2], Gomes KNC[1], Santos PBG[1], Pereira ERM[1], Alexandre HMS[2], Santana JP[1], Januario VHS[1], Silvestre GFG[1], Castro IO[1], Amorim GMW[2], Tavares JF[2], Sobral MV[2], Gonçalves JCR[2]. [1]UFPB, Health Sciences Center, ONCOFAR, Undergraduate in Pharmacy, Brazil. [2]UFPB, Health Sciences Center, PPG in Bioactive Natural and Synthetic Products, Brazil.

10.022 *In vitro* **Screening of Synthetic Compounds with Cytotoxic Activity Against Human Tumor Cells**. Araujo CM[1,2], Oliveira VS[1,2], Souza SF[3], Alves RJ[4], Aquino YS[3], Lavorato SN[3], Soares, MBP[1,2], Meira CS[1,2] [1]Fiocruz-BA, Salvador, [2]SENAI CIMATEC-BA, Salvador, [3]UFOB, Barreiras, [4]UFMG, Belo horizonte.

10.023 **Evaluation of Cytoplasmic SMAD3 Immunoexpression and Its Association with Clinical Outcomes in Inflammatory Breast Cancer**. Teixeira-Filho JIF[1], Batista RER[1], Alves BES[1], Barrozo AEO[1], Maia IFVC[1], Arruda LM[2], Leitão RFC[3], Cavalcante DIM[4], Rogatto SR[5], Lima-Júnior RCP[1], Wong DVT[1]. [1]UFC, Dpt of Physiology and Pharmacology, Lab Inflammation and Cancer Pharmacology, Drug Research and Development Center, Brazil; [2]Haroldo Juaçaba Hospital, Cancer Institute of Ceará, Brazil; [3]UFC, Dpt of Morphology, Brazil; [4]UFC, Dpt of Pathology and Forensic Medicine, Brazil; [5]Unesp, Botucatu Medical School Hospital, Brazil.

10.024 **Use of Antidepressants and Potential Drug Interactions in Oncology Patients - A Bibliographic Review**. Moura AVL[1], Silva HCO[1], Medeiros AC[1], Oliveira IS[2], Lima IPG[3], Ferreira MDL[4] [1]FACENE, Graduação Farmácia, João Pessoa, PB, Brazil; [2]Unileya, Pós Farmácia Clínica Oncológica, João Pessoa, PB, Brazil; [3]FACENE, Saúde da Família, João Pessoa, PB, Brazil; [4]FACENE, João Pessoa, PB, Brazil

10.025 **Extracellular Matrix Changes Associated with Penile Carcinogenesis: A Comparative Study**. Bezerra HRR[1], Belfort MFA[1], Santos CED[1], Bastos HAC[1], Palhano NBM[1], Cavalcante DCS[1], Baltazar RS[1], Viana Sousa F[1], Moreno AVP[1], Medeiros-Fonseca[2], Faustino-Rocha AI[2], Oliveira PA[2], Medeiros R[3], Bastos MMSM[4], Brito HO[1], Gil da Costa RM[1,2,3,4]. [1]UFMA, Research Center For Experimental and Clinical Physiology and Pharmacology (NEC), Bioanalyses Lab (LabIO), Brazil; [2]University of Trás-os-Montes and Alto Douro, Centre for the Research and Technology of

Agroenvironmental and Biological Sciences , Portugal; [3]Research Center of IPO Porto, Molecular Oncology and Viral Pathology Group, Portugal; [4]University of Porto, Lab for Process Engineering, Environment, Biotechnology and Energy, Portugal.

10.026 **A Selenium Compound Induces Apoptotic Cell Death in HeLa Cervical Cancer Cells**. Rodrigues JS[1], Loureiro PBA[2], Farias APGM[2], Amorim GMW[2], Pereira ERM[2], Souza HDS[4], Silva ICF[2], Marques KKG[2], Queiroga LM[2], Scotti L[3], Scotti MT[3], Souza NF[3], Athayde Filho PFA[4], Sobral MV[2], Gonçalves JCR[2] [1]UFPB, Health Sciences Center, ONCOFAR, Undergraduate in Pharmacy, Brazil, [2]UFPB, Health Sciences Center, ONCOFAR, PPG in Bioactive Natural and Synthetic Products, Brazil, [3]UFPB, Health Sciences Center, PPG in Bioactives Natural and Synthetic Products, Brazil, [4]UFPB, PPG in Chemistry, Brazil.

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10.032 **AMTAC-17 Promotes Apoptosis and Modulates Oxidative Status in HCT-116 Colorectal Cancer Cells**. Queiroga LM[1]; Silva DKF[1]; Duarte SS[1]; Dantas MM[1]; Lisboa TMH[1]; Januário VCS[2]; Santana JP[2]; Farias APGM[1]; Ramalho IGS[1]; Ferreira RC[1]; Lyra GB[1], Pinheiro-Segundo MAS[3], Moura RO[4], Gonçalves JCR[1]; Sobral MV[1] [1]UFPB, Health Sciences Center, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]Health Sciences Center, ONCOFAR, Undergraduate in pharmacy, Brazil. [3]UFPE, PPG in Pharmaceutical Sciences, Brazil. [4]UEPB, Dept Pharmacy, Drug Development and Synthesis Lab, Brazil

10.033 **Cytotoxicity of an Indium-Based Coordination Complex in Colorectal Cancer Cell Lines: Evidence of Oxidative Stress Involvement**. Silva ICF[1], Lyra GB[1], Souza RRM[1], Dantas MM[1], Rodrigues JS[2], Amorim GMW[1], Silvestre GFG[1], Ferreira RC[1], Santana JP[2], Gomes KNC[2], Carvalho LR[3], Faria WMA[3], Tavares EC[3], Goncalves JCR[1], Sobral MV[1]. [1]UFPB, Health Sciences Center, ONCOFAR, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]UFPB, Health Sciences Center, ONCOFAR, Undergraduate in pharmacy, Brazil. [3]Unifei, Institute of Physics and Chemistry, LaCSin, Brazil.

10.034 **Selective Cytotoxicity of Novel Thiazole Derivatives Against PC-3 Prostate Cancer Cells**. Paier CRK[1], Brito TL[4], Pessoa CO[2], Almeida MCM[1], Nepomuceno FWAB[1,3], Queiroz BRA[1], Gomes JPP[2], Desiderio GA[2], Oliveira JF[1,3] [1]UFC Graduate Program in Translational Medicine, , Fortaleza, Ceará, Brazil; [2]UFC, Graduate Program in Pharmaceutical Sciences, Fortaleza, Ceará, Brazil; [3]Unilab, Institute of Health Sciences, Redenção, Ceará, Brazil, [4]NPDM-UFC, Lab of Experimental Oncology, Drug Research and Development Center

10.035 **VLA-4 Integrin and VEGFR Blockade Regulates B16F10 Melanoma Adhesion, Migration and Proliferation**. Cavalcante KDM[1], Cavalcante MLS[1], Paixão MS[2], Lima KFN[1], Monte SJH[3], Pereira EM[3], Guimarães PPG[4], Sousa JMC[5], Ferreira PMP[1,6,7], Dittz D[1,5] [1]UFPI, Graduate Program in Pharmacology, Brazil; [2]UFPI, School of Pharmacy, Brazil; [3]UFPI, Immunogenetics and Molecular Biology Lab (LIB), Brazil; [4]UFMG, Dept Biophysics and Physiology, Brazil; [5]UFPI, Dept Biochemistry and Pharmacology, Brazil; [6]UFPI, Experimental Cancerology Lab (LabCancer), Brazil; [7]UFC, Experimental Oncology Lab (LOE), Drug Development Research Center (NPDM), Brazil.

10.036 **Antiproliferative and Acute Toxicological Effects of Antidepressanhts Drugs with Repurposing Potential against Cancers**. Fernandes GS[1], Rocha KF[2,3], Souza RP[1,2], Sousa RWR[1], Freitas MM[1], Almeida ML[1], Esteves JC[1], Barbosa SLM[1], Oliveira AP[2], Oliveira ECA[3], Dittiz D[4]; Ferreira PMP[1,51]UFPI, Lab Experimental Cancerology (LabCancer), Dept Biophysics and Physiology; [2]UFPI, Lab Cardiovascular Pharmacology (Lafac), PPG in Pharmacology; [3]Toxicological Genetics Lab (Labgetox), Dept Biochemistry and Pharmacology; [4]UFPI, Lab Antineoplastic Pharmacology (Lafan), Dept Biochemistry and Pharmacology; [5]UFC, Lab Experimental Oncology (Loe), Dept Physiology and Pharmacology, Brazil

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10.047 **Apoptosis Induction by the Angucycline Saquayamycin B1 in Melanoma Cells: Involvement of Oxidative Stress and MAPK Signaling**. Silvestre GFG[1], Souza RRM[1], Marques KKG[1], Dantas MM[1], Duarte SS[1], Castro IO[1], Ramalho IGS[1], Queiroga LM[2], Araújo YKO[2], Cibulski S[3], Nascimento IJS[4], Moura RO[4], Tavares JF[5], Gonçalves JCR[1], Sobral MV[1]. [1]UFPB, ONCOFAR, PPG of Bioactive Natural and Synthetic Products, Brazil. [2]UFPB, ONCOFAR, Undergraduate in Pharmacy, Brazil. [3]UFRN, FACISA, Faculty of Health Sciences, Brazil. [4]UEPB, LDSF, PPG of Pharmaceutical Sciences, Brazil. [5]UFPB, LMCA, PPG of Bioactive Natural and Synthetic Products, Brazil.

10.057 **Antileukemic Activity of the Isoflavonoid LOE2208: Cell Cycle Arrest and Apoptosis Induction in Acute Myeloid Leukemia Cell Lines**. Sales SLA[1,2], Maranhão SS[1,2], Vieira-Neto JB[1,2]; Caleffi GS[3], Bastos RSB[1,2], Mota JA[1,2], Macêdo SMN[1,4], Oliveira KAF[1,5], Gress LSB[1,2], Desiderio GA[1,2], Santos ACF[1,6], Sasahara GL[7], Pinheiro RF[7,8], Furtado CLM[9], Pessoa C0[1,2] [1]UFC, Experimental Oncology Lab, Center for Research and Drug Development, Brazil. [2]UFC, Dept Physiology and Pharmacology, Graduate Program in Pharmacology, Brazil. [3]UFRJ, Lab Bioorganic Chemistry (LQB), Walter Mors Institute of Natural Products Research, Brazil. [4]UFC, Dept Biochemistry and Molecular Biology, Brazil. [5]UFC, Dept Biology, Brazil. [6]Uninassau, Dept Pharmacy, Brazil. [7]UFC, Cancer Cytogenomics Lab, Brazil. [8] UFC, Graduate Program in Medical Sciences, Brazil. [9]UFMG, Dept Genetics, Ecology and Evolution, Institute of Biological Sciences, Brazil.

10.058 **Antiproliferative Activity and Toxicological Profile of the Hexanic Fraction of *Tocoyena hispidula* Standl. Stems on Eukaryotic Models**. Souza RP[1], Rocha KF[1], Cruz RLC[2], Sousa RCL[3], Esteves JC[4], Sousa EA[5], Freitas MM[3], Sousa RWR[3], Oliveira ECA[2], Ferreira PMP[3],6, Chaves MH[5], Oliveira AP[1] [1]UFPI, Lab Cardiovascular Pharmacology (Lafac), Dept Biophysics and Physiology, PPG Pharmacology; [2]UFPI, Lab Toxicological Genetics (Getox), Dept Biochemistry and Pharmacology; [3]UFPI, Lab Experimental Cancerology (LabCancer), Dept Biophysics and Physiology; [4]UFPI, Lab for Research in Toxicological Genetics (Lapgenic); [5]UFPI, Lab Natural Products, Dept Chemistry; 6UFC, Lab Experimental Oncology (Loe), Dept Physiology and Pharmacology, Brazil.

10.059 **miRNA-181a-5p as a Potential Regulator of the Etoposide Response in Lung Cancer Cells**. Pegado CBS[1,2], Gomes JPA[1,2], Silva BO[1,2], Pereira MC[1,2,3] [1]UFPE, PPG Therapeutic Innovation, Brazil, [2]UFPE, Suely Galdino Center for Research in Therapeutic Innovation, Brazil, [3]UFPE, Dept Physiology and Pharmacology, Brazil

10.060 **Apoptotic and Oxidative Stress-Related Effects of the Organotellurane RF07 in MCF-7 Breast Cancer Cells**. Castro IO[1], Marques KKG[1], Dantas MM[1], Souza RRM[1], Duarte SS[1], Alexandre HMS[1], Ramalho IGS[1], Ferreira[1], RC, Januário VHS[2], Rodrigues JS[2], Santana JP[2], Sousa JMC[3], Cunha RLOR[4], Gonçalves JCR[1], Sobral MV[1] [1]UFPB, ONCOFAR, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil; [2]UFPB, ONCOFAR, Undergraduate in pharmacy, Health Sciences Center, Brazil; [3]UFPI, LAPGENIC, PostgraduateProgram in Pharmaceutical Sciences, Brazil; [4]UFABC, Center Natural and Human Sciences, Brazil.

10.061 **Oral Cashew Gum *Anacardium occidentale* L. Reduces Tumor Growth in a Syngeneic Murine B16-F10 Melanoma Model**. Machado, FS[1]; Alves, GOM[1]; Ribeiro, RMS[1]; Araújo, DD[1]; Aguiar, RPS[1]; Cajado, AG[2]; Lima Junior, RCP[2]; Ribeiro, IS[3],[4]; Paula, RCM[3]; Araujo, AJ[1]; Marinho Filho, JDB[1] [1]UFDPar, Lab Cultura Celular do Delta, Brazil, [2]UFC, Lab Farmacologia da Inflamação do Câncer, Brazil, [3]UFC, Lab Polímeros, Brazil, [4]IFPI, Brazil

10.062 **Cannabidiol Enhances 5-Fluorouracil Efficacy in Colorectal Cancer: Insights into the Molecular Mechanisms Involved**. Iughetti MF, Pereira THR, Zamarioli LS, Smaili SS, Pereira GJS, Bincoletto C Unifesp-EPM, Dept Pharmacology, Graduate Program in Pharmacology, Brazil

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10.073 **B4OCH3 Reduces Colorectal Cancer Cell Viability and Inhibits Tube Formation in HUVECs**. Oliveira MP, Ribeiro RMS, Rodrigues SS, de Sá RE, de Castro LTS, Machado FS, Pérez CN, Valeze AB, Farsky SHP, Scharf PRS, Marinho-Filho JDB, Araújo AJ UFDPar, Lab Cultura Celular do Delta, Brazil, UFG, Instituto de Química, Brazil, IFMT-Cuiabá, Brazil, USP, Lab Inflamação e Imunotoxicologia, Brazil.

10.074 **PD-L1 Gene Editing Modulates Proliferation and Response to Compounds in a Cellular Model of prostate cancer**. Pessoa CÓ[1], Manso MP[2], Correia EM[2], Scandolara TB[1], Pinheiro DP[3], Mota JA[1], Sales SLA[1], Maranhão SS[1], Vieira Neto JB[1], Gress LSB[1], Pereira JVM [1], Furtado GP[3], Bonamino MH[2], Furtado CLM[4] [1]NPDM-UFC, Drug Research and Development Center, Fortaleza, Ceara, Brazil; [2]INCa, Research Center, Rio de Janeiro, Rio de Janeiro, Brazil; [3]Fiocruz-CE, Fortaleza, Ceara, Brazil; [4]UFMG, Belo Horizonte, Minas Gerais, Brazil

10.071 **Selective Cytotoxicity and Apoptosis Induced by a *Croton velutinus* Phenylpropanoid in MCF-7 Breast Cancer Cells**. Farias APGM[1], Abrantes RA[1], Ferreira RC[1], Sousa VM[1], Amorim GMW[1], Silvestre GFG[1], Santana JP[1], Santos PBG[1], Rodrigues JS[1], Abreu LS[2], Velozo ES[3], Silva MS[4], Tavares JF[4], Gonçalves JCR[1], Sobral MV[1]. [1] UFPB, Health Sciences Center, ONCOFAR, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]UFF, Dept Organic Chemistry, Brazil. [3]UFBA, School of Pharmacy, Research Lab in Materia Medica, Brazil. [4]UFPB, Multiuser Lab for Characterization and Analysis, PPG in Bioactive Natural and Synthetic Products, Brazil.

10.072 **APT20TTMG Exhibits Antiglioblastoma Activity by Inducing Intrinsic Apoptosis and Restoring Dysregulated Splicing-Related Gene Expression in U-87 MG Cells**. Silva DKC[1,2], Oliveira VS[2,3], Lobo EB[2,3], Nogueira ML[2], Soares ES[4], Sinatti VVC[4], Silva JC[4], Bottos RM[4], Leal CBQS[4], Meira CS[1,2,3] [1]UNEB-BA, Salvador, [2]SENAI CIMATEC-BA, Salvador, [3]Fiocruz-BA, Salvador, [4]Aptah Bio Inc., San Carlos, CA, USA.

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11.006 **Drugs of Abuse and Exogenous Intoxications of Forensic Interest in Brazil: Toxic Agent, Circumstances of Exposure, and Case Evolution, 2010–2025**. Sousa C, Melo R, Geraldino B Unirio, Centro Universitário Celso Lisboa,

11.007 **A Ferroptosis Resistance Gene Score Linked to KEAP1/NRF2 and Survival in Lung Adenocarcinoma**. Xavier EEP[1,2], Mota JA[1,3], Sales SLA[1,3], Oliveira KAF[1], Soares IF[1], Macêdo SMN[1], Fernandes MCR[1,4], Rocha DD[1], Furtado CLM[1,5], Scandolara TB[1,4], Pessoa CO[1,3]. [1]UFC, Lab Experimental Oncology, Brazil, [2]UFC, Undergraduate Program in Pharmacy, Brazil, [3]UFC, PPG Pharmacology, Brazil, [4]UFC, PPG Translational Medicine, Brazil and [5] UFMG, Dept Genetics, Ecology and Evolution, Brazil.

11.008 **Chronic Toxicity and Transgenerational Effects of Polymethyl Methacrylate (PMMA) in Alternative Animal Model**. Sá MBD[1], Amorim JCG[1], Santos RG[1], Lisboa JS[2], Moura PHM[2], Silva AS[2], Pacheco PGS[2], Barreto MS[2], Souza JB[2], Araújo ZS[3], Guimarães AG[2] [1]UFS, Dept Pharmacy, São Cristovão, Brazil. [2]UFS, Graduate Program in Pharmaceutical Sciences, São Cristóvão, Brazil. [3]UFS, Graduate Program in Health Sciences, Lagarto, Brazil.

11.009 **PK/PD Modeling and Monte Carlo Simulation of β-Lactams Against Pseudomonas aeruginosa and Acinetobacter baumannii Isolates from Hospitalized Patients**. Araujo MLF[1], Ananias CF[1], Fernandes MO[1], Freitas AGS[1], Oliveira KS[1], Pinheiro NM[2], Pontes ER[1], Costa MDR[1], Duque BR[2], Sousa PCP[2], Teixeira IMM[2], Lima DTF[2], Dantas FJL[2], Sampaio TL[1] [1]UFC, Faculty of Pharmacy, Dentistry and Nursing, Dept Clinical and Toxicological Analysis, Brazil; [2]UFC, Faculty of Pharmacy, Dentistry and Nursing, PPG of Pharmaceutical Sciences, Brazil.

11.010 **Weight Loss Pens: the Multisystemic Impact of GLP-1 Analogs on the Liver and Pancreas**. Costa AC[1], Lima ES[1], Moraes TDB[1], Montenegro GMF[1], Silva ALT[2], Costa MMC[3], Guimarães CRA[1] [1]Unichristus, Brazil, [2]UFC Brazil, [3]UNESA Brazil

11.011 **Pharmacological Potential of an Isatin-Derived Oxime against Cellular Oxidative Damage Induced by Subchronic Exposure to Organophosphate Pesticide**. Batista WT, Comis Neto AA, Luzardo BFSL, Gomes J, Rodrigues ES, Fontoura EA, Strebs BL, Rosa SG, Pinton S. Unipampa-Uruguaiana, RS, Brazil.

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11.019 **Subclinical Inflammatory and Endothelial Alterations in Patients Victim of Scorpion Envenomation by** *Tityus stigmurus*. Araújo LM[1], Lopes NC[1], Souza RN[2], Almeida IM[1], Maia KM[3], Magalhães KN[3], Vasconcelos Neto H[3], Landim MJS[4], Oliveira GN[3], Albuquerque PLMM[7], Gonzalez RC[8], Meneses GC[1], Silva-Júnior GB[6], Daher EDF[2], Martins AMC[1] [1]UFC, Faculty of Pharmacy, Dept Clinical and Toxicological Analysis, PPG Pharmacology, Brazil. [2]UFC, Faculty of Medicine, PPG Medical Sciences, Brazil. [3]Dr. José Frota Institute, Toxicological Information and Assistance Center, Brazil. [4]Dr. José Frota Institute, Lab Unit, Brazil. [5]UNIFOR, Faculty of Pharmacy, Brazil. [6]UNIFOR, Faculty of Medicine, PPG Medical Sciences, Brazil. [7]Charles Darwin University, Biomedical Sciences, Australia. [8]UECE, Prof. Dias da Rocha Natural History Museum of Ceará, Brazil.

11.020 **Role of TLR4 Polymorphisms and Gut–Brain Axis Signaling in the Therapeutic Response to Natalizumab in Multiple Sclerosis**. Gimenes BD[1,2], Trefilio LM[1,3], Fernandes GG[1], Mesquita IA[1], Cardoso RC[1,2], Matos MD[1 3], Duarte LA[5,6], Pavani GK[1], Pereira VCSR[4], Domingues VB[4], Fernandez KA[4], Schmidt FR[4], Alves-Leon SV[5,6], Montes GC[1,2,3], [1]UERJ, NeuroPharmacoGenetics Lab, Brazil; [2]UERJ, PPG in Clinical and Experimental Physiopathology, Brazil; [3]UERJ, PPG in Biosciences, Brazil; [4]UERJ, Pedro Ernesto University Hospital, Brazil; [5]UFRJ, Clementino Fraga Filho University Hospital, Brazil; [6]UFRJ, Translational Neuroscience Lab, Brazil

11.022 *In vivo* **Pharmacokinetics Determination of the Anticancer Compound LOE420 by Mass Spectrometry: BioavaiLability and Biodistribution Study**. Bastos RS[1,2], Guimarães CJ[3,5], Sales SLA[1,2], Costa PMS[1,2], Pereira JVM[1,2], Mota JA[1,2], Gress LSB[1,2], Santos JEA[1], Maranhão SS[1,2], Barros-Nepomuceno FWA[1,4], Paier CRK[1,2], Moraes Filho MO[1,2], Pessoa CDÓ[1,2] [1]UFC, Lab. of Experimental Oncology, Drug Discovery and Development Center, Brazil; 2UFC, PPG in Pharmacology, Brazil; [3]Fiocruz, Institute of Pharmaceutical Technology, Brazil; [4]UNILAB, University for International Integration of the Afro-Brazilian Lusophony, Brazil; [5]FCECON, Amazonas State Cancer Control Center Foundation, Brazil

11.023 **Behavioral, Biochemical, and Endocrine Stress Responses in Zebrafish Exposed to Azithromycin, Nimesulide, and their Combination**. Seibel RS[1], Almeida PA[2], Tamagno WA[3,1], Amaral FUI[2], Prado LDSD[2], Lampugnani JAD[4], Rutikoski GW[4], Alves C[5] , FaLabreti C[5] , Tibola GM[5] , Barcellos LJG[1,2,4] [1]UFSM, PPG Ciências Biológicas: Farmacologia, Universidade Federal de Santa Maria; [2]UPF, PPG Bioexperimentação, Universidade de Passo Fundo; [3]Purdue University, School of Health Sciences, West Lafayette, IN, United States of America; [4]UPF, Curso de Medicina Veterinária, Universidade de Passo Fundo; [5]IFRS, Instituto Federal do Rio Grande do Sul.

11.024 **Beyond Addiction: Proteomic Evidence of Neurodegeneration Across Brain Regions in Alcohol Use Disorder**. Hoefel LPL[1,2], Almeida FB[1,3], Schons T[1], Ferreira CF[1], Rosa AR[1], Gomez R[1]. [1]UFRGS, PPG em Farmacologia e Terapêutica (PPGFT), UFRGS, Porto Alegre, RS; [2]UFRGS, PPG em Genética e Biologia Molecular (PPGBM), UFRGS, Porto Alegre, RS; [3]Hospital Moinhos de Vento, Faculdade de Ciências da Saúde Moinhos de Vento (FACSMV), Porto Alegre, RS

Totem 38

11.030 **Single-Dose Oral Toxicity of Coumarin Nanocapsules for Leishmaniasis Treatment: A Preclinical Study**. Gonçalves IFS[1], Araújo AB[1], Almeida JJA[1], Almeida TS[1], Pereira PIO[1], Lopes, AJSB, Colares, NN, Rodrigues NLC[2], Teixeira, MJ[2], Leal LKAM[1] [1]UFC, PPGCF, [2]UFC, Lab. of Parasitology, Brazil.

11.031 **Diesel Exhaust Particles Alter Mitochondrial and cAMP Signaling in Lung Epithelial Cells**. Carvalho AE[1,4,5], Manzano-Covarrubias AL[1,2], Cattani-Cavalieri I[1,3], Dolga A[1,2], Rafie K[1,2], Andrade MF[4,5], Schmidt M[1,2], Kennedy-Feitosa E[4,5] (1)University of Groningen, Molecular Pharmacology, The Netherlands; [2]University Medical Center Groningen, Groningen Research Institute for Asthma and COPD, The Netherlands; [3]Chapman University, Faculty of Pharmacy, Dept Biomedical and Pharmaceutical Sciences, United States; [4]UFERSA, Center for Biological and Health Sciences, Brazil; (5)UERN, Faculty of Health Sciences, Brazil

11.032 **PBPK/PD Model of Levofloxacin: Translational Platform to Predict Tissue Distribution in Humans**. Santos LO[1,2], Santos FL[1,2], Lemos JLS[1,3], Olivo LB[1], Araújo BV[1,2,3] [1]UFRGS, Pharmacokinetics and PK/PD Lab., Brazil, [2]UFRGS, PPG Pharmaceutical Sciences, Brazil, [3]UFRGS, PPG Pharmacology, Brazil

Totem 39

11.034 *in silico* **Screening admetSAR Profiles of the Nicotine: Human Using and Safety Aspects**. Costa AEA[1], Lima EMR[2], Costa CR[2], Siervo JV[1], Taricano ID[3], Silva JLV[1] [1]FMO, [2]USP, [3]UNOESTE

11.035 **Physiologically Based Pharmacokinetic-Pharmacodynamic (PBPK/PD) Modeling as a Tool for the Individualization of Antimicrobial Therapy in the Setting of Sepsis**. Olivo, LB[1]; Lemos, JLS[2]; Rodrigues, VJ[2]; Araújo, BV[1,2] [1]PPG Pharmaceutical Sciences, UFRGS; [2]PPG Pharmacology and Therapeutics, UFRGS

11.036 **Comprehensive Toxicological Assessment of Latanoprost: Safety Considerations for Expanded Therapeutic Use Beyond Glaucoma**. Picada JN[1,2],Bierhals AF1, Grivicich I2, Sousa JT2, Gomez R[1] [1]UFRGS, PPG Farmacologia e Terapêutica, Brazil, [2]ULBRA, PPG Biologia Celular e Molecular Aplicada à Saúde, Brazil.

12. Drug Discovery and Development

Totem 39

12.044 **Safety and Neurobehavioral Evaluation of a Donepezil–Thalidomide Hybrid in *Caenorhabditis elegans***. Arantes LP, Montijo RB, Cordova GL, Campos JP de, Santos AL, Morais RC de, Damasceno ACR, Colombo PC, Ortiz CJC, Viegas Júnior C UEMG, Passos, Research Group in Biochemical Pharmacology and Toxicology, Brazil. UNIFAL, Lab of Medicinal Chemistry, PPG Chemistry, Brazil

12.045 **Development of an LC-HRMS Method for the Analysis of Sickle Cell Disease New Drug Candidates in Pharmacokinetic Studies**. Cerqueira LB[1], Serafim YKBS[2], Custódio RPC[3], Rocha GP[3], Pontarolo R[1], Santos JL[2], Campos ML[3] [1]UFPR, Dept of Pharmacy, Brazil, [2]Unesp, Campus Araraquara, School of Pharmaceutical Sciences, Brazil, [3]UFMT, Campus Sinop, Healthy Sciences Institute, Graduate Program in Health Sciences, Brazil.

12.043 **Nanostructured gamma-Decanolactone Enhances Oxidative Stress Resilience in *Caenorhabditis elegans*: A Model for Healthy Aging**. De Andrade EM, De Souza VL, Garofalo CB, Farias MSR, Santos PA, Pereira P. UFRGS-Institute of Basic Health Sciences, Dept Pharmacology, Lab Neuropharmacology and Clinical Toxicology, PPG in Pharmacology and Therapeutics. Brazil

Totem 40

12.014 **Anti-Inflammatory Activity of the Compound (E)2-cyano-N-3-diphenylacrylamide (JMPR-01)**. Andrade MAJ[1], Rodrigues CVS[1], Costa TB[1], Silva PR[1], De Moura RO[2], Santos VL [11]UEPB, Lab Pharmacological Assays, Brazil, [2]UEPB, Lab Drug Design and Synthesis, Brazil.

12.016 **Formulation and Characterization of Resveratrol-Loaded Cubosomes for Improved Therapeutic Efficacy**. Santos GRA[1], Santos GCM[1,2,3], Pimentel RS[1,3], Bernardi A[1,2,3], Martins MA[1,2,3] [1]Fiocruz, Lab Inflammation, Brazil. [2]Fiocruz, Preclinical Pharmacokinetic Platform, Brazil. [3]Fiocruz, PPG Biologia Celular e Molecular, Brazil.

12.017 **FTIR Spectroscopic Characterization of Folate-Functionalized Liposomes Encapsulating 5-Fluorouracil for Targeted Colorectal Cancer Therapy**. Andrade FGA, Barroso MKA, Petrilli R, Eloy JO UFC, Faculty of Pharmacy Dentistry and Nursing, CEDEFAR/GPNANO, Brazil

12.019 **Deciphering α1A-Adrenoceptor Molecular Recognition Through Quantum Interaction Energy Analysis**. Silva MS, Gavioli EC, Fulco UL, Bezerra KS, Silva-Junior ED. UFRN, Dept Biophysics and Pharmacology, Brazil.

12.020 *In vitro* **and** *in silico* **Evaluation of the Spiro-Acridine AMTAC-18 as a Potential Antileishmanial Compound**. Lima AMAF[1,3], Silva JVV[1,3], Leandro PF[1,3], Lima MKS[1,3], Nobre MSC4, Oliveira MLA[1,3], Fernandes HQA[1,3], Farias AGC[1,2,3], Moura RO[1,2,3], Albino SL[1,2,3] [1]UEPB, Lab Desenvolvimento e Síntese de Fármacos, Brasil; [2]UEPB, PPG em Ciências Farmacêuticas, Brasil; [3]UEPB, Depto Farmácia, Brasil; [4]UFPE, PPG em Ciências Farmacêuticas, Brasil

Totem 41

12.033 **Maximizing Benznidazole Solubility: Optimization of Polymeric Solid Dispersions via Desirability**. França BCS, Amorim IS, Borba LMR, Ferreira IGS, Ferreira AS, Rolim Neto PJ UFPE

12.034 **A Novel cinnamoyl-N-acylhydrazone Compound Attenuates Ulcerative Colitis by Reducing Intestinal Inflammation in Mice**. Lontra, ACP[1], França, PRC[1], Paiva, JPB[1], Castro, FBF[1], Souza, ML[2], Franco, MRR[2], Viegas-Junior, C[2], Fernandes, PD[1] [1]UFRJ, Institute of Biomedical Science, Lab. of Pharmacology of Pain and Inflammation, PPG of Morphological Sciences, Brazil. [2]UNIFAL, Lab. of Research in Medicinal Chemistry, Brazil.

12.035 *in silico* **Evaluation of LOE2208 and Its Derivatives Reveals Predicted Interactions with Tubulin Protein and Suitable ADMET Profiles**. Lima JM[1,2], Da Costa RF[3,4], Bezerra EM[3,4], Viera-Neto JB[1,2], Falcão JS[5,6], Lapa DP[5,6], Costa PRR[5,6], Caleffi GS[5,6], Pessoa C[1,2]. [1]UFC, Lab. of Experimental Oncology, Drug Research and Development Center, Brazil; [2]UFC PPG Pharmacology, Brazil; [3]UFERSA, Lab. of Computational Physics, Brazil; [4]UFERSA, PPG Science and Engineering of Materials, Brazil; [5]UFRJ, Lab. of Bioorganic Chemistry, Research Institute of Natural Products Walter Mors, Brazil; [6]UFRJ, PPG Chemistry of Natural Products, Brazil.

12.036 **Preclinical** *in vivo* **Tests of LOE2026, a Combrestastatin a-4 (CA-4) Analogue Compound, in Zebrafish Embryos and a Xenograft Murine Model Derived from Human Colorectal Cancer Cells**. Motta LCB[1], Raymond J[2], Benedetto MC[2], Woyome VS[1], de Brito Neto JV[1], Nepomuceno FWB[1], Miguel EC[3], Vieira JHA[3], Sampaio, TL[4], Fernandes MO[4], Duarte, ASG[5], Lima LM[6], Pessoa CO[1], de Moraes MO[1], Paier CRK[1] [1]UFC, Lab. of Experimental Oncology, Brazil, [2]Institut Pasteur of Montevideo (IPMon), Lab Animal Biotechnology Unit, Uruguay, [3]UFC, Biomaterials Lab, Brazil, [4]UFC, Lab. of Clinical and Toxicological Analyses, Brazil, [5]UFC, Morphology Dept, Brazil, [6]UFRJ, Lab. of Evaluation and Synthesis of Bioactive Substances, Brazil.

12.037 **Multifunctional Nanocarriers for Local Treatment of Breast and Cervical Cancer: Development and** *In vitro* **Cytotoxicity**. Santos AA[1], Passos JS[1], Araki K[2], Lopes, LB[1] [1]ICB-USP, Dept Pharmacology, Brazil. [2]IQ-USP, Dept Fundamental Chemistry, Brazil.

12.038 **Cannabigerol-Loaded Nanostructured Lipid Carriers for Potential Application in Autism Spectrum Disorder**. Carvalho, FV[1]; Rodrigues da Silva, GH[2]; Paula, RM[3]; Rocco, SA[2]; de Paula, E[1]. [1] Unicamp, Dept of Biochemistry,

Institute of Biology, Brazil. [2]CNPEM, Brazilian Biosc. Natl Lab, Brazil. [3]Unicamp, Fac. Pharmaceutical Sciences, Brazil.

13. Immunology, Microbiology and Parasitology

Totem 42

13.001FR **Analysis of the Antimicrobial Activity of the Ruthenium-Arene Complex Against** *Streptococcus mutans* **Strains**. Sousa SLO[1], Pinheiro AA[3], Oliveira MI[6], Alves EA[1], Malveira EA[4], Holanda AKM[5], Vasconcelos MA[2], Teixeira EH4[4] [1]UFC, Integrated Lab Biomolecules, Dept Pathology and Legal Medicine, Brazil [2]UECE, Faculty of Education of Itapipoca, Brazil [3]UFC, PPG Patholgy, Brazil [4]UFC, PPG Biotechnology of Natural Resources, Brazil [5] UFC, PPG Chemistry, Brazil [6]UFSC, Dept Chemistry, Brazil

13.002FR *In vitro* **and** *in silico* **Evaluation of Hydroxylated Chalcone Derivatives as Antibiofilm Alternatives against** *Staphylococcus aureus*. Alves MF[1], Cunha HAS[1], Fiorin BC[2], Menegatti ACO[1] [1]UFPB, João Pessoa, Dept Molecular Biology, Brazil. [2]UEPG, Uvaranas, Dept Chemistry, Brazil.

13.004FR **Antibacterial Activity of a Pentadentate Copper(II) Complex Against** *Staphylococcus aureus* **Strains**. Alves EA1, Soares PV1, Sousa SLO1, Malveira EA1, Santana FWP3, Holanda AKM3, Vasconcelos MA2, Teixeira EH1 1UFC, Integrated Lab Biomolecules, Dept Pathology and Legal Medicine, Brazil, 2UECE, Faculdade de Educação de Itapipoca, Brazil, 3UFC, Bioinorganic Lab, Dept Organic and Inorganic Chemistry, Brazil

13.005FR **Chemical Characterization and Evaluation of the Antibacterial and Antibiofilm Activity of** *Cymbopogon flexuosus* **Essential Oil Against** *Staphylococcus* **sp. Isolated from Bovine Mastitis**. Zamboti B[1], Feijó FMC[2], Santos JS[3], Rodrigues THS[4], Carmo MK[5], Vasconcelos MA[6], Teixeira EH[1]. [1]UFC, PPG Biotechnology of Natural Resources, Brazil; [2]UFERSA, PPG Environment, Technology and Society, Brazil; [3]UFBA, PPG Teaching, Philosophy and History of Sciences, Brazil; [4]UVA, PPG Biotechnology, Brazil; [5] UFC, PPG Medical Microbiology, Brazil; [6]UECE, Faculty of Education of Itapipoca, Brazil.

13.006FR **Impact of Early Consumption of Ultra-Processed Foods on the Taxonomic Composition of the Gut Microbiota and Insulin Resistance Markers in School-Age Children**. Silva JVG, Clementino LCRF, Neves TAFV, Alves JLB, Martins VJB UFPB, PPG Nutritional Sciences, Brazil

14. Pharmacology: Other

Totem 43

14.005 **Vasodilatory Effect of (E,E)-Farnesol on Excitation–Contraction Coupling in Umbilical Vessels from Women with Preeclampsia**. Araújo ÉRL, Batista PR, Pereira LRS, Bastos CMS, Silva JA, Gonçalves SA, Silva PEO, Sales VS, Tavares AFC, Sousa MJS, Cavalcante JMC, Silva RER, Dias FJ, Sales EPN, Barbosa R. URCA - Excitable Cell Physiopharmacology Lab, Brazil.

14.006 **Influence of Potassium Channels on the Vasorelaxant Effect of Carveol,** *ex vivo***, in human umbilical veins**. Pereira LRS, Batista PR, Cruz JF, Sousa MJS, Bastos CMS, Silva JA, Araújo ERL, Gonçalves SA, Silva FDS, Machado STS, Silva AA, Silva RER, Dias FJ, Calixto GL, Barbosa R URCA, Lab Physiopharmacology of Excitable Cells, Brazil

14.007 **Therapeutic Potential of Polymeric Films Incorporating an N-Acylhydrazone Derivative in Burn Healing**. Silva JF[1], Nascimento BKL[1,2], Sousa BG[1,2], Dantas VG[1], Chaves MJRS[1], Medeiros KA[1,3], Guedes GG[1,3], Oliveira TKB[4], Nonaka CFW[5], Araújo PHL[1], Damasceno BPGL[1,2,3], Cavalcanti ALM[1] [1]UEPB, Lab for the Development and Characterization of Pharmaceutical Products, Brazil; [2]UEPB, PPG Pharmaceutical Sciences, Brazil; [3]UFPB, PPG Development and Technological Innovation in Medicines, Brazil; [4]UNIFACISA University Center, Brazil; [5]UEPB, PPG Dentistry, Brazil

14.008 **Terpinolene induces Vasodilation in Human Umbilical Arteries**. Silva FDS, Machado STS, Pereira LRS, Tavares AFC, Duarte MRS, Cruz JF, Sousa MJS, Sales EPN, Silva AA, Moraes LP, Araújo ERL, Sales SV, Barbosa R URCA, Lab Fisiofamacologia das Células Excitáveis, Brasil

14.009 **Integrated approach of Alternative Methods to Animal Use for the Preliminary Toxicity Assessment of Bioactive Compounds**. Alves AKL[1,2], Dantas MEA[1,2], Brito JM[1,3], Silva AP[1,3], Silva KKF[1,4], Dantas BB[1,5] [1]UFCG, Curimataú Cancer Observatory (OCC), Brazil; [2]PIBIC/UFCG; [3]UFCG, PPGCNBiotec, Brazil; [4]UFPB, Renorbio, Brazil; [5]UFCG, Academic Health Unit, Center for Education and Health, Brazil

14.010 **Adjuvant Effect of Meldrum's Acid Derivatives on Antibiotic Activity against Multidrug-Resistant Bacteria**. Araújo IM, Silva AA, de Morais LP, Machado AJT, Almeida FF, de Matos YMLS, Gondin CNFL, Begnini IM, Rebelo RA, Coutinho HDM URCA, Brazil, FURB, Brazil

15. Neurobiology and Neuronal Diseases

Totem 06

15.011FR **Functional Lateralization of the Medial Prefrontal Cortex Reveals Distinct Contributions of CRF1 and CRF2 Receptors of Cardiovascular and Behavioral Responses to Conditioned Fear in Rats**. Gomes-de-Souza L, Busnardo C, Giatti LO, Ferronato MVS, Tavares LR, Crestani CC. FCFAr-Unesp, Lab Pharmacology, Araraquara, SP, Brazil.

15.012FR **Prebiotics Enhance GPR43 and GPR109A Expression and Protect Against Hypothalamic Neuroinflammation in High-Fat Diet-Fed Mice**. Paiva IHR[1], da Silva RS[2], Peixoto CA[1] [1]IAM/Fiocruz - Lab Ultraestrutura, PPG em Biociências e Biotecnologia em Saúde, Brasil, [2]UFPE - PPG em em Ciências Biológicas, Brasil

Totem 07

15.013FR **Chemogenetic Activation of the Prelimbic–Infralimbic Circuitry Alleviates Dysfunction in Conditioned Fear Processing Following Traumatic Stress in Rats**. Crestani CC[1,], Ragonesi LM[1,] Dunn T[1,] Glorius A[1], Giatti LO[1,], Chambers J[1,] Packard B[1], Oliveira LA[1,], Herman JP[1] [1]University of Cincinnati; Dept Pharmacology, Physiology and Neurobiology; School of Medicine, Cincinnati, OH, USA; [2]FCFAr-Unesp, Lab Pharmacology, Araraquara, São Paulo, Brazil

16. Toxinology, Natural Products and Medicinal Chemistry

Totem 30

16.003FR **Antinociceptive Effect of *Libidibia ferrea* Barks Polysaccharide-Based Orabase in a Rat Model of Traumatic Lesions of the Buccal Mucosa**. Anjos CJF[1], Araújo AM[2], Oliveira LPP[1], Maciel FMS3, Gadelha CJMU[2], Fonseca SGC[4], Assreuy AMS5, Mota MRL[2], Pereira MG[1] [1]UECE/ISCB, Hemostasis and Thrombosis Lab, PPG in Physiological Sciences, Brazil. [2]UFC, Oral Pathology Lab, PPG in Dentistry, Brazil. [3]UECE/FECLESC, Bioactive Polysaccharides Lab, Brazil. [4]UFC, Pharmaceutical Technology Lab, Brazil. 5UECE/ISCB, Lab Physiopharmacology of Inflammation, Graduate Program in Physiological Sciences, Brazil.

Lectures Abstracts

Pre-Congress Course

Active Methodologies in Pharmacology Education: From Theory to Practice with PBL, Problem-Based Learning, and Playful Strategies (Metodologias Ativas no Ensino de Farmacologia: da Teoria à Prática com PBL, Problematização e Estratégias Lúdicas). Francislaine Aparecida dos Reis Lívero – UFPR

Pharmacology education faces important challenges related to the high conceptual complexity of the field, the extensive volume of content, the need to integrate basic and clinical knowledge, and recent changes in the profile of university students. In this context, active learning methodologies have been increasingly incorporated into health education as strategies capable of promoting meaningful learning, critical thinking, intellectual autonomy, motivation, and greater student engagement. Moreover, these approaches contribute to the development of essential competencies in health education, including problem-solving, decision-making, collaborative work, and integration between theory and practice. This pre-congress course aims to discuss theoretical foundations and practical applications of active methodologies in Pharmacology education, integrating scientific evidence from health education with pedagogical workshops. The course will emphasize Problem-Based Learning (PBL), addressing its origins, tutor role, construction of robust problems, assessment strategies, and integration with pharmacological content. The course will also explore Problematization Methodology and the Maguerez Arc, emphasizing conceptual differences between PBL and problematization, as well as the role of social context in learning and its interface with Pharmacology education. In addition, playful teaching strategies and gamification will be discussed, highlighting evidence related to motivation, working memory, and reasoning. By the end of the course, participants are expected to develop skills to design pedagogical products applicable to their institutional realities, including PBL cases, structured problem situations, prototypes of playful educational activities, and lesson plans integrating different active methodologies. The course also aims to strengthen Pharmacology education by promoting pedagogical innovation, didactic training, and integration among faculty members and graduate students interested in teaching and learning practices. **Financial support:** National Council for Scientific and Technological Development (CNPq).

Courses

Cr1 – **Pharmacology-Oriented Metabolomics: Biomarker Discovery and Therapeutic Targets** (Metabolômica Orientada à Farmacologia: Descoberta de Biomarcadores e Alvos Terapêuticos).

This course was designed to provide a comprehensive overview of metabolomics as applied to biomedical sciences and pharmacology. It consists of two lectures, as described below:

Integrated metabolomics: concepts, workflow, and instrumental technologies (**Metabolômica integrada: conceitos, fluxo de trabalho e tecnologia instrumental**). Adriane Ribeiro Rosa, Federal University of Rio Grande do Sul

The fundamentals of metabolomics will be presented, including its definition, historical development, classification of metabolites, and integration with other omics approaches, together with an understanding of the field's workflow, from experimental design to data acquisition and analysis. In this context, the main analytical platforms used in metabolomics will be discussed, with an emphasis on mass spectrometry coupled with chromatographic techniques, such as GC-MS and LC-MS (particularly HPLC), highlighting their applications, advantages, and limitations. Financial Support: CNPq PQ Research Fellowship

Analytical strategies in metabolomics: integrating biostatistics and case studies in pharmacology (**Estratégias analíticas em metabolômica: integrando a bioestatística e estudos de caso em Farmacologia**). Charles Ferreira, Federal University of Rio Grande do Sul

Computational data processing and statistical interpretation of metabolomics data will be addressed, covering essential preprocessing steps in conjunction with the use of established bioinformatics tools and platforms. Univariate and multivariate analysis methods will be explored, together with visualization and interpretation

strategies, such as heatmaps, metabolic networks, and biochemical pathway analyses. Finally, applications of metabolomics in pharmacology will be discussed, with an emphasis on biomarker discovery, identification of therapeutic targets, and the contribution of metabolomics to the development of personalized medicine approaches.

Cr2 – **Introduction to Atomistic Simulations of Biomolecular Systems for Drug Development** (Introdução a Simulações Atomísticas de Sistemas Biomoleculares para Desenvolvimento de Fármacos) Santiago Di Lella (University of Buenos Aires , Argentina)

The course aims to introduce the basic concepts and methods used in atomistic and molecular dynamics simulations applied to biomolecular systems, in the context of drug development. The theoretical foundations of simulations will be covered, including atomic models, force fields and the physical principles governing molecular dynamics, as well as the main steps involved in the preparation, execution and analysis of computational simulations. Methodologies for the study of protein–ligand interactions, docking methodologies, conformational stability and molecular recognition will be discussed, with an emphasis on applications relevant to pharmacological research. As examples, successful cases in computer-aided drug development will be presented, illustrating how simulations have contributed to the identification, optimization and validation of drug candidates. It is expected that by the end of the course, participants will be able to understand and critically evaluate atomistic simulations as strategic tools in the rational development of new medicines or in the identification of potential ligands for cellular targets of interest.

Cr3 – **Statistical Delusions and Questionable Research Practices** (Delírios Estatísticos e Práticas Questionáveis de Pesquisa). Ana Paula Herrmann Depto Farmacologia (UFRGS)

The course aims to explore statistical misconceptions that contribute to the adoption of questionable research practices, a problem frequently discussed in the context of the reproducibility crisis in the biomedical field. Through interactive activities, the first part of the course will focus on the meaning of the p-value along with its interpretations and limitations, with the aim of demystifying common beliefs. The impacts of low statistical power, p-hacking (improperly analyzing data to find statistically significant results, thereby increasing the risk of false positives), HARKing (hypothesizing after the results are known), and publication bias (the influence of experimental results on the decision to publish) on the reproducibility of scientific findings will be discussed. These practices will be critically explored, highlighting how they can distort the scientific record and generate false conclusions that compromise the robustness of the literature. The second part of the course will discuss experimental reproducibility estimates from large collaborative projects, alongside practical examples of failures in translating basic biomedical research findings into novel clinical applications. Participants will have the opportunity to improve their critical skills in planning, executing, analyzing, and disseminating pharmacological studies. By the end of the course, participants will be better prepared to recognize the methodological limitations of experimental assays, interpret results more cautiously, and ultimately adopt more reproducible and transparent research practices. Rather than merely presenting concepts, the course intends to stimulate reflection on common practices embedded in academic research culture and to demonstrate that concrete changes, however small, are within the reach of any researcher willing to contribute to better science.

Cr4 – **Pharmacogenetics, Toxicology, and Clinical Practice** (*Farmacogenética*, *Toxicologia e Prática Clínica*). Paulo Caleb Júnior de Lima Santos (Unifesp-EPM) / José Wilson do Nascimento Correa (UFAM) / Paulo C. Ghedini (UFG)

Individual genetic variability directly influences drug responses, impacting effectiveness and safety. Pharmacogenetics enables understanding of how genetic variants affect pharmacokinetics and pharmacodynamics, contributing to the individualization of therapy. Complementarily, toxicology investigates individual susceptibility to adverse effects and toxicities associated with chemical agents. In this context, the integration of pharmacogenetics, toxicology, and clinical practice enables safer, more effective, and person-centered therapeutic and care decisions, strengthening evidence-based use of interventions. The three research groups develop studies in these areas and may present results, perspectives, and the state of the art of scientific advances in the field.

L2 – **Traveling Along the Neutrophil Recruitment Cascade**. **Markus Sperandio**. Institute of Cardiovascular Physiology and Pathophysiology, Biomedical Center, Ludwig-Maximilians University (LMU), Munich, Germany

Neutrophils are the most abundant circulating leukocytes in humans and act as key effectors of innate immunity. For their recruitment into inflamed tissues, neutrophils rely on various glycosylated surface molecules that fine-tune the recruitment process mediating the different steps along the recruitment cascade including rolling, firm arrest, adhesion strengthening, postarrest crawling and eventually transmigration into the inflamed tissue. Focusing on these steps, I will present recent work on the E-selectin-dependent rapid NLRP3 inflammasome activation pathway in neutrophils and the accompanying release of the DAMP molecule S100A8/A9. Furthermore, I will explore the role of S100A8/A9 in terms of its extracellular and intracellular function and also discuss interesting recent findings on CXCR2-dependent signaling during the recruitment process. Supported by German Research Foundation DFG collaborative research grants TRR359 and TRR332.

L5 – **Human PMN-MDSCs: Novel Insights for Old Unanswered and Newly Emerging Questions**. Marco Antonio Cassatella Department of Medicine, Section of General Pathology, Verona, Italy

Polymorphonuclear neutrophil populations that, once purified from the blood or tissue, prove able to suppress in vitro T cell proliferation and/or T cell activation (i.e., production of IFNγ) are defined as “immunosuppressive”. Among them, the so-called PMN-myeloid-derived suppressor cells (PMN-MDSCs) represent the most investigated type of “immunosuppressive” neutrophils in humans. Human PMN-MDSCs, commonly considered to correspond to the neutrophilic cells known as low-density neutrophils (LDNs), which abnormally sediment within peripheral blood mononuclear cells (PBMCs) after blood density centrifugation, are indeed detectable in patients with cancer and other conditions. The latter includes sepsis, viral infections, severe injury and trauma, neonates, pregnant women, as well as healthy donors (HDs) subjected to G-CSF administration (named as GDs) for transplantation purposes. However, to date, most research on human PMN-MDSCs primarily focuses on their involvement in cancer, as their frequencies—usually ranging between 1 and 10% of total PBMCs—have been demonstrated to negatively correlate with tumor stage, prognosis, and therapeutic response. For years, several factors have impeded a more rapid and detailed molecular characterization of human PMN-MDSCs, including their very low numbers, their heterogeneous composition of mature and immature cells, and the lack of specific markers. Nonetheless, given advances in technology, recent research has provided a more detailed characterization of human PMN-MDSCs, including their origin, composition, transcriptomes, phenotypes, and functions. Hence, in my talk, I will not only discuss how our knowledge of human PMN-MDSCs has advanced, but also address the relationship between human PMN-MDSCs and other types of “immunosuppressive” neutrophils. Furthermore, single-cell RNA sequencing experiments have shown that human mPMN-MDSCs and tumor-associated neutrophils (TANs) share transcriptomic similarities, therefore uncovering a potential relationship between them, which will be hence discussed. This work was supported by grants from AIRC IG-27613 and PRIN20227YR8AW

L6 – **Translational Perspectives on Psychoactive Therapies for Cognitive and Substance Use Disorders**. Samantha K. Saland[1,2], Ryan Harbit[3], Florian Duclot[1,2], Gerald B. Billac[4], Charles D. Nichols[5], David E. Nichols[6], Joel M. Smith[3] & Mohamed Kabbaj[1,2] [1]Department of Biomedical Sciences, [2]Program in Neuroscience, College of Medicine; [3]Department of Chemistry and Biochemistry, Florida State University, Tallahassee, FL, USA. [4]2A Biosciences, New Orleans, LA. [5]Department of Pharmacology and Experimental Therapeutics, LSU Health Sciences Center, New Orleans, LA.[6]2A Biosciences, Chapel Hill, NC.

Alcohol Use Disorder (AUD) is a chronically relapsing and heterogenous disorder, often marked by persistent anhedonia which is difficult to treat with currently available pharmacotherapies. The need to broaden the spectrum of therapeutic options to target both consumption and co-occurring affective symptoms has spurred a resurgence in interest in psychedelics, such as lysergic acid diethylamide (LSD), for the treatment of AUD and other psychiatric

disorders. Though promising, broad utility of LSD as a treatment option is limited by negative side effects, including cardiovascular issues related to activity at the serotonin 5-HT2b receptor. To this end, we have recently synthesized novel LSD derivatives which lack 5-HT2b agonistic activity, including both full (2AB-3006) and partial (2AB-3007) 5-HT2a agonists—the latter of which lacks hallucinogenic potential. Here we compared the effects of these compounds on alcohol consumption and chronic alcohol-induced motivational anhedonia in male and female rats. Overall, our findings support and warrant further investigation into the therapeutic potential of 2AB-3006 for reducing problematic alcohol consumption and use-related anhedonia, and indicate that hallucinogenic properties may play an important role in some of the therapeutic benefits of psychedelic compounds. Ongoing work seeks to generate comparative efficacy and dose-response profiles of the novel derivatives against LSD and identify brain-wide neuronal activation patterns associated with behavioral efficacy to better understand the mechanisms contributing to these promising outcomes. Financial Support: Florida State University Seed Grant

L7 – **Regulation of Cardiovascular Functions during Extreme Conditions in Reptiles**. Tobias Wang. Section for Zoophysiology, Department of Biology at Aarhus University, Denmark

Reptiles were the first group of vertebrates to conquer terrestrial environments Earth around 320 million years ago, and are represented as todays crocodilians, turtles, lizards and snakes. As ectotherms, their body temperature and metabolism depend on the environment, and they exhibit enormous tolerance to extreme fluctuation in oxygen availability, acid-base disturbances, dehydration and starvation. In this lecture I will briefly fundamental aspects on the regulation of cardiac function and vascular tone in reptiles and will then discuss their unique ability to regulate the degree of cardiac shunting through their anatomically undivided ventricle. Out futile attempts to establish a functional role of the cardiac shunt will discussed ,and I will then devote the rest of talk to explain how the cardiovascular system supports the almost ten-fold rise in metabolism when snakes digest their enormous meals. Burggren, Filogonio and Wang (2020). Cardiovascular shunting in vertebrates: a practical integration of competing hypotheses. Biol. Rev. 95, 449-471. Wang and Rindom (021). The physiological response to digestion in snakes: A feast for the integrative physiologist. Comp. Biochem. Physiol. 254, 110891 Wang, Filogonio and Joyce (2023). Evolution of the cardiovascular autonomic nervous system in vertebrates. In Primer of the Autonomic Nervous System.

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LFR1 – **Update on DOHaD Concepts**. Erika Vanesa Cadena-Burbano[1,2]; Ana Elisa Toscano Meneses da Silva Castro[1,2,3,4]; Raul Manhães de Castro[1,2,3] [1]UFPE, PPG Neuropsychiatry and Behavioral Sciences, Center for Medical Sciences, Brazil. [2]UFPE, Studies in Nutrition and Phenotypic Plasticity Unit, Center for Health Sciences, Brazil. [3]Brazilian National Institute of Science and Technology in DOHaD, Brazil. [4]UFPE-Vitória, Nursing Unit, Vitória Academic Center, Brazil.

The Developmental Origins of Health and Disease (DOHaD) framework emerged from research investigating how early-life environmental conditions influence health and disease throughout the life course. The evolution of DOHaD reflects a shift from predominantly genetic and biomedical models toward a multifactorial perspective that integrates genetic, epigenetic, biological, environmental, psychological, and social determinants of health. Current DOHaD concepts emphasize the interaction between genotype and environment and the role of phenotypic plasticity, defined as the capacity of a genotype to produce different phenotypes under different environmental conditions. Epigenetic mechanisms may contribute to these processes by regulating gene expression without altering the DNA sequence and may reflect parental and early-life environmental exposures. The historical development of DOHaD includes the thrifty genotype hypothesis, Barker's hypothesis of fetal origins of adult disorders, the thrifty phenotype hypothesis, and the concept of fetal programming. Together, these perspectives highlight how nutritional and environmental exposures during critical or sensitive developmental periods can produce persistent changes in metabolism, physiology, and susceptibility to chronic diseases. Thus, updated DOHaD concepts reinforce the importance of intrauterine and early-life health, critical developmental windows, maternal nutrition, neurodevelopment, and the prevention of chronic and mental health disorders. This approach

supports interdisciplinary strategies aimed at identifying early-life risk factors and implementing preventive interventions across the life course. Financial support: FACEPE; CAPES; CNPq.

LFR2 – Theranostic Radiopharmaceuticals: The New Frontier of Translational Pharmacology. Fabio Luiz Navarro Marques – Faculdade de Medicina da Universidade de São Paulo

Radiopharmaceuticals are compounds developed through multidisciplinary fields encompassing aspects of molecular biology, synthetic and biological chemistry, and nuclear physics. The complementarity of these fields translates into a new tool for molecular pharmacology and precision medicine. In traditional pharmacology, pharmacokinetics is assessed by collecting and processing fluids to determine excretion and metabolism rates, while organs and tissues are harvested and processed for the subsequent quantification of the drug or its metabolites. With radiopharmaceuticals containing gamma-emitting radioisotopes, pharmacokinetic data, such as hepatobiliary and renal elimination, as well as the distribution of labeled molecules across different compartments, can be determined through real-time imaging and quantification in preclinical and clinical applications, including longitudinal studies. By replacing the gamma emitter with an alpha, beta, or Auger electron emitter in these same molecules, they are transformed into therapeutic products; thus, the theranostic concept is applied. A classic example is the FAPI (Fibroblast Activation Protein Inhibitor) radiolabeled with ^{68}Ga(gallium), which binds specifically to the FAP protein, highly expressed in the stroma of various solid tumors; conversely, when FAPI is radiolabeled with ^{177}Lu(lutetium), it acts therapeutically, destroying the tissue's carcinogenic cells. A non-classical theranostic system involves the use of ^{18}F(fluorine) radiolabeled estradiol, which allows the identification of tumor cells expressing estrogen receptors, thereby making the patient a candidate for hormonal therapy with monoclonal antibodies (mAbs). In this context, the use of mAbs radiolabeled with alpha or beta emitters enhances treatment efficacy through the synergistic action of the immunological component and the particle radiation. Another non-classical theranostic application is the use of radiopharmaceuticals to determine brain receptor occupancy rates, enabling the individualization of dosages for compounds such as benzodiazepines, allowing for better management of tolerance. This highlights the importance of radiopharmaceuticals in the new era of precision molecular medicine.

LFR3 – Medicalization of Suffering and Use of Psychotropic Drugs: An Evidence-Based Analysis. Marcos Rochedo Ferraz Departamento de Farmacologia e Psicobiologia/IBRAG/UERJ

The medicalization of psychological distress has become a defining feature of contemporary societies, accompanied by a substantial increase in psychiatric diagnoses and prescriptions for psychotropic drugs. This raises the question of whether this growing number of diagnoses necessarily indicates a proportional increase in the prevalence of mental disorders. Changes in diagnostic criteria, such as the recognition of previously untreated conditions, the lowering of diagnostic thresholds and the creation of new categories of disorders, may coexist with the increase in human suffering driven by the current neoliberal mode of production. Rising social inequality, unemployment and precariousness in relation to work, transport, security and access to healthcare, as well as human rights violations, violence, a lack of support networks and social devaluation, are the main factors linked to human suffering. We have observed an expansion in the use of psychotropic drugs, such as antidepressants, antipsychotics and anxiolytics. have been used for decades based on the promise of correcting chemical imbalances. Randomized trials and meta-analyses indicate that antidepressants produce effects of modest magnitude, often indistinguishable from a placebo, and that there is substantial inter-individual variability. The traditional hypothesis linking depression to serotonin deficiency lacks consistent evidence to support it. On the other hand, evidence suggests that the continued use of these drugs causes iatrogenic effects, such as antidepressant withdrawal syndrome, post-SSRI sexual dysfunction, hypomania, and cardiac abnormalities. Similarly, antipsychotics have been linked to tardive dyskinesia, dementia, refractory psychosis, insulin resistance, diabetes and an increased cardiovascular risk; and prolonged use of benzodiazepines has been associated with dementia and benzodiazepine-induced neurological dysfunction (BIND). Although psychotropic drugs can be valuable therapeutic tools for some individuals, their use should be guided by the magnitude of the expected

benefit, potential adverse effects, duration of treatment, individual response, psychosocial context and patient preferences.

58th Brazilian Congress of Pharmacology and Experimental Therapeutics

S1 – Molecular Pharmacology: How Fine can We Tune?

Insights into *Mycobacterium tuberculosis* from Computer Simulations: can this Knowledge help New Treatments?
L. Capece* * Universidad de Buenos Aires, Departamento de Química Inorgánica, Analítica y Química Física, Facultad de Ciencias Exactas y Naturales / CONICET, Instituto de Química Física de los Materiales, Medio Ambiente y Energía (INQUIMAE), Buenos Aires, Argentina.

Mycobacterium tuberculosis (Mtb) has developed sophisticated survival strategies to remain in a latent state within the human host by neutralizing the immune response. Central to this defense are truncated hemoglobins, specifically TrHbN and TrHbO.[1] While TrHbN is a highly efficient nitric oxide (NO) detoxifying enzyme that converts toxic NO into nitrate (NO_3^-), TrHbO is involved in oxygen-related metabolism and redox homeostasis. Both proteins are crucial for the pathogen's persistence under the extreme stress of the "oxidative burst" in macrophages. In our research group, we utilize computational tools as a "molecular microscope" to understand these biological processes at an atomic level. Using a combination of computer simulation methods and models, we have dissected the chemical mechanism of NO detoxification[2], we characterize ligand entrance and product release, and determine the kinetic constants that govern these processes.[3] This integrative approach allows us to get a complete molecular, dynamical and thermodynamical description of the biochemistry of these relevant proteins However, translating this knowledge into clinical treatments presents a challenge. Hemoproteins like TrHbN and TrHbO are traditionally considered "undruggable" due to their highly conserved sites. To overcome this, we are exploring the supporting redox machinery that regenerates these proteins. While the specific enzymes responsible for restoring the active ferrous state are still being identified—with potential candidates currently suggested by bioinformatic analyses — this machinery offers more promising sites for small-molecule inhibitors. The transition from understanding protein structure to rational drug design requires increasingly realistic models. Therefore, our research is evolving toward simulating complex biological environments, including interactions with bacterial membranes[4], and the impact of glycosylations[5]. By providing a more accurate picture of Mtb's defense mechanisms in their natural context, these detailed simulations serve as an essential blueprint for identifying novel pharmacological sites, potentially leading to new treatments. Nardini, M.; Pesce, A.; Bolognesi, M. ***Mol. Aspects Med.*** **2022**, ***84*** (101049), 101049. Martí, M. A.; Bidon-Chanal, A.; Crespo, A.; Yeh, S.-R.; Guallar, V.; Luque, F. J.; Estrin, D. A. ***J. Am. Chem. Soc.*** **2008**, ***130*** (5), 1688–1693. Bringas, M.; Lombardi, L. E.; Luque, F. J.; Estrin, D. A.; Capece, L. ***Chemphyschem*** **2019**, ***20*** (19), 2451–2460. Pathania, R.; Navani, N. K.; Rajamohan, G.; Dikshit, K. L. ***J. Biol. Chem.*** **2002**, ***277*** (18), 15293–15302. Arya, S.; Sethi, D.; Singh, S.; Hade, M. D.; Singh, V.; Raju, P.; Chodisetti, S. B.; Verma, D.; Varshney, G. C.; Agrewala, J. N.; Dikshit, K. L. ***J. Biol. Chem.*** **2013**, ***288*** (41), 29987–29999.

Unravelling the Catalytic Mechanism of Thiol-Based Redox Enzymes. Ari Zeida* * Departamento de Bioquímica, Centro de Investigaciones Biomédicas (Ceinbio) and Programa en Alimentos y Salud Humana (PAyS), Facultad de Medicina, Universidad de la República Montevideo, Uruguay.

The presence of highly reactive catalytic cysteines, often embedded within structurally and electrostatically specialized active sites, provides unique opportunities for both covalent and non-covalent drug discovery strategies.[1] In this context, structural biology, combined with detailed mechanistic characterization, has become instrumental for understanding the molecular determinants of catalysis, redox regulation, and ligand recognition in these systems.[2] Elucidating the structural basis of enzyme function and inhibition not only enables the identification of ligandable pockets and reactive hotspots, but also opens new avenues for the rational design of selective modulators targeting thiol-dependent redox proteins.[3] In this talk, I will try to illustrate this concept through two biologically and therapeutically relevant case studies, showing how the integration of structural biology, structural bioinformatics, and computational modeling—combined with complementary experimental approaches—can provide detailed mechanistic insights into thiol-based redox enzymes. First, I will discuss the case of methionine sulfoxide reductases from *Mycobacterium tuberculosis* and their complex chemistry.[4] Then, the possibility of inhibiting cellular SARS-CoV-2 Spike protein recognition by the modification of a particular cysteine residue at the

receptor binding domain (RBD) will be presented.[5] By dissecting how catalytic cysteines shape protein structure, dynamics, reactivity, and ligand recognition, these examples aims to highlight how a deeper understanding of structure–function relationships can guide pharmacological intervention and establish a rational framework for the future design of selective inhibitors and modulators targeting redox-active proteins. Li, B. *et al*. *Signal Transduct*. *Target*. *Ther*. 10, 72 (2025) Nam, K. *et al*. *ACS Omega* acsomega.3c09084 (2024) Xie, S. C. *et al*. *Trends Biochem*. *Sci*. 51, 439–456 (2026) Sastre, S. *et al*. *Biochemistry* 63, 533–544 (2024) Shi, Y. *et al*. *Proc*. *Natl*. *Acad*. *Sci*. 119, e2120419119 (2022)

Engineering antiviral biopharmaceuticals. Roberto Dias Lins Neto (Fiocruz)
The escalating global epidemics of virus infections underscores the urgent need for accurate diagnostics and innovative therapeutic strategies. Leveraging on data and biological samples from clinical studies from our group, the talk will describe our efforts to identify key epitopes and to engineer proteins tailored for both diagnosis, and treatment of flavivirus infections. A machine learning-based model to predict protein-protein binding free energies as a strategy towards highthroughput protein engineering will also be presented.

S2 – Molecular Mechanisms of Neuronal Signaling and Therapeutic Modulation in Brain Function and Disease

Sex-Specific G Protein-Coupled Receptor Signaling in Alzheimer's Disease Mice. Stephen S.G. Ferguson, Department of Cellular and Molecular Medicine, University of Ottawa, Ottawa, Ontario, Canada
Alzheimer's disease (AD) is a progressive neurodegenerative disorder marked by cognitive decline that affects approximately 750,000 Canadians over the age of 65 and disproportionately impacts women. The disease is driven by disruptions in cellular mechanisms underlying learning and memory that are associated with highly neurotoxic Aβ42 and p-tau oligomers that impair synaptic function and ultimately lead to neuronal degeneration. Aβ42 oligomers and cellular prion proteins (PrP^C) form a complex with Group I metabotropic glutamate receptors (mGluR1 and mGluR5) to transduce pathological intracellular signals that impair memory and learning in AD. mGluR5-selective negative allosteric modulators (NAMs) have shown preclinical promise as therapeutic agents to both reverse and treat β-amyloid induced AD progression, whereas the role of mGluR1/Aβ42/PrP^C interactions in AD progression have undergone little investigation. We have reported previously that Aβ42 binds to mGluR5 in male but not female brain tissue resulting in the selective inactivation (increased GSK3β phosphorylation) of a well-defined GSK3β-regulated autophagy pathway that can be reengaged to reduce Aβ pathology following NAM treatment of male mice. This signaling axis is surprisingly absent or functionally uncoupled in females, conferring resistance to mGluR5-dependent pathology. We have now identified both novel (brain enriched E3 ubiquitin ligase Trim9) and known (β-arrestin2) mGluR5 interacting proteins that contribute to male-specific disease pathology in APP/PS1 mice. We hypothesize that AD progression in males is driven by a pathological Aβ42/PrP^C/mGluR5 signaling complex that specifically engages Trim9 and β-arrestin2, leading to inactivation of GSK3β-regulated autophagy, cognitive decline and disease pathology and that Aβ42/PrP^C interactions with mGluR1 may also contribute to AD. This presentation will provide an overview of our progress and results regarding male sex-specific signaling in AD.

mGlur5 Positive Allosteric Modulators To Treat Neurodegeneration. Fabíola Mara Ribeiro (UFMG)
The metabotropic glutamate receptor 5 (mGluR5) plays an important role in neuronal survival and synaptic plasticity. We and others have shown that mGluR5 positive allosteric modulators (PAMs) are biased agonists, triggering the activation of neuroprotective pathways and promoting neuronal survival. Moreover, treatment of mouse models of Huntington's disease (HD) with mGluR5 PAMs, including CDPPB and VU0409551, increases the number of mature spines and ameliorates HD-related memory deficit. As mGluR5 biased pharmacology arises from drug-induced interactions with distinct protein partners, we analyzed the mGluR5 interactome to identify novel binding partners capable of modulating receptor cell signaling. We found that the neuronal growth regulator 1 (NEGR1), a cell adhesion molecule (CAM) important for synaptogenesis, interacts with mGluR5. NEGR1 binding to mGluR5 is important for the synaptic localization of the receptor and for its coupling with Homer, thereby modulating the cell signaling pathways activated by mGluR5. For instance, NEGR1 knockdown leads to decreased

mGluR5-dependent activation of ERK1/2 and reduced expression of ARC/ARG3.1 and BDNF. Importantly, NEGR1 knockdown affects mGluR5 pharmacology, as the neuroprotective effect of VU0409551 is not observed in neurons expressing low levels of NEGR1. These results indicate that NEGR1 is essential for mGluR5 biased activation of neuroprotective cell signaling pathways and for the neuroprotective effect triggered by VU0409551. **Support:** FAPEMIG e CNPq

S3 – **Vascular Signaling in the Gut–Lung Axis during Infectious Disease**

Insights on the Gut-Lung Axis in Pulmonary Arterial Hypertension: a Poorly Investigated Crossroad. Villarreal, Elizabeth Sue[1]#; Loya, Omar[1]; Marinho, Ygor[1]; Aboagye, Samuel Yaw[2]; Costa, Gabriela[3]; Oliveira, Fernanda[3]; Gupta, Muskan[4]; Oliveira, Katia Costa[5]; Silva, Claudia Lucia Martins[6]; Sun, Jun[7]; Erzurum, Serpil Cem[8]; Lutz, Sarah Elizabeth[4]; Williams, David Lee[2]; Oliveira, Rudolf Feitoza Krawczenko[3]; de Jesus Perez, Vinicio[9]; Oliveira, Suellen Darc[1],[10]* [1]Vascular Immunobiology Lab; College of Medicine; Department of Anesthesiology - University of Illinois Chicago (UIC) – IL/USA; [2]Department of Microbial Pathogens and Immunity - Rush University - IL/USA; [3]Department of Medicine, Federal University of Sao Paulo, SP/Brazil; [4]Department of Anatomy and Cell Biology- UIC – IL/USA; [5] Department of Microbiology, Immunology, and Parasitology, Federal University of Sao Paulo, SP/Brazil; [6]Department of Pharmacology and Medicinal Biochemistry, Federal University of Rio de Janeiro, RJ/Brazil; [7]College of Medicine; Department of Medicine- UIC – IL USA; [8]Lerner Research Institute, Cleveland Clinic Foundation, OH/USA; [9]Division of Pulmonary and Critical Care, Stanford University, Palo Alto, CA/USA; [10]Department of Physiology and Biophysics - UIC

Schistosomiasis-associated pulmonary arterial hypertension (Sch-PAH) affects more than 1 million people worldwide, yet disease-specific therapeutic targets remain limited. Our group recently identified gut-lung dysbiosis and increased plasma extracellular vesicle (EV) in a preclinical Sch-PAH model, potentially driven by activation of the death-associated purinergic receptor P2X7 (P2X7R) in lung endothelial cells (ECs). Because cell death and survival are tightly regulated by members of the Inhibitor of Apoptosis Protein (IAP) family, we investigated the role of cellular IAP2 (c-IAP2) in Sch-PAH pathogenesis. We hypothesized that gut-lung dysbiosis promotes P2X7R-mediated endothelial c-IAP2 shedding and enhances immune cell survival in experimental Sch-PAH. Control and endothelial-specific Cdh5creERT2;cIAP1-/-;cIAP2fl/fl mice (male and female), with or without Schistosoma mansoni egg exposure, were evaluated for right ventricular systolic pressure (RVSP), right ventricular hypertrophy (RVH), and cardiac function by echocardiography. Protein expression was assessed by Western blotting, ELISA, and immunohistochemistry (IHC), while microbial composition and metabolites were analyzed by metagenomics and targeted metabolomics. To determine the contribution of P2X7R signaling, mice were treated with the P2X7R inhibitor Brilliant Blue G (BBG; 45.5 mg/kg) prior to egg exposure. Human lung microvascular endothelial cells (HMVEC-L) were also exposed to S. mansoni eggs to evaluate changes in P2X7R expression in vitro. The validated Sch-PAH model demonstrated increased extracellular ATP levels and activation of canonical P2X7R-NLRP3 signaling in lung microvascular ECs, accompanied by enhanced EV release, endothelial apoptosis, and plasma c-IAP2 level. In vitro, P2X7R inhibition prevented ATPinduced endothelial cell death, while in vivo BBG treatment attenuated pulmonary vascular remodeling, reduced EV shedding, and prevented RVSP elevation in female egg-exposed mice, although RVH persisted. Endothelial-specific cIAP2 deficiency resulted in spontaneous upregulation of pulmonary P2X7R expression. Female cIAP2-deficient mice also exhibited reduced pulmonary acceleration time/pulmonary ejection time (PAT/PET) ratios and increased right ventricular free wall thickness compared with males, indicating sex-dependent disease susceptibility. Moreover, c-IAP2 levels were elevated in plasma from female egg-exposed mice and PAH female patients, and preliminary data revealed accumulation of c-IAP2 within immune cells, suggesting an uptake of circulating c-IAP2 may support immune cell survival. Collectively, these findings identify a novel lung P2X7R-c-IAP2 signaling axis and suggest that microbiome dysbiosis-driven P2X7R activation promotes endothelial injury, EV-mediated c-IAP2 shedding, and prolonged inflammatory cell survival in Sch-PH. Targeting P2X7R signaling in patients displaying elevated plasma c-IAP2 level may therefore represent a promising novel therapeutic strategy for preventing progression of sex-linked Sch-PAH.

Caveolin-1–Dependent Endothelial $P2Y_2$–P2X7 Receptors Crosstalk In Intestinal Inflammation Contrasts with $P2Y_6$ Receptor Regulation. Oliveira NF, Mainieri NS, Silva CLM Universidade Federal do Rio de Janeiro, Instituto de Ciências Biomédicas, LFBM

Purinergic signaling is an important mechanism of intercellular communication mediated by extracellular nucleotides. Extracellular ATP conveys intracellular signaling through ionotropic (P2X) or 7TM/G protein-coupled purinergic receptors (P2YRs), which have emerged as promising therapeutic targets in clinical trials. The P2X receptor family (P2X1–P2X7R) assemble as homo- or heterotrimeric, ATP-gated nonselective cation channels. Among these receptors, P2X7R has attracted particular attention due to its unique functional properties and prominent role in inflammation. On the other hand, the P2Y receptor family comprises a group of nucleotideactivated G protein–coupled receptors (GPCRs) characterized by distinct ligand selectivity, G protein coupling, and downstream signaling pathways. $P2Y_2R$ has attracted growing attention as a multifunctional GPCR that integrates extracellular nucleotide signaling with inflammatory, neuroimmune, atherosclerotic and tissue repair responses. In mesenteric endothelial cells, confocal microscopy data showed that both $P2Y_2R$ and P2X7R are co-localized with caveolin-1 (Cav-1), and their co-localization is upregulated during intestinal inflammation. In good accordance, Cav-1 knockdown impaired $P2Y_2R$ and P2X7R crosstalk and function. Moreover, $P2Y_6R$ has emerged as a player of inflammatory conditions, including intestinal inflammation. But in contrast to $P2Y_2R$ and P2X7R, $P2Y_6R$ (either native or transfected) shows a unique model of redox-sensitive regulation, unveiling complementary, but mechanistically distinct, axes of purinergic control in intestinal inflammation. Therefore, although all three receptors have been associated with inflammatory responses, and could represent potential therapeutic targets, their specific contributions may differ according to the context of the disease. **Support:** CNPq (444267/2024-7;312051/2023-9), FAPERJ (204320/2024), INCT SiPu21 (409156/2024-8)

S4 – Cell Communication on Immune Response, Aldosteronism, and Hypertension: Old Questions, New Insights

A Chemogenetic Mouse Model to Uncover the Pharmacological Mechanisms Behind Primary Aldosteronism. Sheerazed Boulkroun Université Paris Cité, Inserm, PARCC, Paris France

Primary aldosteronism is the most frequent form of secondary hypertension, due to autonomous aldosterone producDon by the adrenal gland. The most frequent geneDc cause of aldosterone producing adenoma (APA) are somaDc mutaDons in the *KCNJ5* gene, coding for the potassium channel GIRK4, altering its selecDvity, and promoDng sodium influx leading to cell membrane depolarisaDon, acDvaDon of calcium signalling, the major trigger for aldosterone biosynthesis. To elucidate how *KCNJ5* mutaDons contribute to APA development, we established a mouse model with adrenal cortex-specific expressing of a chimeric ion channel using a Cyp11b2-Cre line generated in our laboratory. This engineered receptor, a7-5ht3r, comprises the ligandbinding domain of the a7 nicoDnic acetylcholine receptor fused to the ion pore domain of the serotonin receptor 5ht3a (a7-5ht3r^{ZG}). SelecDve acDvaDon with PSEM triggers sodium influx, thereby funcDonally mimicking the sodium influx and depolarising effect of *KCNJ5* mutaDons. In an adrenocorDcal cell model, we previously demonstrated that expression of a7-5ht3r induces sodium influx, leading to cell membrane depolarisaDon, increased intracellular calcium levels and sDmulaDon of CYP11B2 expression and aldosterone producDon, while reducing cell proliferaDon and promoDng apoptosis. Transcriptomic and steroidomic analyses revealed unique profile associated with sodium entry. These findings suggest that addiDonal events may be required for the development of an APA with *KCNJ5* mutaDon. In a7-5ht3r^{ZG} mice, four weeks of treatment with PSEM result in increased plasma aldosterone and 18-hydroxycorDcosterone levels, associated with upregulated *Cyp11b2* expression and adrenal cortex disorganisaDon. No concomitant increase in blood pressure, or evidence of cardiac or renal remodelling were detected. Further invesDgaDons, including extended treatment protocols, are ongoing to fully characterize this model. This mouse model, enabling precise modulaDon of calcium entry, represents a powerful tool to dissect the mechanisms driving APA development and to evaluate novel therapeuDc strategies.

S5 – Biomarkers in Cancer: An Opportunity for the Development of New Drugs

Preclinical Models for Functional Precision Medicine in Cancer. Hellen Kuasne[1], Anne Marie Fortier[1], Sandrine Busque[1], Paul Savage[1], Constanza Martinez Ramirez[1], Anie Monast[1], Nebras Koudieh[1], Atilla Omeroglu[2], Lara

Richer[2], Jamil Asselah[3], Nathaniel Bouganim[3], Francine Tremblay[4], Ari Nareg Meguerditchian[4], Sarkis Meterissian[4], Morag Park[1,3,5]. [1]Rosalind and Morris Goodman Cancer Institute, McGill University, Montreal, Quebec, Canada. [2]Department of Pathology, McGill University, Montreal, Quebec, Canada. [3]Department of Oncology, McGill University, Montreal, Quebec, Canada. [4]Department of Surgery, McGill University, Montreal, Quebec, Canada. [5]Department of Biochemistry, McGill University, Montreal, Quebec, Canada.
Functional Precision Medicine (FPM) integrates patient-derived preclinical models, molecular profiling, and drug sensitivity testing to inform personalized cancer treatment strategies. This approach leverages live tumor cells to perform functional assays in real time, exposing them to a panel of therapeutic agents to identify those most likely to be effective. While broadly applicable, my work focuses on rare and hard-to-treat cancers, with particular emphasis, though not exclusive, on rare breast cancer subtypes such as metaplastic breast cancer, a heterogeneous disease with diverse molecular features and limited treatment options. By combining the development of patient-derived models, such as organoids and patient-derived xenografts, and advanced molecular profiling, it becomes possible to identify tumor-specific vulnerabilities, match them to candidate therapies, and functionally validate these responses directly in patient-derived material. This integrated strategy provides a framework for improving therapeutic outcomes. Financial Support: Marathon of Hope Cancer Centres Network, Terry Fox Foundation, RRCancer, Canadian Cancer Society

Marine Natural Products as Inducers of Immunogenic Cell Death in Melanoma: Prospection and pre-Clinical Development of Anticancer Candidates. Diego V. Wilke (UFC).
Advanced metastatic melanoma (AMM) is a highly aggressive skin cancer with a growing incidence worldwide. Immunogenic cell death (ICD) induction is rare, however, it yields better and longer-lasting antitumor responses to chemotherapy due to the activation of a specific antitumor immune response. AMM is incurable for more than half of patients and the discovery of ICD inducers is an interesting drug discovery strategy with high translational potential. Marine microorganisms have emerged as an immeasurable and sustainable source of molecules with anticancer potential. As part of an effort to translate natural products from Brazilian marine biodiversity into anticancer candidates, our group created MicroMarin, a marine bacteria collection with approximately 2,000 isolated strains. To date, 15% of tested crude extracts obtained from MicroMarin showed cytotoxicity *in vitro* against tumor cell lines, and a total of 110 different molecules from active extracts were isolated or annotated. We have identified 5 ICD inducers in melanoma: chromomycins A_{5-8} (CA5-8) and tartrolon D (TRL). Melanoma cells incubated with CA5-8 and TRL exhibited ICD features *in vitro* such as autophagy and apoptosis, externalization of calreticulin, and release of HMGB1. CA5-treated cells also induced ATP release, ERp57 externalization and phosphorylation of eIF2α. Splenocytes from C57BL/6 mice vaccinated with B16-F10 cells preincubated with CA5 or TRL showed an immune antitumor response. Bona fide ICD induction by CA5 was confirmed by vaccination of C57BL/6 mice with CA5-treated B16-F10 cells, which activated both antigen-presenting cells and cytotoxic T lymphocytes and controlled tumor growth when challenged with live B16-F10 cells. Further, we investigated the toxicity and antitumor effect of CA5. A narrow therapeutic window was found due to a vesicant-like effect of CA5. Nevertheless, mice treated intraperitoneally with 300 μg/kg/day CA5 every 3 days (total of 3 administrations) showed a tumor growth inhibition of 60%. CA5 induces bona fide ICD in melanoma and exhibits a potent antitumor effect. We thank the technical support of the multi-user facility of NPDM. Support: CAPES, CNPq, INCT Nature.

S6 – Across Land, Water, and Air: Animal Models in Psychopharmacology

Fast-Tracking Platforms for Screening the *in vitro* and *in vivo* Pharmacological Profile of Cannabidiol in the Context of Autism Spectrum Disorder. Alline Campos- Associate Professor - Depto of Pharmacology- Coordinator- Center for Cannabinoid Research- Ribeirao Preto Medical School- University of São Paulo-Brazil
Autism Spectrum Disorder (ASD) is a neurodevelopmental condition characterized by social communication deficits, repetitive behaviors, and sensory abnormalities. Sodium valproate (VPA) exposure during embryonic development is a well-established preclinical model for ASD, leading to increased oxidative stress in the developing brain, including lipid peroxidation, which affects cell proliferation and organization. During this lecture, we will present how we have been using alternative methods to study the mechanisms of action of cannabidiol (CBD) in

the context of ASD. From the standardization of a quick, efficacious, and cost-effective zebrafish screening platform for new molecules for ASD treatment, to the use of neural stem cells and their communication with microglial cells to improve the distribution of nanoCB, we hope to demonstrate that alternative methods can be used as fast-tracking platforms for evaluating the pharmacological profile of phytocannabinoids and other candidate drugs. These models, in which each protocol lasts approximately 7–10 days, show high reproducibility even in the presence of biological variability, making them particularly valuable for improving statistical power in biological research.

Towards Vertebrates' Replacement in Antidepressant Discovery. Cilene Lino de Oliveira- Full Professor - Depto of Physiological Sciences,Center of Biological Sciences, Federal University of Santa Catarina- CFS-CCB-UFSC, Florianópolis, SC, Brazil

Model organisms are species providing insights into biological mechanisms relevant to human health. The research community has increasingly adopted the principles of the "3Rs" (refine, reduce, replace) to improve animal experimentation. Interest has grown in partial replacement of vertebrates with invertebrates, which allows for assays considering the full complexity of a living organism at scales impractical in mammals. *D. melanogaster* has long been a model in biological research and might be ideal for neuro-psychopharmacology research due to their well-known behavioral repertoire, fully described neuronal wiring, and sequenced genome. D. melanogaster exhibits stress-induced phenotypes similar to those of rodents, such as learned helplessness, characterized by immobility or impaired escape from threat often mitigated by treatment with antidepressants. In this lecture, we present our studies developing models, tests and protocols aiming to establish *D. melanogaster* as an acceptable alternative to vertebrates in antidepressant research. For example, sucrose preference in a lane maze test is highly affect by experimental factors such *as D. melanogaster´* sex and stressor experience, type and duration of stressors, type and dose of antidepressants, and sucrose concentration. These studies took advantage of the inexpensive maintenance costs, short life cycles, and the obvious sexual dimorphism to plan high powered experiments in male and female D. melanogaster. This strategy aims to integrate animal welfare, biologic relevance, and robust experimental design in a low cost system for antidepressant screening.

S7 – Advances in Model-Informed Precision Dosing for Antimicrobials

Preclinical to Clinical Translation of Antimalarial Combinations. Francine Johansson Azeredo Assistant Professor, Department of Pharmaceutics, College of Pharmacy, University of Florida, Orlando, FL, USA

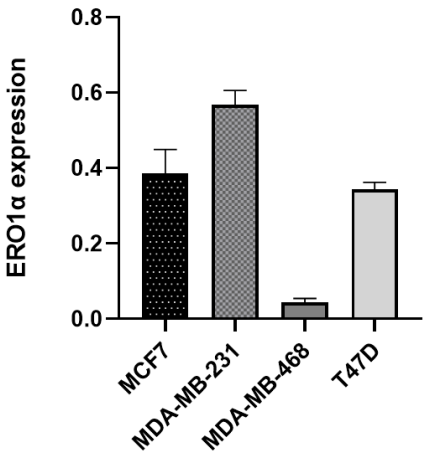
Malaria remains a major global health challenge, particularly in regions affected by drug resistance and limited therapeutic options. Quantitative pharmacology approaches, including pharmacokinetic/pharmacodynamic (PK/PD) and physiologically based pharmacokinetic (PBPK) modeling, have become increasingly important tools for supporting the translational development of antimalarial therapies and optimizing combination regimens. This presentation will discuss recent advances in the preclinical-to-clinical translation of antimalarial combinations through integrated modeling and simulation. First, a PBPK modeling approach for tafenoquine will be presented, focusing on the evaluation of potential drug–drug interactions (DDIs). This work aims to support the safe clinical use of tafenoquine in combination strategies and improve understanding of factors influencing exposure variability and therapeutic response. Then, results from a published PK/PD modeling study of the artesunate–mefloquine combination in *Plasmodium berghei*-infected mice will be presented. The study characterized drug exposure-response relationships and evaluated the translational potential of combination therapy using survival and efficacy endpoints (Mim et al., 2026). Finally, ongoing work using a hollow fiber infection model (HFIM) of *Plasmodium falciparum* will be described. This model evaluates the parasite-killing dynamics of artesunate, its active metabolite dihydroartemisinin (DHA), and mefloquine under clinically relevant exposure profiles. The HFIM platform enables simulation of human-like pharmacokinetics and provides mechanistic insights into mono- and combination-therapy regimens, supporting dose optimization and translational prediction. Overall, this presentation highlights how quantitative translational approaches can support antimalarial drug development, optimize regimens, and facilitate the translation of preclinical findings into clinically meaningful strategies. Financial support: PROSPER

Seed Research Grant, University of Florida; Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq grants nos. 440227/2022-4 and 422821/2025-0).

Pharmacokinetic Modeling Applied to the Prediction of Antimicrobial Exposure in Children and Neonates. Ronaldo Morales Junior. Hospital Sírio-Libanês, São Paulo-SP, Brazil.

The development of new drugs and the establishment of appropriate dosing regimens for children and neonates continue to represent important challenges. In most cases, clinical drug development follows a stepwise process, starting in adults, then progressing to pediatric populations, and only subsequently including neonates. This creates an opportunity to develop methods to predict drug pharmacokinetics and exposure in neonates using data from older populations while accounting for developmental physiological differences. Clinically, optimizing antimicrobial exposure in neonates and children has become increasingly important to improve therapeutic outcomes while minimizing toxicity and the emergence of resistance. Pharmacometric tools, particularly population pharmacokinetic models, can be used to predict antimicrobial exposure in pediatric patients using strategies based on allometric scaling, maturation functions, and organ function biomarkers. The use of maturation-adjusted kidney function metrics is particularly important to distinguish normal physiological renal immaturity from pathological renal impairment. These strategies have practical applications in antimicrobial dose optimization and model-informed precision dosing, including for β-lactam antibiotics in critically ill pediatric populations. Despite the potential utility of extrapolation approaches, pharmacokinetic models must undergo rigorous validation before clinical implementation to ensure adequate predictive performance, reliability, and safety across different pediatric age groups and clinical settings.

Integrating Nonclinical Evidence to Select the Next Successful Regimen in Tuberculosis. Belén P. Solans[1], Anu Patel[2], Rada M Savic[2] [1]Pharmactuarials, LLC. Madrid, Spain [2]University of California San Francisco, San Francisco CA, USA



The development of optimized tuberculosis (TB) regimens increasingly depends on the integration of nonclinical evidence and data to inform clinical design and decision-making. We describe a model-informed translational framework leverages preclinical and disease pharmacokinetic-pharmacodynamic (PK-PD) relationships biology to project the efficacy of novel drug combinations prior to clinical evaluation. Central components include (i) identification of the optimal clinical dose through exposure–response relationships derived from preclinical models, (ii) quantitative characterization and assessment of drug penetration into relevant lesion compartments to ensure target-site exposure and effective drug distribution at sites of infection, and (iii) time to relapse prediction using longitudinal data linked to bacterial burden and sterilizing activity. These elements are integrated within model-based simulation platforms to evaluate candidate combination regimens across dosing strategies. By bridging preclinical evidence with clinical expectations, this approach enables rational prioritisation of regimens with the highest probability of success, supports dose selection, and informs trial design. Ultimately, such model-informed integration strategies provide a rational path toward designing shorter, more effective TB treatments.

S8 – Targeting Cellular Dysfunction in Complex Diseases: From Cancer to Parkinsonism

ERO1α Overexpression in Triple-Negative Breast Cancer Links to EMT and Mitochondria-Dependent Inhibition. Mohamad Aljofan[1,2], Kamilla Khojayeva[1]. Department of Biomedical Sciences, School of Medicine, Nazarbayev University[1], Astana, Kazakhstan; Drug Discovery and Development, Center of Life Sciences, National Laboratory Astana[2], Astana, Kazakhstan.

Introduction. Endoplasmic reticulum oxidoreductin-1α (ERO1α) is an oxidase involved in protein folding and Reactive Oxygen Species (ROS) generation (Shergalis et al, 2020). It promotes epithelial-mesenchymal transition (EMT) (Chen et al, 2024) and links ER redox regulation to mitochondrial function and cancer progression (Bassot et

al, 2023). **Aims**. To evaluate ERO1α expression in breast cancer cell lines and assess the effect of the inhibitor EN460. **Methods**. Western blotting was used to analyze ERO1α expression in MCF-7, T47D, MDA-MB-231, and MDA-MB-468 cells. Treatment with 40 μM of EN460 was tested in normal and mitochondria-depleted MDA-MB-231 cells. **Results**. ERO1α expression was highest in MDA-MB-231 cells, showing a ~1.5-fold increase over MCF-7 and T47D, and ~14-fold higher than MDA-MB-468 (ANOVA, $P < 0.01$). EN460 treatment reduced ERO1α in normal MDA-MB-231 cells to 0.25 ± 0.06 (31% of control, $P < 0.01$), but had no effect in mitochondria-depleted cells. **Discussion**. These findings suggest that ERO1α overexpression drives the aggressive phenotype of MDA-MB-231 cells, and that EN460 inhibits it via a mitochondria-dependent mechanism. Targeting this pathway may offer a strategy to suppress EMT and invasiveness in breast cancer. Bassot A et al (2023) Cell Rep. 42:111899. Chen P et al (2024) J Exp Clin Cancer Res. 43:71. Shergalis AG et al (2020) Pharmacol Ther. 210:107525.

Biochanin A, a Natural Isoflavone, as a Potential Therapeutic Agent in Experimental Parkinsonism. Enilton A Camargo (UFS)

Parkinson's disease is a neurodegenerative disorder characterized by the progressive loss of dopaminergic neurons, formation of Lewy bodies, and the presence of motor and non-motor symptoms. Recent evidence demonstrates that neuroinflammation plays a central role in the pathophysiology of the disease, involving glial cell activation, infiltration of immune cells, and the participation of α-synuclein as a potential autoantigen. Clinical and experimental studies indicate that patients with inflammatory diseases are more susceptible to Parkinson's disease, whereas the use of anti-inflammatory or immunosuppressive drugs may be associated with a reduced risk of developing the disease. In this context, therapeutic strategies aimed at modulating the inflammatory response are of particular interest for treating this condition. Isoflavones, such as biochanin A, are natural compounds with immunomodulatory, anti-inflammatory, and proresolving properties that are promising candidates for testing in parkinsonism models. The use of progressive induction models, such as the reserpine-induced parkinsonism model, offers the advantage of allowing the evaluation of motor and premotor alterations throughout the development of parkinsonism, while also enabling the assessment of neurochemical changes associated with the model. Experimental results from our research group demonstrated that treatment with biochanin A, concomitant with progressive induction of the model, reduced motor symptoms and neurochemical markers associated with impaired dopaminergic transmission. Therefore, relevant preclinical evidence suggests that modulation of neuroinflammation by biochanin A represents a promising strategy for the development of new therapies for Parkinson's disease.

XX FeSBERegional Meeting

SFR1 – Endocrine Disruptors Chemicals and DOHaD

Endocrine Disruptors – Does the Exposure Window Matter? Caroline Serrano do Nascimento Adjunct Professor in the Department of Biological Sciences at the Institute of Environmental, Chemical and Pharmaceutical Sciences (ICAQF), Federal University of São Paulo (Unifesp).

The lecture will address the importance of critical windows of exposure to endocrine disruptors, highlighting how the timing of exposure can be decisive for the intensity, nature, and persistence of their effects on health. Special emphasis will be placed on pregnancy and lactation, periods characterized by intense hormonal activity, rapid growth and cellular differentiation, and high tissue plasticity, in which even small disturbances in endocrine signaling may result in long-lasting consequences. Moreover, the mechanisms by which endocrine disruptors can interfere with hormone synthesis, secretion, transport, metabolism, and action will be discussed, altering essential processes for the development and functional programming of different organs and systems. In this context, exposure during critical periods of development may produce effects that are not always immediately evident, but that may manifest later in life, contributing to increased susceptibility to metabolic, reproductive, neuroendocrine, and cardiovascular alterations, as well as to various chronic diseases throughout life. The lecture will also discuss evidence that some of these alterations may involve epigenetic mechanisms, persistently modifying gene expression and, under certain conditions, contributing to effects observed in subsequent generations. Finally, the importance of understanding not only the dose but also when exposure occurs will be emphasized as a

fundamental element for assessing the risks associated with endocrine disruptors. Financial Support: FAPESP and CNPq.

Endocrine-Disrupting Drugs: Developmental Exposure and Sex-Specific Cardiovascular Effects. Graziela S. Ceravolo, Associate Professor, Department of Physiological Sciences, Center of Biological Sciences, State University of Londrina (UEL), Brazil.
Endocrine disruptors (EDs) are widely used in modern society and continuously released into the environment, where they can persist and bioaccumulate in living organisms. Epidemiological and experimental studies have linked ED exposure to alterations in male and female reproductive systems, as well as to cardiovascular and metabolic disorders, including diabetes and obesity. Cardiovascular diseases (CVDs) are the leading cause of death worldwide, and increasing evidence suggests that early-life exposure to xenobiotics may contribute to their development. Experimental studies indicate that these chemicals can adversely affect cardiovascular health, highlighting the importance of understanding their potential cardiotoxic effects. Sex differences in CVDs have been observed in both humans and experimental animal models, with females generally exhibiting less severe disease phenotypes and lower cardiovascular mortality than males. These differences have been largely attributed to sex hormones, particularly estrogens. Among the health risks associated with ED exposure, cardiovascular effects have received increasing attention. EDs may interfere with critical cardiovascular processes, including lipid metabolism, blood pressure regulation, and endothelial function. Importantly, males and females may experience distinct cardiovascular consequences of ED exposure. Several drugs commonly used in humans may also exhibit endocrine-disrupting properties. Growing evidence suggests that exposure to certain pharmaceuticals can induce physiological alterations similar to those associated with classical EDs, particularly when exposure occurs during critical windows of developmental plasticity, such as childhood and adolescence. Based on this evidence, this presentation will explore the hypothesis that some drugs considered safe for use in children and adolescents may possess endocrine-disrupting properties and consequently affect cardiovascular development and long-term cardiovascular health. Furthermore, it will discuss whether these adverse effects differ between males and females, highlighting the importance of considering sex as a biological variable when investigating the long-term cardiovascular consequences of drug exposure during development.

The danger of Chemical Substances in the Environment, acting on the First Thousand Days of Life, Increases the Risk of Diseases During Development. Egberto Gaspar de Moura – Full Professor of Physiology and Pathophysiology, Department of Physiological Sciences, Institute of Biology, State University of Rio de Janeiro (UERJ).
Nowadays, we are constantly exposed to a variety of chemical agents that affect hormonal regulation and action, increasing the risk of chronic-degenerative diseases. These agents are known as endocrine disruptor chemicals (EDC). Although they act throughout our lives, their action is most critical during gestation, lactation, and up to two years of age. The effects of EDC during this period extend throughout life, through epigenetic alterations. This field of study is called DOHaD (Developmental Origins of Health and Disease). At the Endocrine Physiology Laboratory of UERJ, we study, in murine experimental models, the action of pesticides (organophosphated like glyphosate and acephate and neonicotinoids), plasticizers (different types of bisphenols), micro and nanoplastics that, acting in the first days of life, produce a greater risk of obesity, diabetes mellitus, dyslipidemia, thyroid dysfunction, and behavioral changes, including: increased anxiety and food preference for more sugar and fat. These changes depend on the time the EDC act and are sex-dependent. Although we study each EDC in isolation, it is good to be aware that we are all affected by them simultaneously to varying degrees, according to the region and social class of the population. In this regard, our group has been collaborating with the The Childhood and Environmental Pollutants Project (PIPA), affiliated with the Institute of Studies in Collective Health (IESC/UFRJ), which investigates the effects of pollutants on maternal and child health, spanning the period from pregnancy through the time the children reach four years of age, in different communities of Rio de Janeiro. Financial support: FAPERJ, CAPES, and CNPq

SFR3 – Gut Microbiome and Cardiometabolic Health: Experimental Basis for Nutraceutical Interventions

Gut Microbiome and Cardiometabolic Disease: Mechanisms and Signatures. Paulo César Trindade da Costa Faculty of Medical Sciences of Paraíba (Afya-PB), Cabedelo, Paraíba, Brazil.

The gut microbiome is increasingly recognized as an important regulator of host metabolism and cardiovascular physiology, with growing evidence linking alterations in its composition and function to cardiometabolic diseases. However, understanding these relationships requires moving beyond descriptive changes in microbial taxa toward the identification of biological mechanisms and microbial signatures associated with disease risk. This presentation will provide an overview of the role of the gut microbiome in cardiometabolic health, focusing on the mechanisms through which microbial alterations may contribute to obesity, hypertension, insulin resistance, dyslipidemia, and cardiovascular disease. Particular attention will be given to gut barrier integrity, microbial metabolites, including short-chain fatty acids, bile acid derivatives, and trimethylamine N-oxide, and their interactions with inflammation, immune responses, glucose and lipid metabolism, and cardiovascular and autonomic regulation. The presentation will also explore the concept of microbial signatures associated with cardiometabolic risk, discussing how differences in microbial composition, diversity, functional potential, and metabolite production may characterize specific cardiometabolic phenotypes. Evidence from experimental and human studies will be used to illustrate the challenges of distinguishing associations from causal relationships and of identifying reproducible, biologically meaningful microbiome signatures. Finally, the presentation will discuss current challenges in translating microbiome research into clinically relevant biomarkers and mechanistic models. The talk will emphasize the biological pathways and microbial signatures that may help explain individual differences in cardiometabolic risk and provide a foundation for future translational research. By integrating mechanistic and translational perspectives, this presentation will highlight the gut microbiome as a complex interface between environmental exposures, host physiology, and cardiometabolic disease, while identifying key questions that remain to be addressed in the field.

Development and Characterization of Microbiome-Targeted Nutraceuticals. Fillipe de Oliveira Pereira Academic Unit of Health, Education and Health Center, Federal University of Campina Grande, Cuité, Paraíba, Brazil
Nutraceuticals provide bioactive components beyond basic nutrition that actively promote human health. Currently, the design of microbiome-targeted nutraceuticals represents a rapidly advancing strategy for optimizing gut and systemic health. Among promising food matrixes, edible fungi such as *Pleurotus* species stand out due to their established history of dietary use, simple cultivation, and efficient conversion of lignocellulosic residues into bioactive-rich biomass. Their high nutritional value, recognized safety, and functional properties strongly support their application as versatile raw materials for functional food formulation. This presentation highlights an integrated pathway for developing *Pleurotus*-based nutraceuticals, spanning sustainable agro-industrial cultivation, biological evaluation, and advanced formulation strategies. In our studies, *Pleurotus djamor* powder subjected to simulated gastrointestinal digestion and *in vitro* colonic fermentation selectively expanded *Lactobacillus/Enterococcus* and *Bifidobacterium* populations, reduced *Clostridium histolyticum*, lowered colonic pH, and stimulated short-chain fatty acid production, demonstrating robust prebiotic potential. These insights driven the development of a potentially synbiotic formulation combining *P. djamor* powder with three *Limosilactobacillus fermentum* strains. During 90 days of refrigerated storage, this formulation retained high levels of phenolic compounds, maintained antioxidant activity, and preserved bacterial physiological viability, underscoring the role of processing and storage parameters in product stability. Our current technological pipeline extends to microencapsulated *Pleurotus* powders derived from agro-industrial residues to enhance targeted gastrointestinal delivery. Overall, these findings illustrate how *Pleurotus* can progress from a bioactive food matrix into high-value, microbiome-targeted nutraceuticals. Financial support: CNPq

From Microbiome Modulation to Cardiovascular Outcomes: Translational Applications of Nutraceuticals. José Luiz de Brito Alves Department of Nutrition, Federal University of Paraiba, João Pessoa, Paraíba, Brazil
The gut microbiome has emerged as a key interface between nutrition, metabolism, and cardiovascular health, providing new perspectives on the mechanisms underlying the beneficial effects of nutraceutical interventions. Bioactive compounds and nutritional strategies, including polyphenols, omega-3 fatty acids, dietary fibers and

prebiotics, probiotics, and other naturally derived compounds, may influence cardiovascular physiology both directly and through modulation of the gut microbial ecosystem. This presentation will discuss the translational potential of nutraceuticals in cardiovascular health, with particular emphasis on prebiotic and probiotic strategies and their interactions with the gut microbiome. Mechanistic, experimental, and clinical evidence will be integrated to explore how these interventions can reshape microbial composition and function, modify the production of microbial-derived metabolites, and influence intestinal barrier integrity, systemic inflammation, oxidative stress, metabolic regulation, and vascular function. Particular attention will be given to short-chain fatty acids and other microbiome-related metabolites as potential mediators connecting nutritional interventions to cardiovascular responses. Evidence regarding the effects of nutraceutical interventions on cardiometabolic and cardiovascular risk markers will be critically discussed, bridging findings from experimental models to human studies. Finally, current challenges for clinical translation will be addressed, including interindividual microbiome variability, compound-, substrate-, and strain-specific responses, identification of microbial and metabolic biomarkers, and the development of precision nutraceutical approaches targeting the gut–cardiovascular axis. Financial support: CNPq

SFR4 – Impacts of the Perinatal Environment on Health and Disease

Does Exposure to Vaccines, Pesticides, and Microplastics during Pregnancy and Lactation cause Autism in Offspring? Maria Tereza Nunes, Dept. of Physiology and Biophysics, Institute of Biomedical Sciences, University of São Paulo (ICB-USP-SP)

Autism is a neurodevelopmental disorder arising in childhood that is characterized by impairments in social communication and a pattern of repetitive behavior and restricted interests. The number of individuals diagnosed with autism spectrum disorder (ASD) has been rising. However, studies have measured autism in different ways, limiting comparability, which makes the data on autism a subject of scrutiny and debate. Endocrine disruptors (EDs) are chemicals that are widely spread in terrestrial and acquatical ecosystem and are present in many products used in daily life, and there is growing evidence linking the rising prevalence of autism to increased exposure to EDs. In fact, the exposure to EDs may cause adverse health effects, mainly during periods of vulnerability as pregnancy, in which the development of the fetus organs, especially the central nervous system occurs, and lactation, which is the primary source of energy for development and growth of the offspring. A bunch of studies have been published linking these two topics, and some of them present contradictory results for different reasons, like number of samples, effect size, different times of exposure or concentrations of EDs, among others. In this presentation, we will talk about autism, part of its genetic roots, some genetic risk factors, inherit copy number variants (CNVs), many of which affect genes that encode proteins related to neuronal development, and the reports that present similar or divergent results linking ED and autism or ASD, showing the possible causes underlying their findings. We will also talk about how the data analysis was performed and discuss the results obtained. In particular we will present data about vaccines, pesticides and microplastics exposition in pregnancy and lactation, which are critical biological windows of vulnerability and developmental plasticity, and the mechanisms involved and the effects on the development, growth and metabolism of the progeny, including epigenetic mechanisms. Finally, we will examine the scientific evidences, alerts and myths about endocrine disruption, as well as the methodological limitations inherent in much of the current research, particularly in human studies, which will be essential for an unbiased review of findings and to shape future research.

Anthropometric, Metabolic, and Hormonal Profile of the Mother-Child Dyad of Overweight Children. Vinicius José Baccin Martins[1], Rubia Cartaxo Squizato de Moraes[2], Thallyta Alana Ferreira Viana das Neves[2], Joicy Karla Granjeiro Pereira[2], José Luiz de Brito Alves[3] [1]Department of Biomedical Sciences, Federal University of Paraiba, Joao Pessoa, Brazil, [2]Postgradute Program in Nutrition Sciences, Federal University of Paraiba, [3]Department of Nutrition, Federal University of Paraiba, Joao Pessoa, Brazil;

Childhood and adolescence are critical periods for the development of obesity. Metabolic and endocrine changes described in children with obesity have been associated with cardiometabolic diseases in adulthood. Literature consistently reports increases in glycemia, insulin resistance, and alterations in lipid profiles; however, findings

regarding changes in adrenal function remain inconsistent. Obesity has been associated with changes in cortisol and dehydroepiandrosterone (DHEA) concentrations, as well as increased stress levels and food addiction. We explored changes in morning salivary cortisol and DHEA concentrations in children with obesity and their associations with body composition, metabolic profile, food addiction, and stress in a cross-sectional study. Children with obesity showed lower concentrations of salivary cortisol and DHEA and higher levels of food addiction compared with control children. We also aimed to evaluate the impact of maternal and child stress and food addiction on the nutritional status of children with obesity. Children were divided into a Control Group and an Obesity Group according to their BMI-for-age Z-score (BMI-Z). Mothers were allocated to the respective group of their children. Children with obesity exhibited a significantly higher prevalence of food addiction compared with controls, whereas mothers in the control group showed higher stress levels. Positive correlations were observed between mother–child pairs for body weight and waist circumference. Maternal BMI was the most significant predictor of child BMI-Z, suggesting that maternal BMI may have a greater influence on the nutritional status of children than food addiction or stress levels. This research was supported by Fundação de Apoio à Pesquisa do Estado da Paraiba (Grant 009/2021, Termo 3044/2021).

Maternal Obesity: Metabolic and Mitochondrial Dysfunction in Offspring. Carmen Cabanelas Pazos de Moura, Instituto de Biofisica Carlos Chagas Filho, Universidade Federal do Rio de Janeiro.
Maternal obesity during the perigestational period is associated with metabolic disturbances in offspring at different ages and is considered a predisposing factor for Metabolic Syndrome in adulthood. This raises an additional concern given the high prevalence of overweight among women of reproductive age, including in Brazil. Our group has demonstrated that maternal high-fat diet, even with a relatively low lipid content (29%), induces obesity and metabolic dysfunctions in offspring throughout life. The offspring exhibit fat accumulation in hepatic and skeletal muscle tissues, as well as lower mitochondrial density and mitochondrial damage, which are exacerbated in the presence of a metabolic challenge, such as fructose administration. These alterations were accompanied by changes in lipid synthesis and oxidation pathways, redox imbalance, and impairments in cellular homeostatic mechanisms, including inefficient UPR activation and reduced autophagic flux. Additionally, we investigated the potential preventive effects of n-3 polyunsaturated fatty acids. Supplementation with fish oil, a source of n-3 polyunsaturated fatty acids, during pregnancy was unable to protect the offspring at weaning from systemic metabolic alterations induced by the high-fat diet. However, it had partial protective effects, preventing liver histopathological damage in females and structural alterations in the soleus muscle. Fish oil also partially prevented mitochondrial damage in both tissues in the offspring at weaning. These effects were associated with adjustments in mitochondrial dynamics, particularly an increase in mitochondrial fusion. Additionally, fish oil improved the metabolic profile of these tissues in offspring at birth, particularly in male offspring. Thus, our studies support the evidence that maternal obesity increases offspring susceptibility to metabolic diseases and that n-3 polyunsaturated fatty acids provided during early life may potentially confer benefits by attenuating the detrimental effects of a maternal obesogenic diet. Financial support :: FAPERJ (Fundação Carlos Chagas Filho de Amparo a Pesquisa do Estado do Rio de Janeiro), CNPq e CAPES

SFR5 – Biology of Nicotine and Respiratory Diseases

Systemic Biological Effects of Nicotine. Ingrid D. Taricano Brazilian Society of Science and Technology for Harm Reduction – SBRed
One of the most widely discussed aspects of nicotine is its role in dependence. Neuronal nicotinic acetylcholine receptors (nAChRs) regulate nicotine's rewarding effects through their expression in central reward circuits. α4β2-containing nAChRs constitute major high-affinity nicotine-binding sites in the brain and are densely expressed in neurons involved in reward, particularly dopaminergic, GABAergic, and glutamatergic neurons in the ventral tegmental area (VTA). Nicotine-induced modulation of dopaminergic signaling has also attracted attention because of its potential relationship with symptoms associated with Parkinson's disease. High-affinity nAChRs may incorporate additional subunits, including β3, α6, and α5, generating receptor subtypes with distinct functional properties and different effects on nicotine-induced dopaminergic neurotransmission. Evidence also supports

potential therapeutic effects associated with nicotinic receptor subtypes. Stimulation of α7 nicotinic acetylcholine receptors (α7 nAChRs) by acetylcholine, choline, nicotine, other agonists, and positive allosteric modulators has been associated with reduced production of pro-inflammatory cytokines. These mechanisms may have therapeutic relevance in inflammatory conditions, including inflammatory bowel diseases such as ulcerative colitis and Crohn's disease. Experimental studies have also demonstrated α7 nAChR-mediated effects in rodent models of gastrointestinal disorders, including irritable bowel syndrome and postoperative ileus. Ulcerative colitis is primarily confined to the colon, whereas Crohn's disease may affect any segment of the gastrointestinal tract. As understanding of nicotine's mechanisms of action expands, increasingly selective pharmacological targets are being identified. This evolving knowledge highlights the importance of broadening the scientific discussion of potential therapeutic actions mediated by nicotinic receptors and deepening our understanding of nicotine pharmacology. Financial Support: SBRed

Pharmacological Aspects of Nicotine in the Body. Joelmir Lucena Veiga da Silva Faculdade de Medicina de Olinda, Olinda-PE, Brazil

Nicotine underlies tobacco addiction, influences tobacco use patterns, and is used as a pharmacological aid to smoking cessation. Nicotine exerts complex, bidirectional effects on the human body, acting concurrently as a pathogenic agent and a physiological modulator. The absorption, distribution, metabolism, excretion and disposition characteristics of nicotine from tobacco and medicinal products are reviewed. Regarding the nicotinic acetylcholine receptors (nAChRs) are members of the superfamily of pentameric ligand-gated ion channels and are expressed throughout the body, we will focus on their presence in neural and non-neuronal tissues. Within the cardiovascular system, exposure to nicotine induces premature cellular senescence in endothelial and vascular smooth muscle cells, accelerating arterial stiffness and atherogenesis, while also driving sympathetic hyperactivity and chronic hemodynamic stress associated with tobacco use disorder. Conversely, in the immune system, via the vagal anti-inflammatory pathway suppresses the release of pro-inflammatory cytokines, highlighting a therapeutic potential in modulating systemic inflammation. Within the central nervous system, nicotine exhibits a dual role ("friend or foe"), wherein acute enhancements in attention and working memory contrast with the risks of receptor desensitization, addiction, and neurotoxicity associated with prolonged exposure. Public health initiatives should prioritize combating smoking and its associated risks. Understanding nicotine's complex pharmacological effects is essential for comprehensive research and informed health policies. The purpose will be nicotine spans a spectrum between cardiovascular/neuroadaptive toxicity and neuroimmune modulation, underscoring the necessity for a rigorous evaluation of dosage, delivery route, and exposure duration in clinical and toxicological settings. Financial support: Brazilian Society of Science and Technology for Harm Reduction (SBRed)

Nicotine and Respiratory Diseases. Rodolfo Fred Behrsin. Universidade Federal do Estado do Rio de Janeiro (UNIRIO), Rio de Janeiro, Brazil

Nicotine is the primary addictive component of tobacco products, but its biological and clinical effects should be distinguished from those caused by tobacco combustion and the complex mixture of toxicants present in cigarette smoke. This presentation will review the pharmacology of nicotine with emphasis on its potential effects on the respiratory system. Nicotinic acetylcholine receptors (nAChRs) are expressed not only in the nervous system but also in airway epithelial cells, immune cells, fibroblasts, and other pulmonary tissues, providing biological plausibility for direct respiratory effects of nicotine. Experimental evidence suggests that nicotine may modulate airway inflammation, epithelial repair, mucociliary function, immune responses, fibroblast activation, and signaling pathways involved in tissue remodeling and tumor progression. However, the strength of evidence varies substantially across outcomes, and findings from in vitro and animal models should not be automatically translated into causation of respiratory disease in humans. The presentation will therefore critically examine the evidence linking nicotine itself to asthma, chronic obstructive pulmonary disease, pulmonary fibrosis, infections, and lung cancer, distinguishing mechanistic evidence from demonstrated clinical risk. Human experience with medicinal nicotine replacement therapy will also be considered as an important source of information on nicotine exposure without combustion. Finally, the concepts of hazard, risk, dose, route of administration, and comparative risk will

be discussed. This distinction is essential when evaluating tobacco harm reduction strategies: nicotine is not biologically inert and is responsible for dependence, but its risks should not be considered equivalent to those resulting from inhalation of tobacco smoke. The objective is to provide a balanced, evidence-based framework for understanding nicotine-related respiratory effects and their implications for harm reduction. Financial support: SBred.

SFR6 – **Research in Ecophysiology and Comparative Physiology in the Northeast Region: Challenges and Perspectives**

Diversity and Ecophysiology of Terrestrial Vertebrates in Northeast Brazil. Washington Luiz Silva Vieira Laboratório de Ecofisiologia Animal, Departamento de Sistemática e Ecologia, Centro de Ciências Exatas e da Natureza, Universidade Federal da Paraíba, Campus I, João Pessoa-PB

Northeastern Brazil supports a remarkable diversity of terrestrial vertebrates (tetrapods) across a broad range of ecosystems, including the Atlantic Forest, Caatinga, and increasingly urbanized landscapes. The persistence of these species in heterogeneous environments depends on physiological adjustments to environmental conditions and associated energetic demands. Here, we provide an overview of terrestrial vertebrate diversity in Northeastern Brazil and assess the current state of knowledge on their physiology and ecophysiology. We conducted a bibliographic search of studies addressing physiological and ecophysiological responses in amphibians, reptiles, birds, and terrestrial mammals occurring in the region, using the Web of Science, Scopus, and Google Scholar databases. By 2025, 1,890 terrestrial vertebrate species had been recorded in Northeastern Brazil, including 870 birds, 413 reptiles, 334 mammals, and 273 amphibians. Despite this remarkable biodiversity, research on the physiology and ecophysiology of these taxa remains limited. We identified 29 relevant studies, of which 20 (69.0%) focused on species from the Caatinga and nine (31.0%) on species from the Atlantic Forest. Amphibians (eight and three studies in the Caatinga and Atlantic Forest, respectively) and reptiles (eight and two studies, respectively) accounted for the largest proportion of the available literature. Mammals were represented by four studies in the Caatinga and three in the Atlantic Forest, whereas only one study addressing birds was identified, involving species from the Atlantic Forest. This pronounced geographic and taxonomic research gap is particularly concerning in the context of ongoing climate change, which may intensify the physiological challenges faced by terrestrial vertebrates. Greater investment in ecophysiological research is therefore urgently needed to improve our understanding of species' responses to environmental variation and climate change. By providing baseline information on physiological traits and environmental responses, such research can contribute indirectly to biodiversity conservation and support evidence-based management strategies and conservation planning for terrestrial vertebrates in Northeastern Brazil.

Urban impacts on sandy beaches: insights from mole crabs ecophysiology in Paraíba, Northeastern Brazil. Amado *EM Laboratório de Ecofisiologia Animal*, *Centro de Ciências Biológicas e Sociais Aplicadas*, *Universidade Estadual da Paraíba*, *Campus V*, *João Pessoa*, *PB*, *Brazil*.

Sandy beaches in Northeastern Brazil face growing urban pressures, including stormwater and sewage discharge that locally reduce salinity and introduce contaminants, plus trampling from recreational use. Mole crabs of the genus *Emerita* (Decapoda: Hippidae) are conspicuous, abundant inhabitants of the swash zone and are increasingly recognized as sentinels of these impacts. This talk presents a decade of undergraduate research from our laboratory on *Emerita almeidai* (formerly identified as *E. portoricensis*) on beaches of Paraíba, integrating population, physiological and cellular endpoints. Population surveys showed lower density, abundance and fecundity on beaches with higher human foot traffic. As an osmoconformer, *E. almeidai* tolerates moderate salinity fluctuation through adjustments in tissue hydration and body weight, however, severe hyposalinity (5‰), as may occur near stormwater outfalls, impaired burrowing performance, disrupted ionic balance and increased mortality. Animals from a beach receiving contaminated stormwater showed higher mortality and lower condition factor than those from clean sites, partially reversed after acclimation in clean seawater. At the cellular level, the multixenobiotic resistance (MXR) phenotype showed context-dependent, still inconclusive responses to metals and salinity. Together, these findings support *E. almeidai* as a multi-level bioindicator of urban impacts on sandy

beaches. Our laboratory is now moving toward a new set of studies, combining chemical contaminant analysis with long-term population monitoring, to further consolidate this species as a sentinel of anthropogenic impact on Northeastern Brazilian beaches. Financial support: PIBIC CNPq/UEPB

Research activities at the Animal Ecophysiology Laboratory at Federal University of Paraíba. Paulo Fernando Guedes Pereira Montenegro Animal Ecophysiology Laboratory, Universidade Federal da Paraíba, Centro de Ciências Exatas e da Natureza, Campus I, João Pessoa-PB, Brazil

The Animal Ecophysiology Laboratory has been conducting experiments with animals from different taxa. Some projects use species as study models to address broader research questions, whereas others investigate questions concerning the taxa under study. Another line of research is the use of experiments in educational contexts, employing both animal and physical models. We have carried out projects investigating differences in locomotor performance between albino and pigmented frogs of the species *Lithobates catesbeianus*, *and w*e are currently developing protocols using this species as a model to investigate the effects of abiotic factors on metamorphosis, as well as to validate the use of glucometers in amphibians. We have also studied the role of temperature and hormones in regulating metaorphosis in frogs of the species *Pleurodema diplolister*. Currently, we are developing protocols for studies on estivation in this species, using populations from different ecosystems. We have developed projects investigating thermal biology and water regulation processes in colonies of the termite species *Nasutitermes ephratae*, as well as aspects of nest composition and its effects on colony temperature. More recently, we developed an apparatus for determining the Critical Thermal Maximum (CTmax) in small terrestrial animals and initiated studies with the ant species *Dinoponera quadriceps*. We have also recently developed a protocol for investigating water regulation in small terrestrial animals, validated through a project involving the invasive millipede species *Trigoniulus corallinus*. In an educational context, we have developed simulation models to demonstrate heat exchange processes considering the relationship between surface area and volume in different bodies, as well as models designed to simulate behavioral and physiological responses of animals under scenarios of global warming and ocean acidification. Future projects include expanding CTmax studies to other invertebrate and small vertebrate species, and comparing populations from different ecosystems and under distinct ecological contexts. In addition, we intend to develop further simulation models and simplified protocols for animal-based experiments, aiming their use in undergraduate teaching contexts.

SFR7 Pain, Inflammation and Emotion: Therapeutic Challenges and Opportunities

Chronic Pain and Cognition: Neurobiological Mechanisms and Sex Differences. Marucia Chacur
Department of Anatomy, Functional Neuroanatomy of Pain Laboratory, Institute of Biomedical Science, University of São Paulo

Chronic pain is a complex and persistent condition that extends beyond sensory and nociceptive processing, involving profound alterations in neuronal, glial, immune, metabolic, and cognitive function. Increasing evidence indicates that persistent pain can affect brain circuits involved in learning, memory, attention, emotional processing, and decision-making, while cognitive and affective processes can, in turn, influence pain perception and chronicity. Understanding the bidirectional interaction between pain and cognition is therefore essential for elucidating the mechanisms underlying the transition from acute to persistent pain. Experimental models of neuropathic pain have demonstrated that chronic nerve injury induces sustained changes in peripheral and central nervous system function, including neuroinflammation, altered neuronal excitability, glial activation and mitochondrial dysfunction. These mechanisms may contribute not only to persistent nociceptive hypersensitivity but also to alterations in neural circuits involved in cognitive processing. Importantly, these responses are not necessarily equivalent between males and females. Sex-related differences in immune responses, neuroglial signaling, hormonal regulation, may influence both the development and maintenance of chronic pain and its consequences for cognitive function. Here, we will discuss the neurobiological mechanisms linking chronic pain to cognitive dysfunction, with particular emphasis on neuroinflammation, neuronal plasticity, glial activity, and cellular bioenergetics. Experimental findings from models of neuropathic pain will be used to illustrate how persistent pain alters neural and molecular pathways and how these responses may differ between sexes.

Particular attention will be given to evidence indicating that biological sex can influence nociceptive processing, inflammatory responses, and the response to non-pharmacological interventions. Finally, we discuss the therapeutic implications of these mechanisms, including the potential of photobiomodulation and other non-pharmacological strategies to modulate neuroinflammatory, and neuronal pathways associated with chronic pain. Integrating pain, cognition, and sex as interconnected biological dimensions may provide a more comprehensive framework for understanding chronic pain and for developing more precise and effective therapeutic approaches. Financial Support: FAPESP 2022/08212-6

Sex-based differences in the prevention of stress-induced anxiety: effects of the pro-resolving lipid mediator Resolvin D5. Thalita Suemy Uada[1], Luiza Couto de Avanço[1], Waldiceu Aparecido Verri Jr[2], Joice Maria da Cunha[1], Janaina Menezes Zanoveli[1]*. [1]Laboratory of Neuropsychopharmacology, Department of Pharmacology, Federal University of Paraná, Brazil. [2]Laboratory of Pain, Inflammation, Neuropathy, and Cancer, Londrina State University, Brazil.

Stress and inflammation are closely interconnected in emotional behavior, and impaired resolution of inflammatory responses may increase vulnerability to anxiety. Specialized pro-resolving mediators (SPMs) may restore inflammatory homeostasis. This presentation will discuss our research on Resolvin D5 (RvD5), with emphasis on emoticons and sex as a biological variable. Initial studies showed that RvD5 prevented anxiety- and depressive-like behaviors and reduced IL-1β in the hippocampus and prefrontal cortex of diabetic rats. We subsequently found that repeated RvD5 administration prevented acute restraint stress-induced anxiety-like behavior in male and female rats, without altering basal emotional behavior or locomotor activity. Protection was accompanied by prevention of stress-induced increases in hippocampal IL-1β and TNF-α and modulation of corticosterone. Although protection occurred in both sexes, its persistence after treatment cessation was observed only in females. Importantly, unpublished findings provide preliminary evidence for distinct neuromodulatory mechanisms of RvD5-induced resilience in males and females. Pharmacological blockade indicates a predominant role for CB2 receptors in males, whereas in females the protective effect is attenuated by blockade of CB1, CB2, or 5-HT1A receptors. Thus, the same pro-resolving mediator may recruit distinct cannabinoid and serotonergic pathways depending on sex. Finally, studies with other SPMs, including Protectin DX and lipoxins, will illustrate convergent effects on neuropathic pain, emotional behavior, oxidative stress, and nociception. Together, these findings support resolution of inflammation as a strategy for preserving emotional resilience and highlight sex-dependent mechanisms for therapeutic development. Financial support: CNPq – PIBIC and Research Productivity Fellowship (Call No. 09/2023; Grant No. 307714/2023-3).

Thematic Symposia

TSFR 2 – Developmental Programming of Cardiometabolic Diseases: From Early-Life Insults to Adult Health

Maternal Protein Restriction and Cardiovascular Risk: New Insights into Developmental Programming Mechanisms. Viviane Oliveira Nogueira[1], Aiany Cibelle Simões-Alves[1], Jéssica de Oliveira Campos [1], Euclides da Conceição Guiliche[1 2], Carol Virginia Gois Leandro[1], João Henrique Costa-Silva[1 1]Universidade Federal de Pernambuco (UFPE), Academic Center of Vitória, Vitória de Santo Antão, PE, Brazil. [2]Pedagogical University of Maputo, Maputo, Mozambique.

Abstract: Adverse nutritional exposures during critical developmental windows can induce persistent physiological adaptations that increase cardiometabolic vulnerability later in life. Maternal protein restriction is a well-established model of developmental programming and provides important insights into the mechanisms linking early-life undernutrition to hypertension. Studies from our group have demonstrated that perinatal protein restriction induces early alterations in respiratory control and peripheral chemosensitivity, followed by sympathetic-respiratory overactivity and increased arterial pressure in adult offspring. Mechanistically, these alterations involve enhanced carotid body signaling, HIF-1α-related pathways, oxidative imbalance within brainstem cardiovascular regions, and peripheral activation of the renin-angiotensin system. Importantly, carotid body removal prevents the development of hypertension, supporting a causal contribution of altered chemoreflex signaling to the programmed cardiovascular phenotype. These effects are not necessarily irreversible, as maternal

physical activity attenuates cardiorespiratory, metabolic, and molecular alterations induced by protein restriction. More recent findings extend this developmental perspective toward human populations, linking low birth weight with impaired aerobic fitness in school-aged children and identifying early metabolic signatures associated with cardiometabolic risk. Collectively, these findings support an integrated model in which early nutritional adversity programs neurocardiorespiratory and metabolic pathways, while revealing windows of plasticity that may provide opportunities for early prediction and intervention.
Financial support: CNPq, CAPES, COFECUB and FACEPE.

TSFR 3 - **Neuroimmunology: Basic and Translational Aspects**

Sympathetic modulation of immunity: focus on neutrophil heterogeneity. Alexandre A. Steiner, Instituto de Ciencias Biomedicas, Universidade de Sao Paulo, Sao Paulo, SP, Brazil

Although the sympathetic splanchnic nerve is recognized as a major immunoregulatory pathway, its precise role during infection remains to be defined. Here, we assessed the effects of bilateral ablation of the greater splanchnic nerve (SplancX) on bacterial burden and immune function in a rat model of E. coli–induced septic peritonitis. SplancX markedly reduced bacterial burden within 24 h, lowering by 96% in the peritoneum and by 92% in the spleen. This pronounced reduction was not attributable to major differences in the overall infiltration of innate immune cells, including neutrophils and macrophages, as determined by flow cytometry. Cytokines were not affected by SplancX either. Single-cell RNA sequencing was therefore used to probe for more subtle changes in the activation programs of leukocyte populations. Among the nine cellular clusters identified in the peritoneum of infected rats, three displayed transcriptional profiles consistent with activated neutrophils, whereas two represented quiescent neutrophils with an immunosuppressive signature. SplancX altered the distribution of these neutrophil subsets in a manner indicative of enhanced immunity, increasing activated neutrophils while reducing quiescent neutrophils. The remaining clusters comprised macrophages and erythrocytes, none of which exhibited changes that could explain the enhanced bacterial clearance. Consistent with increased neutrophil activation, protein markers associated with neutrophil degranulation and NETosis were elevated in the peritoneal lavage of SplancX-treated rats. These findings demonstrate that the splanchnic nerve strongly influences bacterial clearance during the acute phase of infection, likely through selective modulation of the balance between microbicidal and quiescent neutrophil subsets. Support: FAPESP, CAPES, CNPq.

TSFR4 – **From Model to Mechanism: The Role of Experimental Choice in Pharmacological Research**

Complement or Replacement? Animal Models and New Alternatives in Drug Research. Maria Martha Campos (PUC-RS)

The development of new therapeutic agents has traditionally relied on animal models to establish proof of concept, characterize pharmacological activity, and assess safety before clinical testing. Meanwhile, rapid advances in new approach methodologies (NAMs), including organoids, microphysiological systems, organ-on-chip technologies, advanced three-dimensional cell cultures, and computational modeling, have transformed preclinical research and strengthened efforts to implement the principles of Replacement, Reduction, and Refinement (3Rs). These innovations have successfully replaced animal testing in certain areas, particularly cosmetic safety assessment. This raises the question of whether a similar shift is feasible for drug discovery and development. Current scientific evidence indicates that, while NAMs significantly enhance human relevance, mechanistic understanding, and screening efficiency, they are not yet able to fully replicate the complex systemic interactions necessary to evaluate pharmacokinetics, efficacy, toxicity, and long-term safety of new therapeutics. This lecture will explore the ongoing debate regarding the translational value of animal models, recognizing their limitations while emphasizing their continued regulatory and scientific importance in pharmaceutical research. Rather than presenting animal and non-animal approaches as opposing strategies, the lecture will argue that they should be viewed as complementary within an integrated preclinical framework. Special attention will be given to drug repositioning, where animal studies often remain essential despite extensive prior knowledge of the compounds involved. Finally, the presentation will discuss the potential scientific and clinical consequences of prematurely eliminating animal

experimentation, including increased uncertainty in efficacy and safety predictions and a potentially higher failure rate during clinical development. Therefore, the future of drug research is unlikely to rely solely on replacement; rather, it will depend on the strategic integration of innovative human-based models with carefully selected animal studies until alternative methodologies can reliably replicate whole-organism physiology.

RT2 – Beyond Academia

Chair: Isis Nem de Oliveira Souza (Coordinator SBFTE Jovem, UFRJ)

The PhD in Pharmacology as a Strategic Differential in Aesthetics: From Academia to Entrepreneurship in Healthcare. Samara Rodrigues Bonfim Damasceno Oliveira Cespu Europa College

The PhD in Pharmacology constitutes a stricto sensu academic training of high scientific complexity, aimed at developing competencies in teaching, research, and innovation. In Brazil, postgraduate programs in Pharmacology are predominantly concentrated in public universities. The most traditional career path for these PhD graduates is entry through competitive public examinations for positions in higher education institutions; however, access is limited and dependent on the restricted expansion of vacancies, faculty replacement through retirements, and institutional restructuring processes. This scenario is reflected in the migration and brain drain of highly qualified researchers trained with national public investment to other countries, as well as in competition for teaching positions in private higher education institutions, whose remuneration is often below the qualification level of these professionals. In parallel, the aesthetic healthcare field shows continuous growth, with increasing use of biomaterials, injectable substances, and technologies based on hyaluronic acid, collagen biostimulators, and other bioactive agents, requiring higher scientific qualification from practicing professionals. In this context, the PhD in Pharmacology provides a relevant technical differential, particularly through in-depth understanding of pharmacokinetic and pharmacodynamic mechanisms applied to products used in aesthetic procedures, contributing to greater safety, predictability, and therapeutic efficacy. Advanced academic training also confers greater technical authority and professional recognition, directly impacting insertion into the aesthetic market and healthcare entrepreneurship, a field that, in addition to being promising, often offers financial returns higher than those of traditional academic careers. Beyond clinical practice, PhD holders in Pharmacology may also engage in teaching activities in undergraduate and graduate programs in aesthetic-related fields, enabling diversification of professional roles, expansion of career pathways, and increased income potential. Thus, the PhD in Pharmacology should not be understood solely as a pathway to public academic positions or traditional university careers, but as a solid foundation for multidisciplinary practice, innovation, and entrepreneurship in contemporary aesthetic healthcare. **Financial support:** Cespu Europa College

Beyond Research: Pharmacology as Cross-Disciplinary Training for Multiple Career Paths in Veterinary Medicine. **Author** Humberto Barbosa da Costa Filho Biotec Group; Animal Facility Center, State University of Ceará (UECE)

Graduate education in Pharmacology is often associated with the training of researchers and academics. However, its contribution extends beyond these traditional roles by fostering essential cross-disciplinary competencies for professional practice across diverse areas of Veterinary Medicine. Scientific reasoning, critical appraisal of evidence, an integrated understanding of biological systems, experimental design, and evidence-based decision-making are skills that significantly broaden veterinarians' professional opportunities. From this perspective, Pharmacology emerges as a field of training that integrates research, teaching, innovation, management, and ethics, enabling professionals to work in a wide range of settings, including laboratory animal facilities, specialized companies, animal ethics committees, professional development programs, and scientific consulting. The application of this expertise to the management and technical supervision of laboratory animal facilities, the refinement of experimental protocols, anesthesia and analgesia in animal models, scientific support for researchers, the training of qualified personnel, and science communication demonstrates that the impact of pharmacological training extends far beyond pharmacotherapy and the study of drugs. Rather than preparing professionals for a single career path, graduate education in Pharmacology cultivates a way of thinking grounded in the integration of science, ethics, and innovation, equipping professionals to address complex challenges and strengthen the interface between academia, industry, and society.

Abstracts

01. Cellular and Molecular Pharmacology

01.001 **Detection of Bacterial DNA in the Plasma of Breast Cancer Patients by qPCR and the Influence of Obesity Phenotype on Bacterial Translocation**. Alves ROF[1], Freitas GL[1], Cajado AG[1], Florêncio KGD[1], Teixeira-Filho JIF[1], Ribeiro MVS[1], Maia DCBSC[2], Vale ML[1], Rocha-Filho DR[3], Arruda LM[4], Lima-Júnior RCP[1],Wong DVT[1] [1]UFC, Lab Inflammation and Cancer Pharmacology, Dept Physiology and Pharmacology [2]Dpt of Pathology and Forensic Medicine, Brazil; [3]HUWC-UFC, Walter Cantídio University Hospital. [4]ICC, Haroldo Juaçaba Hospital, Cancer Institute of Ceará. Fortaleza, Brazil

Introduction: Obesity is recognized as a significant risk factor for the development and poor prognosis of breast cancer, particularly in postmenopausal women. Furthermore, obesity-driven chronic inflammation and gut dysbiosis increase intestinal permeability, which can compromise therapeutic outcomes. **Aim:** To investigate bacterial translocation through plasma detection of 16S rRNA in patients with breast cancer before and after cancer treatment, evaluating its association with the obesity score. **Methods:** This is a prospective study of female patients diagnosed with breast cancer. Bacterial translocation was investigated by detecting the 16S rRNA gene in plasma using qPCR on a QuantStudio3 platform. For this purpose, DNA was extracted on the KingFisher Flex using the MDX Pathogens Kit. The analytical sensitivity of the 16S test was validated using a standard serial dilution curve (*E. coli*, ATCC 2582, 10^7; to 10^1 CFU/ml), and the beta-actin gene was used as an internal control. Initially, the detection of 16S was investigated in an unpaired manner in the pre-treatment (n=154) and post-treatment (n=66) groups. Next, metabolic risk in the pre-treatment group was stratified based on the following indicators: BMI >30 kg/m^2, waist circumference >88 cm, and waist-to- height ratio >0.5, to establish an obesity score ranging from 0 to 3 and to correlate it with the presence or absence of 16S. Analyses were performed using Fisher's exact test, the chi-square test, and the chi-square test for trend, with a significance level of $p<0.05$. Ethics committee approval: number 4,470,803 and 4,664,756. **Results:** The detection limit for 16S in the qPCR assay was 10^2 CFU/mL for qualitative analysis with a Ct of 35 (mean of triplicates + 1 Ct deviation). For 16S detection, 220 patients with breast cancer were evaluated. Of these, a higher prevalence of 16S was observed in the plasma of patients before treatment (30.19%; 48/159) compared to after treatment (16.67%; 11/66), $p<0.0452$. Next, patients were stratified into obesity severity scores as follows: score 0 (20), score 1 (64), score 2 (35), and score 3 (35). It was found that although a substantial proportion of patients began treatment with some degree of obesity impairment ($p<0.00001$), this condition did not initially lead to increased bacterial translocation ($p<0.5852$). It should be noted that this is a preliminary study, with ongoing recruitment and matched longitudinal studies required for causal confirmation. **Conclusion:** Detected bacterial circulation by qPCR-based measurement of plasma 16S rRNA, is prevalent in patients with breast cancer and decreases substantially after chemotherapy treatment. Obesity dysfunction, present in most patients, was not a determining factor for the presence of circulating bacterial DNA.
Funding: CNPq, Capes, Funcap, EBSERH.

01.002 **Quinoxalinylhydrazone As a Potential HDAC Inhibitor in Acute Myeloid Leukemia (AML): Evaluation of Antileukemic Activity and Epigenetic Effects**. Macêdo SMN[1], Sales SLA[1,2], Mota JA[1,2], Gress LSB[1,2], Lima JM[1,2], Oliveira KAF[1], Bastos RS[1,2], Desiderio GA[1,2], Xavier EEP[1], Soares IF[1], Maranhão SS[1,3], Furtado CLM[4] and Pessoa C[1,2]. [1]UFC, Lab. of Experimental Oncology, Drug Research and Development Center, Brazil; [2]UFC, PPG Pharmacology, Brazil; [3]UFC, PPG Translational Medicine, Brazil; [4]UFMG, Dept Genetics, Ecology and Evolution, Institute of Biological Sciences, Brazil.

Introduction: Acute myeloid leukemia (AML) is a hematologic malignancy characterized by molecular heterogeneity and poor response to current therapies. Although its pathophysiology has historically been associated with genetic alterations, recent evidence highlights the important role of epigenetic mechanisms in disease progression, recurrence, and therapeutic resistance. Histone deacetylases (HDACs) are key regulators of epigenetic modulation and are frequently dysregulated in hematologic malignancies, representing promising therapeutic targets. Quinoxaline derivatives exhibit several pharmacological properties, including antitumor activity, and recent studies suggest their potential as HDAC inhibitors. **Objective:** This study aimed to investigate the antileukemic and epigenetic effects of the quinoxalinylhydrazone PJOV56 in human AML cell lines. **Methods:** The cytotoxic activity of PJOV56 was evaluated in AML cell lines using the MTT assay, and MOLM-13 cells were selected for subsequent analyses based on IC_{50} values. Cells were treated with PJOV56 (2 and 4 μM), and morphological alterations were assessed after 24 h by H&E staining. HDAC of class I/IIb activity was determined using the HDAC-Glo™ I/II Assay, while the expression genic of HDAC2, HDAC3, HDAC6, HDAC8, HDAC10, and CDKN1A was analyzed by qPCR after 6 h of treatment using the 2^−ΔΔCq method. Molecular docking was performed to predict the interaction of PJOV56 with HDAC isoforms. **Results:** PJOV56 significantly reduced the viability of AML cell lines, including MOLM-13, OCI-AML3, and MV4-11 cells, presenting IC_{50} values ranging from 1,28 μM to 3,76 μM. In MOLM-13 cells, treatment with PJOV56 induced morphological changes consistent with apoptosis, necrose and senescence, caused by a reduction in cell diameter and area, cytoplasmic leakage, and an increase in cell size compared to the control, respectively. The compound also significantly inhibited HDAC activity by 40% at the lowest concentration tested (0,195 μM) compared with the negative control. Gene expression analysis demonstrated modulation of epigenetic and cell cycle regulators, including decreased expression of HDAC2 (FC=0,15; $p < 0,05$), HDAC6 (FC=0.85), HDAC10 (FC=0.47), and increased expression of HDAC3 (FC=1.31), HDAC8 (FC=1.47; $p < 0,0001$), and CDKN1A (FC=3.10; $p < 0,05$). Molecular docking analyses revealed favorable interactions between PJOV56 and class I and II HDACs, with the highest predicted affinity observed for HDAC2, with a PLP.Fitness score of 72.81. **Conclusion:** Collectively, these findings demonstrate that PJOV56 exhibits significant antileukemic activity associated with epigenetic modulation, highlighting its potential as a promising candidate for further investigation as a therapeutic agent for AML. Ethics and **Financial support:** This study was supported by INCTBIO2, PRONON, Brazilian Ministry of Health, FINEP, CNPq, CAPES, and FUNCAP.

01.003 **6-Nitrodopamine Potentiates Noradrenaline-Induced Intracellular Calcium Signalling Via a Tetrodotoxin-Sensitive Mechanism in Human Aortic Endothelial Cells**. Ribeiro LC[1,2], Britto-Júnior J[1,2], La Scala T[1], Nawaci A[1], De Nucci G[2], Ferro A[1] [1]King's College London, Faculty of Life Sciences and Medicine, London, UK; [2]Unicamp, Dept Pharmacology, Faculty of Medical Sciences, Campinas, SP, Brazil.

Introduction: 6-Nitrodopamine (6-ND) is a recently described endothelium-derived catecholamine involved in cardiovascular regulation (1). Since endothelial intracellular calcium ([Ca^2+]i) is essential for vascular signalling and mediator release (2), we investigated whether 6-ND regulates [Ca^2+]i in human aortic endothelial cells (HAECs), whether it interacts with classical catecholamines, and whether tetrodotoxin (TTX)-sensitive mechanisms are involved. **Methods**: HAECs were cultured in endothelial cell medium and seeded in black, clear-bottom 96-well plates. Live-cell [Ca^2+]i was assessed using fura-2 AM, with fluorescence recorded at 340/380 nm excitation and 510 nm emission at 37 °C (3). Cells were stimulated with 6-ND, noradrenaline (NA), adrenaline (ADR) or dopamine (DA). Responses were quantified as peak increase and area under the curve (AUC). Experiments were also performed in nominally Ca^2+-free HBSS. Synergism was assessed by combining subthreshold concentrations of 6-ND and catecholamines. TTX (10 nM) was used to investigate TTX-sensitive components. **Results**: 6-ND, NA, ADR and DA induced concentration-dependent increases in [Ca^2+]i in HAECs. These responses were significantly attenuated in nominally Ca^2+-free conditions, indicating an important role for extracellular Ca^2+ entry. At 0.1 nM, 6-ND or NA alone produced little or no detectable [Ca^2+]i response. However, combined exposure to 6-ND and NA at these subthreshold concentrations markedly increased [Ca^2+]i, significantly enhancing both peak response and AUC compared with either compound alone. TTX did not affect basal [Ca^2+]i, but significantly reduced 6-ND-induced [Ca^2+]i responses at 100 and 300 nM. In contrast, TTX did not modify NA- or ADR-induced responses, while DA was inhibited only at 300 nM. **Conclusion**: 6-ND acts as an endogenous modulator of endothelial calcium signalling in HAECs. Its potentiation of NA-induced [Ca^2+]i responses at subthreshold concentrations suggest synergism with classical catecholamines. The selective inhibition of 6-ND responses by TTX indicates activation of a TTX-sensitive pathway that differs from the mechanisms underlying NA- and ADR-induced calcium signalling. **References**: 1\. Zatz R, De Nucci G. Physiology. 2024;39:44–59. 2\. Fukao M, et al. Br J Pharmacol. 1997;120:1328–34. 3\. Morgan AJ, Jacob R. J Physiol. 1998;513:83–101.

01.004 **Exploring the Relationship Between PTEN and Klotho in Autophagy**. dos Santos, GRO[1], Berwick, D[2], Kawamoto, EM[1] [1]ICB-USP, Functional and Molecular Biology, Brazil, [2]University of London, City St. George's, School of Health & Medical Sciences, England.

Introduction: PTEN is a tumor suppressor gene that plays an important role in cellular survival, growth and proliferation. PTEN inhibits the PI3K-Akt-mTOR signaling pathway, a highly conserved pathway that negatively regulates autophagy. Similarly, Klotho is a longevity-associated protein that has been shown to downregulate the PI3K-Akt-mTOR pathway. Autophagy is a homeostatic process responsible for the degradation and recycling of proteins and cellular organelles, and it plays an essential role in neuronal development and synaptic plasticity. The autophagy process machinery also involves Rab proteins such as Rab7, which regulates the degradative autophagy. **Objectives:** The main objective of this project was to investigate the relationship between PTEN and Klotho in autophagy-related markers, including ULK1, phosphorylated ULK1 (p-ULK1), and Rab7, in CRISPR-Cas9-mediated PTEN-knockout cells in the presence or absence of Klotho-overexpressing plasmids. **Methods:** HEK293 cells were transfected with CRISPR-Cas9 PTEN plasmids to generate PTEN- KO cells. The efficiency of the PTEN knockout was evaluated by measuring the protein expression of PTEN by Western blot, PCR amplification, and sequencing. PTEN-KO cells were transfected with Klotho (membrane and secreted) and dsRed- tagged Rab7 plasmids to analyze the expression of p-ULK1/ULK expression by Western blot and Rab7 subcellular localization by immunofluorescence. Results The results suggest that PTEN-knockout cells exhibit diffuse Rab7 localization, which may impair Rab7-dependent autophagy processes. In these cells, diffuse Rab7 localization may be attenuated by Klotho treatment ($F(2, 17) = 8{,}141$; $^{*}p = 0{,}0266$; $^{**}p = 0{,}0093$). In contrast, neither PTEN knockout nor Klotho treatment alters ULK protein expression or its phosphorylation. **Conclusion:** These findings provide new insights into the relationship between PTEN and Klotho in the regulation of autophagy using complementary gene-silencing and gene-editing approaches (shRNA and CRISPR-Cas9 technologies).

01.005 **Effects of Endogenous and Exogenous H_2S on the Activity of Antioxidant Enzymes of Cultured Human Umbilical Vein Endothelial Cells** (**HUVECs**). Sebastião MA, da Costa Marques LA, Coavoy-Sánchez SA, Costa SKP, Teixeira SA, Muscará MN ICB-USP, Depto Farmacologia, Lab Farmacologia Bioquímica dos Radicais Livres, Inflamação e Dor São Paulo, SP, Brasil

Introduction: Oxidative stress is a condition present in various chronic diseases and is defined as the imbalance between the production of reactive oxidative species and the ability to be neutralized by the antioxidant defenses of the biological system under study. The antioxidant enzymes superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) are thus crucial for maintaining homeostasis. In addition, H_2S has been shown to exert antioxidant effects, at least partly, via Nrf2 pathway. **Objectives:** In this study, we investigated the effects of endogenous H_2S and exogenous H_2S delivery on the above mentioned enzymes present in cultured HUVECs. **Methods:** Endogenous H_2S generation by HUVEC lysates was assessed by the formation of PbS and in the presence of the H_2S biosynthesis inhibitors aminoxyacetic acid (AOAA), propargyl glycine (PAG) and beta-cyanoalanine (BCA; all at 10 mM). The antioxidant enzyme activities were kinetically measured (UV/vis spectrophotometry) in the HUVEC lysates after incubation of the cells with 10 mM of either AOAA, PAG or BCA, or 10 μM of the H_2S donors, Na_2S and Lawesson's reagent, during 4 h. Activity results are expressed as mean±SEM of percentages relative to respective untreated control cell group. **Results:** H_2S generation by the cell lysates was abolished by AOAA treatment, but unaffected by either PAG or BCA. The antioxidant enzyme activities, as measured in the different treatment groups, are shown in the Table below (*P<0.05, **P<0.01, ***P<0.001 vs. Control).

	Controle	AOAA	PAG	BCA	Na2S
SOD	100,0±4,0	72,9±6,6**	83,7±3,2**	87,4±3,1	90,8±3,83;
CAT	100,0±14,0	24,0±4,7 *	36,8±6,6*	108,7±33,5	90,0±9,6
GPX	100,0±13,6	38,8±0,8*	49,4±1,9*	79,1±6,3	83,3±12,3
GR	100,0±1,5	84,7±6,3	110,9±14,2	109,2±5,5	116,6±7,6
GST	100,0±0,9	108,2±1,4*	110,3±1,7	109,6±1,6	107,1±18,0***

Conclusions: Our results suggest that endogenous H_2S is crucial for maintaining the activity of antioxidant enzymes, while exogenous H_2S donors exert effects depending on their chemical nature and release profile. While RL can activate signaling pathways that promote increased protein expression, Na_2S does not reproduce these effects, probably due to its ionic nature and/or instantaneous H_2S release.**Funding**: FAPESP, CNPq, CAPES, PDCT-Angola

01.006 **APT20TTMG Suppresses Clonogenic Growth and Induces S-Phase Accumulation in U-87 MG Glioblastoma Cells**. Lobo EB[1,2], Oliveira VS[1,2], Silva DKC[1], Nogueira ML[2], Soares ES[3], Sinatti VVC[3], Silva JC[3], Bottos RM[3], Leal CBQS[3], Meira CS[1,2] [1]Fiocruz-BA, Salvador, [2]SENAI CIMATEC-BA, Salvador, [3]Aptah Bio, San Carlos, CA, USA.

Introduction: Glioblastoma (GBM) is the most aggressive primary brain tumor in adults and remains associated with poor prognosis despite treatment with surgery, radiotherapy, and temozolomide (TMZ). RNA-based therapeutics have emerged as a promising strategy to target molecular pathways involved in tumor progression and treatment resistance. APT20TTMG is an oligonucleotide designed to modulate U1-snRNP-associated RNA processing pathways, potentially disrupting mechanisms required for glioblastoma cell survival. **Objectives:** To investigate the effects of APT20TTMG on clonogenic growth, cell cycle progression, and gene expression in U-87 MG glioblastoma cells. **Methods:** U-87 MG cells were treated with APT20TTMG (0.3–30 μM), using TMZ (100 μM) as a reference drug. Antitumor activity was assessed by clonogenic assay and cell cycle analysis by flow cytometry following propidium iodide staining. Gene expression was evaluated by RT-qPCR, focusing on genes associated with tumor survival, adaptability, DNA repair, and stemness (*GFAP* , *MAPT* , *SOX2* , *MLH1* , *MSH2* , *POLK* , and *MGMT*) and cell cycle progression and proliferative signaling (*CCNB1* , *CDK1* , *CDK2* , *CDKN1A* , *MAPK1* , *MAP2K1* , and *EGFR*). **Results:** APT20TTMG significantly reduced clonogenic growth, decreasing colony formation by 47.1%, 73.1% and 80.0% at 0.3, 3 and 30 μM, respectively, compared with untreated cells. For comparison, TMZ (100 μM) reduced colony formation by 90.8%. Cell cycle analysis revealed a marked accumulation of cells in S phase following APT20TTMG treatment. Compared with untreated cells (26.7% S; 65.3% G1), treatment with 3 and 30 μM increased the S-phase population to 47.3% and 52.8%, respectively, while reducing the G1 fraction to 32.5% and 11.6%.Gene expression analysis demonstrated broad transcriptional modulation following treatment with 3 μM APT20TTMG. Notably, genes associated with tumor survival, adaptability, DNA repair, and stemness (*GFAP* , *MAPT* , *SOX2* , *MLH1* , *MSH2* , *POLK* , and *MGMT*) were downregulated. Similarly, key regulators of cell cycle progression and proliferative signaling, including CC*NB1* , *CDK1* , *CDK2* , *CDKN1A* , *MAPK1* , *MAP2K1* , and *EGFR* , were also reduced. These findings suggest that APT20TTMG impairs glioblastoma cell proliferation through coordinated modulation of pathways involved in cell cycle progression, tumor adaptability, and cellular survival. **Conclusion:** APT20TTMG exhibited potent antiproliferative activity in U-87 MG cells by suppressing clonogenic growth, promoting S-phase accumulation, and downregulating genes associated with proliferation, survival, DNA repair, and tumor adaptability. These findings support further investigation of APT20TTMG as a novel oligonucleotide-based therapeutic strategy for glioblastoma.

01.007 **Assessment of the Wound Healing Potential of Dermocosmetics in Fibroblasts** (**L929**). Bertoncelli ACZ[1], Oliveira Mendes TO[1], Livinalli IC[1], Pedrozo ER[1], Peroza LR[1], Augusto RA[2], Milani JA[2], Santoro F[2], Mello GH[3], Cadoná FC[4] [1]UFN, Biomedicine Course, Brazil, [2]Company Smart Gr Lab (Smart Gr Lab - Compounding Lab Ltd.), Brazil, [3]UFN, Graduate Program in Nanosciences, Brasil, [4]UFN, Graduate Program in Health and Life Sciences, Brazil.

Introduction: Skin aging is associated with cellular senescence, oxidative stress, loss of elasticity, and impaired tissue regeneration. In this context, regenerative dermocosmetic compounds such as polydesoxyribonucleotide (PDRN) and exosomes have gained attention due to their anti-inflammatory, antioxidant, and regenerative properties, demonstrating promising applications in skin repair and rejuvenation. **Objectives:** To evaluate the regenerative potential and safety profile of dermocosmetic compounds in L929 fibroblast cells. **Methods:** L929 fibroblasts were exposed to different concentrations of PDRN and exosomes for 24 and 72 hours. Cell viability was assessed using the MTT assay, while oxidative stress parameters were evaluated through reactive oxygen species (ROS) and nitric oxide (NO) quantification. Subsequently, safe concentrations of the compounds were selected for a wound healing assay to investigate cell migration and regenerative activity. **Results:** The tested compounds demonstrated a favorable safety profile at most concentrations evaluated. Exosomes showed cytotoxicity only at the highest concentration tested, whereas PDRN increased cell viability and reduced NO levels, suggesting anti-inflammatory activity. In the wound healing assay, both PDRN and exosomes significantly promoted wound closure and enhanced cell migration when compared to the control group, indicating notable regenerative potential. **Conclusion:** PDRN and exosomes demonstrated significant regenerative activity and satisfactory safety profiles in fibroblast cultures. These findings suggest that such dermocosmetic compounds may represent promising therapeutic strategies for skin regeneration, tissue repair, and prevention of premature skin aging. **Acknowledgments** The authors would like to express their gratitude to the Franciscan University research team for all their help and support.

01.008 **Siglec-10 as a Potential Prognostic Biomarker and Therapeutic Response Marker in Osteosarcoma**. Paz Neta DC[1,2], Santos VL[1,2], Gomes JPA[1,2], Silva BO[1,2], Pereira MC[1,2,3] [1]UFPE, PPG Therapeutic Innovation, Brazil; [2]UFPE, Suely Galdino Center for Research in Therapeutic Innovation, Brazil; [3]UFPE, Departamento of Physiology and Pharmacology, Brazil

Introduction: Osteosarcoma (OS) is a rare and aggressive primary bone malignancy that predominantly affects children and adolescents, accounting for approximately 56% of bone sarcomas and being associated with high mortality rates, mainly due to pulmonary metastasis. SIGLECs comprise a family of transmembrane proteins involved in sialoglycan recognition and immune response modulation. Among them, SIGLEC-10 stands out for its involvement in immune evasion mechanisms in different tumors and for its potential as a target for immunotherapy. Although its role in immunosuppression and tumor progression has already been described in several neoplasms, its involvement in osteosarcoma remains poorly understood. Objective: Therefore, this study aimed to evaluate the gene expression of SIGLEC-10 and its possible involvement in immunomodulatory mechanisms associated with OS for future immunotherapy approaches, using bioinformatic and experimental strategies. **Methods:** *in silico* analyses performed using the STRING and TIMER platforms enabled the evaluation of protein–protein interactions, gene expression profiles, and possible immunological associations related to the SIGLEC-10 gene. For experimental validation, blood samples from OS patients were subjected to total RNA extraction using TRIzol®, followed by cDNA synthesis and analysis of SIGLEC-10 gene expression by real-time polymerase chain reaction (qPCR), using GAPDH as the endogenous control gene. Relative expression was determined using the 2- Δ ΔCt method, and statistical analyses were performed with significance established at $p < 0.05$. **Results:** Protein–protein interaction analysis revealed that SIGLEC-10 is functionally associated with molecules involved in tumor immune evasion and immunomodulatory signaling, including CD24, CD47, SIRPA, and CD274 (PD-L1), suggesting its participation in pathways related to immune checkpoints. Additionally, gene correlation analyses performed on the TIMER platform demonstrated a positive association between SIGLEC-10 and the genes CD274, CD163, and IL10 in sarcomas, indicating a possible involvement in immunosuppressive mechanisms and modulation of the myeloid tumor microenvironment. In the experimental stage, a significant increase in SIGLEC-10 expression was observed in OS patients compared with the control group ($p = 0.0041$). These findings reinforce the *in silico* results, strengthening the evidence for the involvement of SIGLEC-10 in immunomodulatory processes in OS. **Conclusion:** The results suggest that SIGLEC-10 is associated with immune response regulatory processes in OS, interacting with molecules related to tumor immune evasion and immune microenvironment regulation. The integration of *in silico* analyses and experimental validation by qPCR demonstrates that the SIGLEC-10 gene may play a relevant role in modulating the immune response in this neoplasm, highlighting its potential as an immunomodulatory biomarker and possible therapeutic target in OS.

01.009 *in silico* and *in vitro* Analysis of Melittin's Effect on Membranes and Its Regenerative Potential in Muscle Cells. de Souza e Silva S, Boaventura de Oliveira AM, Almeida TC, Sant'anna MBM, Picolo G IBu, Pain and Signalling Lab

Introduction: Chronic wounds affect approximately 2.2 per 1,000 people globally, representing a significant source of persistent pain and infections, imposing substantial economic burden on healthcare systems. Melittin (MEL), the principal bioactive component of bee venom, is an amphipathic cationic peptide with anti-inflammatory, immunomodulatory, antinociceptive, and regenerative properties. Its amphipathic nature allows adsorption and partitioning into cellular membranes in a concentration-dependent manner, potentially modulating mechanosensitive channels involved in proliferation and migration during tissue regeneration. Findings from our group suggest that MEL interferes with muscle injury development in a chronic constriction neuropathy model. Objective: To investigate the effects and interactions of MEL in muscle cells through *in silico* and *in vitro* approaches. Methods: Monolayer and bilayer melittin–membrane systems were assembled using the melittin structure from PDB:2MLT with CHARMM-GUI, PyMOL, and VMD. Initial peptide configurations were defined with the amphipathic helix oriented parallel to the membrane plane, positioning the cationic and polar residues toward the lipid–water interface. Molecular dynamics simulations were performed using GROMACS to evaluate peptide-membrane interactions under different lateral tensions. C2C12 myoblasts cell line was used to assess cell viability through MTT assay. Results: Melittin-membrane simulation systems were successfully parameterized and validated. Analysis of the modeled systems revealed that a lipid-to- peptide ratio of 80:1 best reproduces the sub-lytic conditions targeted in the simulations, consistent with experimentally reported non-lytic concentrations in the literature. Bilayer simulations demonstrated that MEL achieved equilibrium adsorption in a surface-parallel orientation. *In vitro* dose- response assays in C2C12 myoblasts exposed to MEL at 0.25, 0.50, and 0.75 µg/mL revealed no significant cytotoxicity at any concentration tested, establishing the range of no toxic concentrations. Conclusion: The findings establish key parameters for melittin–membrane interactions, including the optimal lipid-to-peptide ratio, equilibrium adsorption behavior, and surface-parallel orientation adopted by MEL under sub-lytic conditions, as well as a non-cytotoxic concentration range in C2C12 myoblasts. These results allow further studies for signaling pathways determination in melittin-membranes interactions. This study was financed by the São Paulo Research Foundation (FAPESP Process Number #2025/28492-1) and Butantan Foundation. Ethics committee approval: not applicable.

01.010 **A BRET-Based Platform for the Study of the Angiotensin II Type 1 Receptor (AT1R) and the Bradykinin B2 Receptor (B2R) Non-Canonical Signaling**. Sousa AC[1], Santos AM[2], Rodrigues FC[3], Bouvier M[5], Parreiras-e-Silva LT[1,2,3,4] [1]FCFRP-USP, PPG Biosciences and Biotechnology, Brazil, [2]FMRP-USP, PPG Pharmacology, Brazil, [3]FMRP-USP, PPG Biochemistry, [4]FCFRP-USP, Brazil, [5]University of Montreal, Institute for Research in Immunology and Cancer, Canada.

Background: G protein–coupled receptors (GPCRs) represent the largest family of membrane receptors and are targets of approximately 35% of currently approved drugs. Traditionally, GPCRs signaling has been described as a process restricted to the plasma membrane. However, emerging evidence demonstrates that these receptors can sustain signaling within intracellular compartments, particularly endosomes. This compartmentalized signaling paradigm has profound implications for cellular responses, pathophysiological outcomes, and drug development. AT1R and B2R, involved in cardiovascular diseases and blood pressure regulation, promote G protein signaling both at the plasma membrane and within early endosomes. **Aims:** The aim of this study was to develop and optimize a robust Bioluminescence Resonance Energy Transfer (BRET)-based platform to characterize the spatiotemporal G protein activation profiles of AT1R and B2R. Specifically, we sought to investigate the activation of Gq/11, Gi/o, and G12/13 subunits at both the plasma membrane and early endosomes to elucidate the non-canonical signaling patterns of these cardiovascular targets. **Methods:** HEK293T cells were transiently transfected with AT1R or B2R together with BRET-based biosensors to detect the activation of distinct Gα subunits: p63-RLucII (Gq/11), RapGAP-RLucII (Gi/o), and PDZ-RLucII (G12/13). Subcellular localization was assessed by monitoring BRET between these biosensors and the compartment-specific fluorescent markers, rGFP-CaaX (plasma membrane) and FYVE-rGFP (early endosomes). Real-time BRET assays were performed following stimulation with angiotensin II (AngII) or bradykinin (BK). **Results:** Optimization of the BRET-based system enabled precise mapping of AT1R- and B2R-triggered Gq/11, Gi/o, and G12/13 activation with high spatiotemporal resolution at both the plasma membrane and early endosomes, validating non-canonical intracellular G protein signaling. Real-time monitoring revealed that endosomal signaling profiles displayed distinct kinetic signatures compared with plasma membrane responses, underscoring the platform's sensitivity for detecting compartmentalized GPCR activity. **Conclusion:** Cardiovascular diseases are the leading cause of death worldwide, and GPCRs such as AT1R and B2R are key therapeutic targets. However, current drugs are not designed to selectively modulate compartmentalized GPCR signaling, potentially contributing to adverse effects and suboptimal therapeutic responses. By elucidating GPCR spatiotemporal signaling, this study may support safer, more effective therapies targeting pathological intracellular pathways. Additionally, BRET-based biosensors will enable identification of biased ligands with compartment-specific signaling profiles. **Acknowledgments:** FAPESP, CAPES.

01.011 *In vitro* Cellular Aging Determines Susceptibility to Cardiotonic Steroid-Induced Epithelial–Mesenchymal Transition in Renal Cells. Barros GMO, Bagri KM, Mermelstein CS, Quintas LEM ICB-UFRJ, PPG in Pharmacology and Medicinal Chemistry, Lab Biochemical and Molecular Pharmacology, Rio de Janeiro, Brazil.

Introduction: Population aging constitutes a major demographic transformation of the 21st century and is associated with an increased incidence of chronic diseases, including chronic kidney disease. In this context, renal tubular epithelial cells exhibit high vulnerability due to their intense metabolic demand and strong dependence on oxidative phosphorylation, factors that promote cellular dysfunction and progressive renal impairment (REX et al., 2023). Moreover, senescent cells remain metabolically active and secrete pro-inflammatory mediators associated with the senescence-associated secretory phenotype (SASP), thereby sustaining chronic inflammation. Among these mediators, TGF-β stands out as an important inducer of epithelial-mesenchymal transition (EMT), characterized by loss of E-cadherin and increased expression of mesenchymal markers (HUANG et al., 2022). Among the mechanisms involved in these cellular responses, Na+/K+-ATPase (NKA) plays a prominent role. Located in the basolateral membrane of renal epithelial cells, NKA is essential for tubular homeostasis and also acts as a signaling platform in caveolae, cholesterol-rich membrane microdomains (QUINTAS et al., 2010). In this context, cardiotonic steroids (CTS), ligands of NKA, have been described as modulators of epithelial phenotypic plasticity. Thus, this study investigated whether susceptibility to bufalin-induced EMT, as well as to other CTS, depends on the degree of cellular aging in LLC-PK1 cells. Methodologys: The expression of cell adhesion and EMT-related markers was evaluated by immunofluorescence in high-passage (P>80) and low-passage (P<40) LLC-PK1 cells treated with bufalin (20 nM) for 48 h. Cell viability and morphological alterations were analyzed by MTT assay and phase-contrast microscopy in P<40 cells exposed to ouabain, marinobufagenin, epoxymarinobufagenin, and telocinobufagenin at concentrations of 20, 50, and 100 nM. Data were expressed as percentage relative to the control group and analyzed using Student's t test($p<0.05$). Results: Bufalin induced significant morphological and molecular alterations in P>80 cells, including marked reductions in pan-cadherin (16.5%; $p=0.0014$) and E-cadherin (70.7%; $p=0.0001$). Tight junction proteins, including occludin, claudin-1, and ZO-2, also showed reduced expression, whereas ZO-1 remained unchanged. In addition, ZEB1 expression was reduced to approximately 45% of the control levels ($p=0.0001$). In contrast, P<40 cells showed no significant morphological or EMT-related changes after bufalin exposure. Only increased α-tubulin expression and perinuclear redistribution of β-catenin were observed. Based on these findings, additional experiments using different concentrations and other CTS were performed to further investigate the susceptibility of LLC-PK1 cells. However, none of the evaluated CTS induced significant morphological alterations or affected cell viability, even at the highest concentrations. Conclusion: The results indicate that susceptibility to CTS-induced EMT depends on the degree of cellular aging, suggesting that replicative aging constitutes a determining factor in epithelial phenotypic plasticity. References: Quintas, L. E. M. et al. Journal of Molecular and Cellular Cardiology, 2010. Huang, W. et al. *Nature Reviews Nephrology*, 2022. Rex, N.; Melk, A.; Schmitt, R. *Clinical Science*, 2023.

01.012 **Gestational Diabetes Mellitus (GDM) Promotes Plasmatic Matrix Metalloproteinase (MMP)-2 Activation and Suggests IR/IGF1R as a Potential Proteolytic Target in Murine Model**. Cantão MBS[1], Nakama RP[2], Sartori DC[2], Castro MM[1] [1]FMRP-USP, Dept Pharmacology, Brazil; [2]FMRP-USP, Dept Biochemistry and Immunology, Brazil

Introduction: Gestational diabetes mellitus (GDM) is characterized by glucose intolerance during pregnancy and constitutes a risk factor for the development of cardiovascular diseases. The hyperglycemic environment can lead to significant dysfunction of the vascular microenvironment. MMP-2 is a protease native to the vascular system that, when activated, promotes the proteolysis of intracellular and extracellular proteins, potentially contributing to various pathological conditions. Therefore, we hypothesize that GDM promotes a state of systemic hyperglycemia resulting in increased MMP-2 activity, which may contribute to the proteolysis of vascular insulin receptors, vascular dysfunction, and maladaptive remodeling. **Objective:** To evaluate the effects of GDM in female mice on systemic MMP-2 activation and to determine whether this effect contributes to alterations in the vascular insulin receptor. **Methods:** This study was approved by the Animal Research Ethics Committee of the Ribeirão Preto Medical School, University of São Paulo (CEUA – Protocol 1419/2025). Six-week-old female C57BL/6 mice were fed a high-fat diet for 4 weeks. Subsequently, at 10 weeks of age, streptozotocin (60 mg/kg, intraperitoneally, for 3 days) was administered to induce diabetes (GDM). Control group animals received a standard diet (ND) and citrate buffer for the same period. The females were placed with males in the afternoon. After the identification of a vaginal plug, the day was designated as gestational day (GD) 0. Females were treated with either doxycycline (to inhibit MMP-2) or a vehicle from GD 13 to 17 and were euthanized on GD 18. We performed intraperitoneal glucose tolerance test (ipGTT) to detect gestational glucose intolerance, gel zymography to assess the gelatinolytic activity of plasma MMP-2 isoforms, and *in silico* prediction of MMP-2 cleavage sites on the insulin receptor (IR) using Cleave Net Predictor software. **Results:** The GDM group exhibited a larger area under the curve in the ipGTT on GD 13 compared to the ND group (60,018 ± 2,481 vs. 29,265 ± 3,210; $p < 0.05$), indicating glucose intolerance. The GDM group displayed a phenotype of persistent hyperglycemia throughout gestation, evidenced by higher blood glucose levels on GDs 0, 7, 13, and 17 compared to the ND group ($p < 0.05$). Furthermore, the GDM group showed increased plasma activity of the 72 kDa MMP-2 isoform (1.096 ± 0.119) compared to the ND group (0.491 ± 0.059; $p < 0.05$), which was reduced by doxycycline treatment (0.513 ± 0.062; $p < 0.05$). *in silico* prediction of potential MMP-2 cleavage sites on the insulin receptor (IR) indicated proteolysis at residues 91–100, 131–140, and 11–21. Cleavage sites on the insulin-like growth factor 1 receptor (IGF1R) were also identified at residues 896–905, 1331–1340, 571–580, and 1076–1085. **Conclusion:** Our results suggest that maternal hyperglycemia in GDM may activate systemic MMP-2 and that IR and IGF1R may be potential targets for cleavage by MMP-2.

01.013 **Role of Dopamine (DA) and 6-Nitrodopamine (6ND) on *ex vivo* α-amylase Secretion by Murine Salivary Glands**. Alves MCO[1], Teixeira SA[1], Costa SKP[1], de Nucci G[1,2], Muscará MN[1] [1]ICB-USP, Lab Farmacologia Bioquímica da Inflamação e Dor, São Paulo, Brasil, PPG Biologia Funcional e Molecular; [2]Unicamp

Introduction: Saliva secretion is essential for oral homeostasis, and this process is regulated by the autonomic nervous system involving both adrenergic and cholinergic receptors. Over the last decade, 6-ND, a dopamine derivative, has been identified as an endogenous mediator in vascular and cardiac tissues. However, its role in glandular protein exocytosis remains poorly investigated. In this study, we investigated the modulatory effects of both DA and 6ND on *ex vivo* α-amylase secretion by murine salivary glands. **Methods:** Submandibular (SM), sublingual (SL), and parotid (PAR) glands were obtained from female Swiss mice (CEUA No. 3188100322). The glands were maintained *ex vivo* in Krebs solution and α-amylase secretion was stimulated with carbachol (CCh, 1 μM) or isoproterenol (ISO, 1 μM), in the presence or absence of either DA or 6ND (at 0.1 μM). α-Amylase activity was spectrophotometrically quantified in the gland supernatants based on the release of 2-chloro-4-nitrophenol (CNP) from the substrate 2-chloro-4-nitrophenol-D-maltotriose. Results were analysed by one-way ANOVA followed by the Tunkey test. Differences among the group means were considered statisticallysignificant at $P<0.05$. **Results:** At 0.1 μM, neither DA nor 6ND alone showed secretory activity significantly higher than baseline. In the parotid gland, DA showed a synergistic effect with carbachol, potentiating its α-amylase secretion (CCh 12,26±1,03 vs. DA 0,098±1,95 vs. CCh + DA 22,95±5,81). In contrast, 6ND markedly inhibited on ISO effects in te submandibulary gland (97.1±45.0 vs. 18.3 ± 8.1 U/10 min) and parotid gland (ISO 9,89±2,70 vs. 6-ND -0,11±0,44). **Conclusions:** These findings demonstrate that both DA and 6ND modulate salivary gland function. 6ND acts predominantly as an inhibitor of protein secretion, possibly by interfering with cAMP-dependent pathways, as suggested by the strong inhibition of ISO-induced responses. Based on these findings, 6ND may represent a novel regulator of salivary secretion and may thus stimulate the development of new pharmacological strategies for treatment of salivar disorders such as xerostomia.

01.015 **Extracellular cAMP–Adenosine Pathway Regulates β2-Adrenoceptor Agonist Anti-Proteolytic Effects in Skeletal Muscle Cells**. Satori NA, Godinho RO. Unifesp-EPM, Dept. of Pharmacology, Div. of Cellular Pharmacology; PPG Pharmacology, São Paulo, Brazil.

Introduction: In skeletal muscle, β2-adrenoceptor activation inhibits catabolism through intracellular cAMP signaling. Previous studies from our group demonstrated that cAMP is released into the extracellular compartment of skeletal muscle fibers and sequentially hydrolyzed by ectoenzymes to AMP and adenosine, which modulates skeletal muscle physiology through activation of adenosine receptors (Chiavegatti, T. Br J Pharmacol, 153:1331, 2008; Duarte, T. *J*. *Pharmacol*. *Exp*. *Ther*.341:820, 2012). Although β2-adrenoceptor/ intracellular cAMP signaling is known to inhibit skeletal muscle proteolysis, the contribution of the extracellular cAMP-adenosine pathway remains unclear. **Objectives:** To evaluate the involvement of the extracellular cAMP-adenosine pathway in the anti-proteolytic effects mediated by β2-adrenoceptor activation in C2C12 myotubes. **Methods:** Differentiated C2C12 myotubes were treated with β2-adrenoceptor agonist formoterol (10 nM), extracellular cAMP (1 μM) or adenosine (0.1 μM) in the presence or absence of the non-selective adenosine receptor antagonist CGS-15943 (20 μM). Intracellular and extracellular cAMP levels were quantified using a TR-FRET immunoassay (LANCE Ultra cAMP Kit, PerkinElmer, USA) (n = 4-6). C2C12 proteolysis was assessed by measuring tyrosine release using a fluorescent assay adapted from Bergantin, LB. J Appl Physiol, v. 111, p. 1710, 2011 for cells cultures (n = 4-6). Statistical analyses were performed using ANOVA followed by Tukey's post hoc test, with significance set at $P \leq 0.05$. **Results:** Formoterol induced a rapid and transient increase in intracellular cAMP levels, followed by a time-dependent cAMP efflux and extracellular accumulation. The cAMP efflux induced by formoterol was concentration-dependent (pEC50 = 9.00 ± 0.12). Formoterol also reduced starvation-induced proteolysis by 73%, consistent with the increased intracellular cAMP levels. In contrast, treatment of C2C12 myotubes with extracellular cAMP or its metabolite adenosine increased tyrosine release by 63% and 196%, respectively, relative to basal levels, indicating enhanced proteolysis. These proteolytic effects were significantly inhibited by CGS-15943. **Conclusion:** Our findings demonstrate that activation of β2-adrenoceptor promotes not only intracellular accumulation of cAMP, but also its extracellular release in skeletal muscle cells. In the extracellular compartment, cAMP and its metabolite adenosine stimulate muscle proteolysis through activation of adenosine receptors. The ability of adenosine receptor blockade to attenuate formoterol anti-catabolic effects indicates that the extracellular cAMP–adenosine pathway plays an important regulatory role in β2-adrenoceptor-mediated anti-catabolic signaling in skeletal muscle.

01.016 **Investigation of Non-Canonical Signaling Triggered by the G Protein-Coupled Receptor HCAR2 (GPR109A)**.
Santos AM[1,2], Sousa AC[1,3], Rodrigues FC[1,4], Cunha TM2, Bouvier M[5], Parreiras-e-Silva LT[1,2,3,4] [1]USP, Ribeirão Preto School of Pharmaceutical Sciences, Lab Molecular Pharmacology of GPCRs, Brazil, [2]USP, PPG Pharmacology, Brazil, [3]USP, PPG Biosciences and Biotechnology, Brazil, [4]USP, PPG Biochemistry, Brazil, [5]University of Montreal, Institute for Research in Immunology and Cancer, Canada

Introduction: The hydroxycarboxylic acid receptor 2 (HCAR2), also known as GPR109A, is a G protein-coupled receptor (GPCR) involved in lipolysis and the treatment of dyslipidemia, with additional anti-inflammatory and neuroprotective effects reported in diverse experimental models. HCAR2 is canonically coupled to Gi/o proteins at the plasma membrane, where it inhibits adenylyl cyclase and reduces intracellular cAMP levels. However, emerging evidence suggests that GPCR signaling may also occur through non-canonical pathways mediated by G proteins activated from intracellular compartments, a mechanism poorly understood for HCAR2. As GPCRs represent major therapeutic targets, a comprehensive understanding of their signaling mechanisms is critical for the development of safer and more selective drugs. **Objective:** This study aims to investigate potential non-canonical G protein signaling pathways associated with HCAR2 using BRET (Bioluminescence Resonance Energy Transfer)-based approaches. **Methods:** Receptor trafficking and G protein activation were monitored in living cells using BRET-based biosensors. In this approach, changes in the proximity between a luciferase-tagged biosensors and compartment-specific fluorescent markers generate signals that report receptor localization and G protein activation at distinct subcellular sites. Receptor internalization was assessed using the HCAR2-RLucII biosensor. Gi/o activation was evaluated using RapGAP-RLucII, a Rap1GAP-derived biosensor that selectively detects activated Gαi/o proteins. Compartment-specific signaling was determined by measuring BRET between these biosensors and fluorescent markers targeted either to the plasma membrane (rGFP-CaaX) or to early endosomes (FYVE-rGFP), allowing real-time assessment of receptor trafficking and Gi/o signaling dynamics at distinct cellular locations. Endogenous ligands, including niacin and butyrate, were evaluated to determine whether distinct agonists promote differential intracellular signaling profiles downstream of HCAR2 activation. **Results:** Niacin stimulation induced receptor internalization and promoted Gi/o activation within early endosomes, whereas butyrate-mediated HCAR2 activation did not appear to trigger endosomal signaling. The findings obtained thus far suggest that niacin and butyrate elicit distinct intracellular signaling signatures downstream of HCAR2 activation. **Conclusion:** The differential signaling profiles observed between niacin and butyrate contribute to the characterization of HCAR2 intracellular signaling mechanisms, particularly non-canonical Gi/o-mediated pathways originating from early endosomes. These findings may provide a foundation for future functional studies investigating compartmentalized HCAR2 signaling and may support the development of novel therapeutic strategies with improved efficacy and safety profiles. **Financial support:** CAPES and FAPESP.

01.017 **Functional Evaluation of miR-181a-5p in the Cisplatin Response in Lung Cancer Cell Lines**. Gomes JPA[1,4]; Pegado CBS[1,4]; Silva MGM[2]; Silva Junior MA[3,4]; Silva JRS[1,4]; Paz Neta DC[1,4]; Silva BO[1,4]; Pereira MC[1,4,5]. [1]UFPE, PPG Therapeutic Innovation, Brazil. [2]UFPE, PPG Genetics and Molecular Biology, Brazil. [3]Unisãomiguel, Brazil, [4]UFPE, Suely Galdino Center for Research in Therapeutic Innovation, Brazil [5]UFPE, Dept Physiology and Pharmacology, Brazil.

Introduction: Lung cancer (LC) is the deadliest neoplasm in Brazil, presenting an unfavorable prognosis due to late diagnosis and high resistance to chemotherapy treatments. Although cisplatin is widely used in the Brazilian Unified Health System (SUS) as a first-line therapy, its efficacy is often limited by toxicity and heterogeneous patient response. In this context, microRNAs (miRNAs) emerge as promising biomarkers for predicting and evaluating therapeutic response, since they play a crucial role in carcinogenesis and chemoresistance mechanisms. Among them, miR-181a-5p stands out as a potential modulator of cisplatin response. Thus, investigating its expression before and after chemotherapy treatment may contribute to the development of innovative therapeutic strategies aimed at reducing tumor resistance. **Objective:** Therefore, this study aimed to evaluate the functional effect of miR-181a-5p on the cellular response to cisplatin treatment. **Methods:** H1299 and A549 lung adenocarcinoma cell lines were cultured and treated with cisplatin at their respective IC50 concentrations (13.57 µM and 16.33 µM). After 8 and 24 hours of exposure, total RNA was extracted and subjected to cDNA synthesis, followed by analysis of relative miR-181a-5p expression by reverse transcription quantitative real-time polymerase chain reaction (RT-qPCR), using U6 snRNA as an endogenous control and TaqMan™ Advanced miRNA Assays according to the manufacturer's recommendations. Subsequently, H1299 cells were transfected with a miR-181a-5p inhibitor to investigate the involvement of this miRNA in the response to cisplatin. Cell viability was analyzed using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay to investigate the effects of miR-181a-5p modulation on cellular sensitivity to the chemotherapeutic agent. **Results:** The results demonstrated increased miR-181a-5p expression in both cell lines after cisplatin treatment, indicating possible modulation of this miRNA in response to the chemotherapeutic agent. In the A549 cell line, the increase in expression was more pronounced after 24 hours, whereas in H1299 cells, overexpression was observed as early as 8 hours and remained elevated after 24 hours. Furthermore, transfection with a specific miR-181a-5p inhibitor combined with cisplatin increased cell viability by 36.39%, while treatment with the inhibitor alone promoted a 42.25% increase in cell viability, suggesting the involvement of this miRNA in the regulation of mechanisms related to cellular survival and chemotherapy response. **Conclusion:** miR-181a-5p demonstrated potential involvement in the cisplatin response in LC cells, suggesting its potential as a molecular target associated with modulation of chemosensitivity.

01.018 **Time-Dependent Modulation of Cardiomyocyte Contractility by Alamandine Involves Different Signaling Pathways**. Monteiro ALL[1], Eliezeck M[1], Scalzo SRA[1], Poletini MO[1], Cau SBA[2], Santos RAS[1], Guatimosim S[1]. [1]ICB-UFMG, ICB, Dept Physiology and Biophysics, Graduate Program in Biological Sciences: Physiology and Pharmacology Brazil. [2]UFMG, ICB, Dept Pharmacology, Graduate Program in Biological Sciences: Physiology and Pharmacology, Brazil.

Our group recently characterized alamandine-(1-7) (ALA) as a time-dependent modulator of cardiomyocyte (CM) contractility, enhancing contractility in the light phase and reducing it in the dark phase. To clarify how the same peptide produces opposing effects at different time points, we characterized the signaling pathway activated by ALA at each phase. CMs from 10-14-week-old male mice were isolated in zeitgebers (ZTs) 02 (light phase) and 14 (dark phase), points at which ALA significantly altered the fractional shortening (FS) of CMs. CMs were incubated with ALA in the presence of antagonists of renin- angiotensin system receptors, and contractile function and NO production were evaluated. Interestingly, at ZT02 the pro-contractile effect of ALA was abolished by the alamandine receptor antagonist (MrgD), D-Pro7 (CTR: 4,3±0,4%; ALA: 7,8±0,6%; ALA+D-Pro7: 4,9±0,5%), as well as by A779 (CTR: 6±0,5%; ALA: 8,5±0,6%; ALA+A779: 5,9±0,4%) and Losartan (CTR: 5,6±0,5%; ALA: 9±0,6%; ALA+LOS: 5,5±0,4%), classic Mas and AT1 receptor antagonists. Additionally, all antagonists diminished ALA-induced NO production, which is crucial for contractile modulation. These data illustrate the complexity of ALA regulation of contractile function in the light phase. Conversely, at ZT14, only D-Pro7 antagonized the reduction in FS induced by ALA (CTR: 8,5±0,5%; ALA: 5,2±0,3%; ALA+D-Pro7: 7,3±0,5%), while A779 and Losartan had no effect, suggesting that at this phase the effect of ALA on contractility is mediated by MrgD. Moreover, NO was not involved in the decrease in CM contractility promoted by ALA during the dark phase, in clear contrast to its role in the light phase. These data highlight the importance of considering time-of-day-dependent mechanisms in ALA-mediated modulation of contractility. Understanding these circadian influences may guide the development of new therapeutic strategies that optimize the efficacy of heart disease treatments.

01.019 **Endothelial P2Y2 and P2X7 Receptors Colocalization with Caveolin-1 Enhances Monocyte Adhesion in Intestinal Schistosomiasis**. Oliveira NF, Mainieri NS, Flores CO, Ribeiro DAS, Silva CLM. ICB-UFRJ, Lab Biochemical and Molecular Pharmacology, Brazil

Introduction: Intravascular infections such as schistosomiasis promote endothelial cell damage and ATP release modulating host immunovascular responses through purinergic P2 receptors. In primed mesenteric endothelial cells, we recently showed a positive cooperation between P2Y2 and P2X7 receptors (P2Y2R/P2X7R) triggering an increased monocyte adhesion during schistosomiasis (Oliveira NF., *et al*, Front. Immunol., 14:1328897, 2024). Caveolin-1 (Cav-1) plays a critical role both in regulating endothelial cell phenotype and integrating complex signaling pathways, but its role to P2Y2R/P2X7R crosstalk remains unclear. **Objectives:** Therefore, our aim was to investigate the endothelial Cav-1 contribution in modulating P2Y2R/P2X7R crosstalk in a model of intestinal inflammation. **Methods:** Primary cultures of mesenteric endothelial cells (MEC) were obtained from control and S*chistosoma mansoni*-infected mice (50-70 days p.i) and used for monocyte adhesion and immunocytochemistry (ICC) assays. Confluent MEC were stimulated with vehicle (basal), UTP (100 µM, 5h) and/or with ATP (500 µM, 10 min) in the presence or absence of siRNA Cav-1 transfection (SI02731813; 1 pmol) for 48h. For the adhesion assays, MEC were incubated with freshly isolated monocytes for 30 min (400X). For ICC double-immunofluorescence staining, MEC were sequentially incubated with primary antibodies anti-Cav-1 (sc-53564), anti-P2X7R (APR-004) or anti-P2Y2R (APR-010) followed by secondary antibodies. Cells were imaged using either a fluorescence microscope (Olympus IX71 equipped with CellSens software) or a confocal microscope (Zeiss Celldiscover 7, LSM 900) for protein expression quantification and colocalization, respectively. Images were analyzed by ImageJ software (NIH) with Puncta Analyzer plugin and data were normalized in relation to basal condition. Data were expressed as mean and SEM. **Results:** We observed a higher P2X7R (311.5% ± 31.5) and P2Y2R (312.6% ± 38.4) colocalization puncta with Cav-1 in the infected than in the control group 100.1% ± 13.5 and 100.0% ± 14.8, respectively, $p < 0.001$, n=4. Moreover, the P2Y2R/P2X7R coactivation increased the P2X7/Cav-1 colocalization compared to basal levels in the infected group (from 100.1% ± 12.6 to 213.2% ± 21.0, $p < 0.001$, n=4). On the other hand, the treatment did not alter protein expression ($p > 0.05$), suggesting a dynamic redistribution of endothelial P2Y2R/P2X7R and Cav-1 into the microdomains of cell membrane. For functional assays, Cav-1 knockdown reduced 70% Cav-1 expression in both groups. Cav-1 knockdown inhibited monocyte adhesion induced by P2Y2R/P2X7R coactivation (from 11.2 ± 1.2 to 5.4 ± 0.3 cells/field; $p < 0.001$, n = 4) only in the infected group. **Conclusion:** In conclusion, our data unveiled a Cav-1-dependent endothelial P2Y2R/P2X7R coactivation due to their higher colocalization during schistosomiasis, which may be an important pathway favoring mesenteric inflammation and morbidity. **Acknowledgments:** FIOCRUZ (RJ).

01.020 **Increased hsa-miR-30e-3p Expression is Associated with Cisplatin Response in Lung Cancer**. Silva BO[1,3]; Gomes JPA[1,3]; Silva MGM[2]; Barbosa FHS[1,3]; Souza GA[1,3]; Silva TD[1,3]; Pegado CBS[1,3]; Paz Neta DC[1,3]; Silva JOR[3]; Pereira MC[1,3,4] [1]UFPE, PPG Therapeutic Innovation, Brazil; [2]UFPE, PPG Genetics and Molecular Biology, Brazil; [3]UFPE, Suely Galdino Center for Research in Therapeutic Innovation, Brazil; [4]UFPE, Dept Physiology and Pharmacology, Brazil

Introduction: Lung cancer (LC) is among the most prevalent and lethal malignancies worldwide, exhibiting high aggressiveness and low survival rates. Although different therapeutic approaches are currently employed for the treatment of this neoplasm, cisplatin-based chemotherapy remains one of the main therapeutic strategies. However, chemoresistance and treatment-related adverse effects still represent major limitations to its clinical efficacy. In this context, the identification of novel biomarkers associated with treatment response has emerged as a promising strategy for the development of more effective and personalized therapeutic approaches. Among these biomarkers, microRNAs (miRNAs) have gained considerable attention as important post-transcriptional regulators involved in cellular proliferation, apoptosis, and therapeutic response. In particular, hsa-miR-30e-3p has attracted interest due to its potential role in tumor progression and modulation of treatment response in different malignant neoplasms. **Objective:** Therefore, this study aimed to evaluate the expression of hsa-miR-30e-3p in an *in vivo* model of lung neoplasia before and after cisplatin treatment. **Methods:** Female BALB/c mice (6–8 weeks old) were subjected to chemical induction of lung neoplasia by intraperitoneal urethane administration and maintained under a 12-hour light/dark cycle with free access to food and water. Tumor induction was carried out for 5 months. After this period, the animals were distributed into three experimental groups: NT (untreated control), LC (urethane-induced lung cancer mice), and CIS (urethane-induced lung cancer mice treated with cisplatin). Animals in the CIS group received cisplatin (5 mg/kg) once weekly for 3 weeks. After treatment, the animals were euthanized, and lung tissues were collected for hsa-miR-30e-3p expression analysis by reverse transcription quantitative real-time polymerase chain reaction (RT-qPCR), using TaqMan™ Advanced miRNA Assays (Thermo Fisher Scientific) and U6 snRNA as the endogenous control. Statistical analyses were performed using GraphPad Prism 9 software with the nonparametric Kruskal–Wallis test, considering $p < 0.05$ as statistically significant. **Results:** Expression analysis demonstrated a significant increase in hsa-miR-30e-3p levels in the lung tissue of cisplatin-treated lung cancer mice compared with the untreated lung cancer group ($p = 0.0012$). **Conclusion:** Taken together, the results highlight the relevance of hsa-miR-30e-3p in modulating the response to cisplatin, contributing to the understanding of molecular pathways associated with lung cancer. Despite these promising findings, further studies are still required to elucidate the mechanisms underlying the role of hsa-miR-30e-3p in the therapeutic response to cisplatin.

01.021 **Impact of Adipose Tissue Secretome on Endothelial Cells in Obesity**. Nascimento-Silva V[1], Souza MJ[1], Rodrigues-Silva G[1], Andrade-da-Costa J[1], Andrade-Santos C[1], Moraes JA[2], Barja-Fidalgo C[1] [1]UERJ, Lab Farmacologia Celular e Molecular, Brasil. [2]UFRJ, Lab de Biologia Redox, Brasil.

Introduction: Adipose tissue (AT) is a metabolically active endocrine organ that secretes several bioactive molecules involved in homeostasis. In obesity, AT acquires a pro-inflammatory profile characterized by increased production of adipokines and cytokines, including IL-6, TNF-α, and leptin, contributing to chronic low-grade inflammation. Cardiovascular diseases are major complications in obesity, and endothelial dysfunctions are the earliest stage of vascular disease, characterized by altered barrier function; impaired nitric oxide (NO) bioavailability; oxidative stress; and abnormal angiogenesis. However, the direct contribution of factors secreted by obese AT to endothelial dysfunction remains incompletely elucidated. **Objectives:** To investigate the effects of soluble mediators released by AT from obese individuals on endothelial functions, focusing on parameters associated with endothelial barrier integrity, oxidative stress, and angiogenic potential. **Methods:** Visceral AT samples were obtained from patients with obesity undergoing bariatric surgery, and subcutaneous AT samples were collected from eutrophic individuals undergoing plastic surgery (UERJ/CAAE 36880914.0.0000.5259). Tissue fragments were cultured for 24h in serum-free medium to generate conditioned media, defined as obese AT secretome (OTS) and lean AT secretome (LTS), respectively. Human microvascular endothelial cells (HMEC-1) were stimulated with OTS or LTS for different time points. Endothelial permeability was assessed by transwell assay with FITC-dextran. VE-cadherin phosphorylation and redistribution, NO production, and reactive oxygen species (ROS) levels were evaluated by Western blotting, immunofluorescence and fluorometric probes. Cell proliferation, invasion, and tubulogenesis were evaluated using BrdU incorporation assay, Matrigel invasion, and tube formation assays, respectively. **Results:** OTS significantly increased endothelial permeability and induced VE-cadherin phosphorylation in HMEC-1 cells compared with LTS. Endothelial cells exposed to OTS also exhibited increased NO production. Furthermore, OTS enhanced endothelial cell invasion, tubulogenesis, and proliferation, indicating a pro-angiogenic phenotype. In addition, OTS increased ROS production, suggesting activation of oxidative stress-related pathways. **Conclusion:** Soluble mediators released by adipose tissue from obese individuals are capable of modulating endothelial cell behavior. OTS promotes endothelial barrier dysfunction, oxidative stress, and pro-angiogenic responses, supporting the concept that obese AT actively contributes to endothelial dysfunction and vascular remodeling. These findings provide mechanistic insights into the association between obesity and cardiovascular disease.

02. Neuropharmacology

02.001 **Investigation of the Neuroprotective Potential of Purple Pitanga** (*Eugenia uniflora*) **Extract on Non-Motor Symptoms of Parkinson's Disease in Female Rats**. Streb BL, Fontoura EA Fidelis EM, Rodrigues ES, Gomes J, Comis-Neto, AA, Batista WT, Pinton S, Rosa SG Unipampa

Introduction: Before the onset of the classical motor signs of Parkinson's Disease (PD), such as tremors, muscle rigidity, and locomotor alterations, the neurodegenerative process may manifest through non-motor symptoms. Among these, behavioral changes associated with depression stand out, being considered one of the most prevalent and debilitating non-motor manifestations in the early stages of PD. In this context, experimental animal models using the neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) have been widely employed due to their ability to induce alterations similar to those observed in humans. Furthermore, natural compounds have been investigated for their neuroprotective potential. Due to its high content of anthocyanins and phenolic compounds, purple pitanga (*Eugenia uniflora*) acts as a potent antioxidant, demonstrating potential in mitigating cellular damage associated with oxidative stress and neurodegenerative processes. **Objectives:** To evaluate the effects of purple pitanga extract (PPE) on depressive-like behaviors in female rats subjected to an experimental PD model induced intranasally (i.n.) by MPTP. **Methods:** Female Wistar rats (CEUA 010/2021) were distributed into the following groups: 1) Control (CON), 2) PPE, 3) MPTP, and 4) MPTP+PPE. The experimental model was induced through intranasal administration of MPTP (1 mg/nostril, 10 µL), while animals in the control group received saline solution. PPE treatment (1000 mg/kg) was administered orally for 28 days. Behavioral tests included the Splash Test, performed on day 7, and the Forced Swimming Test, performed on day 12. Spontaneous locomotor activity was evaluated using the Open Field Test on day 21, after which the animals were euthanized. **Results:** Data were analyzed using one-way ANOVA followed by Tukey's post hoc test. MPTP administration ($p < 0.0018$) reduced self-grooming time in the Splash Test compared with the control group. Treatment with MPTP+PPE reversed this effect. In the Forced Swimming Test, MPTP increased immobility time, and this effect was reversed by PPE treatment. Importantly, administration of PPE alone did not induce behavioral alterations. No significant differences among groups were observed in spontaneous locomotor activity. **Conclusion:** PPE reversed depressive-like and anhedonia-like behaviors induced by the MPTP model in female rats without interfering with locomotor activity. These findings suggest the neuroprotective potential of this natural compound in the management of early non-motor symptoms of PD.

02.002 **Prevalence of the APOE ε4 Allele and its Association with Lipid Markers in Cognitive Decline Profiles**. Canafístula LS[1], Barbosa ISA[1], Oliveira CA[2], Xavier JMC[1], Soares MVR[3], Gonçalves PVS[4], Santos LTR[5], Frota AF[3], Lôbo RR[5], Aires-Peixoto-Júnior A[5], Gaspar DM[3]. [1]UFC, Faculty of Pharmacy, Brazil; [2]UFC, Graduate Program in Pharmacology, Brazil; [3]UFC, Neuropsychopharmacology Lab, Graduate Program in Translational Medicine, Brazil; [4]UFC, Faculty of Medicine, Brazil; [5]UFC, Faculty of Medicine, Dept Clinical Medicine, Graduate Program in Translational Medicine, Brazil.

Introduction: Aging increases the risk of neurodegenerative diseases, influenced by genetic factors. Apolipoprotein E (APOE), which participates in lipid transport and neuronal repair, has three alleles ε2, ε3, and ε4), with the ε4 allele constituting the principal genetic risk factor for sporadic Alzheimer's disease (AD). APOE variants have been associated with lipid profiles and to mild cognitive impairment (MCI) and AD, but Brazilian data remain scarce. Objective: To investigate the frequency of the APOE ε4 allele among controls, MCI, and AD patients and its association with peripheral lipid markers. **Methods:** This cross-sectional study was approved by the local Ethics Committee (No. 8,085,260). Among 175 recruited participants, 133 with comprehensive clinical and neuropsychological assessment underwent APOE genotyping (median age: 75 years; IQR: 69–81): controls (n=30), MCI (n=43), and AD (n=60). This subsample was used for subsequent analyses. APOE genotyping was performed by qPCR, together with lipid profile assessment and measurement of p-Tau181 and GFAP. The frequency of ε4 carriers was compared using Fisher's exact test. Lipid markers were compared using the Kruskal–Wallis test, and multiple linear regression models adjusted for age, p-Tau181, and GFAP were used to evaluate associations between ε4 and lipid markers. **Results:** The sample was predominantly female (66%), with a similar sex distribution across groups (p=0.5). Age did not differ significantly among groups (p=0.8), with median ages of 75.0 years in controls, 71.5 years in MCI, and 73.0 years in AD. The age distribution of the genotyped subsample differed from that of the full cohort, reducing age differences among the analyzed groups. A lower frequency of ε4 carriers was observed in MCI (46.5%; 20/43) than in controls (60.0%; 18/30) and AD (75.0%; 45/60). This finding is descriptive and does not support causal inference. No significant differences in lipid markers were observed between genotypes (total cholesterol: p=0.32; LDL: p=0.70; HDL: p=0.69; VLDL: p=0.40; triglycerides: p=0.43). Likewise, adjusted regression analyses showed no significant association between the ε4 allele and any lipid marker. **Conclusion:** A higher frequency of APOE ε4 carriers was observed in the Control and AD groups relative to the MCI group, though this finding does not establish statistically confirmed causality. A higher frequency of APOE ε4 carriers was observed in the control and AD groups relative to the MCI group, although this finding does not support causal inference. The lack of association with peripheral lipid markers neither confirms nor excludes the involvement of other biological mechanisms, reinforcing the need for further studies in Brazilian populations. **Financial support:** Ceará Foundation for Scientific and Technological Development Support. Ethics Committee: no. 8.085.260

02.003 **Systematic Review and Meta-Analysis of Brain Na^+,K^+-ATPase Activity in Alzheimer's Disease and Epilepsy Preclinical Models**. Carneiro MA[1], Ribeiro LR[1,3], Bariviera JL[1,3], Da Rosa GK[1,3], Ramos RB[1], Freitas JW[2], Oliveira MS[1,3]
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Introduction: Neurological disorders affect over 40% of the global population, with Alzheimer's disease and epilepsy ranking among the most prevalent. A promising pharmacological target for therapeutic intervention is the Na+,K+-ATPase enzyme, regulator of brain homeostasis. While altered enzyme activity has been documented in both Alzheimer's and epilepsy models, the direction and magnitude of these fluctuations vary significantly across specific disease models and experimental contexts. **Objectives:** Our study aimed to quantify the pooled magnitude and direction of Na+,K+-ATPase activity changes, investigate whether enzyme dysfunction is a consistent feature across disease models and identify whether effect sizes vary by model or brain region studied. **Methods:** PubMed, Scopus, and Web of Science databases were searched and a total of 27 studies were included (AD models, n = 9; epilepsy models, n = 18). Peer-reviewed studies assessing brain of Na+,K+-ATPase activity in separate control and untreated chronic animal models of AD (≥ 7 days post-induction or ≥ 6 months for transgenics) and epilepsy (≥ 14 days post epileptogenic insult) were included. Methodological quality was evaluated using the SYRCLE risk of bias tool. Standardized mean differences (Hedges' *g*) were pooled using three-level multilevel random-effects models to separate within- and between- study variance components and account for multiple nested effect sizes per study. Subgroup and moderator analyses across paradigms and brain areas were adjusted via the Benjamini-Hochberg false discovery rate (FDR) procedure. **Results:** Twenty-seven studies were included, comprising 9 Alzheimer's disease (AD) models and 18 epilepsy models; both datasets exhibited very high heterogeneity. For AD models, a global reduction in cerebral Na+,K+-ATPase activity was observed (Hedges' g = -3.100; 95% CI: -4.542 to -1.657), driven by The Aβ injection paradigms (g = -3.02; 95% CI: -4.37 to -1.68) localized primarily in the hippocampus (g = -3.854; 95% CI: -4.995 to -2.714), however transgenic models did not show a statistically significant pooled effect. Conversely, the global pooled effect for epilepsy models was not statistically significant (g = -0.59; 95% CI: -1.32 to 0.130). However, paradigm-specific moderator analysis revealed a significant enzymatic decrease restricted exclusively to focal cortical lesion models (g = -1.30; 95% CI: -2.21 to -0.38). **Conclusion:** Our findings demonstrate that Na+,K+-ATPase activity is markedly and consistently reduced in experimental Alzheimer's disease, whereas its role in epilepsy is strictly governed by the experimental paradigm, evidencing significant impairment only within focal lesion models. These results delineate clear boundaries for targeting Na+,K+-ATPase, strongly supporting its development as a strategic target in preclinical research. **Financial support** Information: CAPES/CNPq.

02.004 **Effects of the β-Carboline Alkaloids Harmine and Harmaline On Scopolamine-Induced Cognitive Impairment**. Rossi NRC, Morales-Lima G, Falconi-Souto A, Mendes FR UFABC Center for Natural and Human Sciences Brazil

Harmine and harmaline are β-carboline alkaloids found in Banisteriopsis caapi (bark and stem) and Peganum harmala (seeds) that exhibit anti-inflammatory, antioxidant, and neuroprotective properties. Scopolamine is a widely used pharmacological model of cognitive impairment associated with Alzheimer's disease due to its anticholinergic activity. Since acetylcholinesterase (AChE) inhibitors are commonly used in Alzheimer's disease treatment and β-carbolines have been reported to inhibit AChE activity, these compounds emerge as promising candidates for preventing or attenuating scopolamine-induced cognitive deficits. In this context, the present study aimed to evaluate the effects of harmine and harmaline on scopolamine-induced cognitive deficits in C57BL/6 mice. Sixty-two male C57BL/6 mice were randomly distributed into six experimental groups (N=9-11/group) and treated daily for 14 days with harmine (4 or 20 mg/kg), harmaline (2 or 10 mg/kg), or vehicle by oral gavage. From day 6 onwards, animals received scopolamine (1 mg/kg) or saline, intraperitoneally. Locomotor activity was assessed using the open-field test (day 5), whereas spatial learning and memory were evaluated using the Morris water maze (days 6-10), and aversive memory was assessed using the passive avoidance test (days 11-14). Statistical analyses were performed through ANOVA (when met the criteria) or Kruskal-Wallis test (non-parametric), followed by the appropriate post hoc test. Significance was achieved when $p<0.05$. Harmaline at 10 mg/kg induced locomotor impairment, as evidenced by reduced total distance traveled and mean speed in the open field test ($p<0.01$, Dunn post hoc test). In addition, scopolamine induced cognitive deficits, characterized by increased escape latency during Morris water maze training ($p<0.05$, Dunnett post hoc test), increased latency to enter the target quadrant ($p<0.01$, Dunn post hoc test), and reduced time spent in the target quadrant during the probe test ($p<0.01$, Sidak post hoc test). Neither harmine nor harmaline attenuated these cognitive deficits. Similarly, scopolamine reduced the aversive memory retention index in the passive avoidance test, and this impairment was not reversed by β-carboline treatment. Taken together, these findings suggest that, under the experimental conditions employed, harmine and harmaline did not attenuate scopolamine-induced cognitive deficits. Additionally, the locomotor impairment observed with the highest dose of harmaline highlights the importance of considering potential motor effects when interpreting behavioral outcomes.

02.005 **Evaluation of Subacute Co-Administration of Oxytocin and Cannabidiol in a Mouse Model of Post-Traumatic Stress Disorder**. Souza MA, Albuquerque EA, Silva RC, Arruda JM, Crispim JG, Lima JPF, Silva RL, Lima CAO, Rosa MM NUPIT-UFPE, PPG in Therapeutic Innovation, Brazil

Introduction: Post-traumatic stress disorder (PTSD) is triggered by traumatic events, causing cognitive and behavioral symptoms such as memory loss, flashbacks, and hypervigilance. Current pharmacological treatments, mainly SSRIs, mitigate anxiety symptoms but lack specific action on the neurobiological mechanisms of traumatic memory. Although MDMA is capable of triggering neuroplasticity and increasing oxytocin levels, contributing to enhanced psychotherapy, its cardiovascular risks and abuse potential restrict clinical use, demanding alternative strategies. **Objectives:** To evaluate the efficacy of combined administration of oxytocin and cannabidiol (CBD) in mitigating PTSD-related symptoms in an animal model. Oxytocin was selected for its role in neuroplasticity, central anti-inflammatory effects, and its ability to destabilize consolidated traumatic memories, favoring reconsolidation. CBD was chosen due to its non-hallucinogenic profile and well-documented anxiolytic properties, aiming to simultaneously address anxiety and cognitive deficits. **Methods:** Male Swiss mice underwent a seven-day subacute treatment with different doses of the CBD+oxytocin combination (5.0 mg/kg or 1 mg/kg CBD; 0.15 IU or 5 IU oxytocin per animal), as well as with the isolated compounds (using PBS/Tween as vehicle), to investigate their ability to prevent the formation of traumatic memory. Animals were subjected to the elevated plus maze (EPM), freezing behavior, novel object recognition (NOR), open field (OF) tests, and contextual fear conditioning extinction. The study was approved by CEUA under protocol number 008/2024, and results were analyzed using GraphPad Prism software, version 8.0.2, by one-way ANOVA. **Results:** When evaluating the effect of the CBD+oxytocin combinations, no significant results were observed for any of the treatments and behavioral assays analyzed. However, there was a trend toward reduced anxiety-like behaviors, according to the EPM, NOR, contextual fear conditioning, and open field tests. The decrease in parameters associated with anxiety-like behavior in these experimental models suggests a potential improvement in PTSD-related symptoms. **Conclusion:** These preliminary findings suggest that combining cannabidiol and oxytocin in an animal model may represent a promising avenue for developing a safer, more efficient, and specific therapy targeting the neurological mechanisms involved in PTSD. Future perspectives include further *in vivo* evaluations to confirm the observed effects in a cohort with greater statistical robustness.

02.006 **Evaluation of the Effect of the P1G10 Proteolytic Fraction of *Vasconcellea cudinamarcensis* on MHV-A59 Infection in a Murine Model of Type 1 Diabetes**. Baptista, ACS[1], Lima ALD[1], Morais ALB[1], Pimenta JC[3], Gonçalves JPCS[1], Queiroz Junior C[3], Litwinski VVC[3], Lopes MTP[2], Vieira, LB[1] [1]UFMG, Neuropharmacology Lab, Dept Pharmacology, PPG Physiology and Pharmacology, Brazil; [2]UFMG, Antitumor Substances Lab, Dept Pharmacology, PPG Physiology, and Pharmacology, Brazil; [3]UFMG, Immunopharmacology Lab, Dept Cell Biology, PPG Biochemistry, Brazil

Introduction: The COVID-19 pandemic highlighted the disproportionate impact of viral infections on individuals with pre-existing comorbidities, particularly diabetes mellitus (DM). Diabetic patients exhibit higher risk of hospitalization, severe complications, and mortality, driven by hyperglycemia, vascular dysfunction, and immunological alterations. The proteolytic fraction P1G10, derived from the latex of *Vasconcellea cundinamarcensis*, has demonstrated anti-inflammatory and antioxidant properties in experimental models, positioning it as a promising candidate for complex inflammatory conditions. **Methods:** Eight-week-old C57BL/6 mice (CEUA protocol number 271/2020) were randomly assigned to the experimental groups by simple randomization and received streptozotocin (STZ, 125 mg/kg) for type 1 DM induction. Blood glucose was monitored weekly. Three weeks post-induction, animals were intranasally infected with MHV-A59 (10^3 PFU). Clinical evaluation was performed daily, due to logistical constraints, blinding of investigators during clinical and behavioral scoring was not feasible, as diabetic and infected animals presented overt phenotypic differences which is acknowledged as a limitation of this study. Animals were euthanized upon 20% body weight loss. P1G10 treatment was initiated on the third day post-infection, with a 1 mg/kg dose. Data were expressed as mean ± SEM and analyzed using two-way ANOVA followed by Bonferroni's multiple comparison test, with statistical significance set at $p<0.05$. **Results:** The experimental model was validated, with diabetic animals displaying metabolic and behavioral alterations consistent with the human disease phenotype, such as increased food and water consumption, significant reduction in body weight ($n=40$, $p<0.0001$) and a marked increase in blood glucose after a 6 hour fast ($n=20$, $p<0.0001$). MHV-A59 infection worsened the clinical condition of diabetic animals, confirming greater susceptibility to severe viral disease. P1G10 treatment significantly reduced mortality, improved clinical and behavioral scores, such as improvement in symptoms related to prostration and in the activity and responsiveness of the animals and attenuated oxidative stress measured by TBARS levels ($n=5$ $p < 0,0001$). **Conclusion:** P1G10 exerts immunomodulatory and antioxidant actions with relevant pharmacological potential in viral coinfection scenarios associated with metabolic dysfunction, warranting further investigation as a therapeutic strategy. **Acknowledgments:** CNPq, CAPES, FAPEMIG, PRPq, UFMG.

02.007 **Effects of Oral Titanium Dioxide Nanoparticle Exposure on Cortical Spreading Depression**. Mousinho EM[1], França BNS[2], Melo SM[1], Gouveia JCA[3], Romero LJZ[4], Baez MC[4], Prieto SCG[1], Guedes RCA[1]. [1]UFPE, Center of Health Sciences, Nutrition Dept, Brazil; [2]UFPE, Center for Biosciences, Dept Physiology and Pharmacology, Brazil; [3]UFPE, Academic Center of Vitória, Vitória de Santo Antão, PE, Brazil; [4]UFPE, Center for Exact and Natural Sciences, Physics Dept, Brazil

Introduction: Titanium dioxide nanoparticles (TiO_2 NPs) are widely used in cosmetic, pharmaceutical, and food products, especially sweets and processed foods, increasing the likelihood of chronic oral exposure. Although TiO_2 NPs may accumulate in peripheral organs after repeated exposure, little is known about their effects on cortical excitability and brain tissue. **Objectives:** To evaluate whether oral exposure to TiO_2 nanoparticles alters cortical spreading depression (CSD) propagation and to investigate the presence of nanoparticles in cortical tissue using transmission electron microscopy (TEM). **Methods:** Male Wistar rats were divided into Control, TiO_2 10 mg/kg, and TiO_2 100 mg/kg groups (n = 6/group). TiO_2 nanoparticles were administered by oral gavage once daily for 15 days. Nanoparticle morphology and size distribution were characterized by electron microscopy, showing a mean particle diameter of ~20 nm. X-ray diffraction analysis confirmed the crystalline structure of TiO_2 nanoparticles. On the last experimental day, animals underwent CSD recordings under urethane/chloralose anesthesia. CSD was elicited by the topical application of 2% KCl to the frontal cortex, and propagation velocity was recorded from parietal cortical electrodes. Cortical tissue was subsequently processed for TEM analysis. **Results:** Oral exposure to TiO_2 nanoparticles did not significantly alter CSD propagation velocity compared with controls. TEM analysis revealed electron- dense nanoparticle-like structures in cortical tissue from exposed animals, suggesting that TiO_2 nanoparticles reached the cerebral cortex after oral administration. **Conclusion:** Repeated oral exposure to TiO_2 nanoparticles did not modify CSD propagation under the present experimental conditions. However, TEM findings suggest that TiO_2 nanoparticles may cross the blood–brain barrier and reach cortical tissue. Further studies are necessary to investigate potential long- term neurobiological effects.

02.008 **Prenatal Sodium Valproate Exposure Impairs Developmental Milestones in Swiss Mice Offspring**. Araújo JR[1], Duarte ALS[1], Herculano-Júnior FS[1], Honório-Júnior JER[4], Lima CBTM[2], Lima LM[2], Lima PJS[2], Pereira JRG[2], Silva SC[2], Sousa FCF[3] [1]UFC, Faculty of Pharmacy, Dentistry and Nursing, Brazil; [2]UFC, Dept. of Pharmacology, PPG in Pharmacology, Brazil; [3]UFC, Center for Research and Development of Medicines, Brazil; [4]Christus University, Brazil.

Introduction: Autism Spectrum Disorder (ASD) manifests through persistent deficits in social communication and interaction, accompanied by restricted behavioral patterns and hypersensitivity to sensory stimuli. Although its etiology is multifactorial, involving complex interactions between genetic and environmental factors, the prenatal sodium valproate (VPA) exposure model in rodents has been widely validated. Consequently, the offspring exhibit marked functional impairments even in the absence of gross neuroanatomical lesions, underscoring the importance of neonatal developmental milestone assessment as a sensitive biomarker of early neurological dysfunction. **Objectives:** To evaluate the effect of prenatal VPA exposure on neurosensory developmental milestones in Swiss mice offspring. Methods. Swiss female mice received VPA (500 mg/kg, i.p.) or saline on gestational day 12.5. Starting on postnatal day 3, pups were assessed daily for eye opening, grasp reflex, crossed extensor reflex, visual placement, and auditory startle response. Differences between groups were analyzed using the unpaired t-test ($p<0.05$). **Results:** VPA exposure resulted in significant delays in physical and motor maturation compared to controls, evidenced by retarded eye opening, grasp reflex, and crossed extensor reflex. In contrast, auditory startle response and visual placement remained preserved, showing no statistically significant differences between groups, although a downward trend was observed in the VPA-treated group. **Conclusion:** Prenatal VPA exposure selectively impaired neurosensory developmental milestones in Swiss mice offspring, with significant delays in grasp reflex, crossed extensor reflex, and eye opening. The persistence of these delays suggests VPA-induced disruption of central nervous system organization. The literature aligns with evidence in humans that the prolongation of primitive reflexes beyond the expected period may reflect delays in brain network maturation, being recognized as a possible biomarker of neurological dysfunction in ASD. Thus, this model is consolidated as a tool for screening neuroprotective strategies and future therapeutic interventions. Animal Research Ethics Committee: CEUA/UFC, protocol no. 138100325-0. **Financial support:** CAPES, CNPq (Grant number 402512/2023-5). Keywords: Autism Spectrum Disorder; Valproic Acid; Neurodevelopment; Primitive, Reflexes; Animal Model.

02.009 **Guarana Extract Modulates Antioxidant Responses and Oxidative Stress Resilience in TDP-43 Depleted Astrocytes**. Piristrello BS[1,2], Dale A[2], Levi J[2], Mendes FR[1], Sattler R[2] [1]Universidade Federal do ABC, São Bernardo do Campo SP, [2]Barrow Neurological Institute, Phoenix AZ

Introduction: Neurodegenerative diseases are characterized by progressive neuronal dysfunction and chronic neuroinflammation, in which astrocytes play a central regulatory role. Dysfunction of the RNA-binding protein TAR DNA- binding protein 43 (TDP-43) is a hallmark of amyotrophic lateral sclerosis and a significant proportion of frontotemporal dementia cases, leading to RNA splicing abnormalities and inflammatory responses in glial cells. Guarana (*Paullinia cupana*), native to the Amazon region, is rich in caffeine and polyphenolic compounds with antioxidant and anti-inflammatory properties. Given the association between oxidative stress and neurodegenerative disease progression, natural compounds may represent complementary strategies to mitigate cellular vulnerability. **Methodology:** Guarana seed powder was obtained from Santos Flora, duly registered on the SISGEN platform (#A415A1E), and used to prepare a hot aqueous extract. Extract cytotoxicity was evaluated using an lactate dehydrogenase assay in human iPSC-derived cortical astrocytes across a concentration range. The expression of antioxidant-related genes (NQO1, TXNIP, and CYP2J2) was assessed by RT-qPCR in healthy astrocytes treated with guarana extract, as well as in TDP-43-depleted astrocytes (via siRNA knockdown) treated with the extract for 24 h. Intracellular ROS levels were also evaluated following a 24-h guarana pretreatment and a 1-h co-treatment with the oxidative stressor H_2O_2. **Results and Discussion**: Guarana showed low cytotoxicity in human iPSC-derived cortical astrocytes, with only approximately 17% cell death at the highest concentration tested (1000 µg/mL). Thus, 300 and 600 µg/mL were selected as non-cytotoxic concentrations. Guarana treatment alone did not alter the expression of NQO1, TXNIP and CYP2J2 in healthy astrocytes. In contrast, TDP-43 depletion altered the expression of these genes, indicating that TDP-43 loss of function affects transcriptional mechanisms associated with the antioxidant response. Interestingly, guarana treatment partially or fully restored these alterations toward control levels, suggesting a modulatory effect on antioxidant responses specifically under conditions of TDP-43 depletion. TDP-43-depleted astrocytes exhibited increased intracellular reactive oxidative species (ROS) accumulation following H_2O_2 exposure compared with control siRNA-treated cells. However, 24-h pretreatment with guarana reduced this difference, suggesting that guarana may improve the ability of TDP-43-depleted astrocytes to cope with oxidative stress. Interestingly, co-treatment with guarana and H_2O_2 resulted in minimal ROS accumulation in both control and TDP-43-depleted cells. This effect may be associated with a direct scavenging or trapping activity of guarana compounds toward the oxidative stressor, potentially neutralizing H_2O_2 before it reaches the cells. **Conclusion:** Guarana extract restored antioxidant responses and reduced oxidative stress susceptibility in TDP-43-depleted astrocytes. These findings highlight its potential to improve cellular resilience under TDP-43-associated stress, although further studies are needed to clarify the underlying mechanisms.

02.010 **Toxicity and Hemolytic Assessment of Novel Peptides with Affinity for Amyloid-β**. Costa CM[1,2], Taveira RAA[2], Camargo LC[2], [1]UCB·2UnB, PPG Patologia Molecular Brasil

Alzheimer's disease (AD) is characterized by the accumulation of beta-amyloid peptide (Aβ) plaques followed by hyperphosphorylated tau tangles, leading to neuronal degeneration and cognitive decline (Deus Vieira et al., 2014; Motta et al., 2023). The sporadic form is the most prevalent, mainly affecting individuals over 65 years of age, and no effective therapy is available to delay disease progression. Two Aβ-binding peptides were developed through *in silico* analyses: alzpeptidina, designed from two wasp venom-derived peptides previously studied by our group, and GLP1-f, derived from an exendin-4 fragment. This study evaluated their safety by *in vitro* cytotoxicity and hemolysis assays. Statistical analyses were performed using ANOVA followed by Dunnett's post hoc test. Cytotoxicity was assessed by the MTT assay (N=3, biological triplicates) using SH-SY5Y cells cultured in DMEM/F12 (50/50) supplemented with 10% fetal bovine serum, 1% Pen/Strep, and 1% L-glutamine. Cells were exposed for 24 h to 0.01, 0.1, 1, 10, and 100 µM of each peptide. Hemolysis assays (N=3) were performed using erythrocytes isolated from eight Swiss mice exposed to 3.125, 6.25, 12.5, 25, 50, and 100 µM of both peptides. None of the tested peptide concentrations showed significant cytotoxicity, whereas Triton differed significantly from the vehicle (Milli-Q water) ($F(12,89)=1882$; $p=0.0472$). Cell viability values were 1±0.23 (vehicle), 0.11±0.01 (Triton), and 0.95±0.29 (untreated). Alzpeptidina showed 0.82±0.17, 0.88±0.13, 0.80±0.06, 0.84±0.15, and 0.81±0.06 at 0.01, 0.1, 1, 10, and 100 µM, respectively. GLP1-f showed 0.91±0.13, 0.88±0.23, 1.10±0.19, 0.88±0.10, and 0.73±0.13. Likewise, none of the tested concentrations showed hemolytic activity, and a significant difference was observed only between distilled water (positive control) and PBS (negative control) (GLP1-f: $F(7,64)=2362$; $p=0.0327$; alzpeptidina: $F(7,82)=2450$; $p=0.0248$). Mean values were PBS 1.22±3.0 and distilled water 15.15±8.1 for GLP1-f, and PBS 1.61±2.93 and distilled water 15.27±7.47 for alzpeptidina. GLP1-f values were -2.63±2.20, -2.41±1.85, -2.69±2.15, -0.84±4.08, -2.55±2.51, and -1.36±2.16; alzpeptidina values were -1.61±2.76, -1.60±3.17, -1.55±2.77, -1.93±3.04, -2.15±3.08, and -1.42±3.08. Both peptides showed no cytotoxicity or hemolytic potential at the tested concentrations, supporting their safety for future therapeutic evaluation.

02.011 **Effects of Lyophilized Hydroalcoholic Extract of *Spondias tuberosa* Arruda on Anxiety-Like Behavior and Brain Lipid Peroxidation in D-Galactose-Aged Wistar Rats**. Souza ETN[1], Araújo AB[1,2], Araújo IGA[1,2], Medeiros IA[1,2], Soares JKB[1] [1]UFPB, Lab Farmacologia Cardiovascular, Instituto de Pesquisa em Fármacos e Medicamentos, Brasil, [2] UFPB, PPG Profissional em Gerontologia, Brasil.

Introduction: Aging is associated with an increased incidence of central nervous system disorders, contributing to the development of anxiety-related behaviors. D-galactose (DGAL) has been widely used as an experimental model of accelerated aging because it induces oxidative damage and neuronal alterations like those observed during physiological aging. In this context, natural compounds as *Spondias tuberosa* Arruda (umbu), a fruit containing bioactive compounds may exert beneficial effects on behavioral alterations associated with aging. Objective: This study aimed to evaluate the effects of lyophilized hydroalcoholic extract from *Spondias tuberosa* bark on anxiety-like behavior and brain malondialdehyde (MDA) levels in male Wistar rats subjected to DGAL- induced aging, using the elevated plus maze test as behavioral assessment. **Methodology:** Groups (n=8/group) were divided: adult control group (ACG), D-galactose group (DGAL), D-galactose + umbu extract 30 mg/kg (FP30), and D-galactose + umbu extract 100 mg/kg (FP100). Animals received the extract by gavage starting at eight weeks of age for 56 consecutive days. All animals were subjected to the elevated plus maze (EPM), for assessing anxiety-like behavior in rodents. The parameters analyzed included time spent in the closed arms, time spent in the center area, and number of head-dipping during a 5-minute session. After euthanasia, brain tissue samples were collected, thawed, and weighed for the MDA assay. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test, and differences were considered statistically significant when $p < 0,05$. **Results:** The FP30 group showed reduced time in closed arms (152.3s) compared with DGAL (202.01s; $p < 0,05$), suggesting increased exploration of the open arms and reduced anxiety-like behavior, meanwhile, FP100 (179,5s) showed no significant difference. Regarding time in the center, FP30 animals remained longer (154.0s) than DGAL (76.67s; $p < 0,05$) and similar to ACG (116.07s), whereas FP100 did not differ from DGAL. In head-dippings, the FP30 also demonstrated increased exploratory behavior (17 dips) compared with the DGAL (12 dips; $p < 0,05$), suggesting a possible anxiolytic, while FP100 showed no statistical difference ($p > 0,05$). FP30 and FP100 groups showed reduction in brain MDA levels compared with the DGAL group ($p < 0,05$), indicating decreased lipid peroxidation. **Conclusion:** These findings suggest that the lyophilized hydroalcoholic extract of *Spondias tuberosa* Arruda bark may exert anxiolytic and neuroprotective effects in rats subjected to DGAL-induced aging. The FP30 group improved behavioral parameters, which was associated with reduced lipid peroxidation in both treated groups, indicating attenuation of lipid peroxidation, mechanisms strongly associated with the aging process.This study was approved by the Animal Ethics Committee of the Federal University of Paraíba (number 6271030725). **Financial support:** UFPB/PROPESQ.

02.012 **Evaluation of the Neuroprotective Effects of Intranasal Octovespin in Alzheimer's Disease Mouse Model**. Aguiar GP, Santos VRM, Camargo LC UnB, Darcy Ribeiro, Biology Institute, Dept Physiological Sciences, Neuropharma Lab, Brazil; UnB, Darcy Ribeiro, Biology Institute, PPG Animal Biology, Brazil; UnB, Darcy Ribeiro, Psychology Institute, Psychobiology Lab, Brazil

Introduction: Alzheimer's disease (AD) is characterized by β-amyloid (Aβ) accumulation, leading to synaptic dysfunction, neuroinflammation, and neuronal death. Since current therapies have limitations, venom-derived peptides have emerged as promising alternatives. Octovespin, a peptide inspired by *Polybia occidentalis* venom, reduces Aβ aggregation and improves cognition in AD mouse models. However, its delivery to the central nervous system is limited, making intranasal administration a potential strategy to enhance its therapeutic efficacy. **Objectives:** To evaluate the neuroprotective effects of Octovespin, via intranasal administration, in Aβ-42-induced AD model in mice. **Methods:** Male Swiss mice were submitted to a neurosurgery where they received a 3µl (400 pmol/mouse) Aβ42 infusion at their left lateral ventricle. Then, animals were treated intranasally with Octovespin synthesized by Pepmic Co., Ltd, in different concentrations (0,2 µg/2µL; 2 µg/2µL and 20 µg/2µL) for 30 days and its behavior were evaluated in the Open Field, Three-Chamber Social Test, Novel Object Recognition Test, Elevated Plus Maze, and Morris Water Maze. Data were analyzed using Anymaze and GraphPad Prism ($p < 0.05$). Statistical analyses included Student's t-test, Mann–Whitney test, and one- or two-way ANOVA, with appropriate post hoc tests. **Results:** In the Three-Chamber Social Test, βA animals showed impaired sociability, whereas treatment with the intermediate dose of Octovespin (2 µg/2 µL) significantly restored social behavior ($p = 0.0074$). The lower and higher doses showed no therapeutic effect. In the Elevated Plus Maze, only the βA and 0.2 µg/2 µL groups differed significantly ($p = 0.0210$). No significant differences were detected in the Novel Object Recognition Test and in the Open Field test. In the Morris Water Maze, no differences were found on the last training day or in spatial and long-term memory tests, although a significant difference between the SHAM and βA groups was observed on the second ($p = 0.0323$) and third training day ($p = 0.0190$). The SHAM and 2 µg/2 µL groups also differed significantly on the third training day ($p = 0.0312$). **Conclusion:** Octovespin mitigated Aβ42-induced behavioral deficits, decreasing anxiety and significantly improving sociability in the Three-Chamber Social Test. Therefore, intranasal administration of Octovespin represents a promising strategy for the treatment of neurodegenerative diseases, such as Alzheimer's disease.

02.013 **Multi-omics Analysis of Molecular Docking and Dynamics of Natural Compounds Targeting Tau Protein Aggregation in Tauopathies**. Farias NR, Souza VL, Andrade EM, Garofalo CB, Farias MS, Pereira P, Santos PA. UFRGS, Institute of Basic Health Sciences, Dept Pharmacology, Lab Neuropharmacology and Clinical Toxicology, PPG in Pharmacology and Therapeutics. Brazil.

Introduction: Tauopathies are characterized by abnormal folding of the tau protein, hyperphosphorylation, and pathological aggregation, resulting in the formation of neurofibrillary tangles and progressive neuronal dysfunction. Integrated multiomics approaches, combining structural modeling and proteomic network analysis, can provide mechanistic insights for therapeutic strategies targeting tau protein aggregation. Natural compounds such as epigallocatechin gallate (EGCG), coumarin, and p-coumaric acid have demonstrated neuroprotective properties; however, their mechanistic effects on tau protein aggregation are not yet fully understood. **Objectives:** To investigate the molecular interactions, structural stability, and systems-level proteomic modulation associated with natural compounds acting on tau protein aggregation in tauopathies, using an integrated *in silico* multiomics approach. **Methods:** A multiomics computational workflow integrating molecular docking, molecular dynamics (MD) simulations, and proteomic network analysis was performed. Molecular docking analyses were conducted using AutoDock Vina against full- length tau protein and aggregation-prone β-sheet-forming domains. Regulatory kinases associated with tau phosphorylation, including glycogen synthase kinase 3β (GSK-3β) and cyclin-dependent kinase 5 (CDK5), were also evaluated. Molecular dynamics simulations assessed complex stability through mean square deviation (RMSD), hydrogen bond persistence, and conformational stabilization analyses. Proteomic enrichment analysis mapped the predicted molecular targets in datasets associated with tau phosphorylation, protein aggregation, cytoskeleton regulation, and proteostasis-related pathways implicated in tauopathies. **Results:** EGCG demonstrated the highest predicted binding affinity for tau domains prone to aggregation and maintained structural stability during molecular dynamics simulations, reducing conformational flexibility in β-sheet forming regions. Coumarin and p-coumaric acid exhibited moderate binding affinity at hydrophobic interfaces associated with initial fibril nucleation. Multiomic proteomic integration revealed convergence in signaling networks involved in the control of tau protein phosphorylation, cytoskeleton organization, proteostasis regulation, and protein quality control systems associated with tau protein aggregation dynamics. The predicted interactions with GSK-3β and CDK5 further corroborated the potential modulation of phosphorylation-dependent tau protein pathology. **Conclusion:** This integrated *in silico* multiomics analysis supports the hypothesis that natural compounds, particularly EGCG, can interfere with tau protein aggregation through structural stabilization of aggregation-prone domains and modulation of proteomic networks associated with phosphorylation and proteostasis. These findings provide mechanistic evidence at the systems level that supports the future experimental validation of therapeutic strategies based on natural compounds for the treatment of tauopathies.

02.014 **Toxicological Evaluation of the Peptide Fraternin-10 Administered Intranasally in Mice** (***Mus musculus***).
Costa MOG[1], Azevedo CVIB[2], Mortari MR[1] [1]UnB, Institute of Biological Sciences, Neuropharmacology Lab., Brazil [2]UnB, Faculty of Health Sciences, PPG in Health Sciences, Brazil

Introduction: Parkinson's disease (PD) is the second most prevalent neurodegenerative disease worldwide, affecting 3% of the elderly population. It is characterized by the degeneration of dopaminergic neurons in the substantia nigra and the acumulation of alpha-synuclein, leading to Lewy body formation and nigrostriatal pathway impairment. Cardinal signs include bradykinesia, resting tremor, and postural rigidity, alongside non-motor symptoms such as sleep disorders, cognitive impairment, and dysautonomia. Motor deficits reflect nigrostriatal dopaminergic loss, making motor coordination a key preclinical readout of neuroprotection in PD. Wasp-venom peptides show high target specificity: the parent peptide Fraternin protected dopaminergic neurons and improved motor deficits in the 6-OHDA model, and its analogue Fraternin-10, related to the neuroprotective peptide exendin-4, likewise improved motor performance, though toxicity was previously reported at all doses. Despite advances, definitive diagnosis still relies on post-mortem autopsy, and many aspects of disease progression remain poorly understood. **Objectives:** To evaluate the toxicity of the peptide Fraternin-10 in *Swiss Mus musculus*mice. **Methods:** The study used 32 male *Swiss Mus musculus*mice, approved by the Animal Ethics Committee (CEUA)/UnB, in accordance with the National Council for Animal Experimentation Control (CONCEA) and the Arouca Law (11.794/2008). Single-dose toxicity assays followed Brazilian Health Regulatory Agency (ANVISA) guidelines, with 4 groups (n=8): vehicle (saline) and three doses of Fraternin-10 (Fra-10) (5, 10, and 20 µg/animal), administered intranasally under isoflurane sedation. Over 14 days, body mass, assessed by the mass variation index (MVI), and motor coordination via the Rotarod test (4–40 RPM, 5 min) were monitored on D1 and D14. At the end, animals were euthanized with thiopental (60 mg/kg, i.p.) and organs (lung, kidney, liver) were processed for hematoxylin-eosin (H.E.) staining and histopathological analysis by optical microscopy. **Results:** Rotarod two-way analysis of variance (ANOVA) revealed a significant difference across days [$F(1.928, 108)=21.47$; $p<0.0001$], with no difference between treatments [$F(7,56)=0.9373$; $p>0.05$]. Tukey post-hoc analysis showed that the Fra-10 20 µg/animal group had greater fall latency on D14 compared to pre-test ($p<0.0001$) and D1 ($p<0.05$), with no signs of toxicity. Body mass showed no significant difference between groups [$F(7,55)=1.575$; $p>0.05$]. Histopathological analysis revealed no morphological alterations in any group. **Conclusion:** Fraternin-10 showed a favorable safety profile at all doses tested, with no changes in motor coordination, body mass, or organ histology, supporting its viability as a therapeutic candidate for preclinical PD studies. **Financial support**: CNPq, FAPDF, and CAPES. Ethics Committee: CEUA/UnB, protocol no. 23106.017341/2024-17.

02.015 **Cannabigerol Modulates Cocaine-Induced Reward in Mice in the Open Field Test**. Souza SS, Manduca CA, Moreira FA and Aguiar DC UFMG, Pharmacology Dept, Lab Neuropsychopharmacology, Brazil

Introduction: Cocaine use disorder (CUD) is a major public health problem in Brazil and is associated with secondary psychiatric conditions. Despite its clinical and social impact, no effective pharmacotherapies are available. Cannabigerol (CBG), a phytocannabinoid and non-psychotomimetic compound derived from *Cannabis sativa*, has demonstrated anxiolytic and neuroprotective effects in preclinical studies and has emerged as a promising therapeutic candidate. **Objective:** This study aimed to investigate whether CBG modifies cocaine-induced reward-related responses in the open field (OF) test. Methods: Adult male and female mice (C57BL/6JUnib) received intraperitoneal injections of CBG at doses of 3,10 and 30 mg/kg and were subjected to the OF test. Subsequently, a 10 mg/kg dose of CBG, which has already been shown to induce antinociceptive and anxiolytic-like effects in mice, was selected for further experiments. We then verified the effects of CBG (10 mg/kg) on both the acute and behavioral sensitization responses induced by cocaine (15 mg/kg) in the OF. **Results:** CBG administration did not alter the total distance traveled by the animals in the OF test, regardless of sex or dose. Similarly, 30 min pretreatment with CBG (10 mg/kg) did not modify the acute hyperlocomotor effect induced by cocaine. However, in the behavioral sensitization test, CBG pre-treatment potentiated cocaine-induced hyperlocomotion in female mice. **Conclusion:** CBG did not modify the acute effects of cocaine but facilitated cocaine-induced behavioral sensitization in females. However, the underlying mechanisms and potential role of sexual dimorphism in sensitization remain to be investigated.

02.016 Neurovespina Reduces Hippocampal Neuronal Death and Microglial Proliferation in a Pilocarpine-Induced Temporal Lobe Epilepsy Model. Fraga CH, Lima LS, Mortari MR. UnB, Darcy Ribeiro, Biology Institute, Neuropharma Lab, Brazil.

Introduction: Neurovespina is na antiepileptic peptide bioinspired by the venom of the social wasp Polybia occidentalis, with neuroprotective and anticonvulsant activity demonstrated in rodent models; however, its specific effects on microglial proliferation in temporal lobe epilepsy (TLE) remain unknown. TLE is the most common form of drug-resistant epilepsy, with approximately 70% of patients unresponsive to current treatments. Hippocampal neurodegeneration and neuroinflammation, particularly microglial activation, play a central role during the latent period following status epilepticus. **Objectives:** To evaluate the effects of Neurovespina on pyramidal neuron death in the hippocampus and microglial proliferation in the pilocarpine-induced temporal lobe epilepsy (TLE) model in mice. **Methods**: Male Swiss mice (*Mus musculus*; 25–46 g; n=4 to 7 per group) received scopolamine butylbromide (4 mg/kg, i.p.) followed, 20 minutes later, by pilocarpine (150 mg/kg, i.p.) to induce status epilepticus (SE), maintained for 180 minutes and terminated by isoflurane anesthesia. From day 2 to day 8, animals received twice-daily subcutaneous injections of vehicle, diazepam (4 mg/kg), or Neurovespina (2.5, 4, or 8 mg/kg). On day 9, brains were cryosectioned (30 µm; −1.34 to −2.30 mm from Bregma). Neuronal density was assessed by fluorescent Nissl staining in the dentate gyrus, CA3, and CA1; microglial proliferation was assessed by Iba-1 immunofluorescence. Optical density and cell counts were quantified using ImageJ. Statistics: Kruskal-Wallis/Dunn or one-way ANOVA/Tukey ($p<0.05$). Ethics: CEUA/UnB No. 23106.044079/2023-01. **Results**: Neurovespina at doses of 4 and 8 mg/kg significantly reduced hippocampal neuronal death compared to epileptic controls [$H(5)=93.65$; $p<0.0001$], with dose-dependent neuroprotection superior to diazepam and Neurovespina 2.5 mg/kg ($p\leq0.0044$). In the CA1 region, Neurovespina 4 mg/kg increased neuronal density compared to the epileptic, diazepam, and 2.5 mg/kg groups ($p<0.0001$; $p<0.0001$; $p=0.0010$); at 8 mg/kg, differences persisted compared to the epileptic and diazepam groups ($p=0.0006$; $p=0.0005$). Regarding microglial proliferation, Neurovespina 4 mg/kg reduced Iba-1-positive cell counts to levels similar to those of healthy animals [$H(5)=50.69$; $p<0.0001$], differing significantly from the epileptic ($p=0.0005$) and diazepam ($p<0.0001$) groups, while doses of 2.5 and 8 mg/kg were ineffective ($p<0.0001$ and $p=0.0062$ vs. Healthy animals, respectively). **Conclusion**: Neurovespina exerts significant dose-dependent neuroprotective effects and selectively reduces microglial proliferation at the 4 mg/kg dose in the pilocarpine-induced temporal lobe epilepsy model. These findings broaden the pharmacological understanding of this peptide and reinforce its potential as a therapeutic candidate for refractory epilepsy. **Financial support:** FAPDF, CAPES, CNPq and UnB. Ethics: CEUA/UnB No. 23106.044079/2023-01.

02.017 **Mulungu** (*Erythrina velutina*) **Infusion Prevents Cholinergic Dysfunction and Oxidative Stress in an Alzheimer's Disease Model in** *Drosophila melanogaster*. Razzera GA[1], Escher ALK[1], Rehbein CP[1], Schmidt JM[1], Silva ES[1], Thom SL[1], Kemmerich C[1], Medeiros CSS[1], Cruz IBM[4], Ribeiro EE[4], Schimith MD[3], Barbisan F[1,2], Musachio E[1,3]
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Introduction: Alzheimer's disease (AD) is the most prevalent form of dementia, characterized by memory loss, oxidative imbalance, and cholinergic dysfunction. Current treatments rely mainly on acetylcholinesterase (AChE) inhibitors with limited efficacy, highlighting the need for new therapeutic strategies. Mulungu (*Erythrina velutina*), a tree native to Northeastern Brazil traditionally consumed as a bark infusion, has antioxidant and neuroactive properties. **Objective:** To evaluate the neuroprotective effects of Mulungu infusion on memory deficits, cholinergic dysfunction, and oxidative stress in an aluminum chloride ($AlCl_3$)-induced AD model in *Drosophila melanogaster*. **Methods:** Wild-type Harwich flies were randomly assigned to four experimental groups: control (standard diet), Mulungu infusion (90 µL/mL), $AlCl_3$ (200 $mg \cdot kg^{-1}$), and $AlCl_3$ + Mulungu, and exposed for 7 days. Sample size was based on previous studies (Schmidt et al. 2026). Each group consisted of 100 flies distributed in four independent replicates the researchers were not blinded to group allocation during the experiments and data analysis. Short-term memory was evaluated using the aversive phototaxis test. AChE activity, marker of cholinergic dysfunction in AD, with spectrophotometric reading at 412 nm. Reactive oxygen species (ROS) levels were evaluated by fluorescence. Data were analyzed using two-way ANOVA to evaluate the effects of $AlCl_3$ exposure and Mulungu treatment, followed by Tukey's multiple comparisons test, considering $p \leq 0.05$ as statistically significant. **Results:** The results demonsterd significant effects of $AlCl_3$ exposure and Mulungu treatment on memory performance, AChE activity, and ROS levels. Tukey's test showed that the $AlCl_3$ group exhibited cognitive impairment compared with the control group ($p < 0.0001$). Mulungu treatment prevented this effect, as the Mulungu and $AlCl_3$ + Mulungu groups showed performance similar to the control group ($p = 0.2550$ and $p = 0.6796$), while the $AlCl_3$ + Mulungu group differed significantly from the $AlCl_3$ group ($p < 0.0001$). AChE activity increased significantly in the $AlCl_3$ group ($p < 0.0001$), whereas the Mulungu and $AlCl_3$ + Mulungu groups remained similar to the control group ($p = 0.0798$ and $p = 0.0861$), suggesting preservation of cholinergic function. ROS levels were elevated in the $AlCl_3$ group compared with the control group ($p = 0.0405$). In contrast, the Mulungu and $AlCl_3$ + Mulungu groups differed significantly from the $AlCl_3$ group ($p = 0.0264$ and $p = 0.0085$), indicating attenuation of oxidative stress. **Conclusion:** Mulungu infusion showed neuroprotective effects in an experimental AD model in *Drosophila melanogaster*, supporting its potential for AD research. However, further studies are needed to elucidate its mechanisms of action and therapeutic applicability.

02.018 **Behavioral and Metabolic Effects of** *Lacticaseibacillus rhamnosus* **64 in a Murine Model of Binge Eating**. Avelar CDFL[1], Malta GFA[1], Parreira, LS[1], Ribeiro, FM[2], Martins, FS[3], Vieira, LB[1] [1]ICB-UFMG, Dept Pharmacology, Neuropharmacology Lab, PPG Physiology and Pharmacology, Brazil; [2]ICB-UFMG, Dept Biochemistry, Neurobiochemistry Lab, PPG Biochemistry and Immunology, Brazil. [3]ICB-UFMG, Dept Microbiology, Biotherapeutic Agents Lab, PPG Microbiology, Brazil.

Introduction: Binge eating disorder (BED) is the most prevalent eating disorder in Western populations and is characterized by recurrent episodes of excessive food intake, particularly highly palatable foods, within short periods of time. BED is commonly associated with anxiety, depression, and increased risk of metabolic disorders. Modulation of the microbiota–gut–brain axis has emerged as a potential therapeutic strategy, as growing evidence indicates that binge-like eating alters gut microbiota composition and that intestinal microorganisms directly influence appetite regulation, body weight, and mood. Therefore, this study investigated the behavioral, metabolic, and molecular effects of the potential probiotic *Lacticaseibacillus rhamnosus* 64 (L64) in a murine model of binge eating. **Methods:** Female C57BL/6 mice aged 6–7 weeks underwent 12 binge-eating sessions, three times weekly for 2 hours, receiving either a control diet (AIN-93G) or a highly palatable diet (HSB). Animals were treated with L64 by oral gavage for seven days after the binge-eating sessions. Behavioral tests assessing binge-like eating, anxiety- and depressive-like behaviors, as well as molecular analyses, were performed. Metabolic parameters, including fasting glucose, body weight, and adiposity index, were also evaluated (CEUA-UFMG Protocol 166/2024). Statistical analyses were performed using GraphPad Prism 9, employing Student's *t*-test, Mann–Whitney, or two-way ANOVA ($p < 0.05$). **Results:** Animals exposed to the HSB diet developed binge-like eating behavior, characterized by higher food intake than control-fed animals ($\Delta = {}^{-}0.3440 \pm 0.05238$; $p < 0.0001$). *Untreated* HSB-exposed mice exhibited increased fasting glucose ($\Delta = 12.33 \pm 3.909$; $p = 0.0102$), anxiety-like behavior in the elevated plus maze (time in open arms: $\Delta = -12.41 \pm 4.224$; $p = 0.0188$) and open field (distance in the center: $\Delta = -2.272 \pm 0.9919$; $p = 0.0477$), and compulsive-like behavior in the marble burying test ($\Delta = 22.50 \pm 8.952$; $p = 0.0307$). L64 treatment reduced highly palatable food intake during the post-treatment binge session compared with HSB-fed animals receiving vehicle alone ($\Delta = 0.5000 \pm 0.06339$; $p < 0.0001$). However, no significant effects were observed in metabolic parameters, and behavioral assessments continued to indicate anxiety- and compulsive-like behaviors. **Conclusion:** These findings suggest a potential anorexigenic effect of L64 in female mice. We hypothesize that the behavioral outcomes may have been influenced by stress associated with gavage. Additionally, the treatment duration may not have been sufficient to induce consistent behavioral effects. These findings contribute to understanding the neurobiological mechanisms underlying binge eating and highlight the importance of longer treatment protocols and less stressful administration strategies.

02.019 **Effects of the Lithium Treatment on Early Stage of Sporadic Alzheimer's (sAD) Disease in Male Rats**. Lima, TF, Kanazawa LKS, Fernandes, SMA, Vital, MABF. UFPR, Pharmacology Dept, Brazil..

Introduction: Alzheimer's disease (AD) is a neurodegenerative pathology that primarily affects cognition, memory, and behavior, representing the most common form of dementia among the elderly. Intracerebroventricular (ICV) injections of low doses of streptozotocin (STZ) are used to mimic sAD in rodents. STZ causes impairments in insulin signaling and has been reported to trigger several alterations in the brain, such as oxidative stress, neuroinflammation, and dysfunctions in adult neurogenesis, which may be involved in cognitive decline and are features of human AD. The aim of this work was to test the hypothesis that oral prolonged low dose of lithium treatment would be able to preserve cognitive functions by inhibiting the GSK3beta in the sAD model induced STZ-ICV. **Objective:** To investigate the prolonged effects of lithium (Carbolithium™) microdoses in a streptozotocin-induced rat model of early-stage Alzheimer's disease. **Methods:** We evaluated the effects of lithium on 3-month-old male Wistar rats (N=41). Animals underwent stereotaxic surgery to receive either STZ (3 mg/kg, i.c.v.) or 0.9% saline (1 mg/kg, i.c.v.) on day one. For the next 21 consecutive days, they received a microdose of 0.1 mg/kg lithium (i.p.), while the control group received 0.9% saline solution (i.p.). Behavioral tests (open field, Y-maze, novel object recognition, and object location) were performed to analyze locomotion, behavior, and memory. For each test, animals habituated to the apparatus for 5 minutes; testing occurred one hour later for a duration of 3 minutes. Following behavioral testing, animals were euthanized, and the prefrontal cortex and hippocampus were collected. These structures were used to quantify phosphorylated GSK-3beta protein via Western blot. All procedures were approved by the Animal Experimentation Committee of the Federal University of Paraná (CEUA, protocol no. 1715). **Results:** prolonged treatment with lithium partially restored short-term spatial memory in male rats in Y maze and novel object location. Furthermore, lithium inactivated GSK-3beta, as evidenced by a higher presence of p-GSK-3beta in the prefrontal cortex of treated animals. **Conclusion:** Therefore, this study demonstrates that chronic microdose treatment with lithium during the early stages of Alzheimer's disease successfully restores spatial memory by inactivating the GSK-3beta protein. **Financial support**: This study was supported by a fellowship from the National Council for Scientific and Technological Development (CNPq, Brazil).

02.020 **BD-8 has no Effect Under Oxidative Stress in the Cerebellum of LPS-Challenged Mice**. Neves EPFI[1], Fonseca MFR[1], Ghedini PC[1], Mazaro e Costa R[1], Villar JAP[2], Barbosa LA[2], Leite JA[1] [1]ICB-UFG, Dept Pharmacology, Goiânia, Brazil; [2]UFSJ, Cellular Biochemistry Lab, Brazil.

Introduction: The biochemical integrity of the brain is essential for normal central nervous system (CNS) function. Oxidative stress, caused by excessive free radicals and inadequate antioxidant response, contributes to brain degradation. This stress is linked to neuroinflammation, with macrophages/microglia and astrocytes producing reactive oxygen species that lead to neurodegenerative and neuropsychiatric diseases. BD-8 is a synthetic cardiotonic steroid derivated from digoxin, which our group has previously found that had a positive response on modulating antioxidant enzymes, such as Superoxide Dismutase (SOD) and Catalase (CAT), as well as reducing Lipid Peroxidation (LPO) and pro-inflammatory cytokines such as IL-6. In that sense, and seeing the important role of the cerebellum on motor parameters, the present study aimed to evaluate if this activity can also be observed on this tissue of mice that were stress induced by LPS. **Methods:** The experimental procedures were approved by the Animal Ethics Committee of the Federal University of Goiás (CEUA/UFG Protocol No. 014/21). Swiss mice were divided randomly into 5 different groups, Control (DMSO; 0.1%), LPS (1mg/kg), BD-8 (0.28 mg/kg), BD-8 (0.56 mg/kg) and BD-8 (1.12 mg/kg) all pre-treated i.p. for 3 consecutive days and 1 hour after the last day of treatment, the animals were challenged with LPS (1 mg/kg i.p.). Antioxidant parameters were evaluated in samples of cerebellum after euthanizing the animals, 24 hours after the LPS challenge. **Results:** BD-8 showed no effectiveness in the cerebellum. The levels of Malondialdehide (MDA), as well as Protein Carbonilation (PC), didn't present a significant response between groups. The same data was also observed in the SOD and CAT evaluation. **Conclusion:** Despite the positive response of this compound in the cortex and hippocampus of mice, the same could not be said for the cerebellum, that despise multiple doses being tested, it has proven itself to be ineffective in this tissue. Further additional studies are necessary to elucidate the reason for why has this effect presented differently in other brain tissues. **Financial support:** CNPq.

02.021 Gamma-Decanolactone Recovers Reserpine-Induced Dopaminergic and Cholinergic Neuronal Damage in *Caenorhabditis elegans*. Farias MS, Souza VL, Andrade EM, Garofalo CB, Santos PA, Pereira P UFRGS, Institute of Basic Health Sciences, Dept Pharmacology, Lab Neuropharmacology and Clinical Toxicology, PPG in Pharmacology and Therapeutics, Brazil.

,Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by dopaminergic neuronal loss, oxidative stress, and motor dysfunction. Current therapies alleviate symptoms but do not prevent neurodegeneration. Natural compounds with antioxidant and neuroprotective properties have emerged as promising therapeutic alternatives. Gamma-decalactone (GD), a naturally occurring lactone, has demonstrated neuroprotective and antioxidant effects in experimental models; however, its mechanisms of action in parkinsonian neurodegeneration remain incompletely understood. Objectives: To evaluate the neuroprotective effects of gamma-decalactone against reserpine-induced dopaminergic and cholinergic neurodegeneration in *Caenorhabditis elegans*. Methods: Wild-type and transgenic *Caenorhabditis elegans* strains expressing green fluorescent protein (GFP) in dopaminergic (BY200), cholinergic (LX929), and oxidative stress-responsive pathways (CL2166 and LG333) were exposed to reserpine (60 µM) to induce PD-like neurotoxicity. GD was administered at concentrations of 75 and 150 µM under pre-treatment and post-treatment protocols. Behavioral assays included locomotor activity, basal slowing response, and pharyngeal pumping. Dopaminergic and cholinergic neuronal integrity was assessed by fluorescence microscopy. Intracellular reactive oxygen species (ROS) levels were quantified using CM-H2DCFDA, while gst-4 and skn-1 expression analyses were performed to investigate antioxidant defense pathways. The use of invertebrates does not require approval by an Animal Research Ethics Committee. Results: Reserpine exposure induced significant locomotor impairment, basal slowing dysfunction, oxidative stress, and dopaminergic and cholinergic neurodegeneration. GD treatment significantly restored dopamine-dependent behavioral responses and reduced locomotor abnormalities, particularly at 150 µM. Morphological analyses demonstrated preservation of cephalic dopaminergic neurons and cholinergic neuronal projections in GD-treated groups. GD also significantly reduced intracellular ROS accumulation and modulated oxidative stress-responsive pathways by decreasing gst-4 activation while increasing skn-1 expression, suggesting activation of endogenous antioxidant defenses through the SKN-1/Nrf2 pathway. Pre-treatment protocols generally produced stronger neuroprotective effects than post-treatment conditions. Conclusion: Gamma-decalactone exhibited specific neuroprotective effects against reserpine-induced neurotoxicity in *Caenorhabditis elegans*, preserving neuronal integrity and attenuating oxidative stress. The modulation of antioxidant defense pathways and restoration of dopamine-associated behaviors support GD as a promising multitarget candidate for neuroprotective strategies in Parkinson's disease.

02.022 **Evaluation of the Toxicity and Neuroprotective Potential of an Isatin Derivative in a *Caenorhabditis elegans* Model for Alzheimer's Disease**. Vieira CFA[1], Marreiro VS[1,2], Sousa LVBS[1], Almeida Filho GP[1], Lima TCBS[1], Carneiro CA[1], Campos CENS[1], Galdino FS[1,2], Costa MESM[1], Diniz MFFM[1,2], Lima-Junior CG[3], Olegário TR[3], Janebro DI[1,2]. [1]UFPB, Toxicological Testing Lab, Brazil, [2]UFPB, PPG in Natural and Synthetic Bioactive Products, Brazil, [3]UFPB, Lab Medicinal Organic Synthesis of Paraíba, Brazil

Alzheimer's Disease (AD) is the leading cause of dementia worldwide, characterized by progressive neurodegeneration associated with the extracellular accumulation of β-amyloid peptide (Aβ) and hyperphosphorylation of the tau protein, events that culminate in synaptic dysfunction and neuronal loss. Currently available therapies are predominantly symptomatic and do not significantly interfere with disease progression, highlighting the need for the development of new compounds with neuroprotective activity. In this context, isatin derivatives have emerged as promising molecules in neuroprotection studies due to their antioxidant and anti-inflammatory properties, as well as their potential ability to modulate multiple targets involved in the pathophysiology of AD. Therefore, the present study aimed to evaluate the toxicity and neuroprotective potential of the isatin derivative 2-3-hydroxy-1-methyl-2-oxoindolin-3-yl acrylonitrile (CH_3ISACN) using the in vivo model of the nematode *Caenorhabditis elegans*. For this purpose, wild-type (N2) and transgenic (CL2006) strains were used, the latter being genetically modified to express the human β-amyloid peptide. The animals were exposed to the compound at concentrations of 240, 1200, and 2400 µM. Toxicological evaluation was performed through egg hatching, survival, and pharyngeal pumping assays, while the neuroprotective effect was investigated using the heat stress-induced paralysis assay. Data normality was verified using the Shapiro-Wilk test and subsequently analyzed by ANOVA followed by Dunnett's post hoc test, adopting $p < 0.05$. The results demonstrated that CH_3ISACN exhibited a low toxicity profile at all tested concentrations, with hatching rates above 95%, survival rates above 90%, and no significant changes in pharyngeal pumping in either strain, indicating preservation of physiological function. In the evaluation of neuroprotective potential. It was observed that the 240 µM concentration significantly reduced the paralysis rate in the CL2006 strain, suggesting a protective effect against Aβ-induced toxicity. Taken together, the findings indicate that the CH_3ISACN compound presents a favorable safety profile and relevant neuroprotective activity in the experimental model used, making it a promising candidate for future studies aimed at the development of disease-modifying therapies for Alzheimer's Disease. Acknowledgments to UFPB, LASOM-PB, and LABETOX.

02.023 **Cytoprotective and Redox-Modulating Effects of** *Achyrocline satureioides* **Infusion in BV-2 Microglial Cells Exposed to Hydrocortisone**. Pulcinelli DLF, Turra BO, Bonotto NCA, Santos É, Escher ALK, Musachio E, Barbisan F
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Introduction: Chronic stress is an important risk factor for neuropsychiatric and neurodegenerative disorders and is associated with persistent activation of the hypothalamic–pituitary–adrenal axis and prolonged release of glucocorticoids, such as cortisol. This environment favours oxidative stress, neuroinflammation, and alterations in neuroplasticity. In this context, exacerbated activation of microglial cells contributes to neuronal damage and the development of neuropsychiatric and neurodegenerative disorders. Natural compounds rich in phenolics and flavonoids have attracted interest due to their antioxidant and anti-inflammatory properties. Among these, marcela (*Achyrocline satureioides*) stands out, being traditionally used in southern Brazil for its potential calming, anti-inflammatory, and gastroprotective therapeutic effects. **Objective:** To investigate the potential cytoprotective and redox-modulating effects of *Achyrocline satureioides* infusion in BV-2 microglial cells chronically exposed to hydrocortisone. **Methodology:** Marcela infusion was prepared according to traditional use and the recommendations of the Brazilian Pharmacopoeia, using 1 g of inflorescences infused for 15 minutes in 150 mL of water at 80 °C. Commercially acquired BV-2 microglial cells were cultured in RPMI-1640 medium supplemented with 10% foetal bovine serum and 1% antibiotic solution and maintained at 37 °C and 5% CO_2. Cells were treated with hydrocortisone at a concentration of 10 µM, previously established through a pharmacological dose–response curve, combined with different concentrations of marcela infusion (10, 50, and 100 µL/mL) for 96 hours. Cell viability was assessed using the ATP CellTiter-Glo® assay, reactive oxygen species levels were determined using the DCFH-DA assay, and BDNF secretion, a neurotrophin related to neuroplasticity, was measured by ELISA. Statistical analysis was performed using GraphPad Prism 8.0 through two-way ANOVA followed by Tukey's post hoc multiple comparisons test, considering $p < 0.05$. **Results:** Marcela infusion significantly increased cell viability even in the presence of hydrocortisone ($p < 0.0001$ for all concentrations). All tested concentrations significantly reduced reactive oxygen species levels compared with the group treated only with hydrocortisone ($p = 0.0011$, $p = 0.0077$ and $p < 0.0001$, respectively). Furthermore, a significant increase in BDNF expression was observed in the co-treated group ($p = 0.0011$, $p < 0.0001$ and $p = 0.0155$, respectively), suggesting a positive modulatory effect on mechanisms related to neuroplasticity. **Conclusion:** *Achyrocline satureioides* infusion demonstrated a potential cytoprotective effect against hydrocortisone-induced damage in BV-2 microglial cells, associated with reduced oxidative stress and increased BDNF levels. These findings reinforce the pharmacological potential of marcela as an adjuvant strategy for modulating redox alterations associated with chronic stress.

02.024 **Integrated Network Pharmacology, Molecular Docking, and Cellular Analysis of beta-Ciclodextrin Complexed 1,8-cineole in Parkinson´s Disease**. Araújo-Monteiro L[1], Carvalhinho-Lopes PS[1], Soares-Silva B[1], Donzelli NIZ[1], Quintans-Junior LR[2], Rando DG[3], Ribeiro AM[1] [1]Unifesp-Baixada Santista, PPG in Bioproducts and Bioprocesses, Brazil; [2]UFS, PPG in Pharmaceutical Sciences, Brazil; [3]Unifesp-Diadema, PPG in Pharmaceutical Sciences; Brazil.

Introduction: Parkinson's disease (PD) is the second most prevalent neurodegenerative disorder and is characterized by progressive dopaminergic degeneration. Current therapies improve symptoms but do not prevent disease progression and may cause adverse effects. Natural compounds are promising therapeutic candidates. The monoterpene 1,8-cineole (CIN), found in several plant species, exhibits antioxidant, anti-inflammatory and neuroprotective properties. Complexation with beta-cyclodextrin (beta-CIN) is a biotechnological approach widely used to improve the physicochemical performance of natural compounds, enhancing aqueous solubility, stability, and protection against volatilization/oxidation, thereby facilitating formulation and increasing the feasibility of translational testing. **Objectives:** To investigate molecular mechanisms associated with the neuroprotective effect of beta-CIN using *in silico* and *in vitro* models of PD. **Materials and Methods:** Potential molecular targets of CIN were identified using PharmMapper and analyzed by network pharmacology with PD-related genes. Gene Ontology (GO), Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment, and molecular docking were performed for caspase-3, PPARgamma, glutathione S-transferase and ERK2. Human SH-SY5Y neuroblastoma cells differentiated into a dopaminergic phenotype were treated with beta-CIN (50-300 μM). Dopaminergic injury was induced using 6-hydroxydopamine (6-OHDA, 100 μM). Cells were exposed to beta-CIN concomitantly or prior to neurotoxin exposure for 24 h. Cell viability was assessed using the MTT assay (n=3). **Results:** Seventy potential molecular targets of CIN were identified, of which 60 were associated with PD. Network analysis revealed three major functional subnetworks related to inflammation, apoptosis and hormonal signaling. Enrichment analysis indicated inflammatory, apoptotic and metabolic pathways associated with neurodegeneration. Molecular docking suggested favorable interactions between CIN and all analyzed targets. One-way ANOVA demonstrated a dose-dependent effect of beta-CIN, with cytotoxicity observed at concentrations ≥250 μM [$F(7,16)=12.21$, $p < 0.0001$]. Treatment with 50 and 100 μM prevented cell death following concomitant 6-OHDA exposure and attenuated lesion exacerbation after prior neurotoxin exposure. **Conclusion:** beta-CIN interacted with multiple PD-related targets and demonstrated cytoprotective effects at lower concentrations, whereas higher concentrations were cytotoxic to SH-SY5Y cells. **Financial support**: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES, Finance Code 001), Fundação de Amparo à Pesquisa no Estado de São Paulo (FAPESP – grant #2020/0915-4 and #2023/11947-0), and Conselho Nacional do Desenvolvimento Científico e Tecnológico (CNPq grant #408377/2021-6, #310403/2021-9, #304572/2025-0). Keywords: 1,8-cineole; neuroprotection; *in silico* analysis; Parkinson´s Disease.

02.025 **Comparison Between Preventive and Concomitant Treatment Effects of Potentially Psychobiotic Bacteria on Ethanol-Induced Conditioned Place Preference Associated with Sleep Deprivation**. Resende GR[1,2], Silva KSO[2], Fighera YCM[2], Souza CS[2], Marinho EAV[4], Berro LF[3], Tamura EK[2,4] [1]UESC PPG in Health Sciences, [2]UESC Chronobiology Research Group, [3]University of Mississipi Medical Center Dept Psychiatry and Human Behavior, [4]UESC Dept Health Sciences

Recent studies have highlighted the role of the microbiota-gut-brain axis in substance dependence. Furthermore, emerging evidence suggests that sleep deprivation (SD) may potentiate drug-related behaviors, increasing susceptibility to addiction. Therefore, this study aimed to compare the effects of concomitant and preventive treatment with *Lactiplantibacillus plantarum* 286 (Lp286) and *Lactiplantibacillus plantarum* 81 (Lp81) on alcohol dependence associated with sleep deprivation. 134 male Swiss mice (3 months old; 25–40g), divided into eight groups, underwent habituation, pre-conditioning, conditioning, and post-conditioning phases on different days. After these stages, animals were treated with vehicle (VEI; saline + 15% skim milk), Lp286, or Lp81 (10^9 CFU; gavage). In the groups receiving bacterial strains, half of the animals underwent preventive treatment, while the remaining half received treatment concomitantly with the conditioning phase. After seven days of treatment, half of the groups were subjected to a sleep deprivation protocol (SD) using the gentle handling method, while the other half remained undisturbed. Sleep deprivation lasted 6 uninterrupted hours (7:00a.m.–1:00p.m.). Animals were subsequently subjected to the ethanol-induced Conditioned Place Preference (CPP) paradigm (ETA; 1.8 g/kg, i.p.) in the afternoon. During CPP, time spent (TS), distance traveled (DT), and number of entries (NE) were assessed. Behavioral sessions were recorded and analyzed using the ANY-maze software. This study was approved by the Institutional Animal Care and Use Committee (CEUA-UESC; protocol nº 026/23). In the pre-treatment protocol, an increase in TS was observed in the VEI-ETA group, with differences also found in the Lp81-ETA and SD-VEI-ETA groups. No differences between pre-cond and post-cond phases were observed in the Lp286-ETA and SD-Lp286-ETA groups. Likewise, no differences between phases were observed in the SD-Lp81-ETA group. Regarding distance traveled, reductions were observed in the VEI-ETA, Lp81-ETA, and SD-VEI-ETA groups. No significant differences were observed in the Lp286-ETA, SD-Lp286-ETA, and SD- Lp81-ETA groups. No differences were found for NE. In the concomitant treatment protocol, regarding TS, significant differences were observed in post-cond 2 in the Lp81-ETA and SD-VEI-ETA groups when compared with their respective pre-cond phases. An increase in TS was also observed in post-cond 2 in the SD-VEI-ETA and SD-Lp81-ETA groups. However, no differences were observed in the Lp81-ETA group between post-conditioning phases. No statistically significant differences were found for DT and NE parameters. Taken together, the data suggest that the Lp286 strain inhibits the establishment of ethanol-induced CPP, both under sleep deprivation and non- sleep deprivation conditions. When comparing the two treatment approaches, concomitant treatment during CPP development proved to be statistically more effective. Further studies are needed to confirm the therapeutic potential of these strains in ethanol dependence and their relationship with sleep deprivation.

02.026 **Purple Pitanga Extract Reduces Neuroinflammation and Motor Impairment in a Postmenopausal Parkinson's Disease Model**. Fontoura EA, Streb BL, Fidelis EM, Da Costa NHC, Rodrigues ES, Gomes J, Comis-Neto AA, Batista WT, Pinton S, Rosa SG Unipampa

Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by dopaminergic neuronal loss, leading to motor impairments, neuroinflammation and oxidative stress. Estrogen deprivation resulting from ovariectomy (OVX) may potentiate these mechanisms in the central nervous system. In this context, the neurotoxin1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) selectively targets catecholaminergic neurons, inducing PD-like symptoms in rodents, which may be aggravated in estrogen-deficient models. Studies have demonstrated that purple pitanga (*Eugenia uniflora*), a fruit rich in phenolic compounds and anthocyanins, modulates pathways related to oxidative stress, apoptosis, and neuroinflammation. **Objective:** To evaluate the purple pitanga extract (PPE)effects on motor behavior and inflammatory markers in the striatum of ovariectomized rats subjected to an experimental PD model. **Methods:** Female Wistar rats (CEUA 010/2021) underwent OVX or sham surgery. After 30 days, the animals received intranasal MPTP (1mg/nostril, 10µL) or saline. PPE(1000mg/kg) or saline was administered for 28 days according to the following groups: 1) Control (CON); 2) PPE; 3) MPTP; 4) MPTP+PPE; 5) OVX; 6) OVX+PPE; 7)OVX+MPTP; 8) OVX+MPTP+PPE.. Motor coordination was evaluated using the rotarodt est on day 28, followed by euthanasia. Striatal IL-10, TNF-α, and IL-1βexpression were assessed By Western Blotting. Data was analyzed using one-way ANOVA followed by Newman-Keuls post hoc test, or Kruskal-Wallis test, with $p<0.05$ considered statistically significant. **Results:** the MPTP and OVX+MPTP groups showed a significant reduction in latency to fall when compared to the CON group. PPE treatment attenuated this locomotor deficit, as the MPTP+PPEand OVX+MPTP+PPE groups showed higher performance compared to their respective non-treated groups. In the striatum, TNF-α levels were significantly increased in the MPTP, OVX, and OVX+MPTP groups when compared to the CON group. PPE reduced TNF-α levels in the MPTP+PPE, OVX+PPE, and OVX+MPTP+PPE groups compared to their respective untreated groups. Regarding IL-1β, the experimental groups showed increased cytokine expression compared to the CON group, including MPTP, MPTP+PPE, OVX, OVX+PPE, OVX+MPTP and OVX+MPTP+PPE, suggesting persistent inflammatory activation. Conversely, IL-10 levels did not differ significantly among the groups. **Conclusion:** MPTP administration combined with OVX induced inflammatory alterations and motor impairments in Wistar rats, evidenced by the increased TNF-α and IL-1β in the striatum and reduced performance in the rotarod test. PPE treatment attenuated TNF-α level sand reverse motor deficits, suggesting neuroprotective and anti-inflammatory effects associated with their phenolic compounds and anthocyanins. These findings reinforce the therapeutic potential of *Eugenia uniflora* against neuroinflammatory alterations associated with PD and estrogen deficiency.

02.027 **iNOS Deletion in Mice Alters CaMKII-alpha S-Nitrosylation and Phosphorylation Dynamics in the Prefrontal Cortex Across Contextual Fear Conditioning Phases**. Silva TA[1], Ferreira BF[2,3], Barbosa KE[1], Meyer E[1], Tella SC[2], dos Santos JE[2], Fronza MG[2,4], Lisboa SF[1] [1]FCFRP-USP, [2]FMRP-USP, [3]University of Quebéc – Tróis-Riviére, Canada, [4]Universitat Autònoma de Barcelona, Spain

Introduction: Nitric oxide (NO) plays a critical modulatory role in fear memory processing. Inducible NO synthase knockout mice (iNOS KO) show fear extinction deficits, a core feature of trauma-related disorders such PTSD, linked to increased prefrontal cortex (PFC) NO signaling. However, downstream molecular mechanisms underlying the behavioral phenotype are unclear. Calcium/calmodulin-dependent protein kinase II alpha (CaMKII-α) regulates synaptic plasticity, whose function can be modulated by phosphorylation and NO-mediated S-nitrosylation. **Objectives:** To assess iNOS deletion effects on CaMKII-α expression, functional activation (phosphorylation at Thr286), S-nitrosylation (SNO-CaMKII-α), and global SNO-proteome in PFC of iNOS KO mice during contextual fear conditioning (CFC) phases. **Methods:** Male wild-type (WT) and iNOS KO mice underwent the CFC protocol and PFC samples were collected right after habituation, conditioning (3 x 0.75mA footshocks), extinction, or extinction retrieval phase. Total /p-CaMKII levels were quantified by Western blot. SNO was assessed by SNO Resin-Assisted Capture (SNO-RAC) assay coupled with multiplex fluorescence (REVERT 700 Total Protein Stain). The Ethical Review Committee of the School of Pharmaceutical Sciences of Ribeirão Preto approved the protocols (CEUA: 24.1.136.60.9). **Results:** Both genotypes acquired fear, but iNOS KO mice showed extinction deficits. Total CaMKII-α expression increased post-conditioning in both groups, indicating preserved basal protein synthesis. However, while WT mice upregulated the total expression of phosphorylated CaMKII-α (pCaMKII-α) during the extinction phase, iNOS KO mice failed to mount this response (significant Genotype x Condition interaction). SNO-RAC revealed global hyponitrosylation in iNOS KO mice (significant main effect of Genotype across all CFC phases). Paradoxically, basal hypernitrosylation of CaMKII-α was seen, which was not observed after acute stress (footshocks). **Conclusion:** iNOS can be a key source of basal S-nitrosylation in PFC. However, CaMKII-α hypernitrosylation suggests compensatory mechanisms to keep this protein function, by recruiting other NOS, such as nNOS. Acute stress prevents this compensation, impairing memory. Notably, rather than a mere baseline deficit, iNOS KO mice fail to upregulate total phosphoCaMKII expression during the extinction phase, unlike the dynamic increase observed in WT controls. This failure indicates that early dysfunctional nitrosylation structurally compromises the enzyme, affecting memory encoding. A possible balance between CAMKII-α nitrosylation and phosphorylation could provide a mechanism for fear extinction memory impairment, as observed in the iNOS KO mice. Direct evidence that restoring CaMKII-α nitrosylation rescues phosphorylation and extinction remains to be established. Keywords: CaMKII alpha, fear conditioning, iNOS, Nitric oxide, PTSD

02.028 **The Role of mGluR5 and the PI3K/AKT/mTOR Pathway in Regulating Body Weight in Obese Mice**. Morais ALBM, Silva LP, Barahuna-Filho PFR, Avelar CDFL, Vieira, LB UFMG, Dept Pharmacology, PPG Physiology and Pharmacology, Brazil

Introduction: Obesity exhibits an energy imbalance that disrupts hypothalamic metabolic regulation. While the phosphoinositide 3-kinase (PI3K)/protein kinase B (AKT)/mechanistic target of rapamycin (mTOR) pathway is a known regulator of energy homeostasis, the specific role of metabotropic glutamate receptor 5 (mGluR5) in feeding behavior and nutrient signaling remains poorly understood. This study investigates whether pharmacological inhibition of mGluR5 modulates hypothalamic and peripheral mTOR signaling in a diet-induced obesity model. **Methods:** Six-week-old C57BL/6 male mice were fed either a high sugar and butter (HSB) diet or the control AIN-93G diet. After 10 weeks, animals received intraperitoneal treatment with 3-((2-Methyl-1,3-thiazol-4-yl)ethynyl)pyridine (MTEP) (5mg/kg), rapamycin (1mg/kg) or saline for 12 days, after which hypothalamus and white adipose tissue were collected (CEUA 217/2019). **Results:** Animals fed with HSB diet showed a significant increase in body weight compared to the AIN93G group starting from the 2nd week of diet ($p<0.05$). Food intake was similar between groups until the 9th week, when AIN93G-fed animals increased feeding. MTEP treatment promoted weight loss compared to HSB-saline group ($p=0.0014$). Rapamycin treatment also induced significant weight loss ($p<0.0001$). The adiposity index was higher in HSB animals than in AIN93G ($p=0.0004$), and treatments reduced overall adiposity. No differences were observed in retroperitoneal adipose tissue weight among groups. However, mesenteric adipose tissue was higher in HSB animals compared to AIN93G ($p=0.0032$). In epididymal adipose tissue, HSB animals showed greater adiposity ($p<0.0001$); In OGTT, fasting glycemia did not differ among groups. However, animals treated with rapamycin showed higher glycemic levels after 30 min compared to saline- treated animals ($p=0.0026$) and MTEP-treated animals ($p=0.0017$), normalizing only after 120 min. **Conclusion:** These results indicate that mGluR5 inhibition via MTEP promotes significant weight loss in obese mice without the glucose intolerance associated with rapamycin treatment. This suggests mGluR5 as a potential therapeutic target for obesity that bypasses certain detrimental side effects of systemic mTOR inhibition. The next steps include Western Blot for phosphorylated extracellular signal-regulated kinase (p-ERK), p-AKT, p-mTOR, and phosphorylated ribosomal protein S6 kinase beta-1 (p-P70S6K), as well as immunofluorescence for p-mTOR, to further characterize the intracellular signaling pathways involved in hypothalamic modulation.

02.029 **Liposomal Nanoencapsulation Potentiates the Anticonvulsant and Neuroprotective Effects of γ-Decanolactone Through GABAergic Pathway Modulation in** *Caenorhabditis elegans*. Souza VL, Andrade EM, Garofalo CB, Santos PA, Pereira P UFRGS – Institute of Basic Health Sciences, Dept Pharmacology, Lab Neuropharmacology and Clinical Toxicology, PPG in Pharmacology and Therapeutics. Brazil.

Introduction: Alterations in GABAergic neurotransmission are strongly associated with neuronal hyperexcitability and epileptic disorders. γ-Decanolactone (GD) exhibits neuroactive and neuroprotective properties; however, limitations related to toxicity and bioavailability may compromise its pharmacological application. Liposomal nanoencapsulation has emerged as a promising strategy to improve compound stability, bioavailability, and therapeutic efficacy. **Objectives:** To evaluate the anticonvulsant and neuroprotective effects of liposomal γ-decanolactone (LP-GD) in *Caenorhabditis elegans* models of pentylenetetrazol (PTZ)-induced hyperexcitability and GABAergic dysfunction. Methods:Wild-type (N2) and GABAergic mutant *C. elegans* strains (unc-25, unc-47, and unc-49) were exposed to free GD or LP-GD (25–200 µmol/mL) for 24 or 48 h. Formulation-induced toxicity was assessed by survival, development, brood size, and pharyngeal pumping. Neuroprotective activity was evaluated in manganese- and methylmercury-induced neurotoxicity models, while anticonvulsant activity was assessed using PTZ-induced neuroexcitation by measuring paralysis, seizure-like behavior, and locomotion. GABAergic mutant strains were used to investigate the involvement of GABAergic signaling in the neuroprotective and anticonvulsant effects of LP-GD. **Results:** PTZ exposure induced progressive paralysis and hyperexcitable phenotypes in *C. elegans*. LP-GD significantly reduced paralysis rates and seizure-like behavior in a dose- and time-dependent manner, particularly after 48 h of exposure, demonstrating greater anticonvulsant efficacy than free GD. In GABAergic mutant strains, increased susceptibility to hyperexcitation was observed, and the neuroprotective effects of LP-GD were markedly attenuated, indicating dependence on intact GABAergic neurotransmission. Evaluation of formulation- induced toxicity showed that LP-GD exhibited lower toxicity than free GD, as evidenced by improved survival, normal developmental progression, preserved reproductive capacity, and maintenance of pharyngeal pumping. Furthermore, in manganese- and methylmercury-induced neurotoxicity models, LP-GD provided greater neuroprotection than free GD, reducing the deleterious effects of metal exposure and preserving normal behavioral responses. **Conclusion:** Liposomal nanoencapsulation significantly potentiated the anticonvulsant and neuroprotective effects of γ-decanolactone in *C. elegans*. The observed effects appear to involve modulation of GABAergic neurotransmission associated with reduced neuronal hyperexcitability. These findings reinforce the translational potential of nanoencapsulated γ-decanolactone as a candidate strategy for the development of safer and more effective anticonvulsant therapies. This work was supported by the Coordination for the Improvement of Higher Education Personnel (CAPES) (number 88887.506777/2020–00); Scholarships from the National Council for Scientific and Technological Development (CNPq). The authors acknowledge the use of public computational platforms and biological databases employed in this study.

02.030 **Role of α1A-Adrenoceptors on Anxiety-Related Behavior in Mice**. Figueredo BS, Gomes LTC, Sena MO, Gavioli EC, Silva Junior ED. UFRN, Dept Biophysics and Pharmacology, Brazil.

Introduction: In recent decades, growing attention has been directed toward the role of α1-adrenoceptors (α1-ARs) in the central nervous system, particularly the α1A-AR subtype, which is the predominant α1-AR expressed in this tissue. Evidence from both human and animal studies indicates that activation of α1-ARs is associated with anxiety-related responses. Nevertheless, it remains unclear which α1-AR subtype mediates these effects, highlighting an important gap in our understanding of the neurobiology of anxiety. **Objective:** To investigate the role of α1A-ARs in anxiety-like behavior using oxymetazoline, a partial agonist of α1A-ARs, in established animal models of anxiety. Material and **Methods:** Male Swiss mice were treated intraperitoneally 60 min before the elevated plus-maze test with a vehicle (control), diazepam 1 mg/kg (anxiolytic), or oxymetazoline at doses of 0.001 mg/kg, 0.01 mg/kg, or 0.1 mg/kg. In this test, the exploration of the open or closed arms was analyzed. **Results:** Mice subjected to pre-treatment with oxymetazoline at 0.001 mg/kg, 0.01 mg/kg, or 0.1 mg/kg showed no changes in the number of entries and the time spent in the open or closed arms of the elevated plus-maze compared to the control group. On the other hand, the group treated with diazepam showed a significant increase in the number of entries into the open arms, indicating an already expected anxiolytic action. **Conclusion:** Pharmacological activation of the α1A-AR with the partial agonist oxymetazoline failed to induce anxiety-like behaviors in the experimental model. Nevertheless, the interpretation of these findings is limited by the lack of receptor selectivity of oxymetazoline, whose off-target effects may have masked potential α1A-adrenoceptor-mediated responses. Further studies employing more selective pharmacological tools are required to clarify the role of this receptor subtype in the modulation of anxiety-related behaviors. Keywords: α1A-adrenoceptors, anxiety, animal model.

02.031 **Genetic Mutations of Na+, K+-ATPase Involved in the Onset of Neurological Disorders – A Systematic Review**. Rosa GK[1,2], Ribeiro LR[1,2], Bariviera JL[1,2], Carneiro MA[2], Vargas, LS[2], Fonseca, CPW[2], Oliveira MS[1,2] [1]UFSM, PPG Pharmacology, Brazil, [2]UFSM, Lab Experimental Neurology

Introduction: Neurological disorders encompass a wide range of severe symptoms and manifestations, many of which are associated with genetic mutations that affect ionic homeostasis. Na+,K+-ATPase, a transmembrane enzyme responsible for maintaining electrochemical gradients in cells, plays a crucial role in neuronal excitability and brain function. Objetives: This systematic review investigates the mutations present in the protein structure and seeks to determine whether there are correlations with neurological pathologies. **Methods:** The review was conducted through a search in the Scopus and PubMed databases. Database-specific search strategies were developed using descriptors such as "Na+,K+-ATPase", "ATP1A1", "ATP1A2", "ATP1A3", "mutations" and "neurological disorders", combined with the Boolean operators "AND" and "OR". The search results were exported to the Rayyan platform. Initially, only the titles and abstracts of the articles were evaluated by two reviewers. In cases of conflict, a third reviewer was consulted. Articles that met the inclusion criteria at this stage were read in full, and the relevant data were organized into tables and visually presented using ChimeraX software. Inclusion criteria included studies conducted in humans, addressing mutations in Na+,K+-ATPase associated with neurological symptoms, published in English and in scientific journals. Conversely, studies in animals, *in silico* models, *in vitro* models, studies that did not address mutations in Na+,K+-ATPase or their neurological outcomes, articles in other languages, and those with unclear methodology were excluded. **Results:** A total of 537 records were identified through the database search, and 61 studies met the inclusion criteria after screening and full-text assessment. Mutations in the ATP1A1 (α1) gene are associated with epilepsy, developmental delays, autism and Charcot-Marie-Tooth disease. Mutations in the ATP1A2 (α2) gene are mainly associated with familial hemiplegic migraine type 2 (FHM2) and sporadic hemiplegic migraine (SHM), epilepsy, polymicrogyria and severe developmental syndromes. ATP1A3 (α3) variants present the broadest phenotypic diversity, including alternating hemiplegia of childhood (AHC), rapid onset dystonia- parkinsonism (RDP), cerebellar ataxia, schizophrenia, and CAPOS syndrome. Furthermore, the Gly41Arg mutation in the FXYD2 gene is implicated in hypomagnesemia with possible neurological effects. **Conclusion:** Our findings reinforce the essential role of Na+,K+-ATPase in neurodevelopment and suggest that its genetic alterations significantly contribute to a spectrum of neurological disorders, especially epilepsy. Understanding these mutations provides insights into disease mechanisms and may inform future therapeutic approaches. **Acknowledgments:** The author acknowledges the financial support of the institutions CAPES and FAPERGS.

02.032 **Effects of Cannabigerol on Sensorimotor Gating and Behavioral Alterations Induced by MK-801 in Mice**. Correa BS, Souza JC, Pereira GJS, Abílio VC Unifesp, Graduate Program in Pharmacology, Brazil.

Introduction: Schizophrenia is a disabling mental disorder that affects approximately 0.31% of the world population. Although current medications are used to treat schizophrenia symptoms, they are associated with serious adverse effects and are mainly effective against the positive symptoms of the disorder. Therefore, new therapeutic alternatives have been investigated by our research group, especially cannabinoid compounds. Cannabigerol (CBG), a bioactive compound derived from *Cannabis sativa*, has pharmacological properties similar to those of Cannabidiol (CBD), including antioxidant, anti-inflammatory, and neuromodulatory effects. **Objectives:** Therefore, considering previous studies that demonstrated the therapeutic and preventive effects of CBD on schizophrenia-related behaviors, this project aims to characterize the behavioral effects induced by CBG administration in an animal model of NMDA receptor antagonism induced by MK-801 in adult mice. **Methods:** For this purpose, male and female C57BL/6J mice were subjected to two experimental protocols. In Experiment 1, mice between postnatal days (PND) 80–90 received an acute dose of CBG (1, 5, or 10 mg/kg, i.p.), followed by an MK-801 challenge (0.5 mg/kg, i.p.). In Experiment 2, mice received CBG for 15 days (1 mg/kg for males and 5 mg/kg for females), while MK-801 (0.25 mg/kg, i.p.) was administered during the last seven days of CBG treatment. After completion of the acute or chronic treatments, all animals underwent behavioral assessments, including spontaneous alternation, open-field locomotor activity, social interaction, and prepulse inhibition (PPI) tests. Subsequently, the animals were euthanized, and the brains were collected for further neurochemical analysis. **Results:** In Experiment 1, significant effects of MK-801 were observed in the behavioral assessments, confirming the induction of schizophrenia-like behaviors in the animals ($p<0.05$, GLM analysis). In Experiment 2, MK-801 also produced significant behavioral alterations ($p<0.05$, GLM analysis). However, CBG treatment reduced rotational behavior in female mice ($p<0.05$, GLM analysis). Furthermore, in the prepulse inhibition (PPI) test, CBG significantly increased PPI responses exclusively in male animals ($p < 0.05$, GLM analysis), suggesting a modulatory effect on sensorimotor gating deficits. **Conclusion:** These findings confirm the validity of the MK-801-induced schizophrenia-like model and demonstrate that CBG modulates sensory gating, highlighting its potential as a therapeutic strategy for schizophrenia-associated alterations. **Acknowledgments:** The authors would like to acknowledge all collaborators who contributed to the development of this project.

02.033 **Formulation and Characterization of an Octovespin Peptide Nanoemulsion for Intranasal Application for Alzheimer's Disease Treatment**. Penha GS[1,2,3], Santos VRM[1,2,3] Mota IFL[1,3], Resende MCS[1], Taveira RAA[1,3], Rabelo GS[1], Gomes CHF[1], Mortari MR[1], Camargo LC[2,3] [1]UnB, Darcy Ribeiro, Biology Institute, Dept Physiological Sciences, Neuropharma Lab, Brazil, [2]UnB, Darcy Ribeiro, Biology Institute, PPG Animal Biology, Brazil [3]UnB, Darcy Ribeiro, Psychology Institute, Psychobiology Lab, Brazil.

Introduction: Alzheimer's disease (AD) is the leading cause of dementia, however treatments are mostly symptomatic, enabling disease progression. Octovespin, a bioinspired peptide from wasp venom (Polybia occidentalis) disaggregates β-amyloid and reduces cognitive deficits but exhibits limited blood-brain barrier permeability. Therefore, intranasal routes and nanotechnologies may be strategies to overcome the limitations as the nasal cavity bypasses the barrier due to the olfactory bulb and trigeminal nerve, enhancing brain drug delivery. **Objectives:** Formulating and characterizing a nanoemulsion containing Octovespin with the aim of enabling its use for intranasal treatment of Alzheimer's disease. **Methods:** Octovespin was synthesized by Pepmic Co., Ltd. Nanoemulsions were adapted from Mota (2024) protocol by mixing lecithin, olive oil, and ethanol for Blank Nanoemulsion (BN) or lecithin, olive oil, ethanol and Octovespin for Octovespin Nanoemulsion (ON), followed by rotary evaporation to form a film. Ethanol volume was adjusted when Octovespin was incorporated. The film was resuspended on PBS containing chitosan and sonicated in an ice bath for the final formulation (6×5minutes, constant pulse, 40% amplitude). Zeta potential, Polydispersity index (PDI), and size were monitored on days 1, 7, 15, 30 and 60 (Zetasizer Nano ZS90). Neurotoxicity was assessed in SH-SY5Y cells via MTT assay with positive/negative controls and 2.5, 5, or 50 µL of BN or ON. The release study on day 30 utilized Amicon Ultra filtration 0.5 mL followed by HPLC and MALDI-TOF analysis. Nasal spray performance (spray pattern at 3 and 6 cm and delivered mass) was evaluated using adapted protocols from Inthavong et al. (2015) and Morita et al. (2025). Statistical analysis was performed via GraphPad Prism ($p < 0.05$). After Kolmogorov-Smirnov normality testing, data were evaluated using Student's t-test, Mann-Whitney, or one/two-way ANOVA (Tukey/Sidak/Holm-Sidak post-tests). **Results:** BN's size remained stable (130 nm) stored at 4 ºC but not at room temperature (P= 0,0438). ON droplet size was larger than BN at 4 ºC (P<0,0001) but remained small enough to reach the brain through the nose (248.2 nm). Both formulations maintained negative zeta potentials and had no significant difference in PDI. In the cell viability assay, negative control reduced cell viability (P=0,0008) when compared to positive control while NB and NO could not reduce cell viability. Octovespin showed sustained release from the nanoemulsion up to 30 days. The spray produced plume diameters of approximately 2 cm (at 3 cm) and 4 cm (at 6 cm), indicating suitability for olfactory bulb targeting. The delivered mass per actuation was 0.0801±0.0324 g (0.1153±0.0466 mL), confirming compatibility with nasal administration. **Conclusion:** The nanoemulsion nasal spray shows great potential for intranasal brain targeting AD treatment. However, long- term stability studies and further spray characterization remain necessary.

02.034 **Evaluation of the Anticonvulsant and Neuroprotective Potential of** *Scenedesmus ecornis* **and** *Limnospira platensis* **in a Chronic Pentylenetetrazol-Induced Kindling Model**. Bentes ILG[1,2], Pantoja EKM[1], Souto TL[1], Nascimento AA[1], Faustino SMM[1], Oliveira EDC[4], Do Nascimento JLM[3], Oliveira FR[1,2] [1]Unifap, School of Pharmacy, Brazil. [2]Unifap, PPG Pharmaceutical Sciences, Brazil. [3]UFPA, PPG Pharmacology and Biochemistry. [4]IEPA, Lab Taxonomy and Ecology of Cyanobacteria and Microalgae, Brazil.

Introduction: Microalgae are photosynthetic microorganisms characterized by rapid growth and ease of cultivation, standing out for the nutritional and therapeutic potential of their biomass. Among them, species such as *Scenedesmus ecornis* and *Limnospira platensis* exhibit antioxidant and neuroprotective properties. In the present study, these species were investigated for their possible anticonvulsant and neuroprotective effects in mice subjected to a pentylenetetrazol (PTZ)-induced kindling model. **Methods:** Female Swiss mice (N = 9 per group) were orally treated with the biomass of *ecornis* and *L. platensis* (100 mg/kg) and sodium valproate (VPA; 300 mg/kg) for 40 days, while the control group received PBS. After the treatment period, all animals received PTZ (35 mg/kg, i.p.) on alternate days and were monitored for 30 min. Behavioral parameters, including latency to myoclonic and tonic-clonic seizures and seizure duration, were evaluated. Nitrite levels and lipid peroxidation were measured in the cerebral cortex. The experimental protocol was approved by the Ethics Committee on Animal Use of UNIFAP under protocol number 02/2025. Data were expressed as mean ± standard error of the mean (SEM). **Results:** The PBS group showed the highest percentage of kindled animals (66.67%) compared with the sodium valproate (VPA), *S. ecornis*, and *L. platensis* groups (22.22%, 44.44%, and 44.44%, respectively), and exhibited the shortest latency to tonic-clonic seizures (706.3 ± 218.6 s) compared with VPA (1557 ± 166.1 s), *ecornis* (1108 ± 273.9 s), and *L. platensis* (1126 ± 266.9 s). Seizure duration was significantly reduced in the VPA, S. ecornis, and *L. platensis* groups (1.1 ± 0.8 s, 2.1 ± 0.8 s, and 1.9 ± 0.7 s, respectively) compared with the PBS group (5.7 ± 1.6 s). Treatment with the microalgae significantly reduced nitrite levels (*S. ecornis*: 2.69 ± 0.39 µM NO/mg protein; *L. platensis*: 2.20 ± 0.32 µM NO/mg protein) compared with PBS (5.807 ± 1.188 µM NO/mg protein), with no significant differences relative to the VPA (2.728 ± 0.2348 µM NO/mg protein) and Sham groups (2.807 ± 0.5506 µM NO/mg protein). Lipid peroxidation was significantly lower in the *L. platensis* group (1.62×10^{-7}; ± 6.62×10^{-8} nmol MDA equivalents/g) compared with PBS (6.55×10^{-7}; ± 1.36×10^{-7}; nmol MDA equivalents/g), whereas no significant differences were observed for VPA (2.85×10^{-7}; ± 1.06×10^{-7}; nmol MDA equivalents/g), *ecornis* (3.30×10^{-7}; ± 9.44×10^{-8} nmol MDA equivalents/g), or Sham (2.82×10^{-7}; ± 1.65×10^{-7}; nmol MDA equivalents/g). **Conclusion:** The biomass of *Scenedesmus ecornis* and *Limnospira platensis* exhibited anticonvulsant and neuroprotective effects in the chronic PTZ kindling model. These effects were associated with a lower proportion of kindled animals, increased seizure latency, reduced seizure duration, and attenuation of oxidative stress markers.

02.036 *Alpinia zerumbet* **Modulates Intestinal Dysbiosis and Cognitive Impairment Induced by Chronic Scopolamine Exposure**. Nascimento JM[1], Ferreira FS[1], Soares SCS[1], Mattos JA[1], Dias KM[1], Lopes CFO[1], Trefilio LM[1], Guimenes BD[1], Fontes-Dantas FL[1], Filgueiras CC[1], Ognibene DT[1], Costa CA[1], Resende AC[1] and Vieira AKG[2], Bem GF[1] [1]UERJ, Roberto Alcantara Gomes Institute of Biology, Research Line in Neuropharmacology and Medicinal Plants, Graduate Program in Clinical and Experimental Pathophysiology, Brazil. [2]UERJ, Professional PPG Biology Teaching, Brazil.

Introduction: Alzheimer's disease (AD) causes cognitive decline, neuroinflammation, and toxic protein buildup. The vagus nerve modulates the gut-brain axis and influences gut microbiota. Recent studies suggest polyphenols, such as those found in plants, may help address these gut-brain changes. Our group has focused on *Alpinia zerumbet* (K.Schum), a medicinal plant included in the National List of Medicinal Plants of Interest to the SUS (RENISUS). Preclinical studies with the hydroalcoholic extract of Alpiniazerumbet (ALE) suggest neuroprotective effects and possible gut-brain modulation in AD. **Objective:** We aimed to investigate changes in the brain-gut axis in C57BL/6 mice following scopolamine administration. **Methods:** Forty male C57BL/6 mice (13 weeks old) were used and distributed into groups: Control; Scopolamine (SCOP, 1 mg/kg/day intraperitoneally for 6 weeks); SCOP+ALE/Preventive (SCOP 1 mg/kg/day and ALE 50 mg/kg/day in drinking water for 6 weeks); and SCOP+ALE/Treatment (SCOP 1 mg/kg/day for 6 weeks and ALE 50 mg/kg/day in the last 3 weeks). In the last week, animals underwent the open field (OF) and object recognition (OR) tests (CEUA/044/2023). Half of the animals were anesthetized and perfused for histological analyses of the ileum and colon, which were stained with eosin, hematoxylin, and alcian blue, respectively. The other half was euthanized by decapitation, and the cecum was frozen for fecal microbiota analysis by real-time PCR. **Results:** In the OF, no significant differences appeared between groups. Values are mean ± SEM: Control (139.4 ± 9.29), SCOP (166.1 ± 20.32), SCOP + ALE/Preventive (158.1 ± 16.65), and SCOP + ALE/Treatment (159.8 ± 11.66). This shows that cognitive tests were not influenced by motor impairments. In the first OR session, using two identical objects, there was no statistical difference in exploration time between groups. In the second session with a new object, the SCOP group showed shorter new object exploration time (p < 0.05) than the control group. In the SCOP+ALE/Preventive and SCOP+ALE/Treatment groups, this exploration time was longer (p < 0.05) than in SCOP. In the colon, mucus production was increased in the SCOP group compared to the control group. Notably, treatment with ALE reversed this increase compared to the SCOP group. In turn, in the microbiota analysis, mRNA expression of the Proteobacteria phylum was higher in the SCOP group than in the control group. In the SCOP+ALE/Preventive group, the increase in expression of this phylum was prevented compared to the SCOP group. There was no significant difference between the groups in mRNA expression of the Actinobacteria and Firmicutes phyla or in the ileum structure measure. **Conclusion:** ALE prevented and reversed cognitive deficits and intestinal dysbiosis induced by scopolamine administration. These preliminary results suggest a potential benefit of ALE on gut-brain axis alterations in AD.

02.037 **Systemic Metoclopramide Modulates Cortical Spreading Depression Parameters in Rats**. Melo SM, Prieto SG, Guedes RA UFPE, Center of Health Sciences, Nutrition Dept, Brazil

Introduction: Metoclopramide (MCP) is clinically used in patients with migraine, particularly in cases refractory to conventional therapy. However, the mechanisms underlying its therapeutic effects are still not completely understood. Previous experimental studies demonstrated that the topical application of metoclopramide, raclopride, and quinpirole, agents that modulate dopamine D2 receptors, alters cortical spreading depression (CSD) parameters. These findings suggest a possible involvement of dopaminergic signaling in the modulation of CSD, an electrophysiological phenomenon associated with migraine pathophysiology. **Objectives:** To investigate whether systemic administration of metoclopramide modulates cortical spreading depression parameters in rats. **Methods:** Adult rats were subjected to baseline CSD recordings before intravenous administration of metoclopramide at two different doses (5 mg/kg and 20 mg/kg) or saline. CSD was elicited and recorded electrophysiologically, and the parameters analyzed included propagation speed, amplitude, and duration. Statistical analysis was performed using one-way ANOVA followed by appropriate post hoc comparisons, and a paired Student's t-test was used for baseline comparisons. Data were expressed as mean ± SEM. **Results:** Systemic administration of MCP significantly altered CSD electrophysiological parameters. The 20 mg/kg dose reduced CSD propagation speed compared with baseline and the other experimental groups ($F(2,21)=9.259$; $p=0.001$). Regarding CSD amplitude, both MCP-treated groups showed significant increases compared with baseline, with a more pronounced effect observed at 5 mg/kg ($F(2,21)=19.056$; $p<0.001$). In addition, CSD duration was significantly increased in both MCP groups compared with saline controls, particularly at 20 mg/kg ($F(2,21)=24.295$; $p<0.001$). These findings indicate dose-dependent modulation of CSD dynamics after systemic MCP administration. **Conclusion:** Systemic metoclopramide modulates cortical spreading depression parameters, reducing propagation speed while increasing amplitude and duration. These results support the hypothesis that dopaminergic D2 receptor-related mechanisms participate in the electrophysiological modulation of CSD and may contribute to the therapeutic effects of metoclopramide in migraine.

02.038 **Acute Naltrexone Effects on Short-Term Memory of Wistar Rats**. Silva-Filho JH, Kanazawa LKS, Lima TF, Pagnussat AL, Vital MABF UFPR, PPG Pharmacology Dept, Brazil

Introduction: Naltrexone is currently used to treat alcohol use disorder and opioid addiction. This drug is a non-selective opioid antagonist with higher affinity for mu receptors and lower affinity for kappa and delta opioid receptors. Recent studies have shown a growing interest in this medication due to its potential to improve cognition in animals. **Objective:** Investigate the acute effects of naltrexone on short-term memory through a dose-response curve. **Methods:** We evaluated the effects of acute naltrexone treatment in 3-month-old male Wistar rats. Three doses of naltrexone were used (2.5 mg/kg, 5 mg/kg, and 10 mg/kg, i.p.). Control group received 0.9% saline solution. The animals underwent behavioral tests (open field test, object recognition test, and object location test) to analyze cognition, locomotion, and behavior. One hour before testing, the animals were habituated to the apparatus for 5 minutes, and they received a naltrexone injection 30 minutes before the test. The tasks were performed with a 24-hour interval between them. All experimental procedures were approved by the Animal Experimentation Committee of Federal University of Paraná (CEUA, protocol no. 1682/2025). Every effort was made to minimize animal suffering and the number of animals used. The results were analyzed using one-way ANOVA. **Results:** Our results showed that acute naltrexone treatment did not change neither locomotion, nor short-term memory. **Conclusion:** Therefore, the present study demonstrated no significant effects of acute naltrexone on cognitive performance with the evaluated doses. Nevertheless, numerous factors regarding the therapeutic potential of this medication still warrant further investigation. **Financial support:** This study was supported by fellowships and grants from the National Council for Scientific and Technological Development (CNPq, Brazil) and the Coordination for the Improvement of Higher Education Personnel (CAPES, Brazil).

02.039 **Impact of Acute and Repeated inhalation of** *Lavandula dentata* **Essential Oil on the Anxiolytic and Antidepressant-Like Behavior of Mice: A Comparative Study with** *Lavandula angustifolia*. Marco MR, Flores VG, Blauth T, Silva GC, Barcellos ES, Prestes RNB, Mattos CB, Betti AH Feevale University, Institute of Health Sciences, Brazil

Introduction: Aromatherapy is a recognized integrative practice in the Brazilian Unified Health System using essential oil (EO). While *Lavandula angustifolia* essential oil (LA) is widely used for its anxiolytic and antidepressant-like effects, the pharmacological profile of *L*. *dentata* (LD), species cultivated in Brazil, remains under-researched. **Objective:** To compare the pharmacological effect of LA and LD after acute and repeated inhalation (28 days) exposure. **Methodology:** Adult male Balb/c mice (n=8/group), divided into control, LA and LD groups, were exposed to the inhalation of 10 drops for 15 minutes. Acute and repeated effects were evaluated through Elevated Plus-maze, Tail Suspension Test, Open Field and Rotarod. Data were analyzed by Two- way RM ANOVA. **Results:** Acute exposure significantly increased the time spent in the open arms for both EOs (LA: P = 0.0406; LD: P = 0.0091) and the number of entries (both P = 0.0019), suggesting an anxiolytic-like effect. However, after repeated exposure, there was a significant decrease in the number of entries into the open arms (LA P = 0.0002; LD P < 0.0001) associated with an increase in closed-arm entries (LA P = 0.0017; LD P = 0.0011) within the treatments themselves, showing a distinct response between acute and repeated dose exposure. The antidepressant-like effect, verified by a decrease in immobility time, was identified for LA after acute exposure (P = 0.0078), which was maintained after repeated exposure (P = 0.0005), differing from LD, whose effect was only identified after repeated exposure (P = 0.0003). Acute exposure also significantly decreased the number of crossings in animals treated with LA (P = 0.0030) and LD (P = 0.0024). Conversely, after repeated exposure, LD significantly increased crossings (P = 0.0358) and rearings (P = 0.0024) compared to the control and its own acute exposure. LD also impaired motor coordination, as evidenced by an increase in the number of falls (P = 0.0025) and a decrease in time spent on the apparatus (P = 0.0083), differing from LA. Taken together, these results suggest a psychostimulant profile with potential neurotoxic effects and stress after repeated doses of LA. **Conclusion:** Therefore, LD demonstrated a distinct pharmacological response compared to LA: despite presenting potential acute anxiolytic and antidepressant-like effects, repeated exposure to the essential oil resulted in a psychostimulant profile accompanied by motor impairment, suggesting potential neurotoxicity. These results caution against the continuous therapeutic use of LD without scientific evidence, considering that it shares the same pharmacological properties as LA. **Financial support:** CAPES and Feevale University. CEUA Feevale nº 02.25.149.

02.040 **Standardized Functional Radioligand Assays for Investigating NeuroVAL Peptide Activity at Dopaminergic Receptors**. Ferreira JW, Mortari MR, Campos GAA, Veras LG UnB, Institute of Biological Sciences, Dept Physiological Sciences, Lab Neuropharmacology, Brazil

Introduction: Binding assays are important drug-discovery tools because they quantitatively evaluate ligand interactions with specific molecular targets. They are especially useful for investigating neurotransmitter systems and supporting new therapeutic strategies. Alterations in dopaminergic signaling have been implicated in several neurological and neurodevelopmental conditions. Autism spectrum disorder (ASD) is one example, as dopaminergic dysfunction has been associated with changes in motivation, reward processing, behavioral flexibility, and responses to social stimuli. However, current therapeutic approaches for ASD are mainly directed toward managing associated symptoms. NeuroVAL is a synthetic peptide derived from mastoparan Agelaia-MP, originally isolated from the venom of *Parachartergus fraternus* Given the neuroactive potential of venom-derived peptides and their ability to interact with membrane-associated molecular systems, we hypothesized that NeuroVAL could interact with dopamine-binding sites and modulate dopaminergic ligand binding. This study therefore aimed to standardize functional radioligand-binding assays for dopaminergic sites and evaluate NeuroVAL's modulatory potential. **Methods:** Synaptosomes were prepared from the cerebral cortices of male and female Swiss mice, according to protocols approved by the Animal Ethics Committee of the University of Brasília (protocol no. 23106.039800/2024-13). Tissue extraction, membrane preparation, protein quantification, incubation time, temperature, and buffer composition were optimized to improve reproducibility. Homologous and heterologous competition assays were performed with tritiated dopamine (^{3}H-dopamine; PerkinElmer, USA). Unlabeled dopamine was the competitor in homologous assays, whereas NeuroVAL was tested in heterologous assays to determine whether it modified ^{3}H-dopamine binding to dopaminergic sites. Nonspecific binding was measured with excess unlabeled dopamine, and total binding without a competing ligand. After incubation, bound and free radioligand were separated by centrifugation, and radioactivity was quantified by liquid scintillation counting. Homologous competition data were analyzed by nonlinear regression; NeuroVAL-treated groups were compared with control by one-way ANOVA followed by Tukey's multiple-comparisons test. Analyses used GraphPad Prism® 8.0, with $p < 0.05$ considered significant. **Results:** NeuroVAL increased radioligand binding to dopaminergic receptors, indicating a possible modulatory action. Instead of the reduction expected for a direct competitive ligand, NeuroVAL markedly increased ^{3}H-dopamine binding, suggesting positive modulation of dopaminergic binding. Standardization of membrane preparation, protein quantification, and incubation conditions also improved protocol reproducibility. **Conclusion:** The results indicate that NeuroVAL is a promising peptide for further pharmacological investigation and may contribute to future therapeutic strategies for neurological and neurodevelopmental conditions associated with dopaminergic dysfunction, like ASD.

02.041 *In vivo* and *in vitro* Effects of Na+/K+-ATPase Activating Monoclonal Antibodies. Bariviera JL[1,2], Ribeiro LR[1,2], Da Rosa GK[1,2], Santos VT[2], Carneiro MA[2], Angelo, IJ[2], Bassoaldo, R[2], Oliveira MS[1,2] [1]UFSM, PPG Pharmacology, Brazil; [2]UFSM, Lab Experimental Neurology

Introduction: The Na+/K+-ATPase (NKA) is a key enzyme responsible for maintaining neuronal electrochemical gradients and excitability. Dysfunction of NKA has been implicated in several neurological disorders, such as epilepsy. Pharmacological modulation of NKA represents a promising therapeutic strategy. The human monoclonal antibody DRhmAb was designed to selectively activate NKA, but until now its effects had not yet been validated in animal models. Intranasal administration offers a non-invasive route for delivering macromolecules, bypassing the blood–brain barrier. Objectives: To evaluate the effects of DRhmAb on NKA activity *in vivo* and *in vitro*, and to assess its distribution in the brain following intranasal administration. Methods: Male Wistar rats (±28 days) were used, under ethical approval. Antibody binding to NKA was assessed by dot blot with hippocampus samples of untreated animals and NKA activity was measured with an enzymatic assay measured with cortex samples of untreated animals pre-incubated with DRhmAb (0.25, 1.0, 2.5, 10, 25 µmol). Additionally, after intranasal administration of DRhmAb (1, 10, and 100 µg/µL) or IgG control (100 µg/µL), animals underwent behavioral tests (open field, marble burying, elevated plus maze, and neuroscore) and were euthanized at 1, 3, and 6 hours. *Post mortem* analyses included ELISA and RT-PCR. Results: Dot blot demonstrated antibody binding to NKA, and enzymatic assays revealed concentration-depending increase in activity *in vitro*. ELISA confirmed DRhmAb presence in the hippocampus; however, no behavioral changes or *in vivo* modulation of NKA activity were observed. Conclusion: DRhmAb activated NKA *in vitro*, reached the central nervous system, but did not produce detectable functional effects *in vivo*. These findings highlight the therapeutic potential of NKA modulation, while indicating the need for further studies to clarify DRhmAb efficacy in animal models.

02.042 Neuroprotective and Antioxidant Activity of Sweet Orange Essential Oil in *Caenorhabditis elegans*. Lisboa JS[1], Sá MEB[2], De Jesus LFS[2], Barreto MS[1], De Souza JB, Silva AS[1], Araújo ZS[3], Pacheco PGS[1], Silva VGO[2], Guimarães AG[2] [1]UFS-São Cristóvão, Graduate Program in Pharmaceutical Sciences, [2]UFS-São Cristóvão, Dept Pharmacy, [3]UFS-Lagarto, Graduate Program in Health Sciences

Introduction: Alzheimer's disease is a progressive neurodegenerative disorder associated with various factors, including oxidative stress and the accumulation of β-amyloid protein, resulting in cognitive and neuronal impairment. In this context, natural compounds with antioxidant and neuroprotective properties, such as terpenes, have attracted therapeutic interest. Given this, *Caenorhabditis elegans* stands out as a suitable experimental model, as it possesses conserved molecular pathways, a well- characterized nervous system, and mutant and transgenic strains associated with neurodegenerative diseases. Objective: To evaluate the neuroprotective and antioxidant activity of sweet orange essential oil in *C. elegans*. Methodology: The worms, cultured in nematode growth medium (NGM) with *E. coli* OP50, were treated for 44 hours prior to conducting survival assays and body size analysis to assess the compound's toxicity. Based on these results, concentrations of 50 and 100 µg/mL were selected for subsequent biological assays. Antioxidant activity was assessed by quantifying reactive oxygen species (ROS). Additionally, the neuroprotective effect of the essential oil on β-amyloid-induced paralysis in *C. elegans* and its ability to modulate cholinergic receptors were investigated. The experiments were performed in triplicate, and for statistical analysis, the Kruskal-Wallis test followed by Dunn's post-hoc test was applied, along with the log-rank test for survival. Results: Treatments with the essential oil resulted in zero mortality at all concentrations; however, they affected development at a concentration of 200 µg/mL. In the antioxidant assay, a reduction in ROS was observed at a concentration of 100 µg/mL ($p<0.005$). Furthermore, regarding neuroprotective activity, a delay in paralysis was observed at concentrations of 50 and 100 µg/mL, and an increase in the branching of cholinergic receptors was observed at concentrations of 50 µg/mL ($p<0.05$) and 100 µg/mL ($p<0.005$). Conclusion: These findings suggest that sweet orange essential oil possesses antioxidant and neuroprotective potential and may help modulate mechanisms involved in the progression of Alzheimer's disease. Funding: This study was supported by the Coordination for the Improvement of Higher Education Personnel (CAPES) and Maratá.

02.043 **Behavioral Profile of Male Offspring from Sedentary Dams Exposed to Prenatal Valproic Acid**. Rodrigues BA, Santiago Prestes TC, Kawamoto EM ICB-USP, Pharmacology Dept. Lab Molecular and Functional Neurobiology.

Introduction: Valproic acid (VPA) is a drug used to treat epilepsy. Prenatal VPA exposure is linked to an increased risk of congenital malformations and neurodevelopmental disorders characterized by cognitive and linguistic impairments, developmental delays, altered behaviors, and an elevated prevalence of autism spectrum disorder (ASD). Maternal physical exercise has been considered a potential neuroprotective strategy; however, despite its well-known benefits, the validation and characterization of baseline behavioral impairments in the offspring are essential for the evaluation of therapeutic interventions. **Objectives:** Therefore, the aim of this study was to investigate the isolated effects of gestational exposure to VPA on the behavioral profile of offspring from sedentary dams. **Methods:** Pregnant female C57BL/6 mice were treated with VPA (300 mg/kg) or saline (vehicle) on embryonic days 10 and 12. During pregnancy, all dams were housed individually in cages containing a locked running wheel, and their body weight and food intake were monitored weekly. At one month old, male offspring (n=6 saline; n=8 VPA) were subjected to behavioral tests: the elevated plus maze (EPM), social interaction (SI), and rotarod (RR) to evaluate anxiety-like behavior, social interaction and motor coordination. Statistical analysis was performed using unpaired Student's T-Test, and two-way ANOVA in the GraphPad Prism. This study was approved by the Ethics Committee on the Use of Animals (nº 3511180925). **Results:** During pregnancy, no differences in body weight or food intake were observed between the groups. In the EPM test, male VPA offspring showed an increase in the time spent in the closed arms ($p=0.0005$; $t=4.735$, $df=12$) and a reduction in the time spent in the open arms ($p=0.0002$; $t=5.165$, $df=12$). No differences were observed in the number of entries into either the closed or open arms. In the SI test, the VPA group showed reduced interaction with an unfamiliar animal ($p=0.0034$; $t=3.631$, $df=12$) and a significant increase in interaction with an object ($p=0.0118$; $t=2.966$, $df=12$) however, no significant differences were found in the time spent in the unfamiliar animal compartment. Finally, RR analysis revealed no differences in average latency to fall between the groups. **Conclusion:** Our findings demonstrate anxiety-like phenotypes and impaired social interaction in male VPA offspring. Financial support by São Paulo Research Foundation (FAPESP).

02.044 **Cannabidiol Nanoemulsion Enhances Permeability Across a Biomimetic Blood-Brain Barrier Model**. Dias KM[1], Dias CMN[1], Montes GC[1], Maluf D 2, Ferreira FS[1], Mattos JA[1], Nascimento JMD-F[1], Soares LN[1], Caetano AC[1], Soares SCS[1], Ognibene DT[1], Costa CA[1], Resende AC[1], Matsuura C[1], Bem GF[1] [1]UERJ, Research Line in Neuropharmacology and Medicinal Plants (NFPM), PPG in Clinical and Experimental Pathophysiology (Fisclinex), Brazil, [2]UFPR, Dept Pharmacy, Graduate Program in Pharmaceutical Sciences, Brazil

Introduction: *Cannabis sativa*, one of the earliest cultivated plants, contains over 400 compounds and more than 60 phytocannabinoids. Its main non- psychoactive component, cannabidiol (CBD), shows significant pharmacological properties, such as antipsychotic effects. Oral administration is common but leads to low bioavailability due to gastric and hepatic processing. CBD inhibits metabolic enzymes (CYP3A4, CYP2D6), raising drug interaction and side effect risks, while some drugs also alter CBD levels. Metabolites may increase side effects like panic and paranoia. Thus, while promising, CBD's oral route faces challenges with central bioavailability and interactions. Nanoformulations could improve central bioavailability and reduce adverse effects. **Objective:** To compare central bioavailability between a CBD nanoformulation and a conventional extract, enabling further investigation in a ketamine-induced schizophrenia model. **Methods:** To obtain CBD nanoparticles, the solvent emulsification method was used, and the final solution was subjected to ultrasonication. The permeability assay was performed using the Parallel Artificial Membrane Permeability Assay for the Blood–Brain Barrier (PAMPA-BBB model), consisting of a lipid artificial membrane sandwiched between a donor and an acceptor compartment. The non-encapsulated extract 47,2%, the extract-loaded nanoemulsion, and low- and high-permeability controls were tested. To confirm the ketamine (KET) concentration to be used for inducing the schizophrenia model, 12 mice were used, divided into: Control (water by gavage for 18 days and intraperitoneal saline from day 8 to day 18) and KET (water by gavage for 18 days and ketamine 20 mg/kg/day intraperitoneal from day 8 to day 18). During the last two days, animals underwent the open field test (OF) and the prepulse inhibition (PPI) test (CEUA 010/2025). **Results:** The CBD nanoemulsion significantly increased permeability, reaching ($p<0.05$) an effective permeability coefficient (Pe) of 1.40×10^{-6} cm/s, approximately 3.5-fold higher than that observed for the free extract (Pe =0.40×10^{-6} cm/s). Furthermore, the nanoemulsion displayed a permeability 1.75-fold higher than that of the low-permeability control (0.80×10^{-6} cm/s). Furthermore, in the CA test, the KET group showed increased hyperlocomotion ($p<0.05$) compared to the control group during the 10-15 and 15-20 minute periods. Finally, there was a reduction in prepulse inhibition ($p<0.05$) by 75 and 80 decibels in the Ket group compared to the control group. **Conclusion:** The CBD nanoemulsion exhibited superior BBB permeability compared with the free extract, indicating its potential to enhance central CBD delivery. Moreover, ketamine administration successfully induced schizophrenia-like behavioral deficits. These findings provide a strong rationale for evaluating whether the increased brain permeability achieved by the nanoformulation translates into enhanced antipsychotic efficacy in experimental schizophrenia.

02.045 **Biochanin A Attenuates Nigrostriatal Degeneration and Motor/Non-Motor Impairments in Progressive Reserpine-Induced Parkinsonism**. Nascimento ACS[1], Souza JLS[2], Mendonça MS[2], Tavares MM[2], França RJO[2], Brito SC[1], Santos GJ[1], Dantas IC[2], Oliveira MCS[2], Santos JR[2], Camargo EA[1]. [1]UFS-São Cristóvão, Dept Physiology, Lab Pharmacology of Inflammatory Process, SE, Brazil; [2]UFS-Itabaiana Behavioral and Evolutionary Neurobiology Lab, Dept Biosciences, SE, Brazil.

Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by degeneration of dopaminergic neurons and accumulation of α-synuclein (α-syn) aggregates. Although levodopa remains the gold standard treatment for PD, its long-term use is associated with adverse effects such as dyskinesias, hallucinations, and wearing-off phenomena. Therefore, the search for novel neuroprotective compounds capable of attenuating disease progression remains essential. Biochanin A (BCA), a plant-derived isoflavone, has demonstrated antioxidant and anti-inflammatory properties and may represent a promising therapeutic strategy for PD. **Objective:** To evaluate the effects of BCA on behavioral and neuropathological alterations in a progressive reserpine-induced model of Parkinsonism. **Methods:** Male Wistar rats received 15 injections of reserpine (RES, 0.1 mg/kg, s.c.) or vehicle every 48 h for 30 days. Simultaneously, animals were treated daily with BCA (12.5, 25, or 50 mg/kg, p.o.) or vehicle. Motor impairments were evaluated using the catalepsy test, open field test (OFT), and tongue protrusion (TP). Anhedonia-like behavior was assessed by the sucrose preference test (SPT). At the end of the protocol, brains were processed for tyrosine hydroxylase (TH) immunohistochemistry in the substantia nigra pars compacta (SNpc), ventral tegmental area (VTA), and striatum, as well as α-syn immunoreactivity in the substantia nigra pars reticulata (SNr) and striatum. **Results:** Repeated RES administration progressively increased the duration of catalepsy from day 12 onward ($p<0.05$). Daily treatment with BCA attenuated this impairment, particularly at 50 mg/kg from day 14 onward ($p=0.01$) and reduced the area under the curve for catalepsy ($p=0.0206$). In the OFT, RES reduced locomotor activity, while BCA (50 mg/kg) increased distance traveled ($p=0.0209$) and reduced immobility time ($p=0.0064$). RES also increased TP frequency, whereas BCA significantly reduced this dyskinetic behavior ($p=0.0009$, $p=0.042$, and $p<0.0001$). In the SPT, RES induced anhedonia-like behavior, which was reversed by BCA at 12.5, 25, and 50 mg/kg ($p=0.0072$, $p=0.0007$, and $p=0.0308$, respectively). Immunohistochemical analyses revealed that RES reduced TH immunoreactivity in the striatum ($p<0.0001$), SNpc ($p=0.0285$), and VTA ($p=0.0110$), while increasing α-syn accumulation in the striatum and SNr ($p=0.0469$ and $p<0.0001$). Co-administration of BCA prevented TH loss in the striatum ($p=0.0008$), SNpc ($p=0.0152$), and VTA ($p=0.0078$), and reduced α-syn immunoreactivity in both analyzed regions (p values ranging from 0.0271 to <0.0001). **Conclusion:** BCA attenuated motor and non-motor impairments, preserved dopaminergic markers, and reduced α-syn pathology in progressive Parkinsonism, highlighting its potential as a neuroprotective strategy for PD.

02.046 **Therapeutic Potential of NeuroVal, a Bioinspired Wasp Peptide, in an Animal Model of Autism Spectrum Disorder**. Veras LG, Ferreira JW, Campos GAA, Mortari MR [1]UnB, Biological Sciences Institute, Neuropharmacology Lab, Brazil, [2]UnB, Faculty of Health Sciences, PPG Health Sciences, Brazil.

Introduction: Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by persistent deficits in communication and social interaction, associated with restricted and repetitive behaviors, presenting high clinical heterogeneity and frequent psychiatric and neurological comorbidities. Despite advances in diagnosis and the understanding of the underlying neurobiological mechanisms, currently available pharmacological treatments remain limited to symptomatic management. Given the limitations of conventional treatments, new strategies have been explored, including the use of bioinspired biomolecules. Molecules inspired by wasp venoms have been used since 1979, and their rational design enables the development of compounds with targeted biological activities. The NeuroVal peptide, inspired by a mastoparan, demonstrated antinociceptive activity through the activation of G protein-coupled metabotropic receptors following intracerebroventricular (i.c.v.) administration. Considering its activity and the fact that neurotransmission alterations involving the opioid system are associated with the pathophysiology of ASD, this peptide was selected for evaluation as a treatment for this disorder due to its potential to modulate social reward. This study aims to assess the safety profile of NeuroVal in mice and its efficacy in an animal model of ASD. The safety methodology consisted of single-exposure treatment at two doses, followed by open field and Rotarod tests. The efficacy methodology evaluated three different doses administered over 15 days, followed by open field and sociability tests. **Results:** Intranasal treatment with NeuroVal, tested at three different doses, was able to reverse sociability deficits in a VPA-induced animal model of ASD without impairing locomotion or inducing significant systemic toxicity. **Conclusion:** Furthermore, it demonstrated a favorable safety profile in a single-exposure model, as recommended by the ANVISA Guide for Conducting Nonclinical Toxicity Studies. Taken together, these results reinforce the potential of NeuroVal as an innovative therapeutic candidate for the management of ASD-associated signs, highlighting the relevance of bioinspired peptides in the development of new pharmacological strategies that are safer and more specifically targeted to the pathophysiology of the disorder. All experimental procedures were previously approved by the institutional Animal Ethics Committee for the Use of Animals (CEUA; protocol no. 23106.039800/2024-13 and 23106.147095/2018-89). This study was supported by FAPDF (Biolearning), CNPq, and CAPES.

02.047 *Alpinia zerumbet* **Reverses and Prevents Cognitive Deficits, Neuroinflammation, and Neurodegeneration induced by Scopolamine Administration**. Ferreira FS[1], Soares LN[1], Mattos JA[1], Nascimento JM[1], Dias KM[1], Lopes CFO[1], Trefilio LM[1], Fontes-Dantas FL[1], Fernandes GG[2], Filgueiras CC[1], Cavalheira MA[1], Ognibene DT[1], Costa CA[1], Resende AC[1] and Bem GF[1] [1]UERJ, Research Line in Neuropharmacology and Medicinal Plants (NFPM), PPG in Clinical and Experimental Pathophysiology (Fisclinex), Brazil, [2]UFJF, Dept Biophysics and Physiology, Brazil

Introduction: Alzheimer's disease (AD) is the leading cause of neurodegenerative dementia worldwide. It causes progressive impairment of memory, learning, and other cognitive functions. No effective treatment is available. Natural compounds attract growing interest for their antioxidant and neuroprotective potential. Our group studied the hydroalcoholic extract of fresh *Alpinia zerumbet* (ALE) leaves. We demonstrated its neuroprotective effect against PCB 126-induced neurotoxicity, an environmental contaminant, suggesting its benefit in AD. **Objective:** We aimed to investigate the preventive and therapeutic effects of ALE on cognitive deficits, neuroinflammation, and neurodegeneration induced by scopolamine administration. **Methods:** Forty male C57BL/6 mice (13 weeks old) were used and distributed into groups: Control; Scopolamine (SCOP, 1 mg/kg/day intraperitoneally for 6 weeks); SCOP+ALE/Preventive (SCOP 1 mg/kg/day and ALE 50 mg/kg/day in drinking water for 6 weeks); and SCOP+ALE/Treatment (SCOP 1 mg/kg/day for 6 weeks and ALE 50 mg/kg/day in the last 3 weeks). In the last week, animals underwent the open field (OF), object recognition (OR), and Y-maze tests. Animals were anesthetized and perfused for immunofluorescence and cresyl violet staining (CEUA/044/2023). **Results:** In the OF, no significant differences appeared between groups. Values are mean ± SEM: Control (139.4 ± 9.29), SCOP (166.1 ± 20.32), SCOP + ALE/Preventive (158.1 ± 16.65), and SCOP + ALE/Treatment (159.8 ± 11.66). This shows that cognitive tests were not influenced by motor impairments. In the first OR session, using two identical objects, there was no statistical difference in exploration time between groups. In the second session with a new object, the SCOP group showed a lower object discrimination index ($p < 0.05$) than the control group. In the SCOP+ALE/Preventive and SCOP+ALE/Treatment groups, this index increased ($p < 0.05$) compared to SCOP. In the Y-maze test, the SCOP group showed reduced ($p < 0.05$) spontaneous alternations compared to the control. Preventive and therapeutic ALE increased ($p < 0.05$) correct alternations. In hippocampal CA1, microgliosis increased ($p < 0.05$) in SCOP versus control. ALE prevented and reversed this change ($p < 0.05$). There was no significant difference in other hippocampal regions. For astrogliosis, there was an increase ($p < 0.05$) in the dentate gyrus, CA1, and CA3 in SCOP compared to control. ALE prevented and reversed this increase ($p < 0.05$) in all regions except the gyrus, where treatment did not differ from SCOP. In the CA3 region, preventive ALE reduced astrogliosis more than treatment alone ($p < 0.05$). Structural disorganization and neuronal degeneration in the hippocampus and prefrontal cortex of SCOP animals were prevented and reversed ($p < 0.05$) by ALE. **Conclusion:** ALE prevented and reversed scopolamine-induced cognitive deficits, demonstrating neuroprotective effects by reducing neuroinflammation and neurodegeneration.

02.048 **Can Cannabidiol Alter Feeding Behavior? A Study of Binge Eating Behavior in C57BL Mice and Cross-Sensitization with Nicotine**. Manduca CA, Marçal AP, Costa RB, Araújo SS, Silva LRO, Moreira FA, Aguiar DC ICB-UFMG, Pharmacology Dept, Lab Neuropsychopharmacology, PPG in Physiology and Pharmacology, Brazil

Introduction: Binge Eating Disorder (BED) is defined by recurrent episodes of intense food consumption in a period of approximately two hours, compared to what most people would eat in a similar timely manner, accompanied by feelings of lack of control and guilt. Several brain systems are involved in BED, often overlapping with psychiatric disorders such as Substance Use Disorder (SUD). SUD is defined as the compulsive use of substances of abuse despite the negative consequences associated with it. Individuals with BED have a lifelong history of substance abuse, with tobacco smoking being highly prevalent. Cannabidiol (CBD), a non-psychoactive component of *Cannabis sativa*, has emerged as a promising alternative for reducing compulsive and anxiety-like behaviors induced by chronic consumption of a high-refined carbohydrate diet in animals, as well as inhibiting hyperphagia induced pharmacologically by type 1 cannabinoid receptor (CB1) agonists. Objectives We investigated the hypothesis that binge eating behavior (BEB) influences the reinforcing effects of nicotine and whether cannabidiol (CBD), which is known to reduce drug- seeking behavior, could decrease the food consumption of binge-eating mice. Methods Male and female C57BL/6J mice underwent intermittent binge-eating sessions with exposure to a control or high-carbohydrate (HC) diet on alternate days over four weeks. During the final week of the protocol, CBD was administered intraperitoneally at 10, 30, or 60 mg/kg. The animals were subjected to the Conditioned Place Preference (CPP) test for nicotine (M=0,5 mg/kg, F=0,25 mg/kg; subcutaneous) to evaluate the drug's reinforcing effects. **Results:** Intermittent HC diet exposure promoted binge eating in both sexes. However, CBD did not alter the feeding behavior. No statistical differences were observed between the control and nicotine groups in the CPP tests. **Conclusion:** Intermittent exposure to the HC diet promoted BEB in both sexes of C57BL/6J mice, whereas treatment with CBD did not attenuate the aforementioned behavior at any of the tested doses. Owing to the statistical variability in nicotine preference tests, it is unclear whether binge eating affects the rewarding effects of drugs.

02.049 **Synergistic Effects of 3-O-Methylquercetin and Polyphenols on Longevity, Healthspan, and Neuroprotection Via FOXO/Nrf2 Pathways in** *Caenorhabditis elegans*. Garofalo CB, Andrade EM, Souza VL, Farias MS, Santos PA, Pereira P. UFRGS, Institute of Basic Health Sciences, Dept Pharmacology, Lab Neuropharmacology and Clinical Toxicology, PPG in Pharmacology and Therapeutics. Brazil

Introduction: Aging is characterized by progressive cellular dysfunction, oxidative stress, and increased susceptibility to neurodegenerative diseases. Polyphenols have emerged as promising geroprotective compounds due to their antioxidant, anti-inflammatory, and cytoprotective properties. Among them, 3-O-methylquercetin (3OMQ) has demonstrated potential biological activity; however, its effects on lifespan, healthspan, and neuroprotection remain incompletely characterized. **Objectives:** To evaluate the effects of 3OMQ and a polyphenolic formulation containing quercetin, luteolin, and 3OMQ on lifespan, healthspan, oxidative stress, and neuroprotection in *Caenorhabditis elegans*. **Methods:** Wild-type and mutant *C. elegans* strains, including daf-2, daf-16, and skn-1 models, were exposed to quercetin, luteolin, 3OMQ, or a combined polyphenolic formulation (FORM). Lifespan and glucose-induced aging assays were performed under standard and hyperglycemic conditions. Worm health was assessed through analyses of motility, lipofuscin accumulation, and red autofluorescence. DAF-16 nuclear translocation, SKN-1 expression, and reactive oxygen species (ROS) production were quantified using fluorescence-based assays. Neuroprotective effects were evaluated through pentylenetetrazole (PTZ)-induced paralysis, methylmercury (MeHg)-induced cognitive impairment, manganese-induced cholinesterase hyperactivity, and neurodegeneration assays. **Results:** 3OMQ and FORM significantly increased lifespan and stress resistance in wild-type worms, extending survival by approximately 20–24%. These effects were maintained in daf-2 mutants but abolished in daf-16 mutants, suggesting dependence on DAF-16/FOXO signaling. Both treatments promoted DAF-16 nuclear translocation and significantly enhanced SKN-1 expression, accompanied by reduced ROS accumulation under oxidative stress conditions. Furthermore, 3OMQ and FORM decreased lipofuscin aggregation and red autofluorescence, indicating attenuation of senescence-associated damage. Behavioral assays demonstrated improved motility and resistance to PTZ-induced paralysis. Neuroprotective analyses revealed attenuation of MeHg-induced cognitive impairment, preservation of nose-touch responses, reduction of manganese-induced cholinesterase hyperactivity, and decreased neurodegeneration scores. **Conclusion:** 3OMQ and the polyphenolic formulation exhibited significant geroprotective and neuroprotective effects in *C. elegans*, predominantly mediated through the DAF-16/FOXO and SKN-1/Nrf2 signaling pathways. The reduction of oxidative stress, improvement of healthspan biomarkers, and preservation of neuronal function support the translational potential of these polyphenols as candidate compounds for healthy aging and neuroprotection strategies.

02.050 **Modulation of Neuroinflammation in BV2 Cells Exposed to *Pseudomonas aeruginosa* and Treated with Omega 3 (DHA)**. Santos FS[1,2,3], Ferreira AMS[2], Reis GLSG[2], Costa MF[2], Silva AR[1,2,3], Castro-Faria-Neto HC[2], Bozza PT[2], Gonçalves-de-Albuquerque CF[1,2,3] [1]Unirio, Immunopharmacology Lab, Dept Physiological Sciences, Rio de Janeiro, Brazil; [2]IOC-Fiocruz, Immunopharmacology Lab, Rio de Janeiro, Brazil; [3]UFF, PPG in Neuroscience), Niterói, Brazil

Introduction: *Pseudomonas aeruginosa* is the main opportunistic pathogen isolated from patients with nosocomial infection. Diseases associated with this bacterium have high mortality rates, mainly in a neuroinflammatory context. Microglia have been highlighted as an important focus of study, revealing that their excessive inflammatory activation is associated with the progression of several neurological diseases, including neuroinfection; therefore, the correct regulation of the microglia response may be an important element for inflammatory regulation. The production of anti- inflammatory and pro-resolving mediators from treatment or supplementation with DHA has been shown to reduce factors related to neuroinflammation, being an important element in the homeostasis of the system. **Objectives:** To observe the anti-inflammatory potential of DHA in BV2 cells during *Pseudomonas aeruginosa* infection. **Methods:** BV2 cell cultures were stimulated with 200 µM DHA one hour before inoculation with bacteria (MOI 1). Cells were incubated with this stimulus for 24 hours for analysis of IL-6 and TNF-α, cell viability, nitrite, morphological analyses by immunocytochemistry using Iba1, β-tubulin, and quantification of NRF2. Western blot analysis of SOD1 and NRF2 was also performed. **Results:** Incubation of BV2 cells with *Pseudomonas aeruginosa* MOI 1 for 24 hours stimulated the expression of the cytokines IL-6 and TNF-α, along with differences in cell morphology, without alterations in cell viability. In cells treated with 200 µM DHA, a reduction in IL-6, TNF-α, and nitrite levels was observed, along with improvements in morphology and cell elongation. Increases in SOD1 and NRF2 concentrations were also observed by Western blot. **Conclusion:** Omega-3 exhibits anti-inflammatory properties in this neuroinfection model; the next step is to analyze additional oxidative stress parameters.

02.051 **Early Pharmacological Intervention with NAC or BBG Produces Persistent Behavioral Improvements with Sex-Dependent Effects in MAM Rats**. Toscano LF[1], Vargas L[1], Ribeiro DE[2], Ulrich H[2], Salum C[1] [1]UFABC, PPG in Neuroscience and Cognition, Brazil; [2]USP, Dept Biochemistry, Institute of Chemistry, Brazil

Introduction: The hypothesis of impaired neurodevelopment in schizophrenia has led to the development of animal models based on perinatal interventions. Among them, the methylazoxymethanol acetate (MAM) model consists of injecting MAM on gestational day 17 in Wistar rats, producing offspring that exhibit behavioral and neurochemical impairments in adulthood, including hyperlocomotion, increased sensitivity to psychostimulants, reduced social interaction (SI), and deficits in prepulse inhibition (PPI). Schizophrenia-like symptoms may also be influenced by the estrous cycle, highlighting the importance of sex as a biological variable in preclinical studies. Recent evidence points to oxidative stress and inflammation as important mechanisms in schizophrenia pathophysiology. Our previous findings showed that treatment in adulthood with the antioxidant glutathione precursor N-acetyl-L-cysteine (NAC) reversed behavioral deficits in the MAM model. Purinergic receptors, particularly P2X7R, also play a key role in neuroinflammation, suggesting that antagonists such as Brilliant Blue G (BBG) may have therapeutic potential. This study evaluated whether pubertal treatment with NAC or BBG (PN45–69) produces behavioral effects in late adolescence/young adulthood (PN60) that persist into adulthood (PN90) in the MAM model. **Methods:** All procedures were approved by CEUA nº 3737171024. Wistar rats were treated with MAM (25 mg/kg, ip) or saline on gestational day 17. After weaning, offspring were separated by sex into six groups (Sal/Sal, MAM/Sal, Sal/NAC, MAM/NAC, Sal/BBG, MAM/BBG; n = 9–12). At PN45, animals received NAC (250 mg/kg, ip), BBG (50 mg/kg), or saline for 15 days. Twenty-four hours after the last treatment, rats underwent locomotor, SI, and PPI tests at PN60. The same tests were repeated at PN90. Data were analyzed using two-way ANOVA followed by Tukey's post hoc test ($p < 0.05$). **Results:** In males, PN60 SI evaluation showed that NAC and BBG treatment reversed the increase in self-grooming observed in MAM/Sal animals ($p = 0.0346$ and $p = 0.0181$, respectively). At PN90, MAM/Sal males showed reduced proximity duration compared to Sal/Sal rats ($p = 0.0052$). BBG treatment increased active interaction and reduced mean distance between subjects compared to MAM/Sal rats ($p = 0.0364$ and $p = 0.0135$, respectively). In females, no significant MAM effect was observed in SI at PN60, although BBG increased proximity duration ($p = 0.035$) and NAC increased mean proximity ($p = 0.010$). At PN90, MAM/Sal females showed reduced active interaction compared to Sal/Sal rats ($p = 0.003$), an effect reversed by BBG treatment ($p < 0.001$). A marginal MAM effect on self-grooming was also observed ($p = 0.071$). **Conclusion:** These findings demonstrate that the MAM model induces social interaction deficits that are attenuated or reversed by pubertal treatment with NAC or BBG, with effects persisting into adulthood. The treatments also produced sex- dependent effects, reinforcing the importance of investigating the mechanisms underlying these differences. Funding: UFABC, CAPES, FAPESP

02.052 **Immunomodulatory Effect of Laminarin in an Animal Model of Corticosterone-Induced Depression**. Nascimento, EF[1]; Batista, PVC[1]; Cunha, CS[1]; Lacerda, LRA[1]; Moura, VC[1]; Sousa, CNS[1]; Honório-Júnior, JER[2]; Chaves-Filho, AJM[3]; Oliveira, TQ[1]; Vasconcelos, SMM[1] [1]UFC, Neuropsychopharmacology Lab, Brazil, [2]Unichristus, Center for Translational Neuroscience, Brazil, [3]HCOR, Brazil.

Introduction: Depression is one of the most prevalent and disabling psychiatric disorders in the world. Biologically, the disorder is associated with neuroendocrine and inflammatory dysfunctions that impair serotonergic neurotransmission in the pathogenesis of depression. In this context, there is a growing interest for therapeutic agents with immunomodulatory action in psychiatric disorders. Laminarin (LAM) is a beta-glucan that modulates the inflammatory response through interaction with the Dectin-1 receptor, which is expressed in immune cells. However, its specific mechanisms of action remain poorly understood in depressive disorder. **Objective:** To elucidate the behavioral and immunomodulatory effects of laminarin in the corticosterone- induced depression (CORT) animal model. **Methodology:** Female BALB/c mice were subjected to a protocol with administration of CORT (20 mg/kg), TWEEN 0.3%, or LAM (20 mg/kg) alone or in combination for 21 days under ethics committee approval number 8339161123. On days 21 and 22, the animals underwent behavioral tests in the open field, elevated plus maze, and forced swim. Immediately after the tests, the animals were euthanized, and samples of hippocampus (HC), prefrontal cortex (PFC), and striatum (SC) were collected for quantification of the pro-inflammatory cytokine IL-1β. **Results:** The forced swim test demonstrated the induction of depressive-like behavior (P<0,0001), which was reversed by LAM (P<0,0001). In the elevated plus maze test, LAM increased the number of entries and time spent in the open arms (P = 0,0437), as well as promoting a decrease in the time spent in the closed arms (P = 0,0035). In the open field test, LAM promoted an increase in the number of crossings and rearings compared to control (P = 0.0023) and CORT (P = 0.0075) respectively. Regarding cytokine levels, LAM reversed the effects induced by CORT in the SC (P = 0,0125), an effect not observed in the PFC (P = 0,0137) and HC (P = 0,0001) regions, although it showed lower levels of IL-1β compared with the CORT group. **Conclusion:** The findings of this study suggest that laminarin represents a promising therapeutic strategy for depressive disorder due to its immunomodulatory properties. **Financial support:** The authors acknowledge FUNCAP for the financial support that made this research possible.

02.053 **Clinical, Cognitive, and Sociodemographic Characterization of Patients with Mild Cognitive Impairment and Dementia Attended at Walter Cantídio University Hospital**. Souza TF[1,2], Ferreira DMA[1,2], Guimarães APDS[1,2], Rosa R[3], Lima DP[3,4,5] Lima AB[5], Miyajima F[1,2] [1]Fiocruz-Ceará, Brasil, [2]ACMELab Lab Analítico de Competências Moleculares e Epidemiológicas, Brasil, [3]UFC, Brasil, [4]Hospital Universitário Walter Cantídio, Brasil, [5]HSM-Messejana, Brasil

Introduction: Mild Cognitive Impairment (MCI) and dementia represent major public health challenges resulting from population aging. The clinical and pharmacotherapeutic characterization of these patients may support future therapeutic strategies. **Objectives:** To describe the clinical, cognitive, sociodemographic and pharmacotherapeutic profile of patients with MCI and dementia treated at the Walter Cantídio University Hospital (HUWC), investigating associations between pharmacological treatment, cognitive performance, and functional severity. **Methods:** This was a cross-sectional observational study including patients diagnosed with MCI or dementia followed at the Neurology Clinic of the HUWC. The study was approved by the HUWC Research Ethics Committee (CAEE 86078325.4.0000.5045). Sociodemographic, clinical, cognitive and medication-use data were obtained through a structured questionnaire, medical records, the Mini-Mental State Examination (MMSE), and the Clinical Dementia Rating (CDR). Statistical analyses included descriptive statistics, Spearman's correlation and Pearson's chi-square test ($p < 0.05$). **Results:** The sample comprised 35 patients recruited between July 2025 and February 2026, with a mean age of 72.21 ± 11.86 years; 63.6% were women and the mean educational level was 9.32 ± 4.61 years. A family history of dementia was reported by 39.4% of the participants. The mean MMSE score was 18 ± 7.45 points. Regarding clinical severity, 39.4% had CDR 0.5, 27.3% had CDR 1, 18.2% had CDR 2, and 9.1% had CDR 3. Memory impairment was the most frequent initial symptom (93.5%), followed by neuropsychiatric symptoms (41.9%) and behavioral changes (29%). Antidepressants were the most commonly used medications (61.3%), followed by anti-dementia drugs (48.4%) and antipsychotics (19.4%). Functional dependence was associated with poorer cognitive performance (rho = -0.394; $p = 0.028$), whereas self-care ability was correlated with better MMSE scores (rho = -0.522; $p = 0.003$). No significant associations were observed between the use of antidepressants, anti-dementia drugs, or antipsychotics and cognitive performance ($p > 0.05$). An association was found between antipsychotic use and clinical severity assessed by the CDR ($p = 0.002$), with more frequent use among patients with CDR 3. **Conclusion:** This study described the clinical, cognitive, sociodemographic and pharmacotherapeutic profile of patients with MCI and dementia followed at a tertiary care center. The findings highlight the clinical heterogeneity of this population, including different levels of functional impairment, neuropsychiatric symptoms, and patterns of pharmacological treatment. Associations were identified between functional status and cognitive performance, as well as between antipsychotic use and greater clinical severity. This characterization provides relevant information for therapeutic management and future investigations in clinical pharmacology related to cognitive impairment.

02.054 **Role of Microglia in Adolescent Stress-Induced Behavioral Impairments and Alterations in Parvalbumin Interneurons and their Perineuronal Nets in Adult Mice**. Hadera V[1], Bobotis B[2], Guimarães FS[1], Tremblay ME[2], Gomes FV[1] [1]FMRP-USP, Dept Pharmacology, Brazil; [2]University of Victoria, Medical Sciences Building, Canada

Background: Trauma during adolescence, a critical period of neurodevelopment, increases the risk of psychiatric disorders. Microglia, the resident immune cells of the brain, play a key role in the response to trauma and may contribute to long-lasting stress-induced alterations. In previous work, we showed that adolescent stress induces behavioral deficits and alters parvalbumin (PV) interneurons and their associated perineuronal nets (PNNs) in the ventral hippocampus (vHip) in adulthood. In the present study, we evaluated the short- and long-term effects of adolescent trauma on microglial activity. In addition, we investigated whether intra-vHip infusion of clodronate disodium (CDS), which induces transient microglial depletion, reverses adolescent stress-induced impairments in adulthood. **Methods:** Male C57BL/6J mice (n=8/group) were subjected to 10 days of footshock stress during adolescence [postnatal days (PD) 31–40]. Behavioral and molecular alterations, including quantification of PV+, PNN+, PV+/PNN+, and Iba-1+ cells (cell number and morphology), were assessed 1, 10, and 20 days after stress exposure. In an independent experiment, mice received a single bilateral intra-vHip infusion of CDS (50mg/mL;500 nL) in PBS one day after stress and were evaluated in adulthood (>PD62). This study was approved by the Institutional Ethics Committee (FMRP 1492/2025). **Results:** Adolescent stress reduced social interaction and novel object recognition and decreased the number of PV+, PNN+, and PV+/PNN+ cells in the vHip, as well as induced alterations in microglial morphology. These effects were more pronounced at early time points (1 and 10 days after stress), whereas partial alterations persisted at later stages (20 days), particularly in PV/PNN populations and in attenuated microglial morphological changes. CDS-induced microglial depletion reversed behavioral deficits as well as cellular and microglial alterations. **Conclusion:** Our findings indicate that adolescent stress induces long-lasting behavioral and cellular alterations, particularly affecting PV interneurons, their PNNs, and microglial homeostasis in the vHip. Local microglial depletion after stress mitigated these effects, highlighting microglia as a potential therapeutic target for adolescent stress-related psychiatric disorders. **Financial support:** FAPESP, CNPq, CAPES, and FAEPA.

02.055 **Negative Correlation Between Cortical Acetylcholinesterase Activity and Spatial Working Memory in STZ-Induced Rats Treated with Probiotic and Postbiotic** *Lactobacillus casei*. Rodrigues ES, Gomes J, Meus SS, Comis-Neto AA, Fontoura, EA, Batista, WT, Streb, BL, Fidelis, EM, Rosa, SG, Pinton S Unipampa-Uruguaiana, RS, Brazil

Introduction: Through the microbiota–gut–brain axis, microorganisms have emerged as potential complementary therapeutic approaches for neurodegenerative diseases, with postbiotics standing out due to their greater stability and safety. Therefore, this study investigated the effects of Lactobacillus casei in probiotic and postbiotic forms on cognitive impairment, cholinergic dysfunction, and neuroinflammation in an intracerebroventricular streptozotocin (ICV-STZ)-induced experimental model of Alzheimer's disease (AD). **Materials and Methods:** Fifty female Wistar rats (110–120 days old) were used in this study. On day 0, animals received bilateral ICV injections of saline or STZ (3 mg/3 µL/kg) (coordinates: AP -0.9 mm, ML ±1.5 mm, DV -;3.6 mm from bregma), according to a protocol approved by the ethics committee (No. 024/2024). After three days of post-surgical recovery, animals were randomly divided into four groups: (i) Control, (ii) STZ, (iii) STZ + Probiotic, and (iv) STZ + Postprobiotic. Oral administrations were performed daily for 14 days using L. casei as probiotic (1×10^9 CFU/kg), or as a heat-inactivated whole-cell postbiotic preparation (100 mg/kg, equivalent to 1×10^9 CFU/kg), or saline solution. At the end of the treatment period, animals performed the Y-maze task and were subsequently euthanized, and cortex tissues were collected for acetylcholinesterase (AChE) activity analysis. Data were analyzed using one-way ANOVA/Tukey and Pearson's correlation analysis. **Results:** In the Y-maze test, STZ-treated animals exhibited a significant reduction in spontaneous alternation behavior compared with the control group ($p = 0.0302$), indicating impairment in working memory. Both postprobiotic and probiotic treatments increased the percentage of correct alternations compared with the STZ group ($p = 0.0068$ and $p = 0.0472$, respectively), suggesting attenuation of STZ-induced cognitive impairment. Cortical AChE activity was markedly increased in the STZ group compared with the control group ($p = 0.0006$). In contrast, both postprobiotic ($p = 0.0014$) and probiotic ($p = 0.0011$) treatments reduced AChE activity relative to the STZ group. Correlation analysis demonstrated a significant negative association between spontaneous alternation performance and cortical AChE activity ($r = -;0.357$, $p = 0.026$), indicating that increased AChE activity was associated with poorer spatial working memory performance. **Conclusion:** These findings suggest that probiotic and postprobiotic treatments modulate AChE activity and attenuate working memory deficits in STZ-induced rats, indicating a potential protective effect against cholinergic dysfunction associated with gut–brain axis communication. Furthermore, these results reinforce the therapeutic potential of microbial-based interventions as complementary strategies for

neurodegenerative disorders such as AD.

02.056 *in silico* and Behavioral Evaluation of Geraniol and Geranyl Acetate Pharmacological Profile in Zebrafish. Bastos LM[1,2], Fuentealba-Villarroel F[1,3], Gallas-Lopes M[1,2], Paulo M[1,2], Patelli-Alves A[1], Cardoso IP[1], Borges GO[1], Portela SM[1], Rosa GO[1], Costa PM[1,5], Herrmann AP[2], Rigo MM[4], Piato A[1,2,3] [1]UFRGS, Porto Alegre, Lab Psicofarmacologia e Comportamento, Brazil; [2]UFRGS, Porto Alegre, PPG Farmacologia e Terapêutica, Brazil; [3]UFRGS, Porto Alegre, PPG Neurociências, Brazil; [4]UFRGS, Porto Alegre, PPG Genética e Biologia Molecular, Brazil; [5]UFCSPA, Porto Alegre, Brazil.

Introduction: Geraniol (Ger) is a terpenoid found in essential oils with reported anxiolytic effects in rodents and fish. Esterification improves bioavailability and drugs' affinity for receptors. This study investigated the pharmacological profile of Ger and its esterified form, geranyl acetate (GerAc), *in silico* and in adult zebrafish (Danio rerio). **Methods:** *in silico* prediction: experiment 1 - molecular docking simulations were performed using the GABAA α1β2γ2 receptor, with GABA and diazepam as controls, alongside Ger and GerAc. Structures were obtained from the Protein Data Bank, PubChem, and Cambridge Crystallographic Data Centre. The receptor was minimized in GROMACS, ligands were prepared in Open Babel and AutoDockTools, and docking was performed in AutoDock Vina using Vina scoring function, a 10 Å grid box, and exhaustiveness of 128. Docking poses were visualized in PyMOL. *In vivo* studies: 333 adult zebrafish of both sexes were used. Experiments 2a-b (anxiolytic effect) - fish were assigned to the groups (n=23-28) 1% DMSO or Ger/GerAc (4, 40, or 60 μM), following block randomization. On the test day, fish were individually exposed to the treatment solutions (10 min) and then allocated to the novel tank test (6 min). Experiment 3a-b (antiseizure effect) - fish were randomly assigned to the groups (n=11-12) 1% DMSO, 50μM diazepam, or Ger/GerAc (60, 120, or 240 μM). Fish were exposed to the treatment solutions (10 min), followed by a 5-min washout, and then exposed to 10 mM pentylenetetrazole (PTZ; 20 min). Behavioral assessments were performed by blinded researchers using ANY-Maze and BORIS software, and analyzed using Kruskal-Wallis/Dunn, One-Way ANOVA/Tukey, and Cohen's d effect size tests. Experiments were approved by CEUA/UFRGS (36307) and preregistered in the Open Science Framework. **Results:** In experiment 1, diazepam showed great affinity for the benzodiazepine-binding site (-9.952 kcal/mol), followed by GerAc (-7.069 kcal/mol) and Ger (-6.367 kcal/mol), while GABA showed no affinity. In experiment 2a, Ger showed no anxiolytic-like effect. In experiment 2b, GerAc (40 and 400 μM) increased the time spent in the upper zone ($p<0.001$ and $p<0.01$, respectively), while 400 μM also increased upper-zone entries ($p<0.01$), without locomotor alterations. In experiments 3a-b, diazepam increased the latency to both clonic ($p<0.0001$ and $p<0.01$) and tonic-like seizure ($p<0.0001$ and $p<0.01$), and decreased seizure intensity ($p<0.0001$ and $p<0.005$), whereas Ger and GerAc did not alter PTZ-induced seizures. **Conclusion:** Docking simulations predicted interactions with the benzodiazepine-binding site, especially for GerAc, suggesting modulation of the GABAergic system. GerAc, but not Ger, induced anxiolytic-like effects in zebrafish without antiseizure activity. These results support GerAc's therapeutic potential. However, pharmacodynamic and pharmacokinetic studies are still necessary to elucidate its effects. **Financial support:** CAPES, CNPq, and PROPESQ at UFRGS.

02.057 **Sodium Valproate and Gabapentin Reduce the Seizure-Like Behavior Induced by Pentylenetetrazol and Mechanical Stress in *Drosophila melanogaster*: Sex Influence on Behavioral Responses**. Santos G, Goes AAD, Oliveira MS, Bressan GN, Fachinetto R UFSM, Centro de Ciências da Saúde, PPG em Ciências Biológicas: Farmacologia, Brasil.

Introduction: Epilepsy is a multifactorial neurological condition characterized by abnormal, recurrent neuronal discharges. The search for new anticonvulsant treatments requires experimental models that replicate the pharmacological responses of drugs commonly used for this condition **Objectives:** This study aimed to evaluate the effect of pentylenetetrazol (PTZ), a pro-convulsant agent, combined with thermal or mechanical stress on seizure-like behavior in female and male D. melanogaster, as well as to determine the response to anticonvulsant drugs. **Methods:** Initially, locomotor activity was evaluated after exposure to PTZ (0.1–60 mM) to rule out baseline locomotor deficits that could interfere with the **Results:** Subsequently, flies were exposed to PTZ for 24 h and subjected to thermal or mechanical stress to induce seizure-like behavior. Based on the results, exposure to PTZ (1 mM) associated with vortex-induced mechanical stimulation was selected for seizure induction in both sexes. Afterwards, flies were treated with the anticonvulsant drugs sodium valproate (0.1, 1.0, 10 mM) or gabapentin (0.5, 1.0, 2.5 mM). **Results:** Both anticonvulsant drugs attenuated the seizure-like behaviors induced by PTZ and mechanical stress, with more pronounced effects observed in male flies. **Conclusion:** PTZ associated with mechanical stress reproduces a phenotype resembling seizure-like behavior in male and female D. melanogaster. Furthermore, the model was responsive to sodium valproate and gabapentin, particularly in males, supporting its translational potential for identifying new anticonvulsant drugs and reinforcing the importance of including sex as an experimental variable. Acknowledgements: The authors acknowledge the financial support provided by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) (ROR identifier: 00x0ma614), which funded the Article Processing Charge (APC) for this publication. This study was also financed in part by CAPES–PROAP–PPG Farmacologia.We also acknowledge fellowships from CAPES–DS (G.S and A.A.D.G.) and CNPq (G.N.B., M.S.O., and R.F. (# number: 309128/2021-8 and # number: 303489/2025-1)).

02.058 **Paraprobiotic Treatment Preserves Striatal TH-Positive Neurons and Modulates Gut Microbiota Following Intranasal MPTP Administration**. Gomes J[1], Rodrigues ES[1], Comis-Neto AA[1], Fontura, EA[1], Evangelista, HC[1], Batista, WT[1], Streb, BL[1], Rosa, SG[1], Ribeiro, AM[2], Pinton, S[1] [1]Unipampa-Uruguaiana, RS, Brazil, [2]Unifesp, São Paulo, SP, Brazil

Introduction: Parkinson's disease (PD) is a neurodegenerative disorder characterized by progressive motor dysfunction and loss of dopaminergic neurons in the striatum (ST) and substantia nigra pars compacta. PD is a multifactorial linked to oxidative stress, neuroinflammation, and gut microbiota dysbiosis. MPTP induces neural and microbial alterations through the gut–brain axis, while paraprobiotics, non-viable probiotic cells, have emerged as a promising strategy to modulate intestinal homeostasis and beneficial microbiota. **Objectives:** Evaluate the effects of a paraprobiotic blend on gut microbiota composition and dopaminergic neuroprotection in an intranasal PD model in female rats. Materials and **Methods:** Female Wistar rats received intranasal MPTP (10 µL, 1 mg/nostril) or saline, followed by 14 days of intragastric treatment with a paraprobiotic blend containing Bifidobacterium lactis, Lactobacillus casei, and Streptococcus thermophilus (100 mg/1 mL/day; 33,33 mg each) (CEUA 003/2024). Animals were divided into groups Control; MPTP; Paraprobiotic; and MPTP+Paraprobiotic. Fecal samples were collected for gut microbiota analysis, and TH immunohistochemistry was performed in the ST following paraformaldehyde perfusion. Data were analyzed by two-way ANOVA with Tukey's post hoc test. **Results:** Two-way ANOVA revealed a significant interaction for TH-positive neurons in the ST. The MPTP group showed reduced TH-positive neurons compared with Control ($p<0.0001$). Paraprobiotic treatment attenuated this effect, increasing TH-positive neuron counts in the MPTP+Paraprobiotics group versus MPTP ($p<0.0001$). Although the Paraprobiotics group also exhibited lower TH-positive neuron counts than Control ($p<0.0001$), values remained higher than in the MPTP group ($p=0.0041$). Relative abundance analysis demonstrated significant modulation of specific microbial taxa following treatment. The MPTP group exhibited increased abundance of Lactobacillus murinus compared with the Control group ($p=0.0134$), whereas the MPTP+Paraprobiotics group showed partial attenuation of this alteration ($p=0.1406$). Additionally, the MPTP+Paraprobiotics group presented increased abundance of the genera Phocaeicola (vs. Control: $p=0.0338$; vs. MPTP: $p=0.0459$), Flintibacter (vs. Control: $p=0.0269$; vs. MPTP: $p=0.0290$), and Limosilactobacillus (vs. Control: $p=0.0597$; vs. MPTP: $p=0.0007$; vs. Paraprobiotics: $p=0.0013$), as well as increased abundance of uncultured Firmicutes bacterium (vs. Control: $p=0.0015$; vs. MPTP: $p=0.0259$) and Bacteroides vulgatus (vs. Control: $p=0.0412$; vs. MPTP: $p=0.0485$). **Conclusion:** Treatment with the paraprobiotic blend prevented MPTP-induced dopaminergic neuronal loss and promoted modulation of gut microbiota composition in female rats subjected to the intranasal PD model. These findings suggest that paraprobiotics may represent a complementary therapeutic strategy with neuroprotective potential, possibly mediated through interactions between the gut microbiota and the gut–brain axis. Key-words: Microbiota-gut-brain axis, Neuroprotection and Prodromal

Parkinson's.

02.059 **Plumieride Attenuates Long-Term Behavioral, Oxidative, Neuronal, and Barrier Dysfunction Following Neonatal Carbonyl Iron Exposure in Rats**. Eisendecker HI[1], Harle M[1], Guimarães GM[1], Sievers J[1], Nilz ACS[1], Malheiros A[1], Dalmagro AP[1,2], Souza MM[1]. [1]Univali, Itajaí, Santa Catarina, Brazil. [2]FURB, Blumenau, Santa Catarina, Brazil.

Introduction: Excessive iron exposure can disrupt redox homeostasis, promote lipid peroxidation, and contribute to neuronal damage, associated with neurodegenerative conditions, involve iron-dependent cell death mechanisms that have also been implicated in the pathophysiology of Parkinson's disease. Plumieride (PLU), an iridoid isolated from *Allamanda cathartica*, has antioxidant, anti-inflammatory, antidepressant, and anxiolytic properties. **Objective:** To investigate the effects of PLU on behavioral, biochemical, histological, and barrier-permeability alterations induced by neonatal exposure to carbonyl iron (CI) in rats. **Methods:** Male (M) and female (F) Wistar rats received CI (30 mg/kg, p.o.) or vehicle on postnatal days 12, 13, and 14. Beginning on postnatal day 120, animals were orally treated for 15 days with vehicle, PLU (1, 5, or 15 mg/kg), or L-DOPA (6 mg/kg). Behavioral assessment included the elevated plus-maze (EPM), splash test (ST), and inhibitory avoidance test (IA). After euthanasia, hippocampal and striatal samples were collected for biochemical and histological analyses. Intestinal and blood–brain barrier (BBB) permeability were also evaluated. The experimental protocol was approved by the institutional ethics committee (015/24). **Results:** PLU did not alter aversive memory consolidation in the IA. Compared with CI-exposed vehicle-treated animals, PLU increased the frequency of open-arm entries in the EPM ($p<0.05$), suggesting an anxiolytic-like effect. In the ST, PLU reduced grooming latency ($p<0.0001$) and increased grooming frequency and total time of grooming ($p<0.05$) in F, whereas no significant antidepressant-like effect was observed in M. Hippocampal superoxide dismutase activity remained unchanged; however, PLU increased glutathione levels ($p<0.01$) and reduced malondialdehyde levels ($p<0.05$) in both sexes. PLU also reduced neuronal death in the hippocampus and striatum of F ($p<0.0001$ and $p<0.001$, respectively) and M ($p<0.0001$ for both regions). Intestinal permeability was reduced in M ($p<0.05$) and F ($p<0.01$), whereas blood–brain barrier permeability was reduced only in F ($p<0.05$). **Conclusion:** PLU attenuated anxiety-like behavior, oxidative damage, neuronal loss, and intestinal barrier dysfunction associated with neonatal CI exposure. Antidepressant-like activity and preservation of BBB integrity were observed only in F, indicating sex-dependent neuroprotective effects. These findings support the potential of PLU to mitigate long-term neurotoxic alterations associated with early-life iron overload. **Acknowledgments:** UNIVALI, CAPES, CNPq, FAPESC.

02.060 **Efficacy and Safety of Cannabidiol plus Δ^9-Tetrahydrocannabinol in Parkinson's Disease: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial**. Ruver-Martins AC[1], Silva ES[1], Matheus FM[1], Recchia MB[1], Cassenotte ACV[1], Franchi C[1], Lopes SC[2], Silva MD[3], Prediger RD[1] [1]UFSC, Experimental Lab Neurodegenerative Diseases, Dept Pharmacology, Center of Biological Sciences, Florianópolis, Santa Catarina, Brazil. [2]UNIDAVI, Research Center in Medical Sciences, Investigations in Health (NPCMed), Faculty of Medicine, Rio do Sul, Santa Catarina, Brazil. [3]UFSC, Lab Neurobiology of Pain and Inflammation, Dept Physiological Sciences, Center for Biological Sciences, Florianópolis, Santa Catarina, Brazil.

Introduction: Parkinson's disease (PD) is a neurodegenerative disorder characterized by bradykinesia, tremor, rigidity, and postural instability. Current therapies, including levodopa and dopamine agonists, improve symptoms but are associated with long-term complications such as dyskinesias and "on-off" fluctuations. These limitations have encouraged investigation of cannabinoids, especially Cannabidiol and Delta-9-tetrahydrocannabinol, due to their potential neuroprotective and symptomatic effects.

Objectives: This study evaluated the effects of combined Cannabidiol and Delta-9-tetrahydrocannabinol treatment in patients with mild to moderate Parkinson's disease receiving standard therapy, including potential sex-based differences in treatment response. **Methods:** The study and the Informed Consent Form (TCLE) were approved by the Ethics Committee of the Universidade Estadual do Paraná (UNIOESTE) under CAAE number 59839722.1.0000.0107 and Federal University of Santa Catarina - UFSC (CAAE 59839722.1.3001.0121), and prospectively registered in the Brazilian Registry of Clinical Trials (RBR-10n7gx74). In this phase 2, double-blind, placebo-controlled trial, 68 patients with mild to moderate PD received placebo or oral Cannabidiol (50 mg/day) plus Delta-9-tetrahydrocannabinol (5 mg/day) for six months. Primary outcomes assessed motor symptoms, while secondary outcomes included quality of life, functional motor performance, and adverse events monitored daily through a mobile application. **Results:** Both groups showed significant improvement in motor symptoms measured by MDS-UPDRS Part III from baseline ($p < 0.001$). However, patients receiving combined Cannabidiol and Delta-9-tetrahydrocannabinol demonstrated earlier clinical benefits, occurring following 30 days in men and 90 days in women, whereas placebo-related improvements appeared only after 180 days. Women in the cannabinoid group also presented greater improvements in total MDS-UPDRS scores ($p = 0.042$) and trunk flexibility ($p = 0.008$) compared to placebo, suggesting possible sex-related differences in response. Treatment was well tolerated, with no severe adverse events reported during follow-up. **Conclusion:** A combination of Cannabidiol and Delta-9-tetrahydrocannabinol accelerated motor improvements and demonstrated sex-specific benefits in individuals with Parkinson's disease. These findings support the need for further clinical trials with optimized dosing strategies and analyses focused on sex-related differences in treatment response.

02.061 **Gene–Environment Interaction in Transgenic Rats Overexpressing Human DISC1: Effects of Early Social Isolation on Behavioral Domains**. Pedroso-Fidelis GS, Ávila FC, Cruz FC, Hayashi MAF. Unifesp-EPM, Depto Farmacologia, PPG em Farmacologia, Brasil.

Introduction: Disrupted-in-Schizophrenia 1 (DISC1) is a protein involved in neurodevelopmental and neuronal signaling processes and has been associated with psychiatric disorders. Transgenic animal models overexpressing human DISC1 reproduce neurobiological and behavioral alterations relevant to schizophrenia-related phenotypes, including dopamine dysregulation and DISC1 protein aggregation. In addition to genetic vulnerability, environmental stressors such as early-life social isolation are known to induce persistent behavioral and neuroplastic alterations. However, the interaction between DISC1 overexpression and early social isolation remains poorly understood. **Objectives:** This study investigated the effects of early-life social isolation on different behavioral domains in tgDISC1 rats during the transition from adolescence to early adulthood. **Methods:** Male Sprague–Dawley wild-type (WT) and tgDISC1 rats were subjected to social isolation immediately after weaning (postnatal day 21) for four weeks. Behavioral evaluation included the Splash Test, Forced Swim Test, Elevated Plus Maze, Open Field Test, and Social Interaction Test. Data were analyzed using unpaired Student's t-test to compare Control and Social Isolation groups within each genotype (WT and tgDISC1). Statistical significance was set at $p < 0.05$. Data are presented as mean ± SEM. Analyses were performed using GraphPad Prism (version 8.0, GraphPad Software, USA). **Results:** Social isolation induced behavioral alterations selectively in WT animals. Isolated WT rats showed reduced grooming time in the Splash Test and decreased latency in the Forced Swim Test compared with control WT animals. In the Social Interaction Test, isolated WT rats exhibited increased social interaction ratio relative to controls. No significant differences were observed in Elevated Plus Maze, or Open Field Test. TgDISC1 rats did not show significant behavioral differences between control and isolated groups in any test evaluated. **Conclusion:** Early-life social isolation induced behavioral alterations in WT rats, whereas tgDISC1 animals did not exhibit significant behavioral changes under the same experimental conditions. These findings demonstrate distinct behavioral responses to early-life social isolation between WT and tgDISC1 rats and contribute to the understanding of gene-environment interactions associated with psychiatric disorder-related phenotypes.

02.062 **Effect of Ibogaine on Hippocampus and Striatum NMDAR and GABAAR Expression in Male and Female Rats after Cocaine-CPP Exposure**. Heidrich N[1], Almeida FB[1], Ávila MS[2], Rocha DP[2], Barth RA[2] Silva IAG[1], Freese L[3], Barros HMT[1,2] [1]UFCSPA, PPG Ciências da Saúde, Brazil, [2]UFCSPA, Neuropsychopharmacology Lab, Brazil, [3]Northwestern University, Feinberg School of Medicine, Augustin Lab, Chicago, USA

Introduction: Cocaine use disorder is a severe condition with no approved pharmacological treatment. Females are particularly vulnerable to the rewarding effects of cocaine, contributing to sex-related differences in addiction. Ibogaine (IBO), a naturally occurring indole alkaloid, has been described as a potential treatment in both humans and animal models. Its effects have been associated with modulation of glutamatergic and GABAergic neurotransmission, involving N-methyl-D-aspartate (NMDA) and γ-aminobutyric acid type A (GABAAR) receptors. The influence of sex on the neuropharmacological effects of ibogaine remains uncertain. **Objectives:** Determine if IBO affects NMDA and GABAA receptor subunit expression in brain structures related to addiction, after the conditioned place preference (CPP) protocol paired with cocaine, in male and female rats. **Methods:** Both sexes Wistar rats received cocaine (15mg/kg i.p. injection, COC+) on alternate days in a 12-day CPP protocol. A saline-only group (COC-) was included for comparison. Rats received two injections of either vehicle or ibogaine (40 mg/kg) via i.p. injection on day 12. After euthanasia, the hippocampi and striata of COC+ versus COC- male and female rats (N = 81) were dissected for mRNA quantification by real-time qPCR analysis of the target genes of NMDAR (GluN2A, GluN2B) and GABAAR (alfa2, δ and γ2) subunits. **Results**: The 3W-ANOVA showed statistically significant differences in the hippocampi for GluN2A (Sexes, Treatment), GluN2B (Treatment). The post hoc test corroborated sex differences for GluN2A (Sex: F(1.41) = 6.341, p = 0.017). These results point to an influence of the male sex on the regulation of GluN2A. Exposure to cocaine showed no effects. Regarding GABA A, only the δ subunit exhibited a pattern of interaction across all factors (p = 0.054), perhaps indicating a tonic inhibition modulation in the hippocampus of these animals, and a difference in treatment for δ. In striata, GluN2A interacts with sex in comparing COC+/COC- (F(1.39) = 5,322, p = 0.028). GluN2B showed an all-factors interaction (F(1,38) = 6.776, p = 0.014), for which males COC+ and females COC+ treated with IBO showed higher means than the controls. **Conclusion:** The results suggest an effect of ibogaine in cocaine neuroplasticity, with a modulating role by sex, especially for glutamatergic receptors. Further research is needed to better determine ibogaine's neurobiological effects. **Animal Research Ethical Committee ****Number** #233/18. **Financial support:** CAPES, FAPERGS, UFCSPA.

02.063 **SARS-CoV-2 Spike Protein Induces Gut–Brain Axis Disruption and Cognitive Decline in a sex-Dependent Manner in mice**. Willrich CH[1], Cazarin CA[1,2], Cury BJ[1], Longo B[1], de Amorim GES[1,2], Machado GM[1], de Oliveira IM[1], Queiroz LY[1], Casimiro LM[1], Santos MR[1], Mariot, LN[1], de Sordi, R[1] Cimarosti HI[1,2], Prediger RDS[1,2], da Silva LM[1,2] [1]UFSC, Dept Pharmacology, Brazil; [2]UFSC, Neuroscience Postgraduate Program, Brazil

Introduction: Long COVID may persist after the acute phase of SARS-CoV-2 infection, with cognitive dysfunction ("brain fog") being one of its most frequently reported manifestations. Persistent neuroinflammation, driven by delayed glial activation, may play a central role in this condition and could be exacerbated by Spike protein-induced disruption of the gut-brain axis. **Objectives:** Investigate whether systemic exposure to the SARS-CoV-2 Spike protein disrupts the gut-brain axis, promoting neuroinflammation and late-onset cognitive decline through increased intestinal and blood-brain barrier permeability and enhanced systemic translocation of LPS. **Methods:** Female and male C57BL/6 mice were assigned to three groups receiving either active Spike protein (Ac-S; 10 µg/5 µL, s.c.), denatured Spike protein (Dn-S; 10 µg/5 µL, s.c.), or vehicle (Veh; 100 µL PBS, s.c.). Behavioral testing during acute phase began three days post-injection (3 dpi) and late (30 dpi) phases using open field (OFT), novel object recognition (NOR) and the Morris water maze (MWM). Brain and intestinal tissues were collected for biochemical analyses. Intestinal barrier permeability was functionally assessed by fluorescein isothiocyanate (FITC)-dextran leakage and indirectly by serum LPS quantification, while BBB permeability was evaluated through Evans Blue (EB) extravasation. **Results:** Ac-S male group exhibited memory impairment in NOR, whereas female showed deficits in MWM task in late phase. Female Ac-S displayed reduced superoxide dismutase (SOD) activity in the hippocampus, whereas male mice showed a marked activity reduction in ileum. NOx levels were elevated in both Ac-S hippocampus. IL-1β and TNF-α levels were increased in the hippocampus and ileum of female mice, while in males, elevated levels were observed only in the ileum. Increased serum FITC-dextran levels were observed exclusively in females, paralleling the increase in EB extravasation in the cortex and elevated serum LPS concentrations. Administration of Ac-S also reduced villus height and crypt depth in the ileum of both sexes. **Conclusion:** These findings support the involvement of gut-derived inflammatory signaling in sex-dependent Spike-induced neurocognitive dysfunction, in which intestinal barrier impairment, elevated systemic LPS levels, and neuroinflammation may contribute to cognitive decline.

02.065 **Topical Modulation of cortical Dopamine D2 Receptors Alters Cortical Spreading Depression Propagation and Neuronal Activation in Rats**. Prieto SG[1], Cabrera-Baez M[2], Guedes RC[1] [1]UFPE, Center of Health Sciences, Nutrition Dept, Brazil, [2]UFPE, Center for Exact and Natural Sciences, Physics Dept, Brazil

Introduction: Cortical spreading depression (CSD) is a propagating wave of neuronal and glial depolarization associated with migraine aura and other neurological brain disorders. Although dopaminergic signaling has been implicated in cortical excitability, the contribution of cortical dopamine D2 receptors (D2R) to CSD modulation remains poorly understood. **Objectives:** To investigate whether topical cortical application of D2R ligands alters CSD propagation dynamics and neuronal activation *in vivo*. **Methods:** Adult male Wistar rats were anesthetized and submitted to KCl-induced CSD recordings. Saline, metoclopramide (MCP), raclopride (RCP), or quinpirole (QNP) (50 mg/ml) were topically applied to the parietal cortex for 5, 10, or 30 min. CSD propagation velocity, amplitude, and duration were analyzed using Ag–AgCl electrodes positioned over the cortex. c-Fos immunohistochemistry was performed in superficial layers of the somatosensory cortex to evaluate neuronal activation. A reaction–diffusion computational model incorporating drug diffusion and receptor occupancy was used to simulate CSD propagation. Statistical analysis was performed using repeated-measures ANOVA, one-way ANOVA, Tukey post hoc test, and Pearson correlation ($p < 0.05$). **Results:** MCP completely blocked CSD propagation at all exposure times and significantly reduced waveform amplitude and duration. RCP produced a biphasic effect, reducing CSD velocity at 5 and 10 min, but increasing propagation after 30 min. QNP transiently increased CSD velocity at 5 min, followed by marked inhibition at longer exposures. Both MCP and QNP significantly reduced c-Fos expression in superficial cortical layers, whereas RCP showed no significant effect. A positive correlation was observed between CSD propagation velocity and c-Fos density ($r = 0.599$, $p = 0.002$). Computational simulations reproduced the experimental propagation profiles and supported a time-dependent modulation of cortical excitability by D2R ligands. **Conclusion:** Topical modulation of cortical D2R signaling alters CSD propagation and neuronal activation in a ligand-specific and time-dependent manner. These findings support a role for dopaminergic signaling in cortical excitability and may contribute to understanding the mechanisms underlying migraine-related cortical dysfunction.

02.066 **Effects of Klotho on cognitive and motor function in a mouse model of LPS-induced neuroinflammation**. Silva JN, Tavares ALPF, Lima TAS, Scavone C, Kawamoto EM. ICB-USP, Dept Pharmacology, Brazil.

Introduction: Klotho is an anti-aging protein implicated in cognitive function and expressed in encephalic regions such as the hippocampus and cerebellum. Studies suggest that Klotho may exert anti-inflammatory and neuroprotective effects. In this context, this study investigated the possible protective role of Klotho in acute lipopolysaccharide (LPS)-induced neuroinflammation, an experimental model associated with cognitive and motor impairments. Understanding the effects of Klotho in this model may provide insights into its potential role in modulating behavioral impairments associated with neuroinflammatory conditions. **Objectives:** To evaluate the effects of Klotho on cognitive and motor parameters in mice subjected to acute neuroinflammation induced by LPS. **Methods:** Adult male Swiss mice (90–120 days old) received saline or Klotho (10 µg/kg, i.p.) for four days, followed by saline or LPS (250 µg/kg, i.p.), generating four groups: saline/saline, saline/LPS, Klotho/saline and Klotho/LPS. Behavioral tests were initiated 24 h after the last injection and included open field, T-maze spontaneous alternation and rotarod tests. Data were analyzed using two-way ANOVA followed by Tukey's post-hoc test, considering $p<0.05$ as statistically significant. The study was approved by CEUA (nº 6850100524). **Results:** In the T-maze, saline/LPS mice exhibited impaired working memory, evidenced by reduced spontaneous alternation compared with saline/saline ($p=0.0006$), Klotho/saline ($p<0.0001$) and Klotho/LPS ($p<0.0001$) groups. No differences were observed between Klotho/LPS and control animals. Saline/LPS mice also showed a lower total number of entries than saline/saline, Klotho/saline and Klotho/LPS groups ($p<0.0001$), indicating reduced exploratory activity, which was attenuated by Klotho treatment. In the open field test, saline/LPS animals exhibited reduced total distance traveled compared with Klotho/saline ($p=0.0070$) and Klotho/LPS ($p=0.0056$). No significant differences were detected in the rotarod test, suggesting that neither LPS nor Klotho affected baseline motor coordination. **Conclusion:** Klotho attenuated locomotor and cognitive impairments induced by LPS, particularly preserving exploratory behavior and working memory. These findings support further investigation of Klotho as a potential therapeutic strategy for neuroinflammation-associated disorders.

02.067 **Antimanic-Like Effect of Dipyridamole in the Methylphenidate-Induced Hyperlocomotion Model**. Kanazawa LKS, Santos AG, Kühl CE, Higashijima AN, de Souza STF, Andreatini R UFPR, PPG Pharmacology, Brazil

Introduction: Increasing evidence suggests that the adenosinergic system is involved in the pathophysiology of bipolar disorder. Drugs that modulate adenosine neurotransmission have shown therapeutic potential as adjunctive treatments for mania. **Objectives:** Therefore, the present study investigated the possible antimanic-like effects of adenosinergic drugs in the methylphenidate (MPH)-induced hyperlocomotion model in mice. **Methods:** Male and female Swiss mice received acute administration of allopurinol (50 or 200 mg/kg, i.p.), dipyridamole (20 mg/kg, i.p.), or inosine (50 mg/kg, i.p.) prior to MPH challenge (5 mg/kg, s.c.). In repeated-treatment experiments, male mice received daily administrations of allopurinol (25 or 50 mg/kg, i.p.), dipyridamole (20 mg/kg, i.p.), or inosine (50 mg/kg, i.p.) for 14 days before MPH administration. To evaluate the involvement of adenosine receptors, animals were pretreated with aminophylline (2 mg/kg, s.c.), a non-selective adenosine receptor antagonist. Locomotor activity was recorded in automated activity chambers during a 20-min session.The experimental protocol was approved by the Ethics Committee for Animal Use of the Federal University of Paraná, protocol n. 1437). **Results:** Acute allopurinol did not alter MPH-induced hyperlocomotion, with a significant MPH effect ($F(1,61)=25.208$, $p<0.0001$) but no treatment or interaction effects. Repeated allopurinol failed to reduce hyperlocomotion despite a significant treatment effect ($F(3,17)=4.497$, $p<0.02$). Acute dipyridamole attenuated MPH-induced hyperlocomotion, showing significant MPH effects ($F(1,41)=57.43$, $p<0.0001$) and MPH×treatment interaction ($F(1,41)=4.60$, $p<0.05$). Post hoc analysis showed reduced locomotion in dipyridamole + MPH vs vehicle + MPH ($p<0.05$), without affecting basal activity. Repeated dipyridamole reduced MPH-induced hyperlocomotion ($F(2,17)=20.78$, $p<0.001$), differing from vehicle + MPH ($p<0.01$). Acute and repeated inosine did not modify MPH-induced hyperlocomotion, although MPH effects remained significant (acute: $F(1,36)=8.153$, $p<0.01$; repeated: $F(2,17)=8.000$, $p<0.01$). Aminophylline blocked dipyridamole effects on MPH-induced hyperlocomotion ($F(3,36)=13.041$, $p<0.01$). As positive control haloperidol prevented MPH-induced hyperlocomotion (interaction: $F(1,34)=9.49$, $p<0.01$) but reduced basal locomotion. **Conclusion:** Dipyridamole produced consistent antimanic-like effects in the MPH-induced hyperlocomotion model, whereas allopurinol and inosine were ineffective under the tested conditions. The blockade of dipyridamole effects by aminophylline supports the involvement of adenosinergic neurotransmission in this response. These findings reinforce the hypothesis that the adenosine system may represent a promising target for the development of novel therapeutic strategies for bipolar disorder. **Acknowledgments and Financial support:** We thank CAPES and CNPq for the financial support.

02.068 **Early Post-Treatment with Beta-Caryophyllene Prevents Motor Deficits and Hippocampal Neuronal Loss after Pilocarpine-Induced Status Epilepticus**. Ribeiro LR[1,2], Bariviera JL[1,2], Da Rosa GK[1,2], Santos VT[2], Carneiro MA[2], Prates DN[2], Furian AF[1,2], Oliveira MS[1,2] [1]UFSM, PPG Pharmacology, Brazil; [2]UFSM, Lab Experimental Neurology

Introduction: Epilepsy affects 1-2% of the global population, and early interventions after an epileptogenic insult are essential to prevent epileptogenesis. Post-status epilepticus (SE) rodent models reproduce features of acquired epilepsy and allow testing of therapeutic strategies. Beta- caryophyllene (BCP) is a natural sesquiterpene with anti-inflammatory, neuroprotective and anticonvulsant properties. **Objectives:** Our study aimed to investigate the effects of post-treatment with BCP on functional and neuropathological outcomes following pilocarpine-induced SE in rats, and to explore the associated transcriptional signatures. **Methods:** SE was induced by pilocarpine in male Wistar rats (21-28 days old). BCP (three doses of 100 mg/kg, i.p.) or vehicle were administered post-SE (at 1, 8 and 16 h) and to animals in the saline control group. EEG was recorded before and during SE induction. Behavioral assessment (pick-up test and Neuroscore) was performed 7 days post-SE. Neuroprotection was evaluated by NeuN immunostaining. An exploratory reanalysis of public datasets (GSE276099: HepG2 cells exposed to BCP / GSE14763: rat hippocampus 7 days post-pilocarpine SE) was conducted to identify differentially expressed genes (DEGs) and overlapping regulatory patterns. The results are presented as the mean ± standard error of the mean (SEM). **Results:** SE induction (n = 14) produced typical epidural epileptiform activity. BCP prevented neuromotor deficits assessed at day 7 by Neuroscore [SE+vehicle vs. SE+BCP: 7.8±0.982 and 11.25±0.479, respectively; $p < 0.001$]. SE induced hippocampal neuronal loss (CA1, CA3, and dentate gyrus hilus), whereas BCP conferred protection particularly in the dentate gyrus hilus [SE+vehicle vs. SE+BCP: 68.125±14.906 and 121.5±13.031, respectively; $p < 0.05$]. Multivariate analysis of pooled NeuN data corroborated this neuroprotective effect. A robust positive correlation was observed between NeuN counts and neuromotor performance [Pearson's r = 0.696; $p < 0.001$]. Transcriptomic reanalysis revealed partially overlapping DEGs between BCP exposure and SE: 19 genes were downregulated and 6 upregulated in both datasets, and two sets of 13 genes each exhibited opposite regulation (pilocarpine vs. BCP). **Conclusion:** Early post-treatment with BCP reduced motor deficits and protected hippocampal neurons (notably in the dentate gyrus hilus region) one week after SE. The correlation between NeuN counts and neuromotor performance supports this neuroprotective effect. Transcriptomic reanalysis indicated overlapping and divergent gene regulation patterns between BCP exposure and SE, consistent with pathways related to synaptic function, cytoskeletal remodeling, lysosomal processing, and inflammatory and ionic mechanisms. These findings highlight the experimental evidence obtained, while further studies are needed to confirm molecular targets and therapeutic relevance. **Financial support** Information: CAPES (Finance Code 001) / CNPq (grants # 308011/2019-8, 309891/2023-0, 444375/2024-4 and 172408/2023-7) Ethical Committee Number: CEUA/UFSM – Protocol 5327190319

02.069 **Serum-Induced TLR3/TLR4 Signaling and Neurotoxicity in Unipolar Depression, Bipolar Disorder, and Attention-Deficit/Hyperactivity Disorder Patients**. de Farias IS[1], Ximenes AX[1], Soares JV[1], Pereira VA[2], Fidalgo T[3], Lima GMA[4], Hayashi MAF[1] [1]Unifesp-EPM, Dept Pharmacology; [2]Institute of Science and Technology; [3]Unifesp-EPM, Dept Psychiatry; [4]Unifesp-EPM, Dept Neurology; São Paulo, Brazil.

Neuroinflammation is increasingly recognized as a key driver in the pathophysiology of major psychiatric disorders. Central to this process are Toll-like receptors (TLRs), which are innate immune sensors that activate NF- κB-dependent inflammatory pathways potentially drive neuronal damage through the release of circulating immune mediators. Although classified as distinct diagnoses in the DSM-5, unipolar depression (UD), bipolar disorder (BD), and attention-deficit/hyperactivity disorder (ADHD), share profound genetic, neurobiological, and clinical architecture. Patients with UD, BD, and ADHD frequently exhibit elevated circulating pro-inflammatory cytokines, particularly IL-6, TNF-α, and IL-1β. This study aimed to evaluate the functional impact of serum on TLR3 and TLR4 activation and on differentiated SH-SY5Y neuronal cells (morphology and citotoxicity) from patients with UD, BD, and ADHD compared to healthy controls (HCs) paired by sex and age. Using hTLR3/hTLR4 reporter assays, we observed disorder-specific immune activation profiles: UD serum increased both hTLR3 (p = 0.0354) and hTLR4 (p = 0.0001) activity relative to HCs. BD serum elevated only hTLR3 (p = 0.0131), with no significant hTLR4 activation (p = 0.3755), whereas ADHD serum induced the most robust increases in both receptors (p <0.001 and p <0.0001, respectively). Cell viability (MTT) assays confirmed these reporter signals in HEK-293 cells were not driven by non-specific cytotoxicity (UD- TLR3: p = 0.4880; UD-TLR4: p = 0.7874; BD-TLR3: p = 0.5030; BD-TLR4: p = 0.7977). However, UD and BD sera exerted robust, neuron-specific toxicity, significantly reducing both neurite density (UD: p = 0.0164; BD: p = 0.0073) and overall cell viability (UD: p = 0.0229; BD: p = 0.0440). Conversely, ADHD serum did not alter neurite density (p = 0.7748) and paradoxically increased cell viability (p = 0.0004). Upregulation of TLR3/TLR4 signaling across these psychiatric conditions shows unique patterns. Taken together, we demonstrate that the circulating immune mediators in UD and BD drive neurotoxicity, whereas ADHD is characterized by a distinct, non-toxic humoral profile. These findings highlight TLR pathways and neuronal integrity as relevant targets for psychiatric pharmacology. **Keywords:** neuroinflammation, toll-like receptors, unipolar depression, bipolar disorder, ADHD.

02.070 **Impact of Prolonged Sweetener Consumption in an Animal Model of Alzheimer's Disease**. Guaita GO[1], Kanazawa LKS[1], Pagnussat AL[1], Hortega JVM[2], Souza RLR[2], Tureck LV[2], Vital MABF[1] [1]UFPR, PPG Pharmacology, Brazil; [2]UFPR, PPG Genetics, Brazil

Introduction: The consumption of artificial sweeteners has increased significantly, driven by the search for healthier alternatives to conventional sugar. **Objective:** The present study investigated the effect of chronic saccharin and sucrose consumption on metabolism, locomotion, cognitive function, oxidative stress, and cholinergic activity in a model of sporadic Alzheimer's disease induced by intracerebroventricular streptozotocin (ICV-STZ) in male Wistar rats. **Methods:** The animals were randomly allocated into 2 groups: STZ (3 mg/kg, n= 7-10 per group) or SHAM (saline, n= 6-10 per group), which were further divided into 3 treatments: water, 1% sucrose, or 0.1% saccharin, provided as a beverage for 35 days. After the treatment period, metabolic parameters (body weight, blood glucose), locomotion and exploration (open field), memory via object location and recognition tests (OLT, ORT), and the Y-maze were evaluated. In addition, the activity of the hepatic antioxidant enzyme superoxide dismutase (SOD) and hepatic and plasma butyrylcholinesterase (BChE) were assessed. Data were expressed as mean ± standard error of the mean (SEM), and statistical analyses were performed using two-way ANOVA followed by Tukey's post-hoc test, with significance set at $p<0.05$. **Results:** Sucrose consumption increased body weight only in the SHAM group. Regarding blood glucose levels, no differences were observed between groups. Animals in the STZ group showed impairment in locomotion and exploration of the central area in the open field compared to the SHAM group, regardless of the sweetener consumed, suggesting an anxiogenic effect. In the memory tests, there was cognitive impairment, evidenced by a lower discrimination index in the OLT and ORT tests and reduced performance in the Y-maze. There was a decrease in hepatic SOD activity in the STZ groups compared to the SHAM group. Furthermore, a significant reduction was observed in the SHAM sucrose group compared to the SHAM water and SHAM saccharin groups, suggesting an alteration in the antioxidant system. Additionally, BChE activity increased in the STZ-lesioned rats. **Conclusion:** In conclusion, ICV-STZ administration induced significant cognitive impairment in spatial, recognition, and working memory, accompanied by a decrease in locomotion and exploration, as well as oxidative and cholinergic imbalance, mimicking deficits characteristic of AD. The consumption of sucrose and saccharin did not aggravate the neurodegenerative phenotype induced by STZ. However, sucrose promoted body weight gain and increased oxidative stress in SHAM group, demonstrating that the metabolic-redox alterations triggered by the diet occur independently of the neurodegenerative pathology. The experimental protocol was approved by the Animal Experimentation Committee of the Federal University of Paraná (CEUA/BIO UFPR 1804). Supported by CAPES.

02.071 **Distinct Behavioral Effects of Short-Term Voluntary Running in Phosphatase and Tensin Homolog Deleted on Chromosome 10 Neuronal Haploinsufficient Mice**. Andreotti DZ[1], Mello NP[1], Paixão AG[1], Scavone C[2], Orellana AMM[2], Kawamoto E[1]. [1]ICB-USP, Lab Molecular and Functional Neurobiology; [2]ICB-USP, Lab Molecular Neuropharmacology

Introduction: Phosphatase and tensin homolog deleted on chromosome ten (PTEN) is a tumor suppressor wich plays several roles, such as cell proliferation, survival, and migration, involved in neurogenesis and synaptic plasticity in the central nervous system. It has been reported that running could have protective effects against the aging process and neurodegenerative diseases. Therefore, we aimed to evaluate the effects of physical exercise on behavioral and biochemical aspects of PTEN-conditioned knockout female mice. **Methods:** Females of the Ptenloxp/+/Nse-Cre+ lineage (WT and HT) were divided in sedentary and exercised individuals. The voluntary physical exercise protocol involved providing a rotating wheel inside the mouse home cage, allowing the mice to engage involuntary physical exercise for 10 days. After this, behavioral tests were performed, starting with the open field test, followed by the elevated plus maze, social behavior, and passive avoidance test. One day after the last behavior test, the mice were euthanized, and the cerebral cortex was dissected and kept frozen at -80°C until protein extraction for western blotting assay. **Results:** Voluntary running positively affected fear memory but caused no changes in anxiety-like behavior. However, it was unable to counteract the social recognition memory deficit in PTEN neuronal haploinsufficient mice. In terms of biochemical aspects, we observed that voluntary running reduced S6 phosphorylation in PTEN heterozygous mice and PTEN protein expression independent of the genotype. In addition, PTEN heterozygous mice presented reduced N-methyl-D-aspartate subunit NR1 protein expression. **Conclusion:** Decreased S6 phosphorylation in HT mice suggest that short-term voluntary running could have induced a protective effect in reducing dysregulated cell growth, possibly related to the downregulation of PTEN. Moreover, running induced distinct behavioral effects in PTEN-conditioned knockout mice. **Financial Support:** CAPES/CNPQ, FAPESP (2016/22996-9). Ethics approval: CEUA ICB/USP, protocol 114/2014

02.072 **Neuroprotective and Anticonvulsant Effects of *Limnospira platensis* Aqueous Extract in Acute Pentylenetetrazol-Induced Seizures in Mice**. Souto TL[1], Almeida LS[1], Bentes ILG[1,2] Nascimento AA[1], Do Nascimento JLM[3], Oliveira EDC[4], Faustino SMM[1], Oliveira FR[1,2]1Unifap, School of Pharmacy, Brazil. [2]Unifap, PPG Pharmaceutical Sciences, Brazil. [3]UFPA, PPG Pharmacology and Biochemistry. [4]IEPA, Lab Taxonomy and Ecology of Cyanobacteria and Microalgae, Brazil.

Introduction: Seizures are major clinical events characterized by involuntary muscle contractions and altered consciousness. The high prevalence of chemoresistance highlights an urgent need for novel therapeutic alternatives. In this context, microalgae emerge as rich sources of bioactive secondary metabolites with human health applications. Notably, phycocyanin, a blue phycobiliprotein, stands out for its well-documented antioxidant, immunomodulatory, and neuroprotective activities. **Objective:** To evaluate the neuroprotective effect of a *L. platensis* aqueous extract (EALP) on a chemically induced seizure in mice. **Methods:** The dry biomass of *L. platensis* was provided by Blue Green Nutrition®. The aqueous extract was obtained using the freeze-thawing method in three 24-hour cycles (18 hours at –80 ºC and 4 hours at room temperature) using distilled water as a solvent in a 3% biomass/solvent ratio and lyophilized. Phycocyanin content, yield and purity was determined by spectrometry. Male mice (*Mus musculus*) (25-30g) were divided into 4 groups (N=10) (0.9% saline solution, Diazepam 2 mg/kg, EALP 50 mg/kg, EALP 100 mg/kg) and 1 SHAM group with 3 animals, maintained in the Laboratory of Animal Experimentation (LEA) of the Federal University of Amapá, in a controlled environment (23–25ºC, 12 h light-dark cycle), free access to food and water. For 7 days, mice were treated orally with 0.9% saline or EALP (50 and 100 mg/kg), or intraperitoneally (i.p.) with Diazepam (2 mg/kg). On the last day, animals were challenged with pentylenetetrazol (PTZ, 60 mg/kg, i.p.). Seizure latency and duration were evaluated as behavioral parameters, followed by nitrite levels in brain samples. The Ethics Committee on Animal Use of the Amapá Federal University approved experimental protocol number 006/2025. **Results:** Phycocyanin content, crude extract yield, and purity were, respectively, 0.2674 ± 0.001 mg/mL, 8.92% ± 0.041, and 0.579 ± 0.005. Diazepam and EALP (100 mg/kg) prevented all seizure episodes. However, EALP (50 mg/kg) increased tonic-clonic seizure latency (432.1 ± 71.50 s vs. 131.9 ± 22.50 s for saline) and reduced duration of seizures (3.80 ± 1.45s vs. 11.14 ± 1.68s for saline). Biochemical data confirmed these effects: nitrite levels were significantly higher in the saline control group (4.46 ± 0.27) than in the Diazepam (3.33 ± 0.26), EALP 50 mg/kg (3.52 ± 0.12), and EALP 100 mg/kg (3.50 ± 0.17) groups, demonstrating a reduction in seizure-induced oxidative damage. **Conclusion:** Treatment with EALP demonstrates significant neuroprotective effects by attenuating both PTZ-induced behavioral seizure parameters and oxidative damage in mice. **Acknowledgments:** The authors thank the National Council for Scientific and Technological Development (CNPq, Brazil) for **Financial support** (grant #444009/2024-8).

02.073 **Anti-Inflammatory and Antiapoptotic Effects of the Bioinspired Peptide Neurovespina in an Experimental Model of Temporal Lobe Epilepsy**. Mortari MR, Oliveira BCC, Camargo LC, Lima LS UnB, Lab Neurofarmacologia, Instituto de Ciências Biológicas, Brasília, DF, Brazil.

Introduction: Temporal lobe epilepsy (TLE) is one of the most common and pharmacoresistant neurological disorders and is strongly associated with neuroinflammation, neuronal death, and progressive hippocampal damage. Current antiseizure therapies are often insufficient to prevent disease progression and may cause significant adverse effects. Bioinspired peptides derived from animal venoms have emerged as promising therapeutic candidates due to their neuroprotective and immunomodulatory properties. Neurovespina, a peptide inspired by compounds identified in social wasp venom, has demonstrated anticonvulsant potential in previous studies; however, its effects on inflammatory and apoptotic pathways in epilepsy remain poorly understood.** Objective **This study aimed to evaluate the anti-inflammatory and antiapoptotic effects of the bioinspired peptide Neurovespina in an experimental model of temporal lobe epilepsy. **Methods:** Male Swiss mice were randomly distributed into four experimental groups: healthy control, epileptic vehicle-treated, Neurovespina-treated (4.0 and 2.5 mg/kg), and positive control. Temporal lobe epilepsy was induced using the pilocarpine model following methyl-scopolamine pretreatment. Neurovespina or vehicle was administered intraperitoneally 60 minutes after *status epilepticus* induction. Histopathological analyses were performed using hematoxylin-eosin staining and immunofluorescence to evaluate neuroinflammatory markers and neuronal damage in hippocampal regions. Interleukin-1 beta (IL-1β) expression was assessed to investigate inflammatory modulation associated with epileptogenesis. **Results**: Neurovespina treatment significantly reduced neuroinflammatory responses and neuronal degeneration in hippocampal regions critically involved in epileptogenesis. Histological analyses demonstrated preservation of neuronal architecture and attenuation of tissue injury in treated animals compared with epileptic controls. In addition, Neurovespina reduced IL-1β expression, indicating modulation of inflammatory pathways associated with seizure-induced neurodegeneration. The peptide also exhibited antiapoptotic effects, suggesting a neuroprotective role against epilepsy-related neuronal death. **Conclusion:** The present findings demonstrate that Neurovespina exerts significant anti-inflammatory, antiapoptotic, and neuroprotective effects in an experimental model of temporal lobe epilepsy. These results support the therapeutic potential of this bioinspired peptide as a promising candidate for the development of disease-modifying therapies targeting the underlying mechanisms of epileptogenesis rather than exclusively seizure suppression.

02. Environmental Biology, Evolution and Comparative Biology

02.001FR **Monitoring of Post-Consumer Medicine Disposal: A Strategy for Mitigating Environmental Risks in Cabedelo, Paraíba, Brazil**. Oliveira RVS[1], Lira JVR[1], De Aróla AB[1], Nunes LFC[2], Martins ERV[3], Vitorino LM[4], Souza CO[4], Honório VM[4], Matos ACL[4], Lima GAS[4], Miranda LRHMB[4], Pontes AS[4], Luckwu RLB[4], Campana EH[5], Jales STL[5]. [1]UFPB, Undergraduate Program in Pharmacy, Brazil; [2]UFPB, Undergraduate Program in Physical Education, Brazil; [3]UFPB, Undergraduate Program in Speech-Language Pathology and Audiology, Brazil; [4]Municipal Health Dept Cabedelo, Brazil; [5]UFPB, Dept Pharmaceutical Sciences, Brazil

Introduction: Pharmaceutical waste is considered an emerging pollutant due to its ability to cause impacts on public health and ecosystems. The improper disposal of medicines contributes to the contamination of soil, surface water, and groundwater, in addition to affecting non-target organisms and promoting changes in ecological processes. The persistence of these compounds in the environment is further aggravated by their limited removal in conventional wastewater treatment systems. In this context, the implementation of reverse logistics systems associated with environmental education actions constitutes a relevant strategy to reduce the release of these contaminants into the environment. **Objective:** To monitor the disposal of household medicines through a reverse logistics system implemented in the municipality of Cabedelo, Paraíba, Brazil, evaluating its contribution to mitigating environmental risks resulting from the improper disposal of pharmaceutical waste. **Methods:** This is a monitoring study developed within the scope of an extension project at the Federal University of Paraíba. Medicine collection points were established in Family Health Units (FHUs) in the municipality, accompanied by environmental education activities conducted both in person in the waiting rooms of the units and through social media. Monitoring was carried out between April 2022 and May 2026 through the quantification of medicines discarded by the population and collected at the collection points. The waste was periodically weighed, and the data was analyzed using descriptive statistics. **Results:** During the evaluated period, 340.7 kg of pharmaceutical waste from post- consumer medicines were collected. The Centro FHU accounted for the highest collected volume, with 261.3 kg, corresponding to 76.7% of the total. The other units presented the following quantities: Jardins FHU (25.9 kg), Renascer FHU (17.2 kg), Leonor Viana FHU (16.8 kg), Siqueira FHU (14.1 kg), Intermares FHU (5.4 kg), and the Psychosocial Care Center (CAPS) (1.7 kg). The differences observed among collection points may be related to factors such as location, duration of collector implementation, user flow, and the reach of educational activities. **Conclusion:** The implementation of reverse logistics for household medicines proved to be a viable strategy for pharmaceutical waste management and for reducing the potential for environmental contamination. The collected volume demonstrates community adherence to the proposed actions and reinforces the importance of maintaining accessible collection points and continuous environmental education activities. Furthermore, the study highlights the role of primary health care in promoting the proper disposal of medicines and strengthening environmental sustainability.

02.002FR **Hypertrophy of the Rectus Femoris and Vastus Lateralis Following Resistance Training with Greater Torque at Lengthened Muscle Positions**. Leite IHA[1], Rodrigues IJS[1], Flora JMG[1], Silva GAB[1], Brandão CFCCM[1], Andrade MJO[2], Drummond LR[1], Lacerda LT[1] [1]UEMG, Dept Physical Education; [2]UEMG Dept Psychology, Brazil

Introduction: One of the main adaptations resulting from resistance training (RT) is muscular hypertrophy. The literature demonstrates that RT performed with a partial range of motion (ROM) at elongated muscle lengths promotes greater hypertrophic responses in the thigh muscles compared to training at shortened muscle lengths. In this context, the CAM device profile, by generating greater torque at longer muscle lengths throughout the full range of motion, may distinctly influence the hypertrophic responses of the biarticular rectus femoris (RF) and the monoarticular vastus lateralis (VL). This response may be related to mechanisms associated with titin and differences in the muscle length×tension relationship. However, evidence regarding the intermuscular effects of resistance training (RT) using a CAM with a resistance profile that promotes greater torque at elongated muscle lengths remains scarce.Parte inferior do formulário **Objective:** To compare the hypertrophic responses of the RF and VL following 12 weeks of training a device that promotes greater torque at lengthened muscle positions. **Methodology:** The study was approved by the Research Ethics Committee of the UEMG de Divinópolis (CAAE: 69318223.0.0000.5115). Ten untrained males were recruited (age: 22.79 ± 2.46 years; height: 176.01 ± 3.32 cm; body mass: 71.97 ± 12.33 kg; BMI: 23.24 ± 3.94 kg/m^2). Training was performed over 12 weeks using knee extension and knee flexion exercises with a descending-radius CAM device attached to the equipment, providing a radius of 36 mm and 18 mm at the beginning and end of the ROM, respectively. The training protocol consisted of 3 sets of 7 repetitions, with a 2-minute rest interval between sets, a repetition duration of 6 seconds (3s concentric action and 3s eccentric action), and an intensity corresponding to 50% of the 1RM test value. Cross- sectional area measurements were obtained at three regions (30%, 50%, and 70% of femur length) of the RF and VL muscles using panoramic-mode ultrasonography (VINNO® V5, Suzhou, China). Data were analyzed using SPSS for Windows version 27.0 (SPSS Inc., Chicago, IL, USA) and expressed as mean ± standard deviation. A two-way repeated-measures ANOVA followed by Bonferroni post hoc tests was used, with significance set at $P \leq 0.05$ and effect size estimated by partial eta squared. **Results:** RT promoting greater torque at lengthened muscle lengths revealed no significant muscle × region interaction, $F(2,54) = 0.820$, $p = 0.446$, $n2p = 0.029$. No main effect of region was observed either, $F(2,54) = 1.099$, $p = 0.340$, $n2p = 0.039$. The main effect of muscle showed a trend toward significance, $F(1,54) = 3.973$, $p = 0.051$, $n2p = 0.069$. **Conclusion:** RT performed at lengthened muscle positions potentiated the hypertrophic response of the RF compared with the VL after 12 weeks of training. This response may be related to the fact that knee extension exercises provided more favorable mechanical conditions for the RF in the hypertrophy response compared to the VL. Foundings: FAPEMIG, CNPq and Pró-Reitoria de Pós-Graduação da UEMG.

03. Psychopharmacology

03.001 **Neuroprotection-Associated Reduction of Anxiety-Like Behavior Induced by *Spondias tuberosa* Arruda in Aged Wistar Rats Assessed by the Light-Dark Box and Open Field Tests**. Lessa IN[1], Souza ETN[1], Costa LL[3], Araújo AB[1,2], Araújo IGA[1,2], Medeiros IA[1,2], Soares JKB[1] [1]UFPB, Cardiovascular Pharmacology Lab, Institute for Research in Drugs and Medicines (IPeFarM), Brazil, [2]UFPB, Professional Master's Program in Gerontology (PPPGERONTO), Brazil, [3]UFCG-Cuité, Graduate Program in Natural Sciences and Biotechnology, Brazil.

Introduction: The aging process is associated with an increased prevalence of neuropsychiatric disorders, especially anxiety disorders, significantly impairing quality of life. D-galactose (D-gal) is widely used to model accelerated aging in rodents. This process culminates in oxidative stress, which intensifies chronic neuroinflammation and contributes to neurochemical alterations associated with anxiety-like behavior. *Spondias tuberosa* Arruda ("umbuzeiro"), rich in flavonoids and organic acids with high phenolic content, is a promising antioxidant source with potential anxiolytic activity. **Objectives:** To investigate the potential neuroprotective effects of the lyophilized hydroalcoholic extract of *Spondias tuberosa* Arruda bark in attenuating anxiety-like and exploratory behavior in male Wistar rats subjected to D-gal-induced aging, using the open field test (OFT) and the light-dark box test (LDB). **Methodology:** The experimental groups (n = 8 per group) were adult control (CG), D-gal, D-gal + umbu 30 mg/kg (FP30), and D-gal + umbu 100 mg/kg (FP100). The treatment lasted 56 days. Following the experimental protocol, the animals were tested in the LDB to assess anxious behaviors. LDB parameters included time spent in the light compartment (TSLC) and the number of transitions between fields. In the OFT, an adaptation of Elliott et al (1993) was used to assess anxious and exploratory behavior in a square black box with side walls and floor markings to delimit areas, under controlled lighting. Parameters evaluated were time in the center, time in the corners, standing on the hind limbs (rearing), and habituation. Each experimental session lasted 10 min. Statistical analysis was performed using one-way ANOVA, followed by Tukey's post-hoc test, with significance set at $p < 0.05$. This study was approved by the Animal Ethics Committee of the Federal University of Paraiba (UFPB) under protocol number 6271030725. **Financial support:** UFPB/PROPESQ **Results:** In the LDB, FP30 showed a significant increase in TSLC compared to the other groups, especially D-gal. In transitions, FP30 and FP100 increased compared to D-gal. In the OFT, FP30 had the longest time in the center. Time in the corners was decreased in FP30 compared to the D-gal group. This demonstrates an anxiolytic effect comparable to the CG group. In rearing, FP30 and FP100 showed a higher frequency compared to the other groups. On habituation, the FP group increased compared to the other groups. This demonstrates greater exploratory behavior, inversely proportional to anxious- type behavior. **Conclusion:** The lyophilized hydroalcoholic extract of *Spondias tuberosa* Arruda bark showed potential anxiolytic and neuroprotective effects in Wistar rats subjected to D-galactose-induced aging. At both FP30 and FP100 doses, the animals demonstrated a reduction in anxious and exploratory behavior, approaching that observed in the control group. Thus, *Spondias tuberosa* Arruda modulates neurobehavioral changes associated with aging.

03.002 **Potential Neuroprotective Effect of Free and Nanoencapsulated THC-Rich** *Cannabis sativa* **extract against nitrosative stress** *in vivo*. Cunha MVS[1,3], Gonçalves MCF[1,2], Silva-Netto LS[1,3], Serra GL[1,3], Almeida JVM[1,3], Teixeira JL[1,3], Neri LCD[1,3], Matos ALLS[1], Dias AL[1,4], Pires HFO[1,4], Cruz LS[2], Silva PR[1,2],4, Xavier-Junior FH[2,3], Santos SG[2,3], Golzio AMFO[1,4,5] [1]UFPB, Psychopharmacology Lab, Brazil, [2]UFPB, PPG Bioactive Natural and Synthetic Products, Institute of Research in Drugs and Medicines, Brazil, [3]UFPB, Health Sciences Center, Brazil, [4]UFPB, PPG Cognitive Neuroscience and Behavior, Brazil, [5]UFPB, Dept Food Technology, Center for Technology and Regional Development, Brazil

Introduction: Nitrosative stress, characterized by an imbalance between reactive nitrogen species (RNS) and the endogenous antioxidant mechanisms responsible for their neutralization, causes damage to lipids, proteins, and nucleic acids, contributing to neurochemical changes associated with disorders such as depression. Despite the growing interest in cannabinoids, the effects of Δ^9-tetrahydrocannabinol (THC) on nitrosative stress markers remain poorly explored, although extracts of *Cannabis sativa* L. rich in THC have already demonstrated neuroprotective properties. In this context, these extracts, evaluated in both free and nanoencapsulated forms, emerge as promising alternatives for investigation. **Objective:** To evaluate the potential neuroprotective effect of *Cannabis sativa* L. extract rich in THC, in its free and nanoencapsulated forms, in an *in vivo* model of dexamethasone-induced depression-like behavior, by quantifying nitrite (NO_2^-) levels. **Methods:** Swiss albino mice were divided into six groups (n=6) and received dexamethasone (64 µg kg^{-1}, subcutaneously, for 21 days) to induce the depression-like model. From day 7 onward, imipramine (30 mg kg^{-1}, intraperitoneally), free THC extracts (5, 10, and 15 mg kg^{-1}, orally), and nanoencapsulated extracts (5, 10, and 15 mg kg^{-1}, orally) were administered concomitantly with dexamethasone. After the treatments, the animals were euthanized, and the prefrontal cortex was isolated for nitrite analysis. The samples were homogenized and centrifuged (10,0 00 rpm, 10 min), and the supernatant was used for nitrite (NO_2^-) quantification by the Griess colorimetric method (absorbance at 546 nm). Data were analyzed by one-way ANOVA followed by Tukey's post hoc test ($p<0.05$). **Results:** Nitrite levels showed a significant increase in the dexamethasone-treated group (11.25 ± 1.05) compared to the control group (5.37 ± 4.08), indicating increased RNS production. In contrast, all groups subjected to the experimental treatments showed lower nitrite concentrations compared to the dexamethasone group. The groups treated with the 5 mg kg^{-1} (E5), E10, and E15 extracts, and the nanoencapsulated 5 mg kg^{-1} (N5), N10, and N15 extracts, exhibited mean values of 6.64 ± 1.90; 3.82 ± 2.15; 4.65 ± 1.99; 5.18 ± 3.53; 4.76 ± 1.20; 7.61 ± 4.83; and 2.82 ± 1.32, respectively. These results suggest that the evaluated treatments attenuated the dexamethasone-induced increase in nitrite levels, indicating a possible protective effect against nitrosative stress. **Conclusion:** The *Cannabis sativa* extracts rich in THC, in their free and nanoencapsulated forms, demonstrated significant neuroprotective potential by attenuating dexamethasone-induced nitrosative stress in the murine prefrontal cortex. These findings highlight the role of cannabinoids as a promising therapeutic alternative for managing nitrosative stress associated with neurodegenerative conditions.

03.003 **Aminothiophene Derivative 7CN03 as a Potential Anti-Inflammatory Agent:** *In vitro* **Analysis of Nitrite and Cytokine Modulation in J774 Macrophage Culture**. Almeida JVM, Mendes LM, Naves FB, Pereira CHL, Alves HAR, Neri LCD, Teixeira JL, Cunha MVS, Barbosa NMMV, Martins AMO, Oliveira LN, Soares MFS, Monteiro AB, Felipe CFB, Silva PR. UFPB, Psychopharmacology Lab

Introduction: The inflammatory process is essential for protecting the body against invading pathogens and cellular damage, and also plays a reparative role in damaged tissues. This process occurs through the release of pro-inflammatory mediators such as prostaglandins, cytokines, and nitric oxide (NO), becoming harmful when there is progression from the acute to the chronic phase. In this context, seeking alternatives that offer safety and fewer side effects, the aminothiophene derivative 7CN03 emerges as a molecule with potential therapeutic activity. **Objective:** To evaluate the cellular toxicity and anti-inflammatory potential of 7CN03 through the quantification of pro-inflammatory cytokines and nitric oxide in J774 macrophage culture. **Methodology:** To determine cell viability, J774 macrophages were incubated in 96-well plates (2×10^5 cells/well) in DMEM medium supplemented with 10% fetal bovine serum and 50 µg/mL gentamicin. 7CN03 was added at concentrations ranging from 3.9 to 1000 µg/mL. Alamar Blue dye was added, and colourimetric readings were taken between 570 nm and 600 nm. Triton X-100 was used as a positive control, and DMSO as the method standard. Subsequently, cells were pre-treated with 7CN03 (3.9 to 500 µg/mL), vehicle (5% DMSO + saline), or Dexamethasone (Dexa, 10 µM) and incubated at 37°C. After 24 hours, the supernatant was collected for nitrite (NO_2^-) quantification using the Griess method, with absorbance measured at 540 nm. Finally, IL-1β and TNF-α quantification was performed following the same protocol, at a 7CN03 concentration of 125 µg/mL. Supernatants were collected after 4 hours, and absorbance was read on a spectrophotometer at 450 nm. Results were expressed as mean ± SEM. For comparisons between groups, one-way ANOVA followed by Tukey's post-hoc test was used. **Results:** In the cytotoxicity assessment, cells treated with Triton X-100 showed a significant decrease in cell viability (5.4 ± 0.32 µM) compared to the control (99.7 ± 0.26 µM). For 7CN03, only the concentration of 1000 µg/mL reduced cell viability (84.1 ± 2.4 µM). An increase in nitrite was observed in the presence of LPS (76.9 ± 1.2 µM) compared to DMSO (13.6 ± 0.1 µM). 7CN03, in turn, reduced these levels at concentrations of 7.9–500 µg/mL (64.9 ± 0.2; 57.2 ± 1.8; 49.9 ± 3.9; 45.5 ± 2.6; 37.8 ± 2.6; 33.6 ± 3.4; 34.6 ± 0.4 µM, respectively), with IC_{50} = 15.8 ± 1.2 µg/mL. The same was observed for Dexa (13.6 ± 0.1 µM/mL). Regarding IL-1β and TNF-α cytokine quantification, no reduction was observed in the presence of 7CN03 at a concentration of 125 µg/mL. **Conclusion:** The aminothiophene derivative 7CN03 presents a safe cellular toxicity profile and a potential anti-inflammatory effect by reducing nitrite concentrations, suggesting a possible modulatory mechanism involving the nitric oxide pathway. Financial support: PIBIC/CNPq, PPgPNSB/UFPB.

03.004 *in silico* and *in vivo* Evaluation of GABAergic Neurotransmission in the Anxiolytic-Like Effect of the Thiophenic Derivative 6CN07. Mendes LM, Naves FB, Almeida JVM, Pereira CHL, Alves HAR , Alves ARS, Teixeira JL, Neri LCD, Barbosa NMMV, Martins AMO, Oliveira LN, Soares MFS, Silva PR, Monteiro AB, Felipe CFB UFPB, Psychopharmacology Lab, Brazil

Introduction: Anxiety disorders are the most prevalent psychiatric conditions worldwide. Modulation of the GABAergic pathway by benzodiazepine (BZP) drugs constitutes an important strategy for relieving acute anxiety symptoms. However, the clinical use of these drugs is limited by their adverse effects and a high risk of dependence. Objectives: To investigate the pharmacochemical profile and interaction of 6CN07 with pharmacological targets involved in the neurobiology and treatment of anxiety disorders, utilizing both *in silico* and *in vivo* approaches. Methods: *in silico* prediction of absorption, distribution, metabolism, and excretion (ADME) parameters was performed using SwissADME and PhaKinPro tools. Molecular docking of 6CN07 at the GABAergic receptor GABA**A **receptor was conducted using Molegro Virtual Docker 6.0 software to determine binding energies. The anxiolytic-like effect was evaluated *in vivo* in Swiss albino mice (*Mus musculus*), with a mean body weight of 25 g, which were distributed into distinct groups (n = 6), using the Elevated Plus Maze (EPM) and Light-Dark Box (LDB) tests. The evaluated parameters included: Number of Entries into Open Arms (NEOA), Time Spent in Open Arms (TSOA), Number of Entries into the Light Compartment (NELC), and Time Spent in the Light Compartment (TSLC). Animals were treated with saline solution (10 mL/kg, p.o.; CG = control group), 6CN07 (50 mg/kg, p.o.), or diazepam (1 or 2 mg/kg, i.p.). To investigate the mechanism of action of 6CN07, animals were pre-treated with flumazenil (20 mg/kg, i.p.). All protocols were approved by the Animal Use Ethics Committee of UFPB (No. 5940100524). Data were expressed as mean ± S.E.M. and analyzed by ANOVA or unpaired t-test ($p < 0.05$). Results: *in silico* analyses demonstrated that 6CN07 exhibited favorable pharmacokinetic properties, including a molecular weight <500 Da, TPSA of 64.39 Å², LogP of 5.08 and high gastrointestinal absorption. In molecular docking, 6CN07 showed strong binding energy to the GABA**A** receptor (score of -52.32 kcal/mol). *In vivo* analysis showed that 6CN07 significantly increased NEOA (6.1 ± 1.0) and TSOA (64.7 ± 9.6) in the EPM compared to the CG (3.3 ± 0,5; 34.7 ± 9.3; respectively). Similarly, an increase was observed for NELC (19.5 ± 1.1) in the LDB when compared to the control (15.8 ± 0.4). Differently, treatment with 6CN07 (124.2 ± 9.5) did not increase TSLC when compared to the control (102.5 ± 5.6). However, when the animals were pre-treated with flumazenil, the observed changes were reversed in NEOA (3.1 ± 0.7), TSOA (39.8 ± 7.8), NELC (12.7 ± 0.9) and TSLC (66.7 ± 3.4), indicating GABA**A** receptor involvement in the anxiolytic-like effects of 6CN07. Conclusions: 6CN07 presents a pharmacokinetic profile compatible with anxiolytic drugs and exerts an anxiolytic-like effect involving, at least in part, GABAergic neurotransmission. Further molecular studies are warranted to clarify the effects of this derivative. Financial support: CAPES, UFPB.

03.005 **Evaluation of the Potential Anxiolytic-Like Effect of the Compound (Z)-N'-(1-Benzyl-2-Oxoindolin-3-Ylidene)-2-Fluorobenzohydrazide (ISA) Through *in silico* and *In vivo* Studies**. Naves FB[1], Mendes LM[1], Pereira CHL[1] Almeida JVM[1], Alves HAR[1], Teixeira JL[1], Barbosa NMMV[1], Martins AMO[1], Oliveira LN[1], Neri, LCD[1], Soares MFS[1], Silva PR[1], Monteiro AB[1], Lima-Junior CG[2], Felipe CFB[1]. [1]UFPB. Psychopharmacology Lab, Brazil. [2]UFPB. Medicinal Organic Synthesis Lab.

Introduction: Anxiety disorders constitute a relevant public health problem due to their high prevalence and significant therapeutic limitations, which justifies the prospection of new pharmacological alternatives. **Objectives:** To evaluate the potential anxiolytic-like effect of the compound (Z)-N'-(1-benzyl-2-oxoindolin-3-ylidene)-2-fluorobenzohydrazide (ISA) through *in silico* and *in vivo* methodologies. **Methods:** For the *in silico* methodologies, molecular docking was performed using AutoDock Vina and GOLD for the 5-HT1A, 5-HT2A, and 5-HT3A receptors. For the *in vivo* methodologies, male Swiss albino mice were used and subjected to the following behavioral tests: the Elevated Plus Maze (EPM) and Light-Dark Box (LDB), which evaluated the anxiolytic-like effect of ISA; the Open Field (OF) test, which evaluated the effect of ISA on the locomotor activity of the animals; and the Rota-Rod (RR) test, which evaluated the effect of ISA on the motor coordination of the mice. In order to investigate the potential mechanism of action of the compound, a pharmacological antagonism test with flumazenil was performed. Data were expressed as mean ± S.E.M. and analyzed by ANOVA or unpaired t-test ($p < 0.05$). **Results:** *in silico* analyses indicated that the compound exhibits stable interactions with serotonergic receptors 5-HT1A (-11.5 Kcal/mol), 5-HT2A (-13.5 Kcal/mol), and 5-HT3A (-12.1 Kcal/mol). In the *in vivo* studies, ISA (2.5 mg/kg, 5 mg/kg, 10 mg/kg, and 20 mg/kg, p.o.) increased the number of entries (7.0 ± 1.4; 4.8 ± 0.7; 6.6 ± 1.6; 5.0 ± 1.0, respectively) and the time spent in the open arms (72.1 ± 13.6; 48.8 ± 9.5; 55.6 ± 13.5; 40.1 ± 10.2, respectively) in the EPM. In the Open Field and Rota-Rod tests, the compound did not alter the locomotor activity or motor coordination of the animals, respectively. In the pharmacological antagonism test, pretreatment with flumazenil (20 mg/kg, i.p.) significantly decreased the number of open arm entries (3.5 ± 0.6) and time spent in the open arms (47.33 ± 8.2) of the animals treated with ISA (2.5 mg/kg, p.o.) compared to the groups that received the compound alone in the EPM. In the LDB, pretreatment with flumazenil (20 mg/kg, i.p.) significantly decreased the number of entries into the light compartment (13.67 ± 1.60) and time spent in the light compartment (96 ± 11.31) of the animals treated with ISA (2.5 mg/kg, p.o.) compared to the groups that received the compound alone. **Conclusion:** ISA appears to present a pharmacodynamic profile similar to anxiolytic drugs, whose effect seems to involve, at least in part, serotonergic and GABAergic receptors, without causing impairment to the motor function of the animals. However, additional studies are necessary for a better understanding of the compound's effects, especially at the molecular level. Animal Research Ethical Committee Number: All protocols were approved by the Ethics Committee on Animal Use of UFPB (no. 2438110524). **Financial support**: PPgPNSB/UFPB and CAPES.

03.006 **Paroxetine Dose-Dependently Attenuated the Impaired Fear Extinction in Female iNOS Knockout Mice**. Barbosa KE, Meyer E, Da Silva TA, Lisboa SF FCFRP-USP, Dept Biomolecular Sciences, Brazil

Introduction: Post-traumatic stress disorder (PTSD) may develop following exposure to traumatic events and is characterized by aberrant fear memories that are intense, inflexible, and resistant to attenuation through extinction. Selective serotonin reuptake inhibitors, including paroxetine, are first-line pharmacological treatments for PTSD. Inducible nitric oxide synthase knockout (iNOS KO) mice present impaired contextual conditioned fear extinction resembling a PTSD phenotype, suggesting their potential as a genetic PTSD model. However, further evidence regarding the pharmacological validity of this strain is lacking. **Aim:** To investigate whether paroxetine attenuates impaired fear extinction in female iNOS KO mice in the contextual fear conditioning (CFC) paradigm. **Methods:** Female C57Bl/6J and iNOS KO mice (8 weeks old) received three footshocks (0.75 mA, 2 s) in the conditioning box. After 24 h, mice received paroxetine (5-20 mg/kg, intraperitoneally) or vehicle 30 min before re-exposure to the box for 20 min to evaluate extinction acquisition. Extinction recall was assessed for 5 min on day 3. Procedures were approved by the Ethical Review Committee of the Pharmaceutical Sciences School of Ribeirão Preto (CEUA no. 22.1.732.60.9). **Results:** Paroxetine reduced CFC expression (first 5 min of extinction acquisition session) in wild type but not iNOS KO mice. iNOS KO mice showed impaired fear extinction, evidenced by elevated freezing during extinction and recall sessions, whereas wild-type groups showed successful extinction recall. Although paroxetine did not facilitate extinction acquisition in iNOS KO mice, the highest dose (20 mg/kg) improved extinction memory recall.. **Conclusion:** Paroxetine facilitated extinction memory recall in iNOS KO mice, supporting the use of this strain as a genetic model of PTSD.

03.007 **Investigation of the Antidepressant-Like Profile of Tetrahydrolinalool in a Lipopolysaccharide-Induced Neuroinflammation Model: an *in vivo* Study**. Neri LCD[1], Gonçalves MCF[1], Cunha MVS[1], Almeida JV[1], Mendes LM[1], Teixeira JL[1], Naves FB[1], Pereira CHL[1], Alves HAR[1], Barbosa NMMV[1], Rêgo IA[1], Monteiro AB[1], Felipe CFB[1,2], Alves ARS[1], Silva PR[1,2]. [1]UFPB, Psychopharmacology Lab, Institute of Drugs and Medicines Research, Brazil, [2]UFPB, PPG in Cognitive Neuroscience and Behavior, Brazil

Introduction: Depression is a multifactorial mental disorder associated with neurochemical, inflammatory, and oxidative alterations. Evidence indicates that neuroinflammation contributes to the development of depressive-like behaviors, making it an important therapeutic target. Tetrahydrolinalool (THL), a synthetic derivative of linalool, has demonstrated pharmacological potential related to neuroprotective and antioxidant properties. **Objectives:** To evaluate the effect of THL on depressive-like behavior in mice subjected to lipopolysaccharide (LPS)-induced neuroinflammation. **Methods:** Thirty-two male *Mus musculus* Swiss mice were used and distributed into four groups (n = 8): Control, LPS (0.5 mg/kg, i.p.), THL (150 mg/kg, p.o. + LPS), and Fluoxetine (10 mg/kg, p.o. + LPS). Treatments were administered for seven consecutive days. Behavioral assessment was performed using the forced swimming test, and immobility time was recorded. Data were expressed as mean ± standard error of the mean (SEM) and analyzed by one-way ANOVA followed by Tukey's post hoc test or Student's *t*-test, considering $p < 0.05$. **Results:** The LPS group showed a significant increase in immobility time (175 ± 16 s) compared with the control group (141 ± 13 s), confirming the induction of depressive-like behavior. THL treatment significantly reduced immobility time (131 ± 18 s) compared with the LPS group ($p < 0.0003$) and did not differ from the control group. Similar results were observed for fluoxetine, used as the reference drug. These findings suggest that THL was able to attenuate the behavioral alterations induced by neuroinflammation. **Conclusion:** Tetrahydrolinalool exhibited an antidepressant-like effect in the LPS-induced neuroinflammation model, significantly reducing depressive-like behavior as assessed by the forced swimming test. These results reinforce the pharmacological potential of THL as a promising candidate for the investigation of novel therapeutic strategies for depressive disorders.

03.008 **Effect of Dietary Inulin Supplementation on the Kynurenine Pathway and the Behavior of Rats Submitted to Alcohol Withdrawal**. Torres CLF[1], Albino MC[1], Oliveira JTA[1], Santos LC[1], Silva MS[1], Silva RT[1], Gavioli EC[1], Ferreira FR[2], Soares VP[1]. [1]UFRN, Dept Biophysics and Pharmacology, [2]Fiocruz, Brazil

Introduction: Behavioral alterations have been observed following different periods of alcohol withdrawal. The kynurenine pathway mediated by enzyme indoleamine 2,3-dioxygenase (IDO) has been suggested as an important modulator of negative emotional states caused by protracted alcohol abstinence. Conversely, inulin has been shown to regulate serotonin metabolism and reduce anxiety- and depressive-like behaviors caused by acute ethanol withdrawal in mice. **Objectives:** Therefore, the present study aimed to investigate whether inulin attenuates anxiety- and depressive-like behaviors induced by protracted alcohol withdrawal through modulation of IDO activity in brain regions associated with emotional regulation in rats. **Methods:** Sixty-eight female Wistar rats (85 ± 5 days old) were divided into four groups: control, ethanol withdrawal, withdrawal treated with 10% inulin, and withdrawal treated with 30% inulin. The experimental protocol consisted of 21 days of ethanol (2, 4 and 6%) as only source of liquid diet, followed by 22 days of abstinence. Inulin treatment was initiated on the 14th day of ethanol exposure and continued for a total of 33 days via gavage. At the end of the protocol, animals were subjected to the elevated plus maze, sucrose splash test, forced swim test, and marble burying test, in addition to biochemical analyses. Data were analyzed using one-way ANOVA followed by Duncan's post hoc test, Kruskal- Wallis's test, or Friedman's test (for marble burying), adopting a significance level of 5% ($p < 0.05$). **Results:** Protracted ethanol withdrawal induced anxiety- and depressive-like behaviors in female rats. In the elevated plus maze, the withdrawal group showed fewer entries into the open arms compared to the control group, with no significant differences in time spent in the open arms. In the marble burying and forced swim tests, the withdrawal and withdrawal + 10% inulin groups exhibited increased marble burying behavior and longer immobility time, respectively, compared to controls. In contrast, treatment with 30% inulin attenuated anxiety- and depressive-like behaviors compared to the other withdrawal groups. No significant differences were observed in the sucrose splash test. Biochemical analyses revealed that kynurenine levels in the frontal cortex, hippocampus, and striatum were not affected by the treatments. **Conclusion:** Chronic ethanol withdrawal induced anxiety- and depressive-like behaviors in female rats without altering IDO activity in the analyzed brain regions. Treatment with 30% inulin partially attenuated these behavioral alterations, suggesting that prebiotics may represent a promising adjunctive strategy in the context of alcohol dependence. Further studies are needed to clarify the role of the kynurenine pathway in the modulation of behavioral changes associated with alcohol withdrawal.

03.009 **Evaluation of the Molecular Mechanisms of the Neuroprotective Action of Cinnamic Alcohol in the Pentylenetetrazol-Induced Chemical Kindling Model**. Alves HAR, Mendes LM, Naves FB, Almeida JVM, Pereira CHL, Neri LCD, Alves ARS, Teixeira JL, Barbosa NMMV, Martins AMO, Oliveira LN, Soares MFS, Silva PR, Monteiro AB, Felipe CFB UFPB, Psychopharmacology Lab, Brazil.

Introduction: Epilepsy affects millions of people and can lead to progressive neurodegeneration after recurrent seizures due to excitotoxicity, oxidative stress, and neuroinflammation. Since current antiepileptic drugs fail to prevent this neurodegeneration and often cause adverse effects, researching new compounds capable of modulating neuronal death mechanisms is essential. In this context, cinnamic alcohol (CA), a phenylpropanoid from the essential oil of Cinnamomum spp. Schaeff (cinnamon), emerges as a promising candidate, as it has demonstrated important anti-neuroinflammatory and neuroprotective activities. **Objectives:** To evaluate the molecular mechanisms of the neuroprotective action of CA in the pentylenetetrazol (PTZ)-induced chemical kindling model. **Methods:** Male Swiss mice (n = 8 per group) were pretreated with CA (0.7 mg/kg, i.p.) and, 60 minutes later, received PTZ (30 mg/kg, i.p.) for 21 consecutive days. The behavioral parameter analyzed was the latency to the first focal bilateral tonic-clonic seizure (LFC). To investigate the mechanism of action of CA, neurochemical analyses of oxidative stress markers (malondialdehyde (MDA) and nitrite), and the activity of the antioxidant enzymes catalase, superoxide dismutase (SOD), and glutathione peroxidase (GSH- Px) were performed, in addition to histomorphometry and immunohistochemistry for IL-1β in hippocampal samples. Statistical analysis was performed by ANOVA followed by Tukey's test ($p < 0.05$). **Results:** Treatment with CA increased LFC (33.9–47.3%) compared to the vehicle group. CA reduced MDA (35.1%) and nitrite (58.7%) concentrations and increased GSH-Px activity (28.0%). Histomorphometry revealed reduced inflammation and greater neuronal preservation (22.2%), evidenced by the absence of vascular reaction and hippocampal neuronal apoptosis. Immunohistochemistry demonstrated diffuse and weak IL-1β immunoreactivity in hippocampal cells of animals pretreated with CA. **Conclusion:** The results indicate that the neuroprotective activity of CA in the chronic model of epileptic seizures involves, at least in part, the attenuation of oxidative stress and neuroinflammatory processes. Moreover, the significant increase in LFC indicates a delay in seizure onset, suggesting reduced neuronal hyperexcitability and reinforcing the neuroprotective effect of CA observed through the biochemical, histological, and immunohistochemical findings. These findings support cinnamon as a natural source of bioactive compounds with pharmacological activity in the central nervous system and potential therapeutic value against epilepsy-associated neurodegeneration. Animal Research Ethical Committee Number: 9590240423. **Financial support:** CNPq.

03.010 **Psychotropic Medication Use Among Medical Students in Paraíba, Brazil**. De Aragão MSO, De Oliveira Neto RG, De Andrade MRD, Viana MS Barbosa JLM1, Barbosa YCM, Lima FJB UNIFACISA, Centro Universitário

Introduction: Mental disorders have become increasingly prevalent in recent years, contributing to a rise in the use of psychotropic medications. In addition, these drugs are frequently associated with self-medication and misuse, even among healthcare students and professionals. Objectives To characterize patterns of psychotropic drug use among medical students in Paraíba, Brazil. **Methods**: A cross-sectional study was conducted through an online questionnaire shared on the researchers' social media platforms. Participants who met the inclusion criteria were encouraged to respond and share the questionnaire with other students, following a snowball sampling strategy. Participants were required to be at least 18 years old and enrolled in a medical degree program in the state of Paraíba, Brazil. Descriptive data were expressed as percentages and mean ± standard deviation. **Results**: A total of 124 medical students from universities located in the cities of João Pessoa, Campina Grande, Patos, and Cajazeiras responded to the questionnaire between May and September 2025. Participants were enrolled from the first to the twelfth semester. The mean age was 25.4 ± 5.6 years. Most participants were women (70.2%), self-reported as White (67.7%), and did not have a formal employment contract (94.4%). The most frequently reported mental health diagnoses were anxiety disorders (51.6%), depression (27.4%), and attention deficit hyperactivity disorder (12.9%). A total of 59.7% of participants (n = 74) reported current or previous use of psychotropic medications since the beginning of medical school. The most used medications included antidepressants (e.g., sertraline), sedative-hypnotics (e.g., clonazepam) and psychostimulants (e.g., methylphenidate). Among psychotropic medication users, 45 (60.8%) reported exclusive use under medical prescription, whereas 29 (39.2%) reported using some or all medications without medical prescription. Antidepressants were the most reported drugs among participants who exclusively used prescribed psychotropic medications (84.4%), followed by sedative-hypnotics (26.7%) and psychostimulants (26.7%). In contrast, participants reporting partial or complete use without medical prescription more frequently reported psychostimulants (58.6%) followed by antidepressants (55.2%) and sedative-hypnotics (48.3%). **Conclusion** Psychotropic medication use was highly prevalent among medical students, including considerable proportion reporting use without medical prescription. The findings reinforce the need for mental health support strategies and rational psychotropic medication use among medical students.

03.011 *in silico* **Evaluation of the Anti-Inflammatory Potential of the Aminothiophene Derivative 7CN03 on COX-2, iNOS, and NF-κB Molecular Targets**. Teixeira JL, Mendes LM, Naves FB, Pereira CHL, Alves HAR, Neri LCD, Almeida JVM, Cunha MVS, Barbosa NMMV, Martins AMO, Oliveira LN, Soares MFS, Monteiro AB, Felipe CFB, Silva PR, UFPB, Psychopharmacology Lab, Brazil

Introduction: Although inflammation is vital for tissue defense, its chronicity is deleterious due to the release of pro-inflammatory mediators. Thus, investigating enzymatic machinery and regulatory transcription factors becomes crucial in the search for safe molecules that can negatively modulate this activity. In this context, the thiophenic derivative 7CN03 emerges as a therapeutic alternative. **Objective:** To investigate the pharmacochemical properties of the aminothiophenic derivative 7CN03 and its interaction with pro-inflammatory targets. **Methodology:** For the *in silico* study, the 3D structure of 7CN03 was modeled in MarvinSketch (v.23.14) and optimized by molecular mechanics in Spartan '14', using mathematical functions that describe the energy of the system as a function of atomic coordinates. The algorithm was validated in Molegro Virtual Docker 6.0 by redocking the co- crystallized ligand, yielding a root-mean-square deviation ≤ 2 Å. The structures of COX-2, iNOS, and NF-κB were obtained from the Protein Data Bank database. Molecular docking was performed without water and cofactors, employing the MolDock SE algorithm (20 runs) and the MolDock Score energy function to calculate the affinity of each generated pose and to filter for internal, torsional, and hydrogen-bonding energies. The affinity grid (radius of 15 Å; resolution of 0.30 Å) was centered on the complexed ligands of COX-2 and iNOS, and on the active site amino acids of NF-κB described in the literature, with analysis of poses and molecular interactions using Discovery Studio Visualizer, referencing celecoxib, dexamethasone, and methylene blue. **Results:** The results present estimates of the binding energy of the ligand–target complexes, with lower binding energy indicating greater expected stability and affinity of the interaction between the ligand and the molecular target. They indicate that with respect to COX-2, although celecoxib (–138.22) and dexamethasone (–109.54) exhibit higher energetic affinity than 7CN03 (–98.47), the latter surpassed them in expressing favorable interactions with critical residues (Ala527, Val349, and Ser530). For iNOS, 7CN03 showed strong anchoring and a lower score (–99.84) than methylene blue (–63.03), binding to essential inhibitory amino acids (Ala351, Tyr347, and Pro350). On the other hand, in NF-κB, the compound also outperformed dexamethasone (–49.65), registering a lower score (–80.89), due to a high density of alkyl and pi- alkyl interactions, which outweigh unfavorable Bump-type interactions. The 7CN03 derivative showed strong molecular affinity for the investigated targets, surpassing the reference drugs for iNOS and NF-κB, and preserved favorable contacts at COX-2 sites. **Conclusion:** The aminothiophenic derivative 7CN03 presents a promising pharmacological profile as a potential anti- inflammatory agent, underscoring the need for continued studies to evaluate its efficacy and safety. **Financial support**: CNPq, CAPES.

03.012 **Effects of *Artocarpus heterophyllus* Seed Core Extract on Behavioral, Metabolic, and Reproductive Parameters**. Alves ALF[1], Oliveira HL[1], Veríssimo TB[2], Alexandre SVD[1], Silva MS[1], Fernandes SEA[1], Costa Pinto MFN[1], Sena MO[1], Carvalho YV[1], Costa ML[1], Silva ED[1], Pedrini MR[2], Matsui KN[2], Soares VP[1]. [1]UFRN, Dept Biophysics and Pharmacology, [2]UFRN, Dept Food Engineering, Brazil.

Introduction: Seeds of *Artocarpus heterophyllus* (jackfruit) contain several bioactive compounds, including phenolic compounds, flavonoids, lignans, saponins, carotenoids, and minerals. Previous studies demonstrated that acute administration of jackfruit seed extract inhibited sexual performance in male rats, an effect attributed to sedation. Therefore, investigating the effects of prolonged exposure to jackfruit seed core extract on behavioral, metabolic, and reproductive parameters is relevant for characterizing its pharmacological and toxicological profile. **Objectives:** To evaluate the effects of treatment with the seed core extract of jackfruit on behavioral, biochemical, and reproductive parameters in male rats. **Methods:** The study used 35 male Wistar rats, aged 3-4 months, divided into control, 0.5 g/kg extract-treated, and 1 g/kg extract-treated groups, administered by gavage for 20 days. Behavioral tests (elevated plus maze, open field and forced swimming tests), biochemical analyses, reproductive function assessment and isolated organ bath experiments were performed. Data were analyzed using ANOVA followed by Tukey's test or Kruskal-Wallis followed by Dunn's test, as appropriate, adopting $p<0.05$. **Results:** Treatment with the jackfruit seed core extract promoted behavioral, metabolic, and reproductive alterations in male rats. Increased immobility time was observed in the forced swimming test, without concomitant alterations in anxiety-related behaviors evaluated in the elevated plus maze and open field tests. In the biochemical parameters, there was a dose-dependent increase in glycemia and a significant reduction in gamma-GT activity, without relevant alterations in AST, ALT, urea, and creatinine. Regarding reproductive parameters, the 1 g/kg dose reduced the number of spermatids and daily sperm production, in addition to promoting slowing of sperm transit, reduction of progressive motility, and increased morphological alterations in the flagellum, without compromising sperm vitality. In the *in vitro* assays, the extract reduced norepinephrine-induced contraction of the vas deferens, suggesting interference in smooth muscle contractility. **Conclusion:** The jackfruit seed core extract exhibited dose-dependent behavioral, metabolic, and reproductive effects in male rats. Treatment with 1 g/kg increased immobility in the forced swimming test, induced hyperglycemia, and impaired sperm production and quality, indicating the need for further studies to clarify the mechanisms underlying these effects and to establish the safety profile of prolonged exposure to the extract.

03.013 **Involvement of Serotonergic Neurotransmission without Anxiolytic-Like Effect of the Thiophene Derivative 6CN07:** *in silico* **and** *in vivo* **Studies**. Pereira CHL, Mendes LM, Naves FB, Almeida JVM, Alves HAR, Alves ARS, Teixeira JL, Barbosa NMMV, Martins AMO, Oliveira LN, Neri, LCD, Soares MFS, Silva PR, Monteiro AB, Felipe CFB. UFPB. Psychopharmacology Lab, Brazil.

Introduction: Anxiety disorders (ADs) are a significant public health problem. Medications used in the management of ADs act through various mechanisms, mainly involving serotonergic neurotransmission. Despite their effectiveness, these medications have a slow onset of action and adverse effects that compromise pharmacotherapeutic adherence. **Objectives:** To investigate the involvement of serotonergic neurotransmission in the anxiolytic-like effect of the thiophene derivative 6CN07. **Methods:** Initially, molecular docking of 6CN07 was performed against serotonergic receptors 5-HT1A, 5-HT2A and the vesicular transporter VMAT2. Subsequently, the anxiolytic-like effect of acute oral administration of 6CN07 (5 mg/kg, i.p.) alone or in combination with ketanserin (5 mg/kg, i.p.), a 5-HT2A receptor antagonist, was evaluated in mice subjected to the Elevated Plus Maze (EPM) and Light-Dark Box (LDC) models, where the number of entries (NEBA) and the time spent in the open arms (TPBA) of the EPM were assessed; Number of entries (NECC) and dwell time in the clear compartment (TPCC) of the CCE (CEUA/UFPB nº 5940100524). Data were calculated as mean ± SEM, analyzed by ANOVA, followed by Tukey's post-hoc test, and expressed as percentage values. **Results:** In the *in silico* approaches, the results obtained showed that 6CN07 presented binding energy support to the 5-HT 1A receptor (-88.63 kcal/mol), 5-HT 2A (-89.57 kcal/mol) and to VMAT 2 (-87.92 kcal/mol) when compared to the co-crystallized positive controls. In the *in vivo* approaches, treatment with 6CN07 alone significantly increased NEBA and TPBA by 83.1% and 94.5%, respectively, in relation to the vehicle; Pretreatment with ketanserin significantly reduced NEBA and TPBA by 82.7% and 86.1%, respectively, and NECC and TPCC by 90% and 92.1%, respectively, compared to the group treated alone with 6CN07. **Conclusion:** 6CN07 appears to possess an anxiolytic-like effect that possibly involves serotonergic neurotransmission and, in particular, the 5-HT2A receptor. However, further studies are needed to broaden the understanding of the anxiolytic-like effect of the thiophene derivative. **Financial support:** CAPES and UFPB. Keywords: Anxiety, Serotonin, Heterocyclic compounds, Molecular docking, 5-HT2A.

03.014 **Distinct Behavioral Consequences of Ethanol Withdrawal in Male and Female Rats: a Focus on Anxiety and Depression**. Jardim ACG, Costa LSR, Silva AJA, Santos RO, Costa Pinto M, Gavioli EC, Soares VP. UFRN, Dept Biophysics and Pharmacology, Brazil.

Introduction: Chronic ethanol consumption followed by abrupt withdrawal are associated with the development of behavioral alterations, such as anxiety and depression. Previous data have been shown sex differences on behavioral tests related to anxiety and depression in rodents. **Objective:** This study aimed to compare the effects of ethanol withdrawal following chronic consumption in male and female rats subjected to behavioral tests associated with anxiety and depression. **Methods:** Male and female Wistar rats (90 days old), with free access to chow, were submitted to the ethanol treatment as the liquid diet source at increasing concentrations (2%, 4%, and 6%) for 21 days. The same animal was evaluated in the Elevated Plus Maze (EPM), Open Field Test (OFT), and Forced Swim Test (FST) after withdrawal periods of 72 hours, 19 days, and 22 days, respectively. Estrous cycle phases were monitored through vaginal smears and females were subjected to behavioral tests using a pooled-phase approach. The data were analyzed using ANOVA followed by Tukey's test or Kruskal-Wallis followed by Dunn's test, as appropriate, adopting $p \leq 0.05$. **Results:** In the EPM ethanol withdrawal did not change both male and female behaviors when compared to control groups ($p = 0.3339$). There was no significant difference in the number of entries into closed arms indicating the absence of locomotor impairment associated with the treatment ($p = 0.1722$). Reinforcing these findings, in the OFT the distance traveled did not differ significantly among groups ($p = 0.4469$). In the FST, males subjected to withdrawal showed a significant increase in immobility time when compared to control males ($p = 0.0034$). No difference was observed between withdrawn females and control females ($p = 0.0786$), nor between withdrawn females and withdrawn males. There was a significant reduction in climbing time between male and female groups exposed to ethanol withdrawal ($p = 0.012$). **Conclusion:** Ethanol withdrawal after 72 hours did not cause behavioral alterations related to anxiety or locomotion in the EPM, and withdrawal for 19 days did not alter locomotion in males and females in the OFT. On the other hand, ethanol withdrawal for 22 days promoted a depressive-like effect in males, but not in females, in the FST. This sex difference was reinforced by the climbing time observed between male and female withdrawal groups. Studies on alcohol dependence and withdrawal should include both males and females in their protocols to improve the understanding of mechanisms involved and the development of sex-specific therapeutic strategies.

03.015 **Evaluation of the Effects of *Artocarpus heterophyllus* Seed Core Extract on Anxiety- and Depression-Related Behaviors and Jejunal Activity in Female Rats**. Alexandre SVD[1], Miguel TBV[2], Alves ALF[1], Oliveira JCA[2], Silva CRL[1], Lima FMS[1], Costa Pinto MFN[1], Silva MS[1], Pedrini MRS[2], Matsui KN[2], Silva Junior ED[1], Soares VP[1]. [1]UFRN, Dept Biophysics and Pharmacology, Brazil, [2]UFRN, Dept Food Engineering, Brazil.

Introduction: Compounds derived from *Artocarpus heterophyllus* (jackfruit) have demonstrated antioxidant, anti-inflammatory, hypoglycemic, neuromodulatory, sedative, and intestinal protective activities in animal models. However, studies investigating the behavioral effects and safety of jackfruit seed-derived products remain scarce. **Objective:** To evaluate the effects of jackfruit seed starch extract on behavioral tests used for screening anxiolytic- and antidepressant-like activities in female rats. Additionally, to assess its effects on jejunal contractility in isolated organ bath experiments, as well as on hematological and biochemical parameters. **Methods:** Jackfruit seed starch was extracted following sodium metabisulfite treatment (0.2%, 24 h), homogenization, filtration, decantation, drying (80 °C, 6 h), and grinding, yielding a product with low water activity (0.320 ± 0.01) and improved stability. Sixty-day-old female Wistar rats (n = 21) underwent daily vaginal smear collection from the first day of treatment (day 1) until euthanasia (day 19) for estrous cycle monitoring. Animals received saline (control, n = 7) or jackfruit seed starch extract at doses of 250 mg/kg (n = 7) or 500 mg/kg (n = 7) by oral gavage (1 mL/kg). On day 15, animals were evaluated in the elevated plus maze (EPM), followed by the open field test (day 16) and the pre-test and test sessions of the forced swimming test (FST, days 17 and 18, respectively). On day 19, animals were euthanized by decapitation, and blood and jejunal tissues were collected for hematological, biochemical, and organ bath analyses. Data were analyzed using ANOVA or Kruskal-Wallis tests, as appropriate, with p < 0.05 considered statistically significant. **Results:** No significant differences were observed in the number of open-arm entries in the EPM [Control: 4.00 (IQR: 3.00–4.00), 250 mg/kg: 1.00 (IQR: 0.00–8.00), and 500 mg/kg: 4.00 (IQR: 2.00–6.00)], distance traveled in the open field [Control: 31.36 (IQR: 9.70–35.90 m), 250 mg/kg: 20.23 (IQR: 7.95–29.17 m), and 500 mg/kg: 27.77 (IQR: 18.80–34.06 m)], or immobility time in the FST [Control: 151.8 ± 21.77 s, 250 mg/kg: 184.4 ± 24.45 s, and 500 mg/kg: 183.8 ± 44.82 s] (p > 0.05). Likewise, isolated organ bath experiments revealed no significant differences in KCl-induced jejunal contractions among groups [Control: 0.9 ± 0.15 g, 250 mg/kg: 1.0 ± 0.06 g, and 500 mg/kg: 1.0 ± 0.17 g] (p > 0.05). No significant differences were detected in the evaluated biochemical parameters. **Conclusion:** The findings suggest that jackfruit seed starch extract, at doses of 250 and 500 mg/kg, did not induce detectable adverse effects or alter anxiety-like behavior, locomotor activity, depression-like behavior, or jejunal contractility in female rats. Further studies are needed to better characterize the therapeutic potential and safety profile of *Artocarpus heterophyllus* seed starch extract in females.

03.016 **Phenacetin as a Cocaine Adulterant: Acute Effects on Anxiety-Like Behavior, Locomotor Activity and Sleep in Mice**. Silva BPH[1], Silva SMC[1], Castro Neto AG[2], Lira VELC[3], Duarte FS[4], Gomes DA[1] [1]UFPE-Recife, Biosciences Center, Dept Physiology and Pharmacology, Lab. of Neuroendocrinology and Metabolism; Center for Medical Sciences, Graduate Program in Neuropsychiatry and Behavioral Sciences, Brazil; [2]UFPE-Recife, Biosciences Center, Dept Biophysics and Radiobiology; [3]Federal Police Dept Pernambuco, Recife, PE, Brazil; [4]UFPE-Recife, Biosciences Center, Dept Physiology and Pharmacology, Lab. of Experimental Neuropharmacology, Graduate Program in Biochemistry and Physiology, Brazil

Introduction: Phenacetin is a prevalent cocaine adulterant in Brazil (10.8% of seized samples in Pernambuco) and has been detected in post-mortem brain tissue from cocaine users. However, its acute neurobehavioral effects remain poorly characterized. **Objectives:** To evaluate the acute effects of phenacetin and cocaine on anxiety-like behavior, locomotor activity and sleep in Swiss mice. **Methods:** Ninety-six male Swiss mice (60-65 days, n=8/group) received i.p. injections: saline (NaCl 0.9%, CTRL-SAL), cocaine 10 mg/kg (COC10), vehicle (carboxymethylcellulose 2%, CTRL-VCL), phenacetin 10, 30 or 60 mg/kg (FEN10, FEN30, FEN60). The open field test assessed anxiety-like behavior (distance traveled in the center zone, distance traveled in the peripheral zone, time spent in the center zone, percentage of time spent in the center zone, number of center entries, time spent in the peripheral zone, total immobility time, immobility time in the center zone, and immobility time in the peripheral zone) during the first 10 min and locomotor activity (total distance traveled and mean velocity) over 110 min in 10-min bins. Isoflurane-induced sleep measured latency to loss of righting reflex (LORR) and total sleep duration. Data were analyzed by one-way ANOVA, two-way repeated measures ANOVA, or Kruskal-Wallis with appropriate post-hoc (α=0.05). **Results:** Cocaine increased locomotor activity during the first 50 min ($p<0.01$), increased center entries (107.9±9.28 vs. 50.1±7.78; $p<0.0001$), and reduced total immobility (218.3±11.66 vs. 340.5±22.92 s; $p=0.0079$) without affecting time spent in the center zone ($p>0.05$), indicating hyperlocomotion without anxiolysis. Cocaine also increased sleep latency (20.77±1.06 vs. 14.16±0.60 s; $p=0.0006$) and total sleep duration (39.99±4.13 vs. 21.62±1.97 s; $p=0.0297$). In contrast, phenacetin (10, 30, and 60 mg/kg) did not alter any behavioral parameter ($p>0.05$ for all comparisons). Locomotor activity curves of phenacetin-treated animals overlapped those of vehicle-treated animals throughout the 110-min session. **Conclusion:** Acute phenacetin administration (10, 30 and 60 mg/kg) produces no detectable effects on anxiety-like behavior, locomotor activity or isoflurane-induced sleep in mice. The behavioral paradigms employed were sensitive to pharmacological manipulation, as demonstrated by the cocaine positive control. These findings indicate that phenacetin alone does not elicit acute neurobehavioral alterations under the experimental conditions tested and contribute to the characterization of the neurobehavioral profile of this common cocaine adulterant.

03.017 **Effects of Learned Helplessness, an Uncontrollable Stress-Based Model of Depression, on Gastric, Intestinal, and Bladder Smooth Muscle Activity in Mice**. Gomes LTC, Gavioli EC, Silva-Junior ED Federal University of Rio Grande do Norte (UFRN), Dept Biophysics and Pharmacology, Brazil.

Introduction: Depression is often associated with somatic symptoms, especially gastrointestinal and genitourinary disturbances. However, the mechanisms underlying these alterations remain poorly understood. **Objectives:** This study sought to evaluate the motor activity of the gastric fundus, duodenum, and bladder from mice exposed to learned helplessness, an uncontrollable stress- based model of depression. **Methods:** Adult male mice were subjected to the learned helplessness protocol and classified as helpless or resilient. A controllable stress and non-stress groups were also included. After euthanasia, fundus of stomach, duodenum, and bladder were isolated for organ bath experiments. Contractile responses to KCl (80 mM) and carbachol (10-7 \- 10-3 M), as well as relaxation induced by isoproterenol (10-10 – 10-4 M), were evaluated. **Results:** In the bladder, KCl-induced contractions were increased in resilient mice (~120%; n = 9) compared with the non-stress-group (n = 8). Maximal bladder contractions induced by carbachol were increased (~95%) in both helpless (n = 6) and resilient animals (n = 5), whereas carbachol potency was 3.5-fold higher in resilient mice compared with the non-stress group (n = 7). In contrast, isoproterenol-induced bladder relaxation decreased by ~30% in both phenotypes (n = 5/group) compared with the non-stress group (n = 8). In the fundus of stomach, maximal effect of carbachol was decreased in helpless (~50%; n = 6) and resilient (~35%; n= 6) mice compared with non-stress group (n = 7). Isoproterenol-induced relaxation of the fundus of stomach decreased by ~20% only in resilient animals (n = 6). In the duodenum, KCl- and carbachol-induced contractions were unchanged (n = 6/group), whereas maximal isoproterenol-induced relaxation decreased by ~30% in resilient animals (n = 5) compared with the non-stress group (n=7). Controllable stress did not alter any parameter compared with the non-stress group (n = 5-7/group). **Conclusion:** Uncontrollable stress, rather than the depressive-like phenotype itself, may be associated with alterations in fundus of stomach and bladder smooth muscle activity. These findings suggest that stress controllability may differentially affect gastrointestinal and genitourinary motility.

03.018 **Spermidine and Arcaine Modulate Defensive Behavior in Mice**. Zambon AF, Timm A, Martins FC, Costa EF, Mello CF UFSM, Dept Physiology and Pharmacology, PPG in Pharmacology

Introduction: Anxiety disorders are among the most prevalent psychiatric conditions worldwide, being associated with significant functional impairment and reduced quality of life. Evidence suggests that endogenous polyamines modulate glutamatergic neurotransmission through interaction with the polyamine modulatory site of the N-methyl-D-aspartate (NMDA) receptor, particularly in receptors containing the GluN2B subunit. However, due to the biphasic nature of this modulation, it remains unclear whether polyamines increase or reduce defensive behavior in animals, a proxy of anxiety in humans. **Objectives:** To investigate the effects of spermidine, an endogenous polyamine, and arcaine, an antagonist of the polyamine modulatory site of the NMDA receptor, on defensive behavior in adult male Swiss mice. **Methods:** In experiment 1, animals received saline or spermidine (1, 3, 10, or 30 mg/kg, i.p.) and were evaluated in consecutive sessions in the open field and elevated zero maze, separated by a five-minute interval. Each session lasted six minutes, assessed in two-minute intervals (0–2; 2–4; 4–6 min). In experiment 2, animals received saline or arcaine (0.1, 1, or 10 mg/kg, i.p.) and were submitted to the same testing protocol. Animal behavior was evaluated by measuring time spent and distance traveled in the central area and rearing responses in the open field, as well as the time spent in the open zone in the elevated zero maze. Data were analyzed by one-way ANOVA for comparisons between dose groups and two-way ANOVA with repeated measures for time intervals, followed by appropriate post-hoc tests. Results with $p < 0.05$ were considered statistically significant. **Results:** Treatment with spermidine (30 mg/kg) decreased the number of rearing responses over time in the open field session ($p < 0.05$) and reduced the time spent in the open zone of the elevated zero maze ($p < 0.05$), both assessed across the 0–2, 2–4, and 4–6 min intervals. Arcaine at the doses of 0.1 and 10 mg/kg increased the time spent in the central area of the open field ($p < 0.05$); the 0.1 mg/kg dose also increased the distance traveled in this region ($p < 0.05$). In the elevated zero maze, arcaine (0.1 mg/kg) increased the time spent in the open zone across the 0–2, 2–4, and 4–6 min intervals ($p < 0.05$). **Conclusions:** These results show that spermidine increases and arcaine reduces measures associated with defensive behavior in mice. The decrease in defensive behavior elicited by arcaine administration suggests that endogenous polyamines are involved in the development of this behavior, likely through the allosteric polyamine site of the NMDA receptor, a finding with potential implications for understanding the neurobiological basis of anxiety in humans. However, further experiments are needed to fully determine the role of endogenous polyamines in this process. Human or Animal Research Ethical Committee Number: 5255170125 **Financial support:** Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES)

03.019 **Effects of Association Between Resveratrol and Ketamine on Behavioral and Biochemical Analysis in Mice**.
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Resveratrol (3,5,4′-trihydroxy-trans-stilbene), a phenol commonly found in grapes and wine, has been associated as protective in experimental models involving alterations in different neurotransmitter systems. However, studies are reporting that resveratrol could have adverse effects. This study evaluated if the association of a low dose of ketamine and resveratrol could induce behavioral manifestations associated with biochemical alterations. Moreover, the effects of treatment with resveratrol and/or ketamine on monoamine oxidase (MAO) activity, oxidative stress markers, and IL-6 levels in the brain were also investigated. Male Swiss mice received a low dose of ketamine (20 mg/kg) for 14 consecutive days, and resveratrol (10, 30, or 100 mg/kg) from day 8 up to day 14 of the experimental period, intraperitoneally. Locomotor, stereotyped behavior, Y-maze, novel recognition object test (NORT), and social interaction were quantified as well as ex vivo analysis of MAO activity, IL-6 levels, and oxidative stress markers (TBARS and total thiol levels) in brain tissues. Ketamine per se reduced the number of bouts of stereotyped behavior on day 8 of the experimental period. Resveratrol per se reduced the locomotor and exploratory activity in the open field, the time of exploration of new objects in the NORT, MAO-A activity in the striatum and increased the IL-6 levels in the cortex. These effects were attenuated when the mice were co-treated with ketamine and resveratrol. There was a decrease in MAO-A activity in the cortex of mice treated with ketamine + resveratrol 100 mg/kg. No significant alterations were found in oxidative stress markers. Resveratrol does not appear to cause summative effects with ketamine on behavioral alterations. However, the effect of resveratrol per se, mainly on locomotor and exploratory activity, should be better investigated.

03.020 **Investigation of the Antinociceptive Effect of the Monoterpene Hydroxycitronellal in mice**. Dias AL[1], Remígio MCRB[2], Pires HFO[1], Gonçalves MCF[2], Neri LCD[1], Salvadori MGSS[1] [1]UFPB, PPG in Cognitive Neuroscience and Behavior, Brazil. [2]UFPB, Psychopharmacology Lab, Institute of Drugs and Medicines Research, Brazil.

Introduction: Pain is a complex experience involving nociceptive stimuli, as well as cognitive and emotional processing. Meanwhile, nociception is characterized by the detection, transduction, and transmission of tissue damage. Approximately 30% of the world's population suffers from some type of recurring pain, which makes research into new pain medications a priority for the pharmaceutical industry, with a demand for more potent drugs that have fewer side effects. Accordingly, this study aims to evaluate the antinociceptive potential of hydroxycitronellal (HC), a monoterpene derived from citronellal, using *in vivo* methodologies. **Methods:** Male Swiss albino mice weighing between 25 and 30 g were used in the studies. To evaluate the antinociceptive effect was evaluated using doses of 12.5, 25, and 50 mg/kg of HC. The acetic acid-induced abdominal constriction test and the formalin test were used. Subsequently, the mechanism of action of HC via the opioid and glutamatergic pathways was investigated. **Results:** The acetic acid-induced abdominal constriction test indicated that all three doses of HC (12.5, 25, and 50 mg/kg) significantly reduced the number of constriction compared to the control group, with no difference observed among the tested doses or compared to the morphine treatment. In the first phase of the formalin test, a statistically significant reduction in paw-licking time was observed in all groups treated with HC compared to the control group, particularly with the 12.5 mg/kg dose, which showed a more pronounced reduction compared to the other doses tested. In the second phase of the test, all three doses maintained a statistically significant reduction in paw-licking time compared to the control group; however, the 25 and 50 mg/kg doses showed a further reduction in paw-licking time compared to the lowest dose. Then, studies were conducted to investigate possible mechanisms underlying the antinociceptive effect of HC using a dose of 12.5 mg/kg. Regarding the involvement of the opioid pathway, the formalin test showed that administration of the opioid antagonist naloxone failed to reverse the antinociceptive effect of HC in either phase of the test. In the glutamate-induced nociception test, HC was able to reduce paw-licking time in both phases of the test, and the combination of HC with the glutamatergic antagonist MK-801 produced a synergistic effect, resulting in a statistically significant reduction in paw-licking time in both phases compared to all other test groups. **Conclusion:** The results showed that HC exhibits an antinociceptive effect in the tests conducted, becoming a promising candidate for new analgesic strategies. Therefore, it is important to conduct further studies to elucidate its entire mechanism of action.

03.021 **Quantification of Neurotransmitters in the Striatum of Rats with Distinct Immobility Profiles in the Forced Swimming Test**. Silva IAG[1], Almeida FB[1], Guasselli MD[2], Nin MS[1,2], Eller SCWS[3], Barros HMT[1,2] [1]UFCSPA, PPG Ciências da Saúde, Porto Alegre, RS; [2]UFCSPA, Lab Neuropsicofarmacologia, Dept. de Farmacociências, Porto Alegre - RS; [3]UFCSPA, Lab Toxicologia Analítica, Central Analítica, Porto Alegre - RS.

Introduction: **and Rationale**: Depression is a multifactorial disorder that still presents many gaps to be investigated. Despite the wide availability of antidepressant drugs, their efficacy compared to placebo in randomized clinical trials remains limited. Therefore, it is evident that monoaminergic neurotransmission, which is the primary target of virtually all currently available antidepressants, is not the only system involved in the psychobiology of depression or in the pharmacology of this disorder. This suggests that additional biological targets should be explored for the development of more effective therapies. selectively bred rats in the fforced swimming have been developed; however, the neurotransmitter profile of these animal models remains poorly understood. **Objective:** To quantify striatal neurotransmitter levels in adult rats exhibiting distinct genetically determined immobility profiles in the Forced Swimming Test, before and after treatment with fluoxetine. **Methods:** Brain regions corresponding to the right and left striata of adult male and female rats, either treated or not with fluoxetine, were analyzed for neurotransmitter quantification. Dopamine, DOPAC, HVA, Serotonin, GABA, and Glutamate levels were determined ex-vivo using high-performance liquid chromatography coupled with tandem mass spectrometry (HPLC-MS/MS). **Results:** Considering the factors: High Immobility (HI)/ Low Immobility (LI), Hemisphere, Sex, and Treatment (FLX20). Serotonin: in the LI + FLX20 (left hemisphere) group, serotonin levels differed between males and females treated with fluoxetine. DOPAC: differences were observed in fluoxetine-treated females, Glutamate: levels were higher in the right hemisphere than in the left hemisphere. Dopamine: In the HI + FLX20 (right hemisphere) male group, dopamine levels differed between males and their corresponding female counterparts in both hemispheres. In addition, HVA, GABA no significant differences were observed. **Conclusion:** The neurotransmitter profile in the striatum of rats displaying different genetically determined behavioral responses to fluoxetine is different according to the sex of the animals and the hemisphere in study.

03.022 **Potential Antioxidant Effect of Free and Nanoencapsulated *Cannabis sativa* L. Extract in a Dexamethasone-Induced Depression Model**. Gonçalves MCF[1,2], Silva-Netto LS[1,3], Cunha MVS[1,3], Serra GL[1,4], Neri LCD [1,4], Matos ALLS1, Dias AL[1,5], Pires HFO[1,5], Cruz LS2, Xavier-Junior FH2,3, Santos SG2,3, Silva PR[1,2],5, Golzio AMFO[1,5,6] [1]UFPB, Psychopharmacology Lab, [2]UFPB, PPG Bioactive Natural and Synthetic Products, Institute of Research in Drugs and Medicines, Brazil, [3]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil, [4]UFPB, Dept Biomedical Sciences, Health Sciences Center, Brazil, [5]UFPB, PPG Cognitive Neuroscience and Behavior, Brazil, [6]UFPB, Dept Food Technology, Center for Technology and Regional Development, Brazil

Introduction: Oxidative stress is characterized by an imbalance between the production of reactive oxygen species and endogenous antioxidant capacity, playing a crucial role in the pathophysiology of neuropsychiatric disorders, such as depression, in addition to contributing to neuroinflammation and neuronal damage. In this context, extracts derived from *Cannabis sativa* L., rich in Δ-9-tetrahydrocannabinol (THC), have attracted attention due to their potential neuroprotective and antioxidant properties. However, the therapeutic application of these compounds is limited by the psychoactive effects of THC, as well as its low stability and limited bioavailability. Therefore, the present study evaluated the effect of a THC-rich C. sativa extract, in both free and nanoencapsulated forms, on reduced glutathione (GSH) levels in the hippocampus of mice subjected to a dexamethasone-induced depression model. **Methodology:** Mice (*Mus musculus*) were divided into six groups (n = 6): free and nanoencapsulated extract (5, 10, and 15 mg/kg; p.o.), dexamethasone (64 µg/kg; s.c.), imipramine (30 mg/kg; i.p.), and vehicle (saline; p.o.). GSH concentration was determined using Ellman's method, based on the reaction of sulfhydryl groups with 5,5′-dithiobis-(2-nitrobenzoic acid) (DTNB), followed by spectrophotometric reading at 412 nm. Results were expressed as ng per gram of tissue. Based on the obtained results, all data were analyzed using the Shapiro-Wilk parametric test. Data were expressed as mean ± standard deviation (SD) and analyzed by one-way ANOVA followed by Tukey's post hoc test. A significance level of $p<0.05$ was considered statistically significant. **Results:** GSH levels were reduced in the dexamethasone-treated group (32.32 ± 12.81) compared with the control group (124.79 ± 87.54), indicating impairment of antioxidant defenses. Compared with the dexamethasone group, all administered treatments increased GSH levels, with values of 43.58 ± 22.24 for imipramine, 47.51 ± 12.44 for E05, 32.88 ± 17.82 for E10, 60.12 ± 46.30 for E15, 49.55 ± 8.01 for N05, 36.30 ± 9.33 for N10, and 114.20 ± 30.15 for N15. Among the evaluated treatments, the N15 group showed the highest GSH levels, approaching those observed in the control group, and was the only group that showed a statistically significant difference compared with the dexamethasone group. These findings suggest that the treatments helped preserve GSH levels despite subchronic dexamethasone administration, thereby contributing to the maintenance of cellular antioxidant capacity. **Conclusion:** The results demonstrate that the nanoencapsulated formulation at the highest dose (N15) reduced dexamethasone-induced oxidative stress in the hippocampus. However, additional studies are needed to elucidate the molecular mechanisms underlying this neuroprotective effect. **Financial support:** UFPB. Ethics committee approval: CEUA/UFPB (certificate no. 9566190623).

03.023 **Evaluation of the Antagonism of Orexin Receptors (Types 1 and 2) During the Discontinuation Phase on Alcohol Preference in the Two-Bottle Choice Model in Swiss mice**. Costa RCA[1], Silva VS[1], Costa EF[1], Silva HC[2], Costa MEB[2], Sena AF[3], Oliveira ICS[1], Zhang Y[4], Malppezi-Marinho E[3], Marinho EAV[2], Berro LF[5], Oliveira-Lima AJ[2]
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Introduction: Alcohol Use Disorder (AUD) is associated with impairments in an individual's daily life; however, current treatment options are limited and are associated with high relapse rates. The orexinergic system is identified as a potential therapeutic target for AUD, as it has been proposed to mediate the reinforcing effects of drugs of abuse. Orexins, neuropeptides expressed by hypothalamic neurons that project to the neuroaxis, are essential for physiological functions such as feeding, arousal, and regulation of the sleep- wake cycle. Furthermore, orexin-1 (OX1) and orexin-2 (OX2) receptors have been extensively implicated in the neurobiological mechanisms associated with alcohol consumption. **Aim:** To evaluate the effect of selective OX1 and OX2 receptor antagonists on alcohol consumption in mice. **Methods:** 58 adult male Swiss mice were divided into 6 groups (n = 9–10 per group). The two-bottle choice (TBC) self-administration protocol included three phases: acquisition, with free access to two bottles (water and 10% alcohol); abstinence (three periods: A1, A2, and A3), during which the mice were treated with vehicle or orexin antagonists according to the experimental groups (vehicle; selective OX1 antagonist, RTIOX-276 (10 or 20 mg/kg, i.p.); selective OX2 antagonist, MK1064 (10 or 20 mg/kg, i.p.); or a combination of the two antagonists (10 mg/kg RTIOX-276 + 10 mg/kg MK-1064, i.p.)); and re- exposure to alcohol, under the same conditions as acquisition, in three periods (R1, R2, and R3), interspersed with abstinence periods. Ethanol consumption was expressed in g/kg/day, and preference (%) for the alcohol bottle over water was calculated as the amount of ethanol consumed / total consumption × 100. Data were analyzed by two-way ANOVA, with $p < 0.05$ considered statistically significant. **Results:** During the acquisition phase, the animals preferred alcohol to water. The analyses indicated a treatment effect associated with the combination of the two antagonists. The Bonferroni post-hoc test indicated a statistically significant reduction in alcohol consumption (g/kg) in R2 (4.33 ± 0.95) and R3 (3.66 ± 0.78) compared to the control (7.98 ± 0.66 in R2 and 7.81 ± 1.33 in R3; $p \leq 0.045$), as well as an intragroup reduction when compared to their own acquisition sessions (last session: [8.02 ± 0.79] g/kg; $p \leq 0.004$). Preference (%) also decreased significantly during the re-exposure periods: R1 (52.52 ± 6.44), R2 (45.17 ± 9.87), and R3 (38.99 ± 7.76) compared to the control (90.48 ± 4.33 in R1, 95.32 ± 2.49 in R2, and 77.94 ± 10.93 in R3; $p \leq 0.045$) and to the acquisition sessions (last session: 86.59 ± 5.84; $p \leq 0.017$). **Conclusion:** The results suggest that treatment with dual orexin receptor antagonists attenuates alcohol consumption and preference in Swiss mice, suggesting that the orexinergic system represents a potential pharmacological target for future therapeutic approaches to alcohol use disorder.

03.024 **Minocycline as a Possible Treatment for Anxiety and Depression Symptoms Associated with Ethanol Withdrawal In Female Wistar Rats**. Costa Pinto MFN, Santos LC, Albino MC, Lima FMS, Moura NPS, Costa JAM, Gavioli EC, Soares VP. UFRN, Biosciences Center, Dept Biophysics and Pharmacology, Psychopharmacology Lab, Graduate Program in Biochemistry and Molecular Biology, Brazil.

Introduction: Previous laboratory data show that ethanol withdrawal causes different behavioral alterations at distinct time points, observed in the same animal. In this context, the tryptophan pathway stands out, in which the enzyme indoleamine 2,3-dioxygenase (IDO-1) converts tryptophan into kynurenine. Alteration of this pathway has been associated with the development of psychiatric disorders, such as anxiety and depression. **Objectives:** To investigate the action of minocycline, an antibiotic that indirectly inhibits the enzyme indoleamine 2,3-dioxygenase, in female rats subjected to short- and long-term ethanol withdrawal after continuous use. **Methods:** Female Wistar rats, 60±5 days old, were distributed into four groups: water-saline, ethanol withdrawal-saline, water+minocycline, and ethanol withdrawal+minocycline. The water-saline and water+minocycline groups received water for 42 days, while the ethanol withdrawal and withdrawal+minocycline groups received ethanol for 21 days, with a gradual increase in concentration from 2% to 6%, followed by 21 days of withdrawal. During the final 21 days, the animals received saline or minocycline 1 mg/kg/mL by daily gavage. After withdrawal, they were submitted to the elevated plus maze (EPM), open field (OF), and forced swim test (FST). Then, they were euthanized, and the prefrontal cortex, hippocampus, and striatum were collected for analysis of IDO-1 activity through kynurenine production using the Lowry technique. Data were expressed as mean ± SEM and analyzed by one-way ANOVA, considering $p<0.05$. **Results:** Ethanol withdrawal reduced the percentage of time and entries into the open arms of the EPM, without altering entries into the closed arms, indicating absence of locomotor impairment. No differences were observed in distance traveled, mean speed, or parameters related to exploration of the central area in the OF. In the FST, there was no difference in climbing time; however, the withdrawal/saline group showed greater immobility time compared to the other groups. Minocycline reversed anxiety and depressive-like behaviors. IDO enzyme activity did not differ significantly between groups in the prefrontal cortex, striatum, and hippocampus. **Conclusion:** Short-term ethanol withdrawal favored the manifestation of anxiety-like behavior, while long-term withdrawal induced depressive-like behavior. These behavioral alterations were prevented by treatment with minocycline 1 mg/kg/mL for 21 days. However, ethanol withdrawal did not alter kynurenine levels in the brain areas evaluated in female rats. These findings suggest that other brain regions may be involved in the participation of the kynurenine pathway in modulating the effects of ethanol withdrawal. In addition, the estrous cycle may be related to the differences observed between males and females. In light of the literature, the kynurenine pathway appears to exert a differential role when comparing results obtained in male and female animals.

03.025 **Acute Buspirone Exposure Increases Shoal Cohesion in Adult Zebrafish**. Müller DV, Gallas-Lopes M, Patelli-Alves A, Portela SM, Piato A, Herrmann AP UFRGS, Dept. of Pharmacology, Brazil

Introduction: Zebrafish are a widely used organism for investigating social behavior, which can be experimentally assessed in the shoal cohesion test. However, the literature is characterized by inconsistent findings and conflicting interpretations regarding this assay. It remains unclear whether shoal cohesion primarily reflects social motivation or is significantly modulated by anxiety-related states, an important distinction for its translational application, given that social withdrawal is a hallmark of various neuropsychiatric disorders. **Objective:** To address this gap, the aim of this study was to evaluate how buspirone, an anxiolytic drug that acts as a partial agonist of 5-HT1A receptors, modulates shoal cohesion in adult zebrafish. **Methods:** The experiment was preregistered (osf.io/jg4r6). A total of 256 adult zebrafish (Danio rerio) of both sexes were randomly assigned to one of the four experimental groups: control, buspirone 3, 6, and 12 mg/L. Shoals composed of four animals were exposed to control or buspirone solutions by water immersion for 20 minutes. Immediately after exposure, the shoals were transferred to the test tanks (n = 16 shoals per group) and recorded for 6 minutes. Screenshots were captured every 15 seconds to quantify mean inter-fish distance (primary outcome), nearest and farthest-neighbor distances, area, and perimeter of the shoal using ImageJ software. Experiments were conducted in two batches, and data were analyzed using Kruskal-Wallis followed by Dunn's post hoc test. **Results:** Acute buspirone exposure reduced mean inter-fish distance, mean farthest neighbor distance, and shoal perimeter at all three concentrations tested. Mean nearest neighbor distance was reduced at the two highest concentrations, whereas shoal area decreased only at the highest concentration. **Conclusion:** Our findings show that buspirone administration increased shoal cohesion in adult zebrafish, particularly at the highest concentration tested, suggesting a dose-dependent effect. This apparent pro- social effect of buspirone may actually be a confounder driven by its anxiolytic properties, as a reduction in bottom-dwelling naturally leads the animals to spend more time in the upper zone of the tank, thereby limiting the occupied area and artificially increasing shoal cohesion metrics. Further studies are needed to disentangle the effects of anxiolytic and anxiogenic interventions on shoal cohesion to differentiate true social alterations from spatial exploration artifacts.

03.026 **Rapid-Acting Antidepressants in the Prophylaxis of Inescapable Stress-Induced Behaviors in Mice: A Comparative Study between Esketamine and Dimethyltryptamine** (**DMT**). Marques VB[1], Silva ANS[1], Moura CA[1], Torres CIO[1], Silva JMNS[1], Da Silva Jr ED[2], Gavioli EC[1] [1]UFRN, Dept Biophysics and Pharmacology, PPG Psychobiology, Brazil. [2]UFRN, Dept Biophysics and Pharmacology, PPG Biochemistry and Molecular Biology, Brazil.

Introduction: Exposure to inescapable stress does not produce uniform outcomes, resulting in distinct profiles of vulnerability or resilience. The rapid-acting antidepressant esketamine promotes acute neuroplasticity and exerts prophylactic effects on stress-induced depressive-like phenotype. However, the preventive effects of dimethyltryptamine (DMT) on stress have not yet been investigated. **Objective:** This study aimed to compare the prophylactic effects of esketamine and DMT on inescapable stress-induced behaviors in mice. **Methods:** Male Swiss mice received a single intraperitoneal dose of esketamine (30 mg/kg), DMT (10 mg/kg), or saline 24 h before the inescapable stress footshocks (performed on two consecutive days), and the frequencies of and latencies to escape from the electrified chamber were registered on day 3. Phenotypes were defined using k-means clustering (k=2) in the control group, and treated groups were classified according to Euclidean distance to the centroids. Behavioral performance after inescapable stress was assessed using the Tail Suspension Test (TST; at 3, 4 and 7 days after treatment) and Contextual Fear Conditioning (CFC; at 4 and 7 days after drug administration). Statistical analyses included Fisher's exact test with Monte Carlo simulation, Firth logistic regression, the Kruskal-Wallis test, and Dunn's post-hoc test with Bonferroni correction (α=0.05). **Results:** In the cluster analysis of the saline group, a clear separation was observed between two behavioral groups, resilient and helpless mice (silhouette=0.55; Cohen's d: escapes=-2.89; latency=2.97). Preliminary data showed that the percentage of resilient animals was 30.0% in the saline group (n=20), 42.9% in the esketamine group (n=14), and 57.1% in the DMT group (n=14), with no significant difference between groups (Fisher: p=0.295). The effect magnitude, estimated by Firth's penalized logistic regression, indicated that animals in the esketamine group had 1.59 times greater odds of exhibiting a resilient phenotype compared to the control group (OR=1.59; 95% CI 0.40–6.52; p=0.512), while the DMT group had 2.72 times greater odds (OR=2.72; 95% CI 0.70–11.42; p=0.152). In the TST, only esketamine reduced immobility time 7 days after treatment compared to saline (Kruskal-Wallis: p=0.02). In the CFC test, no significant differences were detected between groups. **Conclusion:** The findings, with marginal statistical significance, indicated an increased probability of resilient phenotype associated with esketamine, with DMT showing a trend in the same direction, though more pronounced. These results reinforce the relevance of direct comparisons between these compounds and point to the need for studies with greater sample power.

03.027 **Effects of Spermidine on Alcohol Consumption in a Two-Bottle Choice Model in Mice**. Costa EF[1], Zambon AF[2], Costa RCA[1]., Silva VS[1], Sena AF[3], Silva HC[4], Dias, ES[4], Schat LES[5], Macedo IK[6], Marinho ELM[5], Lima AJD[4], Marinho AVL[4], Mello CF[2] [1]UESC, PPG in Health Sciences; [2]UFSM, Dept Physyology and Pharmacology, PPG in Pharmacology; [3]UESC, PPG in Biology and Biotechnology of Microorganisms; [4]UESC, Dept Health Sciences; [5]UESC, Dept Biological Sciences; [6]UESC, Dept Agricultural and Environmental Sciences

Introduction: Alcohol Use Disorder (AUD) is characterized by impaired control over alcohol consumption. Although approved pharmacotherapies are available, treatment adherence remains limited, largely because of adverse effects. N-methyl-D-aspartate (NMDA) receptors play a central role in the neurobiology of AUD, and their hyperactivity has been associated with increased ethanol consumption and relapse vulnerability. Polyamines, such as spermidine (SPD), modulate NMDA receptors and may therefore influence alcohol-related behaviors. **Objectives:** To investigate whether 10 or 30 mg/kg SPD alters ethanol consumption and alcohol preference in the intermittent-access two-bottle choice paradigm. **Methods:** 76 adult male Swiss mice were used. Animals underwent a 30-day acquisition period, during which they had access to two bottles: one containing 10% ethanol and other with water for 15 h on alternate days. After the eighth drinking session (Day 15), animals consuming <1.5 g/kg/day of ethanol were excluded. The remaining animals (n=44) continued to access ethanol up to day 31, when the first abstinence period began. Pharmacological treatment initiated on day 32 with 0.9% NaCl (10 mg/kg, i.p., n = 13) or 10 mg/kg SPD (n = 14) or 30 mg/kg SPD (n = 17) every other day for 14 days (up to day 44). On day 45 animals initiated first ethanol re-exposure for 6 days, in alternate days, up to day 50. Thirty-two hours later (on day 51) the animals started receiving the same previous pharmacological treatment every other day, up to day 58. On day 59 initiated the second re- exposure period, which extended up to day 64. On day 65, the animals initiated the third and last abstinence period (with concomitant respective pharmacological treatment), up to day 72. On day 73, the animals initiated the third and last re-exposure, up to day 78. Ethanol and water consumption was measured throughout the experiment. Ethanol intake (g/kg/day) and alcohol preference (%) were analyzed using two-way repeated-measures ANOVA during acquisition and repeated-measures ANCOVA adjusted for baseline values during re-exposure. **Results:** During acquisition, ethanol consumption did not differ among groups ($p>0.05$). During re-exposure, ANCOVA revealed a significant effect of treatment on ethanol consumption ($F(2,40) = 6.19$, $p = 0.006$), with baseline consumption as a significant covariate ($F(1,40) = 13.80$, $p = 0.001$). Adjusted means showed higher ethanol consumption in the SPD 30 mg/kg group (8,16 g/kg) than in the SPD 10 mg/kg group (5,18 g/kg) throughout re-exposure, but no significant differences compared with the control group (6,74 g/kg). Adjusted alcohol preference ($F(2,40) = 5.76$, $p = 0.006$) was higher in the SPD 30 mg/kg group (71.5%; $p = 0.048$) when compared with control group (55.3%) and the SPD 10 mg/kg group (52.2%; $p = 0.008$). **Conclusion:** Baseline ethanol consumption predicted subsequent ethanol intake during re-exposure. Spermidine (30 mg/kg) increased ethanol preference compared with control and 10 mg/kg group. It also increased ethanol consumption compared with the 10 mg/kg group, but not with control. These findings suggest that a high dose of SPD increases ethanol preference.

03.028 **N,N-dimethyltryptamine Reduced Anxiety-Like Behaviors in Escapable Stressed Mice Later After Administration**. Lima VVF, Sousa-Silva AN, Moura CA, Torres CIO, Gavioli EC. UFRN, Dept Biophysics and Pharmacology, PPG in Psychobiology, Natal, RN, Brazil.

Introduction: Psychedelics have emerged as promising strategies for relieving anxiety and depressive-like behaviors in stress-related psychiatric disorders. N,N-dimethyltryptamine (DMT), a serotonergic psychedelic compound, has recently gained attention as a potential rapid-acting antidepressant with anxiolytic properties reported for humans and rodents. **Objectives:** This study aimed to investigate the effects of DMT on escapable stressed mice assessed in behavioral tests from 24 to 72 h after drug administration. **Methods:** Male Swiss mice were exposed on day 1 to escapable footshock sessions (30 cycles; 0.5 mA, shocks from 1-10 s, 20 s intertrial interval), and immediately after, they were treated with saline or DMT (10 mg/kg, ip). Head-twitch responses were registered immediately after drug treatment to detect the 5-HT2A receptor activation, as classically observed with psychedelics. On day 2, animals were again exposed to escapable footshock stress (similar to day 1), and then, the immobility time was measured in the tail suspension test. On day 3, the mouse behavior was assessed in the open field and forced swimming tests. On day 4, at 72 h after DMT treatment, animals were exposed to the novelty-suppressed feeding behavior test. Data were analyzed using Student t test and Pearson's correlation. **Results:** Mice treated with DMT increased head-twitches responses assessed in the first 15 min after drug injection compared to saline ($P<0.05$). In the tail suspension and forced swimming tests, performed at 24 and 48 h after drug administration, respectively, DMT did not affect immobility time compared to saline ($P>0.05$). However, a significant moderate negative correlation between frequency of head-twitches and immobility time in the tail suspension test was detected in escapable stressed mice ($r=-0.71$, $P=0.02$). This finding suggests that acute central 5-HT2A receptor activation by DMT is inversely related to the passive coping strategy (i.e., immobility) assessed 24 h after. Interestingly, the treatment with DMT did not change spontaneous locomotion assessed in the open field test. By contrast, mice treated with the psychedelic, 48 h after injection, displayed increased exploration to the central area of the apparatus compared to saline ($P<0.05$), thus supporting an anxiolytic profile. Similarly, 3 days after administration, DMT reduced the latency to eat food in an unfamiliar environment compared to saline ($P=0.05$), being consistent with an anxiolytic action. **Conclusion:** The treatment with DMT 10 mg/kg evoked head-twitch responses in mice, which negatively correlates with immobility in the tail suspension test. Additionally, DMT evoked sustained anxiolytic actions in escapable stressed mice observed up to 3 days after a single administration. These findings reinforce the sustained anxiolytic actions of DMT in stressed mice.

03.029 **Behavioral and Neuroinflammatory Effects Caused by Lipopolysaccharide Application in Mice Exposed to CO_2.** Corsi LAF, Nascimento-Silva JM, Cabral BC, Rocha-Gomes A, Zangrossi-Júnior H USP, Lab. of Behavioral Pharmacology, PPG in Biological Sciences (Pharmacology), Brazil

Introduction: Panic disorder (PD) is a chronic and disabling disorder characterized by the recurrence of panic attacks (PA), which occur unexpectedly, whose underlying pathophysiological mechanisms have not yet been elucidated. Inhalation of high concentrations of CO2 evokes panic attacks in humans and defensive behaviors associated with panic, such as the escape response, in mice. The dorsal periaqueductal gray matter (DPAG) in the midbrain has been critically implicated in mediating these effects of CO2 and, consequently, in the pathophysiology of PD. In our laboratory, we observed that exposure to 20% CO2 generates an escape response in mice, and evidence shows that this challenge triggers the activation of microglial cells in the locus coeruleus, a region also involved in panic attacks. Microglia plays a critical role in maintaining neural homeostasis, including the regulation of local inflammatory processes and neuronal metabolism. **Objective:** In this work, we investigate the behavioral and neuroinflammatory consequences resulting from immune activation caused by the administration of lipopolysaccharide (LPS) in male C57BL/6J mice subjected to exposure to 20% CO2. **Methods:** Animals were injected intraperitoneally with LPS (0.1, 0.5, or 1 mg/kg) or saline and, 24 h later, exposed to CO2 (20%) for 7 min. After the test, the brain was removed and sections were processed for immunofluorescence detection of Iba-1 (microglia marker) and for cytokine dosage in areas associated with panic, such as the DPAG, dorsal raphe nucleus, and medial hypothalamus. **Results:** The results obtained demonstrated that LPS, at doses of 0.5 mg/kg and 1 mg/kg, increased the number of jumps in mice during CO2 exposure, indicative of a panicogenic effect. At the highest dose, the toxin also impairs locomotor function. Currently, analyses of the Iba-1 immunolabeled slides and tissue processing are being carried out. **Conclusion:** Our results show that immune activation with LPS increases the panicogenic effect caused by CO2 exposure. Ongoing studies will indicate whether this behavioral effect is related to changes in microglial profile in regions critical to the pathophysiology of panic, as well as in the expression of cytokines in these regions.

03.030 **Physiological and Behavioral Characterization of the Effects of the Chronic Social Defeat Stress Model: Preliminary Findings**. De Souza D, Poian LR, Chiavegatto S. ICB-USP, Dept Pharmacology, Functional and Molecular Biology Post Graduation Program, Brazil.

Stress promotes physiological and psychological adaptations; however, when prolonged, it may contribute to the development of psychopathologies. The chronic social defeat stress (CSDS) model has high ethological validity and reproducibility for investigating processes involved in susceptibility and resilience to psychosocial stress. Here, we employed the CSDS protocol for 10 consecutive days using C57BL/6 male mice and evaluated behavioral alterations through the social interaction test, splash test, and sucrose preference test, as well as physiological measures of body weight and temperature. This protocol consisted of daily pairings between C57BL/6 mice and previously selected aggressive CD-1 mice for 5 minutes. These pairings promoted attacks or chasing and the establishment of CD-1 dominance over the C57BL/6 mouse, resulting in social subjugation. We used 29 C57BL/6 mice, divided into 19 experimental animals (subjugated) and 10 control. Experimental animals were subjected to CSDS, while controls were housed in similar cages but were not exposed to agressive encounters. All assessments were performed before and after the stress protocol. Preliminary results indicated a significant increase in body temperature after stress in the subjugated group (35.93 ± 0.18 °C vs. 34.67 ± 0.20 °C; $p < 0.0001$), as well as a significant increase in the subjugated group compared with post-protocol controls (35.93 ± 0.18 °C vs. 34.55 ± 0.14 °C; $p = 0.0004$). In the social interaction test, subjugated animals showed a longer latency to initiate social interaction compared with post-protocol controls (84.61 ± 12.35 vs. 23.05 ± 9.59 seconds; $p = 0.003$), although total interaction time was not significantly different. Grooming frequency increased after the stress period in the subjugated group (10.05 ± 0.74 vs. 6.053 ± 0.65 events/5 min; $p < 0.0001$), and was higher in subjugated animals than in post-protocol controls (10.05 ± 0.74 vs. 7.10 ± 0.78 events/5 min; $p = 0,0128$). The ratio between total grooming time and grooming frequency was significantly lower in subjugated animals compared to controls (8.89 + 0,77 vs. 12.39 + 1,6 seconds/event/5min; $p = 0.0179$). All results are expressed as mean and standard error of the mean. No significant differences were observed in body weight, total social interaction time, total grooming time, or sucrose preference up to this point. Therefore, the preliminary results suggests that the stress protocol was effective in inducing physiological and behavioral alterations consistent with expected phenotypes following chronic social stress. These findings support the use of this experimental model and provide a behavioral basis for subsequent molecular analyses.

03.031 **Effects of Neonatal Immune Challenge with Lipopolysaccharide on Panic-Related Behaviors in Adult Sprague Dawley Rats**. Aguiar L, Rocha-Gomes A, Nascimento-Silva JM, Hernandes PM, Zangrossi-Júnior H FMRP-USP, Dept. of Pharmacology, Lab. of Behavioral Pharmacology, PPG in Biological Sciences (Pharmacology), Brazil.

Introduction: Panic disorder (PD) is characterized by recurrent, unexpected panic attacks and is frequently associated with significant psychiatric comorbidities. Neonatal stressors have been shown to strongly promote behavioral changes in offspring, potentially modulating the neuroimmune system and increasing vulnerability to psychiatric disorders throughout life. Previous studies from our laboratory demonstrated that maternal deprivation induces defensive escape responses (panic-associated behavior) to respiratory challenges, such as hypoxia. Given that lipopolysaccharide (LPS) is a potent immune activator capable of inducing panic-related behaviors, we investigated its role as a neonatal stressor. **Objective:** To evaluate the behavioral and neuroinflammatory effects of neonatal LPS administration in rats and its contribution to vulnerability to PD. **Methodology:** Sprague Dawley rats were obtained by mating males and females maintained at a 1:2 ratio for 10 days under controlled temperature and humidity conditions, and a 12 h/12 h light/dark cycle, with ad libitum access to food and water. On postnatal day 11 (PND11), litters were adjusted so that half of the pups (2 males and 2 females) received an intraperitoneal injection of LPS (0.05 mg/kg), while the remaining pups received saline as a control. Injections were performed using Hamilton syringes fitted with 30G gingival needles. On PND60, animals were exposed to hypoxia challenge (7% O_2), an experimental model used to induce panic-related behaviors (e.g jump). Following exposure, animals were anesthetized and transcardially perfused at two different time points (1 h and 6 h post-test). Brains were then removed and processed for morphological analysis. Immunofluorescence labeling of glial and astrocytic cells was performed in sections containing the dorsal periaqueductal gray, dorsal raphe nucleus, medial hypothalamus, and locus coeruleus, in which morphological analyses are currently ongoing. **Results:** Both female and male rats subjected to neonatal LPS administration showed a significant increase in the number of jumps when exposed to the hypoxia challenge in adulthood when compared to control group, indicating increased susceptibility to panic-like responses. **Conclusion:** The results indicate that neonatal exposure to LPS increases behavioral reactivity to respiratory challenges in adulthood, suggesting greater vulnerability to panic-like responses. These findings support the hypothesis that early-life immune activation promotes long-lasting alterations in the neuroimmune system, potentially contributing to the development of PD. Ongoing morphological analyses may further elucidate the neuroinflammatory mechanisms involved in this process.

03.032 **Effects of Antagonism of Orexin Receptors, Administered during the Acquisition Phase, on Alcohol Preference in the Two-Bottle Choice Model in Swiss Male Mice**. Silva VS[1], Costa RCA[1], Costa EF[1], Ferreira KR[1], Santos RS[2], Carneiro DM[2], Zhang Y[3],Marinho ELAM4, Marinho EAV[2], Lima AJO[2], Berro LF5. [1]UESC, PPG Health Sciences, Brazil, [2]UESC, Dept Health Sciences, Brazil, [3]Research Triangle Institute, USA, [4]UESC, Dept Biological Sciences, Brazil, [5]University of Mississippi Medical Center, USA

Introduction: Alcohol use is a major contributor to morbidity and mortality worldwide. While treatments for alcohol use disorder (AUD) exist, relapse rates remain high. As an alternative, treatments targeting the orexinergic system, which regulates arousal and reward mechanisms, have been proposed as new pharmacotherapies for AUD, particularly antagonists of orexin-1 (OX1) and orexin-2 (OX2) receptors. However, findings on the effects of selective OX1 and OX2 antagonists on alcohol drinking have been inconsistent. **Objective:** Evaluate the effects of selective OX1 and OX2 receptor antagonists on alcohol consumption in male mice using the two-bottle choice model (TBC). **Methodology:** The study used 60 adult male mice (3 months old). The protocol was divided into 3 stages: acquisition—intermittent access to ethanol (10% v/v) in a TBC procedure for 30 days, with treatment with vehicle or orexin compounds being administered before acquisition sessions; discontinuation—animals remained undisturbed in their home-cages for 15-9-9 days (interspersed with re-exposure), with no treatment;re-exposure—similar to acquisition, without pretreatment. RTIOX-276 (OX1-selective antagonist) and MK-1064 (OX2-selective antagonist) were chosen for these studies for their high potency and greater selectivity. Pretreatment was administered i.p. according to the following groups (n=10/group): vehicle; 10 mg/kg RTIOX-276; 20 mg/kg RTIOX-276; 10 mg/kg MK-1064; 20 mg/kg MK-1064; 10 mg/kg RTIOX-276+10 mg/kg MK-1064. Parameters evaluated were ethanol intake (g/kg/day) and preference for the ethanol bottle compared to the water bottle (%). For statistical analysis, one- and two-way ANOVAs were performed, and $p < 0.05$ was considered a statistically significant difference. **Results:** During acquisition, the lowest dose of RTIOX-276 (10 mg/kg) decreased alcohol drinking (P=0.0040) and preference (P=0.0034) compared to vehicle- treated animals. The lowest dose of MK-1064 (10 mg/kg) selectively decreased alcohol preference (P=0.0261) vs vehicle. The combination RTIOX-276+MK-1064 reversed the effects of the drugs alone on both alcohol intake and preference (P's>0.05 vs vehicle). During re-exposure, 10 mg/kg RTIOX-276 (P<0.0191) and MK-1064 (P=0.0169) decreased alcohol consumption, while preference was only decreased by 10 mg/kg MK-1064 (p=0.0226). No significant differences compared to vehicle were observed for the combination RTIOX-276+MK-1064. **Conclusion:** Selective OX1 and OX2 receptor antagonists dose-dependently reduced alcohol consumption and preference in male Swiss mice, demonstrating their potential as a therapeutic option for the treatment of AUD. The combination of the two antagonists reversed the effects of the drugs alone, suggesting a complex interaction between the two receptor systems on alcohol drinking.

03.033 **N,N-Dimethyltryptamine Did Not Affect Associative Memory and Footshock Responses in Mice**. De Macedo SPF, Sousa-Silva AN, Moura CA, Torres CIO, Lima VVF, Gavioli EC. UFRN, Dept Biophysics and Pharmacology, PPG in Psychobiology, Natal, RN, Brazil.

N,N-dimethyltryptamine (DMT), a serotonergic psychedelic compound, has recently gained attention as a potential rapid-acting antidepressant in humans. Recently, our research group showed sustained antidepressant-like effects of DMT in the learned helplessness model, observed 24 h after administration. However, potential confusing effects of DMT, such as footshock sensitivity and effects on associative memory deserves investigation. **Objectives:** This study aimed to investigate the effects of DMT on footshock reactivity and associative memory in mice. **Methods:** Male Swiss mice were treated with saline or DMT (10 mg/kg, ip) 24 h prior to tests. Footshock sensitivity was investigated measuring the vocalization, jump and flinch threshold in the footshock chamber, following crescent footshock amperage (0.1, 0.3, 0.5 and 0.7 mA). Associative memory was assessed investigating the frequency of escapes and latency to escape from the electrified side of the chamber following 30 cycles of footshocks (0.5 mA; 1-4 s duration; delivered within the first 10 s of each trial; mean intertrial interval: 20 s) during a first session without drug, and two subsequent sessions, which happened 24 h and 72 h after treatment. Data were analyzed using Student t test and ANOVA followed by Dunnett's post-hoc test. **Results:** In the footshock sensitivity test, the administration of DMT did not change the estimated shock threshold for vocalization, jump and flinch responses compared to saline ($P>0.05$). In the associative memory task, saline-treated mice, in a time-dependent way, learned to escape from the side of the chamber in which a footshock was delivered, as measured by average of latency to and frequency of escapes. The administration of DMT, immediately after the first escapable footshock session, did not display significant differences in the acquisition of associative memory compared to saline ($P>0.05$). **Conclusion:** The treatment with DMT neither affected sensitivity to footshock nor changed the acquisition of associative memory in mice. These findings exclude any potential confusing effects of DMT, thus reinforcing genuine antidepressant actions of this psychedelic compound in the learned helplessness model.

03.034 **Role of 5-HT7 Receptors in the Dorsal Periaqueductal Gray in the Modulation of Anxiety-Like Behavior**. Souza AF[1,2], Silveira MA[1], Gavioli, EC[1], Soares VP[1,2] [1]UFRN, Center for Biosciences, Dept Biophysics and Pharmacology, Brazil. [2]UFRN, Center for Biosciences, Dept Morphology, PPG Structural and Functional Biology, Brazil.

Introduction: Anxiety is an emotional state of considerable adaptive value that plays an important role in survival. The serotonergic system plays an important role in the modulation of anxiety-related behaviors. The dorsal periaqueductal gray (DPAG), a brain region critically involved in defensive responses, expresses serotonin 5-HT7 receptors, although their contribution to anxiety-like behavior remains poorly understood. **Objective:** To investigate whether pharmacological manipulation of 5-HT7 receptors within the DPAG modulates anxiety-like behavior in rats. **Methods:** Wistar rats (90 ± 5 days old) underwent stereotaxic surgery and were subjected to two experimental protocols. In Experiment 1, animals received an intra-DPAG administration of vehicle or the 5-HT7 receptor agonist AS-19 (0.05, 0.1, or 0.2 μg) and were tested in the elevated plus maze (EPM), followed by the open-field test 24 h later. In Experiment 2, animals received the 5-HT7 receptor antagonist SB-269970 (5, 10, or 20 nmol) or vehicle, followed by AS-19 (0.1 μg) or vehicle before behavioral testing. Data are expressed as mean ± SEM and were analyzed by one-way ANOVA (Experiment 1) or two-way ANOVA (Experiment 2), followed by Tukey's post hoc test when appropriate. Significance was set at $p < 0.05$. This study was reviewed and approved by the Animal Use Ethics Committee of the Federal University of Rio Grande do Norte (CEUA/UFRN; protocol no. 029/2012). This study was supported by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES, Brazil). **Results:** In Experiment 1, AS-19 at 0.1 μg significantly decreased the percentage of open- arm entries [$F(3,43) = 5.17$, $p = 0.004$] and time spent in the open arms [$F(3,43) = 4.68$, $p = 0.007$] compared with vehicle, indicating an anxiogenic- like effect. No significant changes in locomotor parameters were observed ($p > 0.05$). In Experiment 2, SB-269970 at 10 nmol increased the percentage of time spent in the open arms, indicating an anxiolytic-like effect, which was reversed by AS-19 (0.1 μg). A significant effect was also observed for SB-269970 at 20 nmol [$F(7,67) = 7.42$, $p < 0.001$]. A significant agonist–antagonist interaction was detected for the percentage of open-arm entries [$F(7,67) = 3.57$, $p = 0.002$]. **Conclusion:** These findings suggest that 5-HT7 receptors within the DPAG are involved in the modulation of anxiety- related responses. Activation of these receptors produces an anxiogenic-like effect, whereas their blockade favors an anxiolytic-like response. Together, these results support a role for DPAG 5-HT7 receptors in the serotonergic regulation of defensive behavior and suggest that blockade of this receptor subtype may contribute to anxiolytic-like effects.

03.035 **Anticonvulsant and Neuroprotective Effects of Hydroxycitronellal in Experimental Models of Epilepsy**. Pires HFO[1,2], Dias AL[1,2], Gonçalves MCF[1,3], Neri LCD[1], Silva PR[1,2], Salvadori MGSS[1,2,3] [1]UFPB, Psychopharmacology Lab, Institute of Drugs and Medicines Research, Brazil, [2]UFPB, PPG in Cognitive Neuroscience And Behavior, Brazil, [3]UFPB, PPG in Bioactive Natural and Synthetic Products, Brazil.

Introduction: Epilepsy is a chronic neurological disorder affecting nearly 70 million people worldwide and is characterized by recurrent, unprovoked seizures. Although currently available antiseizure medications can reduce seizure frequency, they are not curative and are often associated with adverse effects and treatment refractoriness.. Among the compounds investigated for this purpose, monoterpenes have attracted considerable interest due to their potential neuropharmacological properties. Therefore, the present study aimed to evaluate the anticonvulsant and neuroprotective potential of the monoterpene hydroxycitronellal in animal models of epilepsy. **Methods:** Acute oral toxicity and median lethal dose (LD_{50}) were determined in male Swiss albino mice (25–30 g) according to OECD guideline 423. The anticonvulsant activity of hydroxycitronellal was evaluated using both the pentylenetetrazole-induced acute seizure model and the pentylenetetrazole chemical kindling model. Neuroprotective effects were further assessed through biochemical and histopathological analyses. **Results:** Acute toxicity assessment demonstrated that hydroxycitronellal was well tolerated following oral administration with LD_{50} >2,000 mg·kg^{-1}. The pentylenetetrazole-induced acute seizure model revealed significant anticonvulsant and neuroprotective effects at doses ranging from 12.5 to 200 mg·kg^{-1}, with the 100 mg·kg^{-1} dose producing the most pronounced response. In contrast, 6.25 mg·kg^{-1} was identified as the threshold dose for loss of anticonvulsant activity under the experimental conditions employed. Treatment with hydroxycitronellal also increased hippocampal levels of reduced glutathione, suggesting an antioxidant effect. In the kindling model, the compound delayed epileptogenesis, as evidenced by increased latency to the first seizure and prolonged survival. Furthermore, histopathological analysis demonstrated preservation of neuronal architecture and a reduction in glial nodule formation compared with untreated animals. **Conclusion:** These findings demonstrate that hydroxycitronellal exhibits anticonvulsant and neuroprotective properties and may represent a promising candidate for the development of new therapeutic strategies for epilepsy. Nevertheless, further studies are required to elucidate its mechanisms of action and fully characterize its pharmacological potential.

03.036 **Behavioral and Biochemical Effects Of N,N-Dimethyltryptamine (DMT) and S-Ketamine in a Mouse Model of Glucocorticoid-induced Depression**. Torres CIO[1], Marques VB[1], Silva ANS[1], Moura CA[1], Silva JMN[1], Lima VVF[1], De Macedo SPF, Da Silva Jr ED[2], Gavioli EC[1] [1]UFRN, Dept Biophysics and Pharmacology, PPG Psychobiology, Brazil. [2]UFRN, Dept Biophysics and Pharmacology, PPG Biochemistry and Molecular Biology, Brazil.

Introduction: Major Depressive Disorder (MDD) is a highly prevalent and disabling psychiatric condition, frequently associated with therapeutic resistance and the delayed onset of conventional antidepressants. In this context, rapid-acting antidepressants such as S-ketamine and N,N-dimethyltryptamine (DMT) have gained attention due to their potential to promote rapid and sustained antidepressant responses. **Objectives:** This study aimed to evaluate the behavioral and biochemical effects of DMT and S-ketamine in a mouse model of depression induced by repeated exposure to hydrocortisone (HC) in drinking water. **Methods:** Male Swiss mice were exposed to hydrocortisone (HC; 8 mg/kg/day, p.o.) for 28 days to induce a depressive-like phenotype. After 21 days of HC exposure, animals were subjected to the sucrose preference, open field, marble burying, forced swimming, and novelty- suppressed feeding tests. Subsequently, they received an acute administration of DMT or S-ketamine (both at 10 mg/kg, i.p.) or vehicle. Behavioral analyses were performed immediately after administration and again after 24 h and 120 h. During the protocol, body weight, water and food intake were monitored. At the end of the experiment, serum oxidative stress markers were evaluated using protein carbonylation and TBARS assays. Data were analyzed using One-way or Two-way ANOVA followed by Tukey's Test. **Results:** Chronic HC exposure reduced body mass (approx. 10% of initial weight) (One-way ANOVA, $F(3,55)=11.29$, $p<0.05$). and sucrose preference, indicating anhedonia-like behavior, without significant alterations in the other behavioral parameters or serum oxidative stress markers. Five min after DMT administration behavioral alterations compatible with central activation were registered (i.e., increased time stopped, and reduced rearings and grip the lid) ($p<0.05$). Both DMT and S-ketamine reversed anhedonia-like behavior, increasing sucrose preference after 120 h (Two-way ANOVA, effect of time: $F(3,132)=5.49$, $p<0.05$; effect of treatment: $F(3,132)=5.50$, $p<0.05$; interaction: $F(9,132)=2.27$, $p<0.05$). However, only DMT significantly reduced immobility time in the forced swimming test after 24 h (One-Way ANOVA, $F(3,54)=3,68$, $p=0,02$). Neither treatment promoted consistent changes in locomotor or anxiety-related parameters, nor in the biochemical markers evaluated. **Conclusion:** The oral HC exposure model proved suitable for studying anhedonia associated with MDD. DMT produced rapid and sustained antidepressant-like effects, which were evident 24 h after administration and remained detectable up to 120 h later. These findings highlight the therapeutic potential of DMT as a rapid-acting antidepressant, with effects comparable to those observed with ketamine. Further studies are needed to elucidate the underlying mechanisms and improve the translational relevance of these findings.

03.037 **N,N-dimethyltryptamine Produces Sustained Antidepressant- and Anxiolytic-Like Effects in Helpless Mice: Comparison with S-Ketamine**. Sousa-Silva AN, Moura CA, Torres CIO, Marques VB, Silva JMN, Gavioli EC. UFRN, Dept Biophysics and Pharmacology, PPG in Psychobiology, Natal, RN, Brazil.

Introduction: Rapid-acting antidepressants have emerged as promising strategies for stress-related psychiatric disorders. Although ketamine induces rapid clinical improvement, its use remains limited by adverse effects and abuse liability. N,N-dimethyltryptamine (DMT), a serotonergic psychedelic compound, has recently gained attention as a potential rapid-acting antidepressant; however, its behavioral effects in translational models of depression remain poorly characterized. **Objectives:** To investigate the antidepressant- and anxiolytic-like effects of DMT in helpless mice and compare its behavioral profile with S-ketamine. **Methods:** Group- and single- housed helpless mice received saline, DMT (10 and 25 mg/kg), or S-ketamine (10 and 30 mg/kg). Depression-like behaviors were evaluated 24 h post-treatment using the learned helplessness paradigm, sucrose preference test (SPT), and tail suspension test (TST). Anxiety-like behavior and locomotor activity were assessed using the elevated plus maze (EPM) and open field test (OFT), respectively. Data were analyzed using ANOVA and mixed-effects models followed by Dunnett's post-hoc test. **Results:** In group-housed helpless mice, but not in isolated animals, DMT and S-ketamine (both at 10 mg/kg, ip, 24 h prior the test) increased escape behavior during learned helplessness. In single-housed helpless mice, S-ketamine (30 mg/kg, ip) reduced immobility only 28 h after administration ($p<0.05$), whereas DMT (10 mg/kg, ip) reduced immobility at 28 h ($p<0.05$) and showed sustained effects, with trends toward reduced immobility at 5 and 8 days after treatment. Additionally, both drugs prevented helplessness-induced anhedonia 5 days after treatment (RM ANOVA, $F(2,16)=3.71$, $p=0.04$). In the OFT, DMT (10 mg/kg), but not S-ketamine, significantly increased spontaneous locomotor activity 30 h post-treatment ($p<0.05$), thus reversing helplessness-induced hypolocomotion. No significant correlations were detected between locomotion and immobility or escape, ruling out hyperlocomotion as a confound. In the EPM, 5 days after administration, DMT (10 and 25 mg/kg), but not S-ketamine, increased time spent in open arms (ANOVA, $F(2,18)=4.13$, $p=0.03$), without affecting closed arm entries. **Conclusion:** DMT produced rapid and sustained antidepressant-like effects comparable to S-ketamine, while additionally evoked anxiolytic-like effects in helpless mice. These findings reinforce the transdiagnostic potential of DMT as a promising rapid-acting therapeutic strategy for stress-related neuropsychiatric disorders.

03.038 **Effects of Aromatherapy with *Citrus bergamia* Essential Oil on Stress, Anxiety, and Depression in Public School Teachers: a Randomized Crossover Clinical Trial**. Sobral R[1], Santos HLS[1], Santos AF[2], Silva GNB[1], Silva BM[1], Sette-de-Souza PH[2], Albuquerque PBSA[1,2]. [1]UPE, PPG Biologia Celular e Molecular Aplicada, Brazil, [2]UPE, PPG Saúde e Desenvolvimento Socioambiental, Brazil.

Introduction: Disorders such as stress, anxiety, and depression have significantly impacted the mental health of public school teachers, ranking among the primary complaints that compromise their quality of life and professional performance. In this context, aromatherapy emerges as a promising complementary strategy, notably using bergamot essential oil (*C. bergamia*), which is recognized for its calming and anxiolytic effects. **Objective:** This study analyzed the effects of aromatherapy through the inhalation of bergamot essential oil on the psychological and physiological parameters of public-school teachers. **Methods:** This is a randomized, crossover, single-blind clinical trial conducted with 44 public school teachers. Participants were selected based on inclusion and exclusion criteria, completed all stages, and served as their own controls. Participants were randomly subjected to three sessions of inhalation aromatherapy with bergamot essential oil and three control sessions with *Melaleuca alternifolia*, in distinct periods separated by a seven-day washout interval. Physiological parameters, including heart rate, blood pressure, and peripheral oxygen saturation, were evaluated before and after each session. Levels of stress, anxiety, and depression were measured using the Depression, Anxiety, and Stress Scale-21 (DASS-21), administered at the beginning of each session. **Results:** A progressive reduction in the median scores of stress, anxiety, and depression was observed throughout the sessions with bergamot essential oil: stress decreased from 25 to 16, anxiety from 21 to 13, and depression from 16 to 11. In contrast, the control group showed slight variations without relevant clinical improvement. Paired analyses demonstrated statistically significant reductions following the intervention ($p < 0.05$). In the intergroup comparison at the end of the protocol, an increase in effect size was observed, with moderate magnitude for stress (rrb = 0.45) and a large effect for anxiety (rrb = 0.50). Regarding the physiological parameters evaluated, no statistically significant changes were observed during the experimental period. **Conclusion:** Inhalation aromatherapy with bergamot essential oil proved effective in reducing symptoms of stress, anxiety, and depression in public school teachers, establishing itself as a promising complementary strategy for promoting mental health within the school environment.

03.039 **Antinociceptive Effect of Cinnamaldehyde in Male Mice: an *in silico* and *In vivo* Mechanistic Investigation**. Rêgo RIA[1], Pires HFO[1], Dias AL[1], Remigio MCRB[1], Andrade HHN[2], Silva PR[1], Sousa NF[1], Scotti L[1], Scotti MT, Salvadori MGSS, Castro RD[1]. [1]UFPB, PPG in Natural and Synthetic Bioactive Products, João Pessoa, Paraíba, Brazil; [2]PeFarM-UFPB, Institute of Research in Drugs and Medicines, João Pessoa, Paraíba, Brazil

Introduction: Cinnamaldehyde (CA), the major bioactive constituent of essential oils from *Cinnamomum* spp., has demonstrated several pharmacological properties, including potential analgesic effects. However, the mechanisms underlying its acute antinociceptive activity remain incompletely understood. **Objectives:** To investigate the antinociceptive effect of cinnamaldehyde and its possible mechanisms of action through *in silico* and *in vivo* approaches. **Methods:** Molecular docking analyses were performed to evaluate possible interactions between CA and nociception-related targets. Behavioral and antinociceptive effects were assessed in male Swiss mice using the open field, rota-rod, formalin, glutamate, capsaicin, and hot plate tests. Pharmacological antagonism protocols were additionally conducted to investigate the involvement of opioid and adrenergic pathways. **Results:** Docking simulations demonstrated favorable interactions between CA and κ- and δ-opioid receptors, as well as NMDA, AMPA, and TRPV1 targets, suggesting a multimodal mechanism of action. In behavioral assessments, CA reduced locomotor activity in the open field test without impairing motor coordination in the rota-rod test. In nociception models, CA significantly inhibited nociceptive behavior in both phases of the formalin test, in addition to reducing glutamate- and capsaicin-induced nociception. In the hot plate test, CA increased response latency at 30 mg/kg, indicating participation of central mechanisms. Furthermore, naloxone completely reversed the antinociceptive effect of CA, while yohimbine partially blocked its action, suggesting the involvement of opioid and α_2-adrenergic systems. **Conclusion:** Cinnamaldehyde exhibited robust acute antinociceptive activity without causing motor impairment. The findings suggest that its effects involve opioid and adrenergic pathways, possibly associated with interactions with glutamatergic and TRPV1-related targets, highlighting CA as a promising candidate for the development of new analgesic agents.

03.040 **Meningeal Inflammatory Responses and Long-Term Behavioral Alterations Induced by Adolescent Stress**. Coelho S, Pigatto G, Meschick CG Verza FA, Freitas IS, Grigório-de-Sant'Ana M, Guimaraes FS, Cunha TM, Gomes FV. FMRP-USP, PPG em Farmacologia , Brasil

Introduction: Exposure to stressful events during critical periods of neurodevelopment, along with an imbalance between excitatory and inhibitory networks, is associated with the development of psychiatric disorders. GABAergic interneurons expressing parvalbumin (PV+) play a central role in regulating neural circuit synchrony and are consistently impaired in psychiatric disorders such as depression and schizophrenia. Our group has observed that exposing rodents to stressors during a period corresponding to adolescence results in behavioral and circuit deficits associated with PV+ interneuron dysfunction. Peripheral immune activation, particularly at the meningeal level, may influence these circuits through inflammatory mediators. **Objective:** Investigate whether the meningeal immune response mediates long- term behavioral impairments induced by stress exposure during adolescence. **Methods:** Male C57BL/6 mice were subjected to a stress protocol from postnatal day (PND) 31 to 40, which consisted of 15 randomized footshocks per day (0.75mA, 2s duration, randomly distributed). The animals were euthanized the following day (PND41) to assess changes in meningeal and brain parenchymal cells and cytokine levels. Another group was maintained until early adulthood (PND60) for behavioral testing and the same molecular analyses described above. **Results:** Analysis of the meninges 24 hours after the stress protocol revealed an increase in total CD45+ (Naïve, $6.66x10^4±1.25x10^4$, n=6; Stress, $1.32x10^5±1.81x10^4$, n=7,*p=0.006) and myeloid cells (Naïve, $1.40x10^4±2.74x10^3$, n=6; Stress, $2.36x10^4±2.20x10^3$, n=7,*p=0.01). This accumulation of immune cells remained restricted to the meninges, as no significant increase was observed in the brain parenchyma for total CD45+ (Naïve, $3.94x10^4±3.30x10^2$, n=6; Stress, $2.43x10^4±2.73x10^2$, n=7, p=0.06) or myeloid cells (Naïve, $1.44x10^4±2.60x10^3$, n= 6; Stress, $1.11x10^4±1.41x10^3$, n=7, p=0.9). Also, 24 hours after the stress protocol there was an increase in mRNA expression of Il2 (Naïve, 1.02±0.27, n=6; Stress, 3.00±1.78, n=7,*p=0.01), Il10 (Naïve, 1.05±0.31, n=6; Stress,1.49±0.29, n=7,*p=0.01), Il6 (Naïve, 1.03±0.28, n=6; Stress, 1.57±0.48, n=7,*p=0.01), Ifnγ (Naïve, 1.04±0.32, n=6; Stress, 2.54±0.99, n=7,*p=0.002), Il17 (Naïve, 1.02±0.23, n=6; Stress, 1.92±0.58, n=7,*p=0.002), and Ccl2 (Naïve, 1.05±0.32, n=6; Stress, 1.39±0.23, n=7,*p=0.02). For the adult animals exposed to adolescent stress, it was found a reduction in social interaction (Naïve: 0.52±0.06; n=11; Stress: 0.31±0.05; n=12,*p=0.005), social discrimination (Naïve: 0.53±0.06; n=10; Stress: 0.09±0.09; n=13,*p=0.001), and object recognition ability (Naïve: 0.50±0.07; n=12; Stress: 0.28±0.05; n=13,*p=0.002). Despite the behavioral impairments, the increase in immune cells and inflammatory mediators observed 24h after stress exposure was no longer detected in adulthood. **Conclusion:** Repeated stress during adolescence induces a short-term compartmentalized inflammatory response restricted to the meninges, which may contribute to the behavioral alterations observed in adulthood. Funding: FAPESP, CAPES, CNPq, and FAEPA.

03.041 **Sex-Independent Recruitment of the Dorsal Periaqueductal Gray in Fear Memory Expression, Consolidation, and Generalization**. Zanoveli JM, Cunha JM, Oliveira PHA, Silva AHBL UFPR, Dept Pharmacology, Brazil.

Introduction: Stress-related anxiety disorders involve dysregulation of neural circuits associated with emotional processing, particularly the endocannabinoid and serotonergic systems. Specialized pro-resolving mediators (SPMs), derived from omega-3 fatty acids, have emerged as potential modulators of neuroinflammation and emotional behavior. Resolvin D5 (RvD5), a DHA-derived lipid mediator, has shown neuroprotective and anxiolytic-like properties, although its preventive effects against stress-induced anxiety and the mechanisms involved remain unclear. This study investigated whether repeated RvD5 treatment prevents stress-induced anxiety-like behavior in male and female rats and evaluated the involvement of cannabinoid CB1, CB2, and serotonergic 5-HT1A receptors. **Methods:** Adult male and female Wistar rats received daily intraperitoneal injections of RvD5 (1 ng/animal) or vehicle for 10 days. Basal anxiety-like behavior was evaluated in the light–dark transition (LDT) test on day 8. On day 9, animals were exposed to 2 h of acute restraint stress. On day 10, rats received WAY-100635 (5-HT1A antagonist), AM251 (CB1 antagonist), or AM630 (CB2 antagonist) before evaluation in the elevated plus maze (EPM). Sustained or withdrawal-related effects were assessed in the novelty-suppressed feeding test (NSFT) on day 17. **Results:** Repeated RvD5 treatment did not alter basal anxiety-like behavior in the LDT. However, RvD5 prevented stress-induced anxiety-like behavior in the EPM in both sexes. In males, this effect was blocked only by CB2 antagonism, whereas in females it was prevented by CB1, CB2, and 5-HT1A antagonists, suggesting sex-dependent receptor mechanisms. No behavioral alterations were observed in the NSFT after treatment interruption. **Conclusion:** Repeated RvD5 treatment produced preventive anxiolytic-like effects specifically under stress conditions without affecting basal emotional behavior. These effects involve cannabinoid and serotonergic mechanisms in both sexes, supporting RvD5 as a promising preventive strategy for stress-related anxiety disorders independent of sex.

03.042 **Modulation of Social Behavior in Adult Zebrafish: A Systematic Review and Meta-Analysis**. Gallas-Lopes M[1,2], Müller DV[1,2], Abreu MB[1,3], Arbo BD[1,2], Bastos LM[1,2], Fröhlich NT[1,4], Marcon M[1,5], Moraes IB[1,6], da Silva LCCP[1,7], Zurchimitten GR[1,8], Herrmann AP[1,2] [1]BRISA ColLaboration, Brazil, [2]UFRGS, Dept. of Pharmacology, Brazil, [3]UFRJ, Institute of Biophysics Carlos Chagas Filho, Brazil, [4]UFRGS, Dept. of Biochemistry, Brazil, [5]UFTM, Dept. of Biochemistry, Pharmacology and Physiology, Brazil, [6]UFOB, Center of Biological and Health Sciences, Brazil, [7]Fiocruz, Institute of Science and Technology in Biomodels, Brazil, [8]UFSC, Dept. of Pharmacology, Brazil

Introduction: Adult zebrafish (Danio rerio) are widely used to investigate the neurobiological mechanisms of social behavior and to screen interventions with potential effects on sociability. Social preference and shoal cohesion are among the main assays to evaluate zebrafish social behavior; however, the available literature remains heterogeneous, limiting reproducibility and generalizability. **Objectives:** To evaluate how pharmacological and stress- related interventions modulate social preference and shoal cohesion in adult zebrafish, and their association with anxiety-like behavior. **Methods:** This review was registered in OSF (osf.io/x95w6). We searched Embase, PubMed, and Web of Science up to October 25, 2024. After deduplication, records underwent eligibility assessment by independent reviewers. Controlled studies assessing social preference or shoal cohesion in adult zebrafish exposed to pharmacological or stress-related interventions were included. Risk of bias was assessed using SYRCLE's tool. Standardized mean differences (SMD) were calculated and pooled using multilevel and multivariate random-effects models and robust variance estimation. Prediction intervals estimated expected effects in future studies. **Results:** We retrieved 3,177 records; 1,719 were screened, 1,131 underwent full-text assessment, and 108 studies were included. Social preference was evaluated in 65 studies, shoal cohesion in 30, both paradigms in 13, and anxiety-like behavior in 63. In social preference, significant reductions were observed for pro- dopaminergic agents (SMD=-0.56; 95% CI -1.02 to -0.10), ethanol (SMD=-0.65; 95% CI -0.84 to -0.46), N-methyl-D-aspartate receptor antagonists (SMD=-1.89; 95% CI -3.24 to -0.55), and stress-related interventions (SMD=-0.61; 95% CI -1.14 to -0.09). Ethanol concentration significantly moderated social preference, with higher concentrations associated with greater reductions in this behavior. In shoal cohesion, only stress-related interventions showed a significant increase (SMD=0.94; 95% CI 0.20 to 1.68). No consistent effects were detected for anxiety-like behavior. Most analyses showed substantial heterogeneity, and prediction intervals were consistent with both increased and decreased sociability. Risk of bias assessment indicated frequent unclear reporting of randomization, blinding, and sample size, and a high risk for pseudoreplication. **Conclusion:** Social behavior in adult zebrafish is modulated by pharmacological and stress-related interventions, but effects differ between social preference and shoal cohesion, supporting these assays as complementary rather than interchangeable outcomes. The evidence highlights the translational value of zebrafish for neurobehavioral research while underscoring the need for better reporting, bias control, and standardized analysis.

03.043 **Dealing with the Enemy: Antidepressant-Like Effects of N-Acetylcysteine Treatment in Vulnerable Rats to Social Defeat Stress**. Morais-Silva G[1,2], Giatti LO[2], Martins LLS[2], Marin MT[2]. [1]UEM, Dept. of Pharmacology and Therapeutics, Graduate Program in Pharmaceutical Sciences, Brazil. [2]Unesp, School of Pharmaceutical Sciences of Araraquara, Lab Pharmacology, Interinstitutional Graduate Program in Physiological Sciences UFSCar/Unesp, Brazil.

Introduction: Despite the recent advancements regarding neurobiology and treatment of stress-related psychiatric diseases, they are still highly prevalent and represent an important burden to public health. Such disorders still present relevant therapeutic limitations, including low efficacy, high rates of relapse, and therapeutic-limiting adverse effects. Thus, it is imperative to develop new therapeutic strategies to circumvent such limitations. Recent results suggest that glutamatergic neurotransmission is implicated in stress-related psychiatric disorders, uncovering the potential of drugs that regulate synaptic glutamate release as antidepressant agents. N-Acetylcysteine (N-AC), acting as a modulator of the astrocytic cystine-glutamate exchanger (xCT), could have potential use in the treatment of stress-related psychiatric disorders, including depression. **Objectives:** This study aimed to evaluate the effects of N-AC treatment on stress-related behavioral alterations in vulnerable rats (VUL) to social defeat stress (SDS). **Methods:** Male Wistar rats (n=60, CEUA/FCF/CAr 01/2017) were exposed to 7 days of SDS (4 agonistic encounters with a male Long Evans rat, every other day), after which their SDS coping phenotype [resilient (RES) or VUL] was identified using the k-means clustering of the interaction ratio (IR) obtained in the social interaction test (SIT). Control (CON) animals were not exposed to SDS. Twenty-four hours later, animals were treated for 16 days with N-AC (60 mg/kg, i.p., twice a day). In the last 3 days, animals were tested regarding anxiety-like behaviors in the elevated plus maze (EPM) and depressive-like behaviors in the forced swim test (FST). Data were analyzed by two-way ANOVA followed by the Newman-Keuls test, considering $p \leq 0.05$ as significant. **Results:** VUL and RES rats were identified based on the presence of social avoidance in the SIT. VUL rats showed a decrease in the % of time spent in the open arms (%OAT) of the EPM, which was reversed by N-AC treatment. ANOVA showed a significant effect for the interaction between phenotype and N-AC factors ($F_{2,57} = 3.22$; $p<0.05$) for the %OAT. Vehicle-treated VUL rats (VUL-VEH) spent less time in the open arms relative to all the experimental groups ($p<0.05$). Moreover, VUL rats showed an increase in time spent immobile (IMMO) and a decrease in swimming time (SWIM) in the FST, which were reversed by N-AC. ANOVA showed a significant effect for the interaction between phenotype and N-AC factors ($F_{2,54} = 4,04$; $p<0.05$) for the IMMO. VUL-VEH rats spent more time immobile relative to all the experimental groups ($p<0.05$). ANOVA showed a significant effect for the interaction between phenotype and N-AC factors ($F_{2,54} = 3,53$; $p<0.05$) for the SWIM. VUL-VEH rats spent less time swimming relative to all the experimental groups ($p<0.05$). **Conclusion:** We showed that chronic N-AC treatment reversed stress-induced behavioral alterations related to anxiety and depression in VUL rats to SDS. **Financial support:** CAPES financial code 001; Grant #2015/25308-3, São Paulo Research Foundation (FAPESP).

03.044 **Octovespin Ameliorates Cognitive Impairment and Amyloid-β Aggregation in Experimental Alzheimer's Disease**. Camargo LC[1], Alves LG[2], Veras LG[2], dos Santos VRM[2], Só YAdO[3], Costa CVS[3], Gargano R[3], Mortari MR[2]
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Introduction: Alzheimer's disease (AD) is the most common neurodegenerative disorder, and no current therapy can cure or effectively slow its progression. Peptides have emerged as promising therapeutic candidates due to their specificity and versatility. Venom derived molecules represent a particularly valuable source of bioactive compounds, since was shaped by evolutionary pressure to target precise biological pathways. **Objective:** In this study, we investigated the therapeutic potential of octovespin, a peptide inspired by the venom of *Polybia occidentalis*, against Amyloid β (Aβ), a central hallmark of AD. **Methods:** *In vitro* assays were conducted to evaluate the effects of octovespin on amyloid-β (Aβ) aggregation using the Thioflavin T assay, as well as its antioxidant activity and cytotoxicity in SH-SY5Y cells, including protection against 6-hydroxydopamine-induced toxicity. Hemolytic and neurotoxic effects were assessed across all tested doses. *In vivo*, an Aβ- induced cognitive impairment model was established in Swiss male mice, which received intracerebroventricular administration of octovespin (0.15 nmol/animal) for seven consecutive days. Cognitive performance was evaluated using the Morris Water Maze and Novel Object Recognition tests. Similarly, octovespin treatment was also evaluated subcutaneouly (4 mg/kg). Additionally, molecular docking and molecular dynamics simulations were performed to investigate the interaction between octovespin and Aβ(17–42) fibrils as well as Angiotensin-converting enzyme (ACE), Beta-secretase 1 (BACE1), Glycogen synthase kinase-3 (GSK-3), Tumor necrosis factor-α–converting enzyme (TACE) and Acetylcholinesterase (AChE). **Results:** Octovespin inhibited Aβ aggregation and antioxidant activity *in vitro*. No hemolytic or neurotoxic effects were observed. *In vivo*, octovespin treatment significantly improved memory deficits and behavior alterations in Aβ-injected mice when injected i.c.v however, no improvement was observed after subcutaneous treatment. Computational analyses showed that octovespin remained stably bound to Aβ(17–42) fibrils throughout the simulations, indicating a strong disaggregation potential. Moreover, Octovespin exhibited greater flexibility throughout the simulated trajectories for AD targets such as ACE, BACE1, GSK-3 and TACE. **Conclusion:**Overall, octovespin appears to be a promising candidate for AD therapy due to its ability to inhibit Aβ aggregation and reduce Aβ induced cognitive decline although alternative routes of administration and treatment strategies still need to be investigated.

04. Inflammation and Immunopharmacology

04.001 **Anti-Inflammatory Activity of Methyl 2-(3-hydroxy-1-methyl-2-oxoindolin-3-yl) acrylate (MISACM) in Murine Acute Lung Injury**. Mota PRV, Pordeus GM, Silva TGd, Félix MJD, Rodrigues MRF, Laurentino MVS, Moura BVS, Oliveira JB, Gadelha FAAF, Vieira GC, Dejani NN. UFPB, Lab Immunopharmacology, Brazil.

Introduction: Acute lung injury (ALI) is a multifactorial condition characterized by alveolar and endothelial damage within an inflammatory context. The pharmacotherapy of ALI involves the administration of anti- inflammatory agents to reduce the recruitment of inflammatory cells and alveolar damage, but their spectrum of use remains limited due to adverse effects and variations in efficacy among patients. Morita-Baylis-Hillman adducts (MBHA) are molecules that are attracting growing pharmacological interest due to their biological activity, including antimicrobial, antitumor, and anti-inflammatory effects. The synthetic molecule methyl 2-(3-hydroxy-1-methyl-2-oxoindolin-3-yl) acrylate (MISACM) is an MBHA derived from isatin that has already been evaluated for antitumor effects but has not demonstrated significant therapeutic efficacy. However, its anti-inflammatory effect remains unexplored. **Objectives:** To evaluate the anti-inflammatory effects of MISACM in a murine model of ALI. **Methodology:** Swiss mice were treated orally with 100 µL of MISACM at doses of 6 mg/kg, 12 mg/kg, and 25 mg/kg. After 1 h, ALI was induced via intranasal instillation of 40 µL LPS at dose of 5 mg/kg. After 24 hours, the animals were euthanized, and their lungs were removed for processing and histological evaluation of common ALI changes. A statistical score was calculated based on the American Thoracic Society criteria. Total protein levels in bronchoalveolar lavage fluid (BALF) were quantified using a colorimetric assay, and cell counts were assessed. Additionally, TNF levels in BALF were measured using an ELISA assay, while phosphorylation of NF-κB was evaluated by flow cytometry. **Results:** Compared to the ALI group, treatment with MISACM reduced alveolar edema, hemorrhage, alveolar inflammatory cell infiltration, and hyaline membrane formation, with the 25 mg/mL concentration having the greatest effect. In BALF, MISACM treatments decreased protein exudate, the total number of inflammatory cells, including neutrophils, and also the amount of TNF-α. Furthermore, MISACM reduced phosphorylation of p65 NF-κB. **Conclusion:** MISACM demonstrated anti- inflammatory potential in the ALI model, proportional to the dose increase, as it minimized inflammation and lung injury in the animals. Animal Research Ethics Committee Number: 8246070825\. **Financial support:** Coordination for the Improvement of Higher Education Personnel (CAPES). **Acknowledgments:** To UFPB and the Immunopharmacology Laboratory.

04.002 **Structural and Quantum Perspective on the Potential Anti-Inflammatory Mechanisms of Caulerpin as a TLR2 Modulator**. Coringa WV[1], Assunção AS[1], Paiva EA[1], Santos BVO[5], Menezes GL[3], Sena CPS4, Vieira D S4, Fulco UL[3], Bezerra KS[2,3], Souto JT[1]. [1]UFRN, Lab Immunopharmacology, Brazil. [2]Unicamp, Gleb Wathing Institute of Physics, Brazil. [3]UFRN, Dept Biophysics and Pharmacology, Brazil. [4]UFRN, Institute of Chemistry, Brazil. [5]UFCG, PPG in Development and Technological Innovation in Medicines, Brazil.

Structural and quantum perspective on the potential anti-inflammatory mechanisms of caulerpin as a TLR2 modulator. Coringa WV[1], Assunção AS1,2, Paiva EA[1], Santos BVO3, Menezes GL4, Fulco UL4, Sena CPS5, Vieira DS5, Bezerra KS4,6, Souto JT1,2. [1]UFRN, Laboratory of Immunopharmacology, Brazil. [2]UFRN, PPG in Parasitic Biology, Brazil. 3UFCG, PPG in Development and Technological Innovation in Medicines, Brazil. 4UFRN, Department of Biophysics and Pharmacology, Brazil. 5UFRN, Institute of Chemistry, Brazil. 6Unicamp, Gleb Wathing Institute of Physics, Brazil. **Introduction:** Natural products, such as the alkaloid caulerpin found in marine algae of the genus Caulerpa, exhibit anti-inflammatory activity. Studies using murine models of peritonitis and generalized inflammation induced by zymosan have pointed to the inhibitory potential of this molecule on cell migration to the infection site. **Objective:** In this context, the present study aimed to investigate, through *in silico* approaches, the possible molecular mechanisms associated with the biological activity of caulerpin. **Methods:** Initially, molecular docking studies were performed between caulerpin and the Toll-like receptor 2 (TLR2), which is responsible for recognizing zymosan and fungal components. The most favorable conformations obtained were subjected to molecular dynamics simulations to evaluate the structural stability of the protein-ligand complex over time. Additionally, quantum mechanics calculations based on the Molecular Fragmentation with Conjugate Caps (MFCC) methodology combined with Density Functional Theory (MFCC/DFT) were employed to quantify and characterize the energetic contributions of the amino acid residues involved in the interaction with caulerpin. **Results:** The docking results revealed a high affinity of caulerpin for the TLR2 binding site. Molecular dynamics simulations indicated that the conformational stability of the complex was maintained throughout the simulated trajectory, demonstrating the persistence of the key protein-ligand interactions. The MFCC/DFT quantum calculations allowed the identification of specific receptor residues that contribute significantly to the stabilization of the complex, providing a detailed description of the interactions responsible for molecular recognition. **Conclusion:** Together, the results suggest that caulerpin may act by modulating TLR2 activation, offering a molecular explanation for the experimentally observed anti-inflammatory effects and pointing to this receptor as a potential therapeutic target for the molecule. Animal Ethics Committee: CEUA/UFRN (013/2023). **Financial support:** CAPES, CNPq e Propesq/UFRN.

04.003 **Role of the Endogenous Hydrogen Sulfide (H_2S) in the Inflammatory Response Induced by Bacterial Membrane Lipopolysaccharide (LPS) in cultured THP-1 Macrophages**. Rodrigues JLG, Coavoy-Sánchez SA, Teixeira SA, Costa SKP, Muscará MN ICB-USP, Pharmacology Dept, Lab Free Radicals, Inflammation and Pain.

Introduction: **and Objectives:** Hydrogen sulfide (H_2S) is a gaseous mediator produced endogenously by several cells, including macrophages, through the enzymes cystathionine β-synthase (CBS), cystathionine γ-lyase (CSE), and 3-mercaptopyruvate sulfotransferase (3-MST). Evidence indicates that H_2S can exert modulatory effects on the inflammatory response, but the mechanisms involved in regulating the activation of THP-1 macrophages are not yet fully understood. Thus, this project aims to investigate the role of endogenous H_2S in the inflammatory response in differentiated THP-1 macrophages and to characterize the enzymes involved. Materials and **Methods:** Human monocytic THP-1 cells were differentiated into macrophages by treatment with 10 ng/ml phorbol 12-myristate-13-acetate (PMA) for 48 h, followed by 24 h in PMA-free medium for phenotypic stabilization. H_2S production was quantified in THP-1 macrophage homogenates using the lead sulfide (PbS) formation method. This production was analyzed in the presence of inhibitors of H_2S-producing enzymes (aminoxyacetate—AOAA, β-cyano-L-alanine—BCA, and DL-propargylglycine—PAG) at concentrations of 1, 3, and 10 mM. Cell viability was assessed after incubation with the various treatments using the MTT assay. Data are expressed as mean ± SEM. Differences between group means were analyzed by one-way ANOVA, followed by Dunnett's multiple comparison test, with differences considered significant at $P < 0.05$. **Results:** The values of the standardization of endogenous H2S production quantification correspond to the increase in H2S production relative to the reading taken after 2 h of incubation, which was used as a reference (baseline) for subsequent analyses. For all total protein amounts tested, a linear increase in H2S production was observed over the analysis time; for subsequent assays, 200 µg of total protein were used during 4 h of incubation. When analyzing the effects of the inhibitors on endogenous H_2S production in THP-1 macrophage homogenates, the results shows that AOAA (10 mM) significantly reduced H2S production compared to the control group (C (-)) ($P<0.0001$; N = 6). However, BCA and PAG, selective inhibitors of the CSE enzyme, did not promote a significant reduction in H_2S production at any of the concentrations evaluated. In the MTT assay, that treatment with AOAA for 4h did not alter cell viability at any of the concentrations tested. In contrast, there was a significant increase in cell viability after incubation with BCA at a concentration of 10 mM (*$P<0.05$; N = 6). Similarly, occurred during the 4-hour treatment with PAG also promoted a significant increase in cell viability at different concentrations (3 mM: $P<0.001$; 10 mM: $P<0.0001$; N = 6), compared to the control. **Conclusions:** The analysis of the effects obtained by the treatments in THP-1 macrophages under basal conditions allowed the **Conclusion:** that the inhibitor AOAA (10 mM) is the most suitable for subsequent experiments. These aim to associate the determinations regarding the role of H_2S in cells, under basal conditions, with the modulation of the inflammatory response in macrophages activated by bacterial membrane lipopolysaccharide (LPS). Finnancial support: The project is funded by FAPESP. **Acknowledgments:** The main author acknowledges all the other authors, FAPESP, family and friends for the support during the project.

04.004 **Therapeutic Modulation of NF-κB and p38 MAPK Signaling by ZIB Reduces IL-6 Expression in LPS-Stimulated RAW 264. 7 Macrophages**. Pordeus GM[2], Moura BVS[1], Laurentino MVS[1], Rodrigues MRF[1], Oliveira JB[1], Mota PRV[2], Lima-Júnior CG[3], Gadelha FAAF[2], Dejani NN[2]. [1]UFPB, Immunopharmacology Lab, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]IPeFarM-UFPB, Immunopharmacology Lab, Institute of Pharmaceutical and Medicinal Research-, Brazil. [3]UFPB, Medicinal Organic Synthesis Lab Paraíba, Brazil.

Introduction: Excessive activation of pro-inflammatory intracellular signaling pathways is a key driver of acute inflammatory disorders. In macrophages, lipopolysaccharide (LPS) stimulation activates the NF-κB and p38 MAPK pathways, promoting the production of inflammatory mediators such as IL-6 and contributing to tissue damage and immune dysregulation. Pharmacological modulation of these pathways represents a promising therapeutic strategy, particularly after the onset of inflammation. In this context, (Z)-N'-(1-(3-methylbut-2-en-1-yl)-2-oxoindolin-3-ylidene)benzohydrazide (ZIB) emerges as a potential therapeutic candidate capable of selectively targeting key intracellular mediators involved in inflammatory signaling. **Objectives:** To evaluate the therapeutic immunomodulatory potential of ZIB in an acute inflammation post-treatment model by assessing its ability to modulate key intracellular inflammatory signaling pathways, specifically NF-κB and p38 MAPK, and to regulate IL-6 gene expression in LPS-stimulated RAW 264.7 macrophages. **Methodology:** RAW 264.7 macrophages were cultured in supplemented DMEM and stimulated with LPS (1 μg/mL). After 2 h, ZIB (5 μM; 0.2% DMSO) was administered under a therapeutic post-treatment protocol. After 24 h, the percentage of cells positive for total and phosphorylated NF-κB and phosphorylated p38 MAPK was determined by flow cytometry. IL-6 expression was quantified by RT-qPCR (Δ ΔCt), using β-actin as control. Statistical analysis was performed by one-way ANOVA followed by Dunnett's post hoc test ($p < 0.05$). **Results:** Therapeutic intervention with ZIB promoted significant modulation of key intracellular signaling pathways involved in the inflammatory response, reinforcing its potential as a targeted pharmacological agent. Within the NF- κB pathway, ZIB significantly reduced the percentage of cells positive for phosphorylated NF-κB, indicating attenuation of pathway activation while preserving total NF-κB expression, which suggests a selective immunomodulatory mechanism rather than nonspecific suppression of cellular signaling. ZIB exerted an inhibitory effect on the p38 MAPK pathway, significantly decreasing the frequency of cells positive for phosphorylated p38, demonstrating direct interference with a critical signaling axis associated with inflammatory amplification and cytokine production. Importantly, the coordinated modulation of these intracellular pathways was accompanied by a significant downregulation of IL-6 gene expression, highlighting the functional impact of ZIB on the control of established inflammatory responses. **Conclusion:** ZIB demonstrated significant therapeutic potential by selectively modulating key inflammatory signaling pathways, attenuating NF-κB and p38 MAPK activation and consequently reducing IL-6 gene expression. These findings highlight its immunomodulatory profile and support its potential as a promising pharmacological candidate for the treatment of acute inflammatory disorders.

04.005 *in silico* Analysis of *Chlamydia trachomatis* MOMP Protein for the Identification of Immunogenic Epitopes.
Pinheiro IC[1], Conceição LS[2], Costa LFA[3], Sousa LR[4], Cartagenes MSS[5], Andrade MS6[1]UFMA, PPG Adult Health, Brazil, [2]UFMA, Biological Sciences Course, Brazil, [3]UFMA, Pharmacy Course, Brazil, [4]UFMA, PPG Adult Health, Brazil, [5]UFMA, Dept Physiological Sciences, PPG Health Sciences, Brazil, 6UFMA, Center for Biological and Health Sciences, Dept Physiological Sciences, PPG Adult Health, Brazil.

Introduction: Chlamydia trachomatis is the most common bacterial sexually transmitted infection worldwide and is associated with pelvic inflammatory diseases, ectopic pregnancy, and infertility. The MOMP protein, the main component of the outer membrane, is an important vaccine target due to its exposure to the immune system. In this context, reverse vaccinology allows the identification of epitopes with immunogenic potential, aiding in the selection of vaccine candidates. Objective: To identify *in silico* immunogenic epitopes of the C. trachomatis MOMP protein using immunoinformatics tools. Methods: The C. trachomatis serotype E MOMP protein sequence was obtained from UniProt. TMHMM was used to identify transmembrane regions, while physicochemical properties were evaluated using ProtParam. Transmembrane topology and the presence of a signal peptide were predicted by Phobius, and conserved domains were analyzed using InterProScan. The prediction of cytotoxic T lymphocyte (MHC-I), helper T lymphocyte (MHC-II), and B lymphocyte epitopes was performed using the IEDB MHC I (NetMHCpan EL), NetMHCIIpan-4.1, and BepiPred 2.0 servers. The selected epitopes were evaluated for homology with human proteins using BLASTp. Those approved for antigenicity, allergenicity, and toxicity were used to construct a multi-epitope vaccine. The 3D structure of the vaccine protein was predicted by AlphaFold2 and refined using GalaxyRefine. Results: MOMP showed physicochemical parameters indicating a moderately thermostable, stable, and hydrophilic protein. No transmembrane helices were identified, and it is indicated that part of the protein is non-cytoplasmic, suggesting its outer membrane localization and secretion. These results are compatible with a typical porin β-barrel structure, making MOMP accessible to immune recognition. The presence of the ChlamOMP domain confirms the structural conservation of MOMP among serotypes. Eighty-one candidate epitopes were identified for CD8+ T lymphocytes and about 40 for CD4+ T lymphocytes, from which four of each were selected based on the highest rank% and an antigenic, non-allergenic, and non-toxic profile. Following these criteria, three linear and two conformational B lymphocyte epitopes were also selected. Based on these results, a multi-epitope vaccine was constructed, including the β-defensin adjuvant and epitopes connected by linkers. The protein showed a molecular weight of 28.39 kDa, a pI of 9.04, a hydrophilic profile, and structural stability. The 3D modeling showed high confidence in the adjuvant region and greater flexibility in the regions composed of epitopes and linkers. Conclusion: The selected epitopes of the MOMP protein presented favorable antigenicity, safety, and conservation characteristics, demonstrating potential to compose a multi-epitope vaccine. The results reinforce the efficiency of immunoinformatics in identifying vaccine candidates and highlight the need for experimental validations.

04.006 **Effect of Silymarin** (*Silybum marianum* L.) **on Adipocytokines in High Fat Diet-Fed C57BL/6 Mice**. Carvalho JPAQ[1], Ferreira ALN[1], Sousa GA[1], Costa SGA[1], Canafístula LS[1], Oliveira KS[1], Barbosa ISA[1], Silva FRC[2], Silva ME[2], Bezerra VM[2], Martins BVB[2], Yaochite JUN[2], Martins AMC[2], Sampaio TL[2], Menezes RRPPB[2] [1]UFC, Faculty of Pharmacy, Dentistry and Nursing, Dept of Clinical and Toxicological Analysis, Brazil; [2]UFC, Faculty of Pharmacy, Dentistry and Nursing, Dept of Clinical Analysis and Toxicological, PPG of Pharmaceutical Sciences, Brazil

Introduction: Obesity has become a public health problem and is considered a risk factor for the development of pathological conditions due to inflammation and oxidative stress resulting from excess adiposity. Despite its prevalence, pharmacotherapeutic options remain limited and are associated with side effects. Therefore, the search for new anti-obesity compounds is necessary, with silymarin standing out as a promising candidate. Silymarin is the main component extracted from the seeds and fruits of *Silybum marianum* L. and exhibits properties such as preventing lipid peroxidation in hepatocyte structures, in addition to anti-inflammatory and immunomodulatory actions. Thus, this study aimed to investigate the anti-inflammatory potential of silymarin in mice exposed to a high-fat diet. **Methods:** Male C57BL/6 mice (CEUA-UFC, nº 9214030622) were divided into 7 groups (n = 10/group; Control, Silymarin, Obesity, Orlistat 30 mg/Kg, Silymarin 100, 10 and 1 mg/Kg) and received either a standard diet (SD) or a hypercaloric diet (HD) for 55 days. Treatment with vehicle (saline), orlistat, or silymarin began on the 6th day after HD administration and continued for the remaining 50 days. Body mass and average water and food intake per group were measured daily. At the end of the protocol, the animals were euthanized and subjected to surgical procedures for the collection of both adipose and hepatic tissues. Tissue samples were stored at -80°C for subsequent measurement of cytokines. Frozen samples were weighed and homogenized in phosphate buffer solution (pH 7.4); the homogenates were centrifuged, and the supernatant was used for the assays. From the homogenates, interleukin-1β (IL-1β) (in liver and adipose tissues) and adiponectin (in adipose tissues) levels were measured using enzyme-linked immunosorbent assay (ELISA) kits and expressed as pg/mg and ng/mg, respectively. **Results:** In hepatic tissue, treatment with silymarin at all three doses reduced IL-1β levels (84–95 pg/mg) compared with the Obesity group (160.1 ± 13.8 pg/mg), while remaining similar to the Control group (79.9 ± 7.6 pg/mg). In adipose tissue, IL-1β levels did not differ from the Control group (162.7 ± 33.8 pg/mg), but prevented the increase observed in the Obesity group (454.9 ± 34.1 pg/mg). Regarding adiponectin, the silymarin-treated groups remained comparable to the Control group (1,147 ± 44.4 ng/mg), whereas reduced levels were observed in the Obesity group (426.9 ± 45.3 ng/mg). **Conclusion:** Therefore, silymarin proved to be effective in regulating adipocytokines associated with obesity, highlighting its potential as a promising therapeutic agent for the treatment of obesity and its comorbidities. **Financial support**: FUNCAP.

04.007 **Investigation of the Immunopathogenesis Mediated by NETs (Neutrophil Extracellular Traps) in Chikungunya**. Barbosa ISA[1], Leal ARSN[2], Cesário IBB[1],Carvalho JPAQ[1], Costa SGA[1], Canafístula LS[1], Oliveira KS[1], Rodrigues RO[1], Barreto FKA[3], Silva TN[3], Cavalcanti LPG[3], Siqueira AM[4], Yaochite JNU[1]. [1]UFC, Faculty of Pharmacy, Dentistry, and Nursing, Dept Clinical and Toxicological Analysis, Brazil; [2]UFC, Faculty of Pharmacy, Dentistry, and Nursing, Dept Clinical and Toxicological Analysis, Graduate Program in Medical Microbiology, Brazil; [3]UFC, Faculty of Medicine, Brazil; [4]Fiocruz, Brazil

Introduction: Chikungunya, caused by the Chikungunya Alphavirus (CHIKV), is a critical public health issue due to chronic, disabling arthralgia. The innate immune response attracts inflammatory cells to the site to control viral spread, and neutrophils are a key component of this defense. They release neutrophil extracellular traps (NETs), composed of genetic material and antimicrobial proteins. However, excessive NET production can trigger exacerbated inflammation and systemic damage. The objective was to investigate the role of NETs in the immunopathogenesis of CHIKV infection in women. **Methodology:** This is a longitudinal, retrospective study (2021–2024) involving 40 women who tested positive for IgM/IgG and 10 healthy controls. Myeloperoxidase (MPO), elastase (EN), and citrullinated histone H3 (H3cit) were quantified by ELISA, and cell-free DNA (cfDNA) by fluorimetry. Statistical analysis employed the Friedman, Mann-Whitney, and Spearman tests ($p < 0.05$). Study approved by the Research Ethics Committee of the Federal University of Ceará (UFC) (CAAE: 75466723.2.0000.5054). **Results:** The sample consisted predominantly of women aged 50–59 years. MPO and cfDNA levels peaked on Day 0, followed by a decline; MPO levels rose again on Day 360. MPO, EN, and cfDNA levels in infected individuals were lower than those in controls ($p < 0.05$). H3cit remained persistently elevated compared to the control group (D0 to D360, $p < 0.05$). Positive correlations between MPO and EN were observed on D0, D90, and D180. There was no difference when stratified by chronic pain, comorbidities, or medication use. **Conclusion:** The findings show that CHIKV induces the release of NETs. Non-lytic NETosis suggests a host effort to contain the virus, but the persistence of these markers may mediate chronic inflammation and be associated with arthralgia. The results reinforce the need for immunomodulatory interventions that balance protection and tissue damage without compromising antiviral immunity. **Financial support:** J.B.S S.A.

04.008 **Evaluation of the *In vitro* Cytotoxicity and Pharmacokinetic Properties of a New Green Synthetic Acetanilide with Potential Application in Neuroinflammation**. Silva TG[1], Sousa M. [1], Luís LRCS[1], Falcão MEES[1], Gadelha FAA[1], Dejani NN[1], Fiss GF[2], Luís JAS[2], Vieira GC[1]. [1]UFPB, Research Institute of Drug and Medicines, Lab. of Immunopharmacology, Brazil. [2]UFPB, Lab. of Bioenergy and Organic Synthesis Research, Brazil.

Introduction: Inflammation and neuroinflammation play central roles in the pathophysiology of several chronic diseases and are associated with persistent activation of pro-inflammatory pathways. Although current anti-inflammatory drugs are therapeutically effective, adverse effects associated with prolonged use highlight the need for novel bioactive molecules with improved safety profiles. In this context, N-phenylacetamide (acetanilide) derivatives have attracted interest due to their structural scaffold and potential immunomodulatory properties. **Objective:** To investigate the *in vitro* cytotoxicity profile and the *in silico* pharmacokinetic properties of compound 2D, a green synthetic N-phenylacetamide derivative. **Methods:** Murine RAW 264.7 macrophages were seeded overnight in 96-well plates (1×10^4 cells/well) and maintained at 37 °C in a humidified atmosphere containing 5% CO_2. Cells were exposed to increasing concentrations of compound 2D (25–400 µg/mL) for 24 h. Cell viability was determined using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) colorimetric assay, based on the ability of metabolically active cells to reduce MTT into formazan crystals. Statistical analysis was performed relative to the untreated control. Data were expressed as mean ± SEM from three independent experiments and analyzed using one-way ANOVA with Dunnett's post hoc test. CC_{50} values were estimated by nonlinear regression using GraphPad Prism. Pharmacokinetic properties were predicted using SwissADME. **Results:** Compound 2D maintained cell viability at concentrations up to 100 µg/mL. At higher concentrations, significant cytotoxicity was observed, with cell viability reduced to 51.3% at 200 µg/mL ($p < 0.001$) and 11.0% at 400 µg/mL ($p < 0.0001$), compared with the control group (99.3%). The estimated CC_{50} value was approximately 198 µg/mL, indicating a concentration-dependent cytotoxic effect at higher doses. *in silico* pharmacokinetic analysis predicted high gastrointestinal absorption, blood–brain barrier permeability, and the absence of P-glycoprotein substrate characteristics. Additionally, selective inhibition of CYP1A2 was predicted, with no relevant interactions with the other evaluated cytochrome P450 isoforms. These findings suggest favorable systemic bioavailability and the ability to reach the central nervous system, supporting future investigations in neuroinflammatory models. **Conclusion:** Therefore, *in vitro* cytotoxicity assays demonstrated that the 2D synthetic compound maintained cell viability above 80% at concentrations up to 100 µg/mL, with a CC_{50} of 198 µg/mL, indicating an initial safety profile. Additionally, predicted *in silico* pharmacokinetic properties, including high gastrointestinal absorption and blood-brain barrier permeability, support its potential as a candidate drug for neuroinflammatory diseases. Together, these findings justify further preclinical studies to confirm its therapeutic potential.

04.009 **Differential Effect of Fluoxetine in the Febrile Response Induced by Lipopolysaccharide in Male and Female Rats**. Pereira V, Alencar TS, Schneider RC Schneider VMM, Borges AP, Costa RA, Baggio D, Zampronio AR UFPR Inflammation and Fever Lab Dept Pharmacology Brazil

Introduction: Systemic infectious diseases present signs such as fever, hyperalgesia, and lethargy, which are modulated by the hypothalamus. During this response induced by the injection of lipopolysaccharide (LPS) from Gram- negative bacteria, there is a reduction in serotonin (5-HT) levels in the hypothalamus of male rats, while in females there is an increase (Costa et al., J Neuroimmunol. 394:578427, 2024). The release of 5-HT in the hypothalamus by LPS modulates the inflammatory reflex, which is a descending sympathetic pathway responsible for controlling the cytokines levels in internal organs such as the spleen and liver. Therefore, the reduction of 5-HT in males produces a less intense inflammatory reflex and, therefore, a more intense febrile response. **Objective:** Evaluate the effect of acute administration of fluoxetine, a selective 5-HT reuptake inhibitor (SSRI), on the LPS-induced febrile response and hypolocomotion in male and female rats. **Methodology:** Male and female Wistar rats, 90 days old, received a remote temperature recorder implanted in the peritoneal cavity. After 7 days, the animals were treated with Fluoxetine (10 mg/kg) or water by oral route, and after one hour, an intraperitoneal injection of LPS (100 µg/kg) or saline was done. Body temperature was assessed for 5 hours at 15-minute intervals. Subsequently, locomotion was evaluated using the open field test for 3 minutes. The procedures were approved by the ethics committee CEUA/UFPR (#1601/2024). **Results:** After the LPS injection, both male and female rats pre-treated with vehicle demonstrated a significant increase in body temperature of approximately 1.5°C. Fluoxetine administration significantly reduced the febrile response in male rats but did not change LPS induced fever in female rats. No statistically significant differences were observed in locomotor parameters between the groups, although the Fluoxetine + LPS group showed numerically lower values, suggestive of hypolocomotion in male rats. **Conclusion:** LPS induced a febrile response in both male and female rats. The febrile response in males was reduced by a single dose of the SSRI fluoxetine, suggesting that this reduction is related to increased 5-HT levels in the hypothalamus. On the other hand, the absence of fluoxetine effect in females suggests that, since 5-HT levels are already elevated after LPS, a further increase did not affect fever, highlighting sexual dimorphism with respect to medication. These possible changes in 5-HT levels in the hypothalamus will be confirmed. However this dose of fluoxetine was not sufficient to promote significant changes in locomotion of the animals.

04.010 **Healing Effect of Alginate Biomembrane with Biochanin A in Mice**. Brito SC[1], Aragão JMDA[1], Biano LS[1], Nascimento ACS[1], Ramos LS[1], Sales MR[1], Santos GJ[1], Vasconcelos ABS[1], Albuquerque-Júnior, RLC[2], Grespan R[1], Camargo EA[1] [1]UFS-São Cristovão, PPG Physiological Sciences, Lab Pharmacology of the Inflammatory Process, Dept Physiology, SE, Brazil; [2]UFSC, Dept Pathology, Lab Oral Pathology

Introduction: Cutaneous wound healing represents a challenge in clinical practice. Therefore, there is a growing interest in treatments that promote better quality healing. Technological advancements in the development of biomaterials allow the incorporation and gradual release of bioactive compounds at the injury site. Thus, natural products like Biochanin A (BCA) have gained attention for their anti-inflammatory and antioxidant properties. Objetive: Thus, we aim to investigate the effect of a biomembrane containing BCA on cutaneous wound healing. **Methods:** Female Swiss mice (25 - 30g) were used. The animals were divided in: untreated group (UT); group treated with 2% alginate membrane (ALG); or group treated with alginate membrane containing 1% BCA. The biomembranes were prepared using the casting technique. Excisional wounds were created with (6 mm) on day 0, and treatments were applied covering the entire wound area on days 0, 3, 7 and 14. The wound area was evaluated on days 0, 3, 7 and 14, and the percentage of healing was calculated. On the seventh day, the wounds were collected using a punch (8 mm) and divided for analysis of cytokine (IL-6, IL-1β, and TNF-α), myeloperoxidase (MPO) activity, gene expression of Arg1, Nos2, Vegf, Pparγ, and Col3 and histopathological analysis. On fourteenth day, the wound was collected for histopathological analysis. We used GraphPad Prism 8.4.3, for data analysis. We performed a normality test, and based on the result an appropriate test was used. Results with $p<0.05$ were considered significant. **Results:** After 7 days, the BCA 1% membrane had the highest percentage of healing compared to ALG or UT group (p=0.018 and p=0.011, respectively). Nevertheless, MPO activity was reduced compared to ALG and UT groups (p=0.0002 and p=0.0006, respectively). The concentration of the cytokine IL-6 was also reduced compared to the ALG or UT group (p=0.0084 and p=0.024, respectively). The other cytokines did not change among the groups. Gene expression analysis showed reduced Nos2 (p=0.0156) and increased of Vegf (p=0.0159), Pparγ (p=0.0028), and the M2/M1 ratio (Arg1/Nos2; p=0.0003) compared to ALG group. However, no differences were observed in the degree of healing in the histology on the seventh day (p=0,0834), but on the fourteenth day, the BCA 1% membrane improved the degree of healing (p=0,0449). **Conclusion:** Therefore, we can conclude that the BCA compound can improve the wound healing process by accelerating inflammation resolution and enhancing wound quality.

04.011 **Impact of Diabetes and Annexin A1 Deficiency on Intact Skin Architecture**. Oliveira SS[1], Oliveira SM2, Gil CD[1], Silva RA[1], Ferreira LPS[1], Santos DD[1], Mimura KKO[1 1] Unifesp, São Paulo - SP, Brasil. [2] UFMT-Pontal do Araguaia – MT, Brasil.

Introduction: Individuals with diabetes mellitus (DM) present impaired cutaneous wound healing, which may be associated with pre-existing alterations in intact skin. Annexin A1 (AnxA1) is a protein involved in the modulation of inflammatory responses and tissue homeostasis; however, its contribution to skin integrity under diabetic conditions remains poorly understood. **Objective:** To evaluate whether diabetes and AnxA1 deficiency promote basal structural alterations in intact skin that could negatively affect tissue repair capacity. Materials and **Methods:** Wild-type (WT) and AnxA1 knockout (KO) C57BL/6 mice were subjected to streptozotocin-induced diabetes (DM) or received vehicle (CT). Animals were distributed into four experimental groups: CT WT, DM WT, CT KO and DM KO. After 90 days, skin samples were collected for histological and morphometric analyses, including measurements of epidermal and dermal thickness, collagen types I and III deposition by picrosirius staining, and hair follicle quantification. All experimental procedures were approved by the Ethics Committee (CEUA nº 8518230821). **Results:** Streptozotocin administration promoted persistent hyperglycemia in both genotypes. The CT WT group exhibited increased epidermal and dermal thickness compared with the other experimental groups, which did not differ significantly from each other. Collagen type I deposition was higher in the CT KO group, while similar levels were observed among the remaining groups. No significant differences were detected for collagen type III deposition and hair follicle quantification among the experimental groups. **Conclusion:** Diabetes and AnxA1 deficiency are associated with structural alterations in intact skin, including reduced epidermal and dermal thickness and selective modulation of collagen type I deposition. These findings suggest that diabetic conditions impair basal cutaneous structural homeostasis, while AnxA1 appears to play a role in maintaining skin integrity.
Keywords: Diabetes mellitus; Annexin A1; Skin; Collagen; Extracellular matrix.

04.012 **Effect of the Phenylacetamide Derivative JM-01 on Leukocyte Migration in a Zymosan-Induced Peritonitis Model**. Silva Netto LS[1], Serra GL[2], Ferreira Gonçalves MC[3], Neri LCD[2], Souza Cunha MV[1], Freire Macêdo ME[2], Stiebbe Salvadori MGS[3,4,5], Moura RO[6], Santos VL[6], Villarreal CF[7], Oliveira Golzio AMF[5,8], Silva PR[5] [1]UFPB, Pharmacy, Brazil; [2]UFPB, Biomedicine, Brazil; [3]UFPB, PPG Natural and Synthetic Bioactive Products, Brazil; [4]UFPB, CCHLA, Dept. Psychology, Brazil; [5]UFPB, PPG Cognitive Neuroscience and Behavior, Brazil; [6]UEPB, PPG Pharmaceutical Sciences, Brazil; [7]Fiocruz, Instituto Gonçalo Moniz, Brazil; [8]UFPB, Dept. Food Technology, Brazil

Introduction: Acute inflammation is an essential biological response for maintaining homeostasis, characterized by leukocyte recruitment to the site of injury or infection. Although fundamental to host defense, its exacerbation may contribute to the development of various inflammatory diseases, involving mediators such as eicosanoids and platelet-activating factor (Rodríguez, M. Biochem. Pharmacol., v. 102, p. 78, 2016). Currently available drugs have proven efficacy but are frequently associated with adverse effects that limit their prolonged use, highlighting the need for new molecules with anti-inflammatory potential and improved safety profiles. **Objectives:** To evaluate the anti-inflammatory activity of the phenylacetamide derivative 2-cyano-N-phenylacetamide (JM-01) in a zymosan-induced peritonitis model in mice, assessing its effect on leukocyte migration to the peritoneal cavity. **Methods:** The anti-inflammatory activity of JM-01 was investigated using the zymosan-induced peritonitis model in mice, a well-established experimental system for the study of acute inflammation (Cash, JL. Methods Enzymol., v. 461, p. 379, 2009). Animals were divided into experimental groups and treated orally with saline solution (negative control), indomethacin (10 mg/kg; positive control), or JM-01 at doses of 5, 10, and 50 mg/kg. After 30 minutes, inflammation was induced by intraperitoneal administration of 2% zymosan. Four hours after induction, animals were euthanized and the peritoneal exudate was collected by washing the abdominal cavity with phosphate-buffered saline. The total number of migrated leukocytes was determined by counting in a Neubauer chamber. Data were subjected to statistical analysis, with significance set at $p<0.05$. **Results:** Treatment with JM-01 significantly reduced leukocyte migration to the peritoneal cavity compared to the control group, demonstrating anti-inflammatory activity in a dose-dependent manner, with more pronounced effects at the highest doses evaluated. The reduction in cellular recruitment suggests that JM-01 interferes with inflammatory mediators involved in the acute phase of inflammation, including prostaglandins (Lima, JBM. J. Physiol. Sci., v. 67, p. 673, 2017). Although the observed effect was lower than that of the most active compound in the series, the results confirm the pharmacological potential of JM-01 as a modulator of the inflammatory response. **Conclusion:** The phenylacetamide derivative JM-01 exhibited significant anti-inflammatory activity in the zymosan-induced peritonitis model, evidenced by the reduction of leukocyte migration to the peritoneal cavity, reinforcing its potential as a candidate for the development of new anti-inflammatory agents and justifying further studies to elucidate its mechanisms of action. Ethics Committee:CEUA/ICS UFBA: 135/2018.

04.013 **Anti-Inflammatory and Antioxidant Effect of Glycitein in a Mouse Model of Ear Edema**. Sales MR, Nascimento ACS, Santos GJ, Souza DA, Nunes ERS, Brito SC, Grespan R, Aragão JMDA, Camargo EA. UFS, PPG Physiological Sciences, Brazil.

Introduction: Inflammation is a physiological defense response, but it can cause tissue damage when excessive. Given the inflammatory nature of skin diseases and the limitations of their conventional treatments, it is of interest to explore topically administered therapies. In this sense, glycitein, a soy isoflavone, may be a promising alternative. **Objectives:** This study aimed to investigate the anti-inflammatory and antioxidant effects of glycitein in a mouse model of acute inflammation. **Methods:** The animals received a topical administration of TPA (12-O-tetradecanoylphorbol 13-acetate; 1 µg/ear) in the right ear to induce inflammation, followed by topical treatment with glycitein (0.3, 1.0, or 3.0 mg/ear), vehicle (acetone), or dexamethasone (0.05 mg/ear), five minutes later. Mice were euthanized after 6 hours, and 6-mm ear punch biopsies were used to evaluate edema, myeloperoxidase (MPO) activity, levels of IL-6, IL-1β, and TNF-α, histological analysis, and oxidative stress. **Results:** We found that glycitein decreased ear edema (24.2%, p=0.036; 36.8%, p=0.0002 and 33.2%, p=0.001), MPO activity (90.1%, 87.2% and 72.1%, p<0.0001 each) compared with the vehicle group. It also reduced tissue concentrations of IL-6 (p=0.0007, p=0.0006, and p<0.0001), IL-1β (p=0.0002; p=0.0002 and p<0.0001) and TNF-α (p=0.011, p=0.002, and p=0.002), for 0.3, 1.0, and 3.0 mg/ear, respectively, compared with the vehicle group. In the histological evaluation, less intense edema and dermo-epidermal thickness were observed with doses of 1.0 and 3.0 mg/ear (p<0.0001 for each), but not with the 0.3 mg/ear dose, compared with the vehicle. Furthermore, treatment with glycitein reduced the total hydroperoxide concentrations in 60.1% (p=0.014) and 81.4% (p=0.0004) for 1.0 and 3.0 mg/ear, respectively, when compared with the vehicle group. Furthermore, glycitein at 1.0 mg/ear was tested for antioxidant enzyme activity and it increased catalase activity in 55.8% (p=0.009) and superoxide dismutase activity in 76.3% (p=0.001) compared with the vehicle group. **Conclusion:** Glycitein exhibited significant anti-inflammatory and antioxidant effects in the TPA-induced ear edema model, supporting its potential as a candidate for the development of topical therapies for inflammatory skin disorders.

04.014 **Functional Study of 7-Nitroindazole Derivative Compounds on Edema and Vascular Smooth Muscle**. Santiago MLA[1], Costa MEP[1], Pereira, LK[1], Pinto CCC[2], Souza E[3] [1]UNINTA, Faculdade de Medicina, [2]UNINTA, Faculdade de Medicina, Lab Microbiologia, [3]UFC, Faculdade de Medicina, Depto Morfologia, PPG de Ciências Morfofuncionais

The nitric oxide synthases (NOS) enzymes hyperactivity impairs body functions, since NO is divergent in actions. Potent and selective inhibitors of those enzymes become essential, like 7NI, which has been considered a selective nNOS inhibitor *in vitro*, and has become a useful tool for studies with this isoforms. However, this selectivity has been discussed in the literature since some bioassay experiments demonstrated inhibitory activities both for constitutive as for inducible enzymes. In order to look for more potent and selective analogues for the isoforms, it was studied the functional effects of the 7NI and its analogues in two experimental models: 1. inflammation *in vivo* carrageenan-induced paw edema) for nNOS evaluation (initial phase) and iNOS (late phase and 2. contractility *in vitro* (isolated aorta rings) for eNOS evaluation. Male rats weighing between 150 and 200 g were housed in cages and provided with food and water ad libitum. In the paw edema experiments, the animals received a vehicle or the analogs (5–25 mg/kg) intraperitoneally 30 minutes prior to the injection of 1% carrageenan into the paw. Paw volume was assessed via plethysmography by measuring fluid displacement following paw immersion in the chambers, with readings taken hourly for up to 6 hours. The area under the curve (AUC) was calculated for the first 3 hours (early phase) and the last 3 hours (late phase). For contractility studies, rat aortas were isolated—with the endothelium intact—and maintained in isolated organ baths. The protocol involved the application of phenylephrine (1 µM) followed by carbachol (1 µM); 10 minutes later, the analogs (0.1–100 µM) were added to the bath. *In vivo*, 7NI (15 mg/Kg), 7AI (15mg/Kg), 1Me5NI (25mg/Kg), 1Me6NI (25 mg/Kg) and 2Me5NI (25mg/Kg) inhibited nNOS in 67, 58, 38, 40 and 60%, respectively, and iNOS in 33, 67, 41, 34 and 66%. *In vitro*, only 7NI (0,1 – 100µM), inhibited eNOS (IC50 of 2,64 µM), about 94%. We concluded that: 1. 7NI was a potent inhibitor of eNOS, contrary to literature; 2. Replacement of the nitro group for the amino group (7AI) turned out the molecule less selective for nNOS and iNOS, and ineffective for eNOS; 3. Methylation of 1 or 2 positions plus nitro group displacement promoted loss of selectivity of the 7NI molecule for nNOS and iNOS.

04.015 **Evaluation of Cell Viability and Nitrite Production by the Phenylacetamide Derivative JM-01 in J774 Macrophages**. Serra GL[1], Silva Netto LS[2], Gonçalves MCF[3], Neri LCD[1], Cunha MVS[2], Macêdo MEF[1], Salvadori MGSS[3,4,5], Moura RO[6], Santos VL[6], Villarreal CF[7], Golzio AMFO[5,8], Silva PR[5] [1]UFPB, Curso de Graduação em Biomedicina, Brazil, [2]UFPB, Curso de Graduação em Farmácia, Brazil, [3]UFPB, PPG em Produtos Naturais e Sintéticos Bioativos, Brazil, [4]UFPB, Centro de Ciências Humanas Letras e Artes, Depto Psicologia, Brazil, [5] UFPB, PPG em Neurociência Cognitiva e Comportamento, Brazil, [6]UEPB, PPG em Ciências Farmacêuticas, Brazil, [7],Fundação Oswaldo Cruz, Instituto Gonçalo Moniz, Brazil, [8]UFPB, Depto Tecnologia de Alimentos, Brazil.

Introduction: Inflammation is a biological response mediated by the production of pro-inflammatory compounds, including cytokines and nitric oxide (NO). The exacerbated production of these mediators is associated with the pathophysiology of several inflammatory diseases (Wang J. Int. J. Mol. Sci., v.20, p.1, 2019). Although currently available treatments show clinical efficacy in controlling these conditions, their prolonged use may be associated with important adverse effects, reinforcing the need to develop new therapeutic alternatives with improved safety profiles. In this context, phenylacetamide derivatives represent promising compounds for modulating the inflammatory response. **Objectives:** To evaluate cell viability and the effect of the 2-cyano-N-phenylacetamide derivative (JM-01) on nitrite production in murine J774 macrophages stimulated with lipopolysaccharide (LPS) and interferon-gamma (IFN-γ). **Methods:** Cell viability was determined in J774 macrophages using the Alamar Blue® colorimetric assay (Mosmann T. J. Immunol. Methods, v.65, p.55, 1983; Rampersad SN. Sensors, v.12, p.12347, 2012). Cells were cultured in 96-well plates and treated with JM-01 (6.25; 12.5; 25; 50 and 100 μM), followed by assessment of metabolic activity by spectrophotometric reading between 570 and 600 nm. For nitrite quantification, cells stimulated with LPS (500 ng/mL) and IFN-γ (5 ng/mL) were treated with non-cytotoxic concentrations of JM-01. After 24 hours, supernatants were collected and analyzed using the Griess method (Green LC. Anal. Biochem., v.126, p.131, 1982). Dexamethasone (40 μM) was used as a positive control. Data were analyzed by ANOVA followed by Tukey's test, considering $p<0.05$. **Results:** JM-01 exhibited low cytotoxicity in J774 macrophages up to 50 μM, maintaining cell viability similar to that observed in the control group. However, at the concentration of 100 μM, a significant reduction in cell viability was observed ($p < 0.05$), characterizing a concentration-dependent cytotoxic effect. Regarding nitrite production, JM-01 promoted a significant reduction ($p < 0.05$) in the levels of this inflammatory mediator at the concentration of 50 μM when compared with the group stimulated only with LPS and IFN-γ. This result demonstrates the ability of the compound to modulate macrophage activation and reduce nitric oxide production associated with the inflammatory response. **Conclusion:** The phenylacetamide derivative JM-01 showed a satisfactory safety profile in J774 macrophages at concentrations up to 50 μM and was able to significantly reduce nitrite production in stimulated cells, demonstrating potential *in vitro* anti-inflammatory activity. These findings reinforce the relevance of JM-01 as a candidate for further pharmacological studies.

04.016 **Multitarget *in silico* Evaluation of Novel Green Synthetic Acetanilides and Acetanilide–Theobromine Hybrids Targeting COX, iNOS, PDE and TLR4 Pathways**. Luís LRCS[1], Sousa M[1], Silva TG[1], Falcão MEES[1], Gadelha FAA[1], Dejani NN[1], Fiss GF[2], Luís JAS[2], Vieira GC[1]. [1]UFPB, Research Institute for Drugs and Medicines, Lab. of Immunopharmacology, Brazil. [2]UFPB, Lab. of Bioenergy and Organic Synthesis Research, Brazil.

Introduction: The dysregulation of inflammatory pathways is involved in the pathophysiology of neurodegenerative diseases, mental disorders, and other immune-related conditions. In this context, compounds with multitarget activity have emerged as a promising strategy for the development of novel anti-inflammatory agents. Acetanilide and theobromine derivatives exhibit relevant pharmacological properties, making molecular hybridization an attractive approach for obtaining candidates with multitarget anti- inflammatory potential. **Objective:** To investigate the multitarget anti- inflammatory potential and physicochemical profile of two series of synthetic compounds (2a-2f and 3a-3f) through *in silico* analyses, including molecular docking studies. **Methods:** Two series of previously synthesized and characterized compounds were evaluated: acetanilide derivatives (series 2a-f) and acetanilide–theobromine hybrids (series 3a-f). Molecular docking simulations were performed using Molegro Virtual Docker 6.0 against hENT1, adenosine receptors (A1A, A2B, and A3A), COX-1, COX-2, PDE3A, PDE4D, GABA-A, iNOS, and TLR4 targets. Drug-likeness properties, toxicological risks, and physicochemical parameters were assessed using the Osiris Property Explorer and SwissADME platforms, including cLogP, topological polar surface area (TPSA), molecular weight, blood–brain barrier (BBB) permeability, and compliance with Lipinski's rule of five. **Results:** Series 3 compounds exhibited superior binding affinities (-90 to -134 kcal·mol-^{1}) across all evaluated targets when compared with Series 2 compounds, suggesting a favorable multitarget profile. Among them, compounds 3a and 3e displayed the most balanced profiles, combining high binding affinities, elevated drug scores (0.90 and 0.88, respectively), and physicochemical parameters consistent with desirable drug-candidate characteristics. Although compound 3d showed the lowest docking energies, its lower drug-likeness score suggests potential limitations. SwissADME analysis indicated that Series 3 compounds possess higher TPSA values (~90 Å^{2}) and lack predicted BBB permeability, suggesting a predominantly peripheral mode of action. In contrast, Series 2 compounds exhibited lower TPSA values (~29 Å^{2}), predicted BBB permeability, and lower molecular weights, indicating potential central nervous system exposure despite their weaker binding affinities. Within this series, compound 2f displayed the most balanced overall profile. **Conclusion:** The integrated *in silico* analysis revealed two distinct pharmacological profiles. Series 3 compounds, particularly 3a and 3e, exhibited characteristics consistent with potential multitarget peripheral anti-inflammatory agents, whereas Series 2 compounds, especially 2f, demonstrated properties suggestive of central nervous system exposure. These findings provide support for future structural optimization and experimental validation of the identified candidates. Keywords: Molecular docking. Drug-likeness. Molecular hybridization. Blood–brain barrier. Computational pharmacology.

04.017 **Renin-Angiotensin System Modulators Alter the Neutrophil-to-Lymphocyte relationship in Smokers but not in COPD Patients**. Medeiros VLD, Freitas JLC,Paiva YMA, Bezerra GB, Martins NRS, Kennedy-Feitosa E, Silva FS. UFERSA, Mossoró, Morphophysiopharmacology Lab.

Introduction: The Neutrophil-to-Lymphocyte Ratio (NLR) is a widely available marker of systemic inflammation. It has been used in smokers and COPD patients as a biomarker which is able to indicate the possibility of exacerbation. Smoking activates the Renin-Angiotensin System (RAS), increasing ACE activity resulting in pro-inflammatory activity contributing to chronic obstructive pulmonary disease (COPD) pathogenesis. Therefore, the NLR may represent a sensitive hematological readout of RAS-mediated immune modulation in smoking- related pulmonary conditions. **Aim:** To evaluate whether RAS modulators alter the Neutrophil-to-Lymphocyte Ratio (NLR) in current smokers. **Methods:** A cross- sectional study included current smokers (n=10), former smokers (n=12), and COPD patients (n=10). Within each clinical group, participants were stratified according to the use of Renin-Angiotensin System modulators (RASm) or non-use of these medications (Non-RASm). Linear regression analyses were performed to evaluate the relationship between neutrophil (%) and lymphocyte (%) counts (NLR). Regression slopes were subsequently compared between RASm and Non-RASm subgroups within each clinical group, with statistical significance set at $p < 0.05$. **Results:** A strong negative correlation in NLR was observed in all groups ($r = -0.80$ to -0.99; $p < 0.05$). Among current smokers, the RASm subgroup showed a steeper inverse relationship (slope = -1.146; $r = -0.98$; $p = 0.003$) than the Non-RASm subgroup (slope = -0.616; $r = -0.93$; $p = 0.02$), with a significant difference between slopes ($p = 0.04$). No significant slope differences were observed in former smokers ($p = 0.182$) or COPD patients ($p = 0.969$). The overall analysis without stratification also showed no difference between RASm and Non-RASm groups (slopes -0.84 vs. -0.83; $p = 0.949$). **Conclusion:** RAS modulator use was associated with a steeper inverse NLR in current smokers without differences among smokers, former smokers, and COPD patients receiving RAS modulators.

04.018 **Preliminary Study of the Cytotoxicity Profile and Pharmacokinetic Characteristics of a Green Synthetic Acetanilide with Potential Application in Neuroinflammation**. Falcão MEES[1], Sousa M[1], Silva TG[1], Luís LRCS[1], Gadelha FAA[1], Dejani NN[1], Fiss GF[2], Luís JAS[2], Vieira GC[1]. [1]UFPB, Research Institute for Drugs and Medicines, Lab. of Immunopharmacology, Brazil. [2]UFPB, Lab. of Bioenergy and Organic Synthesis Research, Brazil.

Introduction: Neuroinflammation refers to a cellular immune response in which glial cells are activated in response to a noxious stimulus. However, when chronic, it leads to lesions that cause neuronal loss, playing a significant role in the pathophysiology of neurodegenerative diseases. The development of novel molecules with immunomodulatory potential and favorable safety profiles represents a promising strategy. Among these compounds, green synthetic acetanilides obtained through sustainable approaches have emerged as attractive candidates. **Objective:** To investigate the *in vitro* cytotoxicity and *in silico* pharmacokinetic properties of compound 2A, a green synthetic acetanilide derived from N-phenylacetamide. **Methods:** Cell viability was evaluated using the MTT assay on murine RAW 264.7 macrophages seeded in 96-well plates (1×10^4 cells/well) and incubated overnight at 37°C and 5% CO_2. They were exposed to increasing concentrations of compound 2A (25–400 µg/mL) for 24h, followed by incubation with 3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide (MTT). After 4h of incubation, the formazan crystals were solubilized in dimethyl sulfoxide (DMSO) and absorbance was measured at 570 nm. Data were expressed as mean ± SEM from three independent experiments and evaluated using one-way ANOVA followed by Dunnett's post hoc test. Pharmacokinetic properties were predicted *in silico* using the SwissADME platform. IC_{50} values were determined by nonlinear regression using the GraphPad Prism. **Results:** Compound 2A maintained cell viability at concentrations up to 200 µg/mL. At 400 µg/mL, cell viability decreased to approximately 60% compared with the untreated control group (100%). *in silico* , pharmacokinetic analysis predicted high gastrointestinal absorption, blood- brain barrier permeability and the absence of P-glycoprotein substrate characteristics. Selective inhibition of the CYP1A2 isoform was also predicted, with no relevant interactions with other cytochrome P450 isoforms. The estimated IC_{50} value was 316.23 µg/mL, indicating low cytotoxicity in the experimental model employed. A concentration-dependent effect on cell viability was observed, with significant reductions ($p < 0.01$) at higher concentrations. These findings suggest favorable systemic bioavailability and the ability to reach the central nervous system. **Conclusion:** Compound 2A, a green synthetic acetanilide, exhibited favorable predicted pharmacokinetic properties *in silico* , including potential blood-brain barrier permeability, and low cytotoxicity at concentrations up to 200 µg/mL. The IC_{50} value obtained reinforces its preliminary safety profile and pharmacokinetic characteristics predicted *in silico* support further investigation in studies targeting the modulation of neuroinflammatory processes. Collectively, these findings highlight compound 2A as a promising candidate for the development of novel pharmacological approaches based on the acetanilide chemical scaffold.

04.019 **Anti-Inflammatory and Antioxidant Effects of the Total Polysaccharides of *Caesalpinia ferrea* Bark and Pod in Intestinal Mucositis Induced by 5-Fluorouracil**. Costa MEP[1], Santiago MLA[1], Pereira LK[1], Pinto CCC[3], Souza, EP[2,], [1]UNINTA, Faculdade de Medicina, [2]UFC, Faculdade de Medicina, Depto Morfologia, PPG de Ciências Morfofuncionais, [3]UNINTA, Faculdade de Medicina, Lab Microbiologia.

Intestinal mucositis is a disorder that appears as adverse effect of treatments of radiation and chemotherapy in cancer patients. 5-fluorouracil (5-FU) is one of anticancer drugs widely used in cancer chemotherapy treatments. Caesalpinia ferrea, popularly known as Juca or ironwood, is a widely used plant widely for the treatment of organic disorders such as diabetes, dysentery, allergies, ulcers, respiratory diseases and cancer. The antioxidant and antiinflammatory activities of this plant have been scientifically proven. This study evaluated the effects of treatment with total polysaccharides (PLT) C. ferrea bark and pod in the inflammatory response, antioxidant and morphofunctional modifications in the intestinal mucositis induced by 5-FU in mice. The animals were randomly divided into eight groups (n=8 per group), were treated for 4 days (d0-d3) by C. ferrea PLT bark and pod in three different doses (1 mg/kg, 5 mg/kg and 15mg/kg). On day 0 all animals, except control group, were treated with a single intraperitoneal dose of 5-FU (450 mg / kg). On day 4 (d4), all mice were sacrificed by cervical dislocation and jejunum and ileum fragments were extracted for morphological analysis, histological and biochemical parameters. We evaluated animal weight change, total count of blood leukocytes, concentration of sulfhydryl groups (GSH), malondialdehyde (MDA), myeloperoxidase (MPO), cytokines (TNF-α and IL-1-β), nitrite and immunohistochemistry (TNF-α), histopathology and morphometry in the jejunum and ileum portions. Our results showed that in the fifth experimental day, after treatment with 5-FU, there was a loss of integrity of the intestinal mucosa, with a significant shortening of the villi in the jejunum and ileum, leukopenia toxicity and weight loss, increase in the neutrophilic infiltrate in the jejunum, increased oxidative stress GSH, MDA and nitrite in both segments and immunostaining for TNF-α. The treatment with the pod shell and the PLT significantly increased the length of villi in intestinal segments both the three doses evaluated. The PLT (bark and pods) at all three doses reduced the oxidative stress by reversing the increased MDA levels and tissue levels of nitrite and nitrate (bark: 5 mg/kg in the jejunum and ileum). The PLT reversed the increased levels of MPO (pod: 15 mg/kg, jejunum) and reduced immunostaining for TNF-α (bark: 5 mg/kg and 15 mg/kg, jejunum and ileum). It is concluded that the bark PLT and C. ferrea pod reduced damage caused to the intestinal mucosa of animals treated with 5-FU, which together with the gastrointestinal symptomatology compromise the quality of life of patients undergoing treatment with this drug.

04.020 **Sexual Dimorphism in Viral Inflammatory Responses**. Schneider VMM, Alencar ST, Costa RA, Borges AP, Pereira V, Malheiros MB, Baggio FD, Zampronio RA UFPR

Introduction: Inflammatory diseases exhibit sex-related differences both in terms of prevalence and underlying pathophysiological mechanisms a pattern also observed during the COVID-19 pandemic, in which men presented with more severe symptoms and higher mortality rates. Most of the studies evaluate sex differences related to inflammatory diseases using lipopolysaccharide (LPS), which is a model for bacterial infection. Previous studies (Costa et al., J. Neuroimmunol. 394:578427,2024) showed that male rats display a more intense LPS-induced febrile response compared to females, suggesting differences in central mechanisms, particularly within the hypothalamus. Males exhibit reduced hypothalamic serotonin (5-HT) levels, whereas females demonstrate an increase in this neurotransmitter after LPS injection, suggesting that they differentially regulate descending inhibitory pathways. Despite these differences, LPS induces similar systemic hyperalgesia and hipolocomotion in males and females. The present study aimed to investigate the systemic hyperalgesia, hypolocomotion, and alterations in hypothalamic 5-HT release in a model of systemic viral infection induced by polyinosinic-polycytidylic acid (Poly IC) at pyrogenic doses in male and female rats. **Methods:** For the experiments, 90-day-old male and female Wistar rats were used and received intraperitoneal (i.p.) injections of Poly I:C (300 or 600 µg/kg). Hyperalgesia was assessed using the electronic Von Frey test at 1, 3, and 5 hours after Poly I:C administration. At the end of this period, the animals were subjected to the open field test to evaluate locomotor activity. Subsequently, the hypothalamus was collected for quantification of serotonin (5-HT) and its metabolite, 5-hydroxyindoleacetic acid (5-HIAA), using high- performance liquid chromatography (HPLC). This project was approved by the Animal Research Ethics Committee of the Federal University of Paraná (Protocol No. 1658/2025). **Results:** Intraperitoneal injection of poly I:C at 300 or 600 µg/kg induced similar hyperalgesia in both sexes. Male rats exhibited a greater reduction in mechanical threshold at the 600 µg/kg dose at 1 h and 5 h compared to the 300 µg/kg dose. Female rats showed a reduction in mechanical threshold at the 300 µg/kg dose starting at 3 h and persisting until 5 h. Hypolocomotion (reduced crossing, speed and distance travelled in the open field test) was observed only in female rats. Hypothalamic levels of 5-HT was reduced and the 5-HIAA/5HT turnover was significantly increased in males. No changes were observed in hypothalamic 5-HT in females at the lower dose. **Conclusion:** These results showed that at pyrogenic doses, the injection of Poly I:C induces systemic hyperalgesia in males and females. However, hypolocomotion seems to occur only in females. Conversely, only males showed changes in 5-HT hypothalamic levels at these doses of Poly I:C. Altogether, these results suggest that there are sex differences in viral responses between males and females rats. **Financial support:** CNPq and UFPR.

04.021 **Investigation of the Immunomodulatory Potential of the Alkaloid 6,6a-Dihydrodismethoxyguadiscine Isolated from** *Guatteria friesiana*. Neto AC[1], Cezar IS1,2, Ramos KS2,3, Silva DKC2,3, Gonçalves RS4, Soares MBP1,2, Costa EV5, Meira CS1,2,3. 1 Fiocruz-BA, Salvador, 2 SENAI CIMATEC-BA, Salvador, 3 UNEB-BA, Salvador, 4 UFPR-PR, Palotina, 5 UFAM-AM, Manaus.

Introduction: Modulation of the inflammatory response by natural compounds represents a promising approach for the development of safer immunomodulatory therapies. Species of the genus *Guatteria* are recognized as important sources of bioactive alkaloids with diverse pharmacological activities. Among these metabolites, 6,6a-dihydrodismethoxyguadiscine (DHG), isolated from *Guatteria* friesiana, has been poorly investigated with respect to its immunomodulatory potential. **Objective:** To investigate the immunomodulatory activity of DHG using *in silico* , *in vitro*, and experimental endotoxemic shock approaches. **Materials and Methods:** Initially, the toxicological and pharmacokinetic properties of DHG were predicted using the ProTox 3.0 and ADMETlab 3.0 platforms. Subsequently, cytotoxicity, hemolytic activity, nitric oxide production, and the levels of IL-6 and IL-10 were evaluated in LPS- and IFN-γ-stimulated RAW 264.7 macrophages. In parallel, the expression of inflammation-related genes (Ptgs2, Nos2, Arg1, Cd206, Il10, Il1β, Il6, Nfκb1, and Tnfα) was determined in RAW 264.7 macrophages by qRT-PCR. Immunomodulatory activity was further assessed in murine splenocytes through lymphoproliferation assays and quantification of IL-2 and IFN-γ production. Finally, the therapeutic potential of DHG was evaluated in a murine model of LPS-induced endotoxemic shock. **Results:** *in silico* analyses predicted a favorable safety profile for DHG, with no relevant toxicological liabilities. Consistent with these findings, the compound exhibited no cytotoxic or hemolytic effects under the tested conditions. In stimulated RAW 264.7 macrophages, DHG (20 μM) significantly suppressed the production of inflammatory mediators, reducing NO levels by up to 78%. Moreover, treatment at 20 μM decreased IL-6 production by approximately 65% while increasing IL-10 levels by 55%. Gene expression analysis performed in RAW 264.7 macrophages further supported its immunoregulatory activity, revealing downregulation of pro-inflammatory markers and significant upregulation of Il10 expression, suggesting a shift toward an anti-inflammatory phenotype. In murine splenocytes, DHG significantly inhibited lymphocyte proliferation, reaching 76% inhibition at a concentration of 20 μM. Additionally, the compound reduced IL-2 and IFN-γ production by approximately 89% and 88%, respectively. Finally, DHG demonstrated protective effects *in vivo*, significantly improving survival in mice subjected to LPS-induced endotoxemia, with survival rates reaching 80% following oral administration at 10 mg/kg. **Conclusion:** DHG demonstrated pronounced immunomodulatory activity, reducing inflammatory mediators and improving survival in experimental LPS-induced endotoxemic shock. These findings highlight its potential as a promising candidate for the development of novel immunomodulatory therapies.

04.022 **Hydroethanolic Extract from** *Selaginella selowii* (**EHSS**) **reduces** *In vitro* **Neutrophil Chemotaxis without Inducing Cytotoxicity**. Diniz FS, Machado LL, Lossavaro PKMB, Fernandes, MML, Toffoli-Kadri MC, Silva-Filho, SE. UFMS, FACFAN

Introduction: Several plants are used in medicine to treat inflammatory conditions and pain, yet many lack scientific validation. Plants of the genus Selaginella have shown antiviral, anti-inflammatory, and antidepressant properties. **Objectives:** This study evaluated the *in vitro* anti-inflammatory activity and cytotoxicity of the hydroethanolic extract of Selaginella sellowii (EHSS) by *in vitro* chemotaxis induced by N-formyl-methionyl-leucyl-phenylalanine (fMLP) and cell viability by MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) tests. **Methods:** The experimental protocol was approved by the Ethics Committee on Animal Use of UFMS under registration Nº. 1.414/2026. Leukocytes were obtained from the peritoneal cavity of mice 4 h after an intraperitoneal injection (i.p.) of 1 mg of zymosan diluted in saline. Animals were euthanized, and the peritoneal cavity was washed with PBS, and the collected cells were centrifuged, washed, and resuspended in RPMI-1640 medium. For cytotoxicity evaluation, leukocytes (2x106 cells/mL) were exposed to EHSS (1, 30, 10, 30, 60, and 90 µg/mL) for 90 min, followed by MTT incubation. Cell viability was determined by absorbance at 550 nm. For the neutrophil chemotaxis assay (1x106 leukocytes/mL), leukocytes were exposed to the same extract concentrations and subjected to a modified Boyden chamber assay against 10-6 M fMLP, which was used as the chemotactic stimulus. After incubating the chamber for 1 hour, the polycarbonate membrane separating the upper and lower compartments was removed and stained to determine cell migration by counting cells under an optical microscope. Data were expressed as mean ± S.E.M. and analyzed by one-way ANOVA followed by Tukey's test ($p<0.05$). **Results:** EHSS showed a cell viability of 100% in all concentrations tested, indicating that the extract did not present *in vitro* cytotoxicity. In the chemotaxis assay, fMLP induced neutrophil migration (25.97 ± 2.99 cells/field) compared to the RPMI-1640 medium (14.68 ± 1.44 cells/field). EHSS significantly reduced neutrophil migration at all concentrations tested, with inhibition percentages of 48.09% (1 µg/mL), 43.39% (3 µg/mL), 60.53% (10 µg/mL), 63.17% (30 µg/mL), 58.60% (60 µg/mL), and 81.97% (90 µg/mL). **Conclusion:** EHSS presents *in vitro* anti-inflammatory activity by inhibiting neutrophil chemotaxis without inducing cytotoxicity, supporting further investigation of its therapeutic potential in inflammatory conditions.

04.023 **A Role for Protease-Activated Receptor (PAR) 4 on the Impairment of LPS-Induced Nitric Oxide Production by P1G10 Proteolytic Fraction Obtained from** *Vasconcellea cundinamarcensis* **in Macrophages**. Silva CR[1], Torres MPB[1], Lopes MTP[2], Klein A[1] [1]ICB-UFMG, Lab Inflamação e Proteases, [2]ICB-UFMG, Lab Substâncias Antitumorais, Depto Farmacologia, Belo Horizonte, MG, Brasil.

Introduction: Protease-activated receptors (PARs) are a family of four G-protein coupled receptors (PAR1-4), activated through the proteolytic and irreversible cleavage of a particular amino group in the extracellular N-terminal domain of receptor, unmasking a novel anchored fragment that acts as a ligand on the receptor itself. We have shown PAR2 and 4 mediating LPS-induced nitric oxide (NO) production in RAW 264.7 cells, and anti-inflammatory, trombolytic and healing activities in the proteolytic fraction obtained from *Vasconcellea cundinamarcensis* P1G10. However, the underlying mechanisms of anti-inflammatory activities of P1G10 has not been fully understood. **Objective:** Investigate the role for PAR2 and 4 on the inhibition of nitric oxide production mediated by P1G10 in LPS-stimulated RAW 264.7 cells. **Methods:** 105 RAW 264.7 cells were suspended in DMEM containing 1% fetal bovine serum, placed in 24-well plates and incubated at 37 °C at 5% CO2. After 4 h , adherent cells were incubated with LPS (1-100 ng/well) with or without P1G10 (6µg/well) before or after the addition of the PAR2 antagonist GB83 (10-6 M) or PAR4 antagonist ML354 (10-9 – 10-7 M) for 8 – 48 h, and NO production was indirectly measured by Griess reaction. The results are expressed as the mean ± standard error of the mean of 4 wells per group and representative of 2 independent experiments. Comparisons between groups were performed using one-way ANOVA, and differences among groups were assessed using the Tukey posttest. The viability of cultured macrophages was determined by 3-(4,5-dimethylthiazol- 2-yl)- 2,5-diphenyltetrazolium bromide (MTT) assay. **Results:** P1G10 IC50 in cultured macrophages was determined as 5.25ug/well. LPS induced a time and dose-dependent nitrite production in RAW 264.7 cells, peaking 48 h and P1G10 pre-incubation abolished this effect. PAR4 antagonist ML354, not PAR2 antagonist GB83, restores the level of LPS-induced nitrite production in P1G10 treated macrophages. **Conclusion:** This study provides evidence for PAR4 mediating P1G10 effects in macrophage response triggered by LPS. Alhtough more studies are necessary to clarify the relevance of PAR4 to others innate response mechanisms such as reactive osxigen species and phagocytosis, this is the first study demonstrating a role for PAR4 in P1G10 activity. **Financial support:** FAPEMIG (APQ 0238-18/APQ-01758-22), CNPq (408730/2025-0).

04.024 **Evaluation of the Effects of Docosahexaenoic Acid (DHA) and DHA-Loaded Nanocapsules on the Endothelium in *In vitro* and *in vivo* models**. Gomes-Reis GLS[1], Moraes BPT[2], Saraiva JSG[2], Cunha CMC[1], Ferreira-Costa M[1], Santos FS[3], Ferreira AM[1], Bozza PT[1], Castro-Faria-Neto HC[1], Ferrarini SR[4], Silva AR[1], Gonçalves-de-Albuquerque CF[12]. [1]IOC-Fiocruz, Immunopharmacology Lab and PPG in Cellular and Molecular Biology, Rio de Janeiro, Brazil; [2]Unirio, Immunopharmacology Lab and PPG in Molecular and Cellular Biology, Rio de Janeiro, Brazil; [3]UFF, PPG, in Neuroscience, Niterói, Brazil; [4]UFMT-Sinop, PPG Health Sciences, Brazil

Introduction: Sepsis is an organ dysfunction caused by a dysregulated host response to infection. During sepsis, the endothelial integrity is compromised, resulting in increased vascular permeability. Among the factors that promote endothelial dysfunction, reactive oxygen species (ROS) can dysregulate the expression of tight junction proteins, such as claudin, occludin, and zonula occludens-1 (ZO-1). However, compounds with antioxidant potential can neutralize free radicals and minimize damage caused by oxidative stress. Therefore, new therapeutic approaches are being explored to contribute to endothelial homeostasis. Docosahexaenoic acid (DHA) is an omega-3 with anti-inflammatory and antioxidant functions that may contribute to the positive regulation of tight junction proteins. Furthermore, nanosystems are used as a strategy to enhance the bioavailability of active ingredients, such as DHA. **Objectives:** We aimed to evaluate the effects of DHA on endothelial cells stimulated with *E. coli* and the effects of lipid-core nanocapsules containing DHA (LNC DHA) in a murine model of experimental sepsis. Methods: bEnd.3 cells were plated for 48h, followed by 3h of starvation and 1h of pretreatment with DHA (10 µM or 100 µM), then stimulated with *E. coli* (MOI 100). Cells were evaluated for cell viability by resazurin, reactive oxygen species (ROS) production by DCFH-DA, and occludin expression by western blotting. *In vivo*, male Swiss mice were pretreated with LNC DHA (3 mg/kg) for 7 days and then subjected to the cecal ligation and puncture (CLP) model (CEUA/IOC license: L-027/2022). Clinical score, survival, and plasma urea concentration were evaluated. **Results:** *In vitro*, all experimental groups remained viable. Stimulation with *E. coli* induced ROS production, whereas pretreatment with 10 µM DHA minimized it. Occludin protein expression was reduced in the stimulated group and preserved in the group that received the pretreatment. *In vivo*, animals subjected to CLP and pretreated with LNC DHA had lower clinical sign scores and greater survival over 7 days, as well as lower plasma urea concentrations compared with untreated animals. **Conclusion:** Pretreatment with DHA preserved occludin expression and minimized ROS production in *E. coli*-stimulated bEnd.3 cells, indicating its antioxidant effects and preservation of endothelial integrity. LNC DHA improved survival and minimized clinical score and plasma urea concentration in animals undergoing CLP, suggesting its therapeutic potential.

04.025 **Anti-Inflammatory and Anti-Hyperalgesic Effect of the New Isoxazole Analogue Based in the Celecoxib and Neolignans in Experimental Models**. Machado LL, Costa PAN, Lossavaro PKMB, Diniz FS, Venancio GSO, Lencina JS,Toffoli, Kadri MC, Baroni ACM, Silva-Filho SEU FMS, FACFAN, Pharmaceuticals Science

Introduction: Nonsteroidal anti-inflammatory drugs are widely used for the treatment of inflammatory disorders; however, their use is associated with important adverse effects, including gastric injury and renal and cardiovascular complications. In this context, the development of new therapeutic alternatives with improved safety profiles has become increasingly relevant. **Objectives:** The present study aimed to investigate the effects of a novel hybrid isoxazole analogue derived from celecoxib and neolignans (LASQUIM-PC-2) on carrageenan-induced mechanical hyperalgesia and paw edema during acute inflammatory responde. **Methods:** The experimental protocol was approved by the Ethics Committee on Animal Use of UFMS under registration No. 1.347/2024. Male Swiss mice were orally treated with LASQUIM-PC-2 (1, 3, or 10 mg/kg), celecoxib (10 mg/kg, reference drug), or vehicle (1% DMSO solution, control group) (n = 5-7 animals/group) 1 hour before the intraplantar injection of carrageenan (300 µg/paw) into the right hind paw. The contralateral paw received 0.9% saline solution. Edema formation was evaluated by measuring the volume difference between the right and left paws using a digital plethysmometer at 0.5, 1, 2, and 4 hours after carrageenan injection. Mechanical hyperalgesia was assessed using a digital analgesimeter (Von Frey test), which records the force applied until paw withdrawal, at 3 and 4 hours after carrageenan administration. **Results:** Oral treatment with LASQUIM-PC-2 at doses of 1, 3 and 10 mg/kg did not reduce the edema formation in the time of 30 minutes. There was reduction of edema in 1 hour (in 37.5, 65, and 70%, respectively), in 2 hours there was reduction in the doses of 1 and 10 mg/kg (in 52,65, and 54.5%, respectively), and 4 hours (56.1, 35.13 and 70.27%, respectively), compared to the control group. The celecoxib reduced the edema formation in all times tested. The LASQUIM-PC-2 treatment, in all doses tested reduced the mechanical hyperalgesia in time of 3 hours, and in the time of 4 hours, the LASQUIM-PC2 reduced mechanical hyperalgesia at doses of 3 and 10 mg/k. Celecoxib reduced mechanical hyperalgesia at all tested time points. **Conclusion:** In conclusion, LASQUIM- PC-2 exhibited both anti-inflammatory and anti-hyperalgesic activities during the acute inflammatory response.

04.026 **Chronic Kidney Disease and Cognitive Impairment from the Perspective of Neuroinflammation: Evaluation of the Exposure of Healthy Astrocytes to Uremic Serum**. Custodio GT[1], Russo FB[2], Beltrão PCB[2], Kawamoto EM [1]
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Introduction: Chronic Kidney Disease (CKD) can lead to cognitive impairment by compromising the central nervous system (CNS). This may occur due to uremic toxins from organic waste accumulation and pro-inflammatory cytokines that cross the blood-brain barrier. To understand this relationship, cultures of healthy astrocytes derived from human induced pluripotent stem cells (iPSCs) were exposed to uremic serum from CKD patients. **Objectives:** To study the effects of serum from healthy volunteers and CKD patients before and after hemodialysis on healthy astrocytes functioning, expanding the understanding of neuroinflammation in CKD. **Methodology?** Astrocytes derived from human iPSCs (CEP CAAE 67426623.0.0000.5467), generated from tooth pulp, were exposed to concentrations 0.1%, 0.5%, 1%, 5%, and 10% of three serum types: (I) healthy, (II) pre- and (III) post-hemodialysis. Three healthy volunteers (H1-H3) and five CKD patients participated; blood was collected pre- (PR1-PR5) and post- (PO1-PO5) hemodialysis. Cytotoxicity was analyzed via LDH assay. ELISA assays measured pro-inflammatory cytokines tumor necrosis factor (TNF)-α, interleukin (IL)-6 and IL-1β in raw serums and astrocyte supernatants to observe if uremic serum alters astrocyte functioning. All data were analyzed using One-Way ANOVA (GraphPad Prism), representing preliminary findings. **Results:** In the LDH assay, at 0.1% concentration ([$F(13.5)=12.34$, $p<0.05$]), patient 3 pre-hemodialysis (PR3) serum showed a cytotoxic effect compared to control. Significant differences were also found between PR5 and control ($p<0.05$) and PO5 and control ($p<0.05$). At 1% concentration ([$F(13.6)=7.820$, $p<0.05$]), only PR5 showed a significant difference from control. Other concentrations showed no significant differences. In ELISA assays, raw serum results showed high TNF-α in H2 and PR1; IL-6 was quantified only in H2, and in PR3, PR5, PO3 and PO5; IL-1β was detected in H2 and H3. Before hemodialysis, only PR1 showed IL-1β; while after it, low amounts appeared in PO1 and PO2. Regarding astrocyte treatment, TNF-α graphs demonstrated a more inflammatory profile for PR1 and PO1; IL-6 levels were apparently higher in 5% concentration of PO1; IL-1β was detected at 1% in H1, H2, PR1, PR2, PO1 and PO2. In other samples, this cytokine was undetected. **Conclusion:** Regarding the LDH partial results, it is suggested, up to this point, that in human astrocytes that were exposed to uremic serum there is an apparent greater cytotoxicity in cells treated with serum before hemodialysis. For the ELISA assays, the preliminary results showed a great variability concerning the levels of some pro-inflammatory cytokines that may have an important role in CKD neuroinflammation. Human Research Ethical Committee Number 67426623.0.0000.5467. **Financial support**: CAPES, CNPq and FAPESP (process number 2023/15619-8).

04.027 **Sex-Dependent Effects of Tirzepatide on Fever and Inflammatory Mediators during Systemic Inflammation**. Aguiar SCR, Oliveira BCC, Cruz EKM, Sousa GLS, Londe ABR, Alves GS, Trindade KP, Gomes BRB, Souza FHV. UnB, Faculty of Health Sciences and Technologies, Lab. of Experimental Biomodels, Brazil, UnB, Institute of Biology, Lab. of Protein Chemistry and Biochemistry, Brazil, UnB, PPG Parmaceutical Sciences, Brazil.

Introduction: Systemic inflammation induced by bacterial lipopolysaccharide (LPS) triggers the release of pro-inflammatory mediators that promote fever through activation of hypothalamic prostaglandin E_2 (PGE_2) synthesis. Although fever is an important component of host defense, excessive inflammatory responses may contribute to tissue damage and adverse outcomes. Recent evidence demonstrated that liraglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist, attenuates LPS-induced fever through sex-dependent neuroimmune mechanisms (Sousa, GLS. Pharmaceuticals, v. 18, p. 1738, 2025). Tirzepatide (TZP), a dual GLP-1/GIP receptor agonist widely used for obesity and type 2 diabetes, also exhibits anti-inflammatory properties; however, its effects on fever and inflammatory mediators during LPS-induced systemic inflammation remain poorly understood. Furthermore, potential sex-dependent differences in the antipyretic mechanisms of TZP have not yet been investigated. **Objectives:** To investigate the effects of TZP on LPS-induced fever and inflammatory mediators in male and female rats. **Methods:** Male and female Wistar rats received pretreatment with TZP (1.0 mg/kg, i.p.) or vehicle, followed 1 h later by LPS administration (50 µg/kg, i.p.). Body temperature was continuously monitored, and the febrile response was assessed using the thermal index, calculated as the area under the temperature-time curve between 2 and 6 h after TZP administration. Hypothalamic PGE_2 concentrations and serum IL-10 levels were quantified by ELISA. Data were analyzed using two-way ANOVA followed by Tukey's post hoc test, with statistical significance established at $p < 0.05$. **Results:** LPS significantly increased the thermal index in both sexes, from 3.098 to 6.663 °C·min in males and from 3.200 to 7.311 °C·min in females. Pretreatment with TZP significantly attenuated fever, reducing the thermal index by approximately 72% in males and 80% in females ($p < 0.05$). LPS markedly increased hypothalamic PGE_2 concentrations in both sexes, with levels in LPS-treated males (7329 pg/g tissue) being nearly three-fold higher than in females (2589 pg/g tissue). In male rats, TZP reduced PGE_2 concentrations by 36%, from 7329 to 4699 pg/g tissue ($p < 0.05$). In contrast, TZP did not significantly affect PGE_2 concentrations in female rats ($p = 0.996$). LPS increased serum IL-10 levels in both sexes, but TZP did not significantly alter IL-10 concentrations in either sex. **Conclusion:** TZP attenuated LPS-induced fever in both sexes, but reduced hypothalamic PGE_2 concentrations exclusively in males. These findings indicate that suppression of PGE_2 may contribute to the antipyretic effect of TZP in males, whereas alternative mechanisms are likely involved in females.

04.028 **Integrated** *In silico*, *In vitro*, **and** *In vivo* **Evaluation of the anti-inflammatory Potential of Magnolin Isolated from** *Annona pickelii*. Ramos KS[1,2], Cabral Neto A[3], Lobo EB[2,3], Silva DKC[1,2,3], Cezar IS[2,3], Dutra LM[4], Barreto BC[1,3], Souza CVC[5], Santos-Filho OA[5], Gonçalves RS6, Soares MBP[2,3], Costa EV7, Meira CS[1,2,3]. [1]UNEB-BA, Salvador, [2]SENAI CIMATEC-BA, Salvador, [3]Fiocruz-BA, Salvador, [4]UFS-SE, São Cristóvão, [5]UFRJ-RJ, Rio de Janeiro, [6]UFPR-PR, Palotina, [7]UFAM-AM, Manaus.

Introduction: Natural products represent an important source of bioactive molecules with potential applications in the treatment of inflammatory disorders. Magnolin, a lignan isolated from Annona pickelii, has been reported to exhibit anti-inflammatory properties, however, its immunomodulatory effects on innate and adaptive immune responses remain poorly characterized. **Objectives:** To investigate the immunomodulatory activity of magnolin using integrated *in silico* , *in vitro*, and *in vivo* approaches. **Methods:** Toxicological and pharmacokinetic properties were initially predicted using the ProTox 3.0 platform. Cytotoxicity and hemolytic activity were evaluated in RAW 264.7 macrophages and human erythrocytes, respectively. Anti-inflammatory activity was assessed by measuring nitrite production, cytokine secretion, and inflammatory gene expression in LPS/IFN-γ-stimulated macrophages. Immunomodulatory effects on splenocytes were evaluated through lymphoproliferation assays and quantification of IL-2 and IFN-γ in Con A-stimulated murine splenocytes. Molecular docking analyses were performed against NF-κB and IκB kinase (IKK). Acute toxicity was assessed following oral administration of magnolin (50 mg/kg) in C57BL/6 mice. Finally, therapeutic efficacy of magnolin was evaluated in a murine model of LPS-induced endotoxemic shock. **Results:** *in silico* analyses predicted a favorable safety profile for magnolin, with low probabilities of hepatotoxicity, neurotoxicity, mutagenicity, and cytotoxicity. Consistently, magnolin showed low cytotoxicity in RAW 264.7 macrophages and no hemolytic activity in human erythrocytes. In activated macrophages, magnolin significantly ($p < 0.05$) reduced nitrite production and suppressed IL-1β, IL-6, IL-12, and TNF-α secretion. Gene expression analyses demonstrated downregulation of inflammatory mediators and signaling-related genes, including Nfkb1, Il1β, Tnf, Nos2, Ptgs2, Cxcl9, and Cxcl10. In activated splenocytes, magnolin significantly ($p < 0.05$) inhibited lymphocyte proliferation and reduced IL-2 and IFN-γ production without affecting cell viability. Molecular docking revealed favorable interactions with NF-κB- and IKK-associated binding sites. *In vivo*, acute oral administration of magnolin (50 mg/kg) produced no signs of toxicity, whereas treatment significantly improved survival in endotoxemic mice, reaching 60% survival at 10 mg/kg. **Conclusion:** Magnolin exhibited potent anti-inflammatory activity by suppressing inflammatory mediators associated with both innate and adaptive immune responses, while demonstrating a favorable preliminary safety profile. These findings support further investigation of magnolin as a promising natural-product-derived immunomodulatory agent for inflammatory disorders.

04.029 **A Ni(II) Complex with a Schiff Base Derived from Meldrum's Acid Reduces Lipopolysaccharide-Induced Acute Lung Injury in Mice**. Cândido JPS[1], Ramalho ABF[3], Santos, ABR[1], Pessoa WFB[2], Ferrari JS[3], Alves AF[1] [1]UFPB, PPG Produtos Naturais e Sintéticos Bioativos, Brasil [2]UFPB, Depto Ciências Biomédicas, Brasil, [3]UFPB, Depto Química, Brasil.

Introduction: Acute Respiratory Distress Syndrome (ARDS) is a severe inflammatory lung disease associated with high mortality. Experimental models of Acute Lung Injury (ALI) are widely used to investigate its mechanisms and potential treatments, since current therapies remain limited. Schiff bases and their metal complexes have shown promising antioxidant and anti-inflammatory activities. However, the effects of the Ni(II)-Melophen VI complex have not yet been evaluated *in vivo*. Therefore, this study investigated the therapeutic potential of Melophen VI and its nickel(II) complex in LPS-induced ALI in mice. **AIM:** Evaluate the therapeutic effects of Melophen VI and its nickel(II) complex in a murine model of lipopolysaccharide (LPS)-induced ALI. Methods: Forty male Swiss mice were used, of which five animals were randomly distributed into five experimental groups..: healthy control, acute lung injury (ALI), ALI treated with Melophen VI, ALI treated with the Ni(II)-Melophen VI complex, and ALI treated with dexamethasone (ALI+DEXA). ALI was induced by intranasal administration of LPS by a single application at a dose of 5 mg/kg under anesthesia. Melophen VI and the nickel complex were administered orally at a single dose of 100 mg/kg, one hour before ALI induction, while the control group received DMSO as vehicle. The ALI+DEXA group received a single dose of dexamethasone one hour after induction. At the end of the experiment, animals were euthanized and the lungs were collected for macroscopic evaluation, morphometric analysis, wet weight determination, and histological processing with hematoxylin and eosin staining. Statistical analyses were performed using one-way ANOVA followed by Tukey's post hoc test, considering $p < 0.05$ as statistically significant. **Results:** The LPA group showed marked macroscopic and microscopic pulmonary alterations, including edema, hemorrhagic areas, inflammatory infiltrate, and reduced alveolar spaces. In contrast, the groups treated with DEXA, Melophen, and Nickel Complex demonstrated improved lung morphology, with reduced lesion areas, smaller lung size, and lower wet lung weight compared to the untreated LPA group. These findings suggest that Melophen VI and especially the Ni(II)-complex exert protective anti-inflammatory effects against LPS-induced acute lung injury, reducing pulmonary edema and tissue damage. **Conclusion:** Melophen VI and its Ni(II)-complex reduced inflammation and lung damage in LPS-induced acute lung injury, with the nickel complex showing the strongest protective effect. These findings suggest their potential as therapeutic agents for inflammatory lung diseases.

04.030 **Evaluation of the Anti-Inflammatory Potential of Morita-Baylis-Hillman Adduct CISACN in Acute Lung Injury-an *in vitro*, *in vivo* and *in silico* study**. Rodrigues MRF[1], Oliveira JB[1], Lima LM[2], Vieira CID[2], Ferreira LKD[2], Moura BVS[1], Laurentino MVS[1], Pordeus GM[2], Mota PRV[2], Gadelha FAAF[2], Lima-Júnior CG[3], Dejani NN[2], Piuvezam MR[2] [1]UFPB, Immunopharmacology Lab, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]UFPB, Immunopharmacology Lab, Institute of Pharmaceutical and Medicinal Research, Brazil. [3]UFPB, Medicinal Organic Synthesis Lab Paraíba, Brazil.

Acute lung injury (ALI) is a syndrome of severe respiratory failure resulting from an intense and diffuse inflammatory response in the lung tissue, characterized by edema and reduced lung compliance, leading to respiratory failure. Currently, there is no effective standard pharmacotherapy for this condition. Recent studies have demonstrated that the Morita-Baylis-Hillman adduct 2-(3-hydroxy-1-methyl-2-oxoindolin-3-il) acrylonitrile(CISACN) exhibits anti-inflammatory activities in a model of combined allergic asthma and rhinitis syndrome and also presents low toxicity and good oral availability. Therefore, this study aimed to investigate the anti-inflammatory activity of the adduct CISACN in a ALI murine model (approved under certificate number 7316150420) and *in vitro* with RAW 264.7 cell line. Additionally, an *in silico* molecular docking analysis was performed. BALB/c mice were challenged by nasal instillation with LPS (2.5 mg/kg) and orally treated with CISACN (6.25, 12.5, or 25 mg/kg). Twenty-four hours later, bronchoalveolar lavage fluid (BALF), serum, and lung were collected. RAW 264.7 were stimulated with LPS (1µg/mL) and treated with CISACN (5, 10, 20µM) under pre-treatment and post-treatment conditions. Data were analyzed by GraphPad Prism software (9.0) and values with $p < 0.05$ were considered significant. All results presented were obtained from experiments performed in triplicate and were expressed as mean ± standard error of the mean and analyzed using the one-way ANOVA statistical test followed by Tukey's or Bonferroni's tests. In the ALI model, treatment with CISACN significantly reduced lung inflammation, as evidenced by decreased cell migration, levels of TNF-α, IL-1β, and IL-6, as well as reduced protein exudate in BALF. Additionally, it decreased serum TNF-α levels and attenuated histopathological alterations in the lung, such as edema, inflammatory cell infiltration, and hemorrhage. *in silico* analysis, showed a high binding energy of the CISACN with TLR4/p38 MAPK molecules. *In vitro*, the adduct was able to significantly reduce the NO production by the Raw cell line after stimulation with LPS in both pre- and post-treatment conditions at all concentrations tested. Also both treatments with CISACN significantly reduced the mean fluorescence intensity (MFI) for Phospho-p38 compared to the LPS-stimulated cells, confirming the *in silico* analysis. Therefore, this study highlights the anti-inflammatory potential of CISACN by inhibiting a key inflammatory pathway, although further studies are needed to investigate its anti- inflammatory effects.

04.031 **Type 1 Diabetes Negatively Modulates Th2-Driven Airway Inflammation in a Murine Asthma Model**. Leutz MC, Barbalho TM, Oliveira AL, Horioka CP, Medeiros ML, Antunes E Unicamp, School of Medical Sciences, Lab. of Pharmacology of the Urogenital Tract and Inflammation, PPG Pharmacology, Brazil

Asthma is an immunological allergic disorder characterized by chronic airway inflammation and airway hyperresponsiveness. Its classic phenotype, known as type 2 asthma, is defined by the prominent role of eosinophils in its pathogenesis, which are closely linked to the elevated production of Th2 cytokines (IL-4, IL-5, and IL-13) and eotaxin. Preclinical and clinical studies show that obese and type 2 diabetic (T2D) individuals experience exacerbated asthma compared to normoglycemic individuals, which may be due to accumulation of glucose-derived methylglyoxal and activation of receptor for advanced glycation end-products (RAGE). In contrast, asthma in individuals with type 1 diabetes (T1D) is attenuated, suggesting that T1D exerts a “protective” effect against allergic airway diseases, but this is still poorly investigated. Therefore, this preliminary study aimed to investigate the allergic airway inflammatory response in a classical murine model of T1D. Adult male C57BL/6Unib mice (8 weeks old) were submitted to multiple low doses of streptozotocin (STZ 50mg/kg, i.p, 5 days). Diabetic and non-diabetic animals were immunized twice with grade V ovalbumin (OVA, 100 µg) and then intranasally challenged with this antigen (10 µg, four times). At 48h after the first challenge, animals were euthanized by isoflurane overdose, followed by the collection of bronchoalveolar lavage fluid (BALF) and lung tissue for total and differential cell counting. Data (mean values ± SD) were analyzed using ANOVA followed by Bonferroni’s post-hoc test. Compared with control group, STZ administration significantly increased blood glucose levels (163.7±29.6 and 369.5±18.7 mg/dl, respectively) and water consumption (6.20 and 16.80 ml/animal/day, respectively) concomitant with a reduction in body weight (27.00±1.0 and 17.3±1.73 g, respectively), confirming the efficacy of T1D model. In control mice, OVA-challenge induced a marked infiltration of total cells (1.72±0.92×106/BAL) and eosinophils (0.64±0.12×106/BAL), both of which were nearly suppressed in STZ group ($P<0.05$). OVA-challenge also discreetly increased the number of neutrophils in BAL at 48h, but no significant differences between STZ and control groups were observed (0.19±0.08 and 0.21±0.11×106/BAL, respectively). Similarly, the number of mononuclear cells in BALF did not significantly differ between control and STZ groups. Our findings show that STZ-induced diabetes down-regulates classical Th2-driven eosinophilic airway inflammation impairing cellular recruitment into the airways, thus confirming that metabolic and immunological environment associated with T1D negatively modulate allergic airway responses. The underlying mechanisms involved in such down-regulation is under current investigation. This study was performed in accordance with the protocols and guidelines approved by CEUA/UNICAMP (nº 6788-1/2025) and was financially supported by CAPES.

04.032 **Pulmonary Effects of Nicotine Exposure from Cigarette Smoke and E-Cigarette Vapor in Experimental Allergic Asthma**. Rocha BM[1,2], Santos GCM[2,3,4], Motta DSE[2], Oliveira MECL[2], Santos GRA[2], Santana ACC[2], Arantes ACS[2], Ferreira TPT[2], Silva PMR[2], Martins MA[2,3,4] [1]ICB-UFRJ, , PPG Pharmacology and Medicinal Chemistry, Brazil; [2]IOC-Fiocruz, Lab Inflammation, Brazil; [3]Fiocruz, Preclinical Pharmacokinetic Platform, Brazil; [4]IOC-Fiocruz, PPG Biologia Celular e Molecular, Brazil.

Introduction: The tobacco epidemic remains a major public health concern. Furthermore, the increasing use of electronic cigarettes may increase nicotine delivery to lung tissue and exacerbate chronic pulmonary diseases, including asthma. This work aimed to investigate and compare how nicotine exposure from conventional cigarette smoke (CS) and electronic cigarette (e-cig) aerosol affects airway inflammation in a mouse model of allergic asthma. **Methods:** Female C57BL/6 mice (n = 7/group) were subcutaneously sensitised with ovalbumin (OVA) and aluminium hydroxide on days 0 and 13. From days 17 to 27, the mice were exposed to ambient air, conventional cigarette smoke (Marlboro Red), nicotine-containing e-cig aerosol (e-liquid: 20 mg/mL nicotine, PG/VG 50:50), or e-cig aerosol without nicotine (e-liquid: PG/VG 50: 50) for 1.5 h/day for 11 consecutive days. Allergic asthma was induced by intranasal OVA challenges from days 21–27, while control groups received saline. Bronchoalveolar lavage fluid (BALF) was collected 24h after the final exposure for analysis of leukocyte infiltration. Concurrently, lung samples were collected to quantify nicotine and cotinine levels using an in-house-developed bioanalytical LC–MS/MS method (linear range: 1.0–125 ng/mL). Procedures were approved by the FIOCRUZ Ethics Committee (L-002/2020-A9). **Results:** Allergen challenges induced intense airway inflammation in asthmatic mice exposed to ambient air, characterized by increased total leukocyte counts and marked eosinophilia. However, exposure to nicotine-containing e-cigarette aerosol, but not nicotine-free e-cigarette aerosol or CS, further increased total leukocyte counts. Notably, differential cell counts revealed that this enhanced inflammatory response was associated with a marked increase in neutrophil recruitment (17.2 ± 4.8 vs. 6.1 ± 1.9 × 10^5 cells/BALF compared with asthmatic non-exposed mice; $p < 0.001$), accompanied by a reduction in eosinophil numbers (1.2 ± 0.6 vs. 7.0 ± 1.4 × 10^5 cells/BALF compared with asthmatic non-exposed mice; $p < 0.05$). In another setting, lung homogenates from asthmatic mice exposed to nicotine-containing aerosol showed higher nicotine concentrations than non-asthmatic controls (10. 1 ± 2.4 vs 3. 5 ± 0.1 ng/g; $p <$ 0\. 01). The asthmatic CS group showed a similar, but non-significant, trend. **Conclusion:** These results suggest that the inhaled nicotine accumulates in allergen-inflamed lungs at higher levels than in negative controls. Furthermore, even short-term exposure to nicotine-containing e-cigs aerosol was sufficient to exacerbate and shift the inflammatory response phenotype, replacing eosinophils with a surge in neutrophils. Importantly, neutrophilic asthma is generally more severe and potentially associated with corticosteroid resistance, the mainstay of asthma treatment, highlighting the risks of e-cig exposure in pre-existing respiratory diseases.

04.033 **Anti-Inflammatory and Antioxidant Effects of *Solanum stipulaceum* Willd. ex Roem. & Schult on Cutaneous Inflammation in Mice**. Nunes ERS[1], Biano LS[1], Ramos LS[1], Sales MS[1], Souza DA[1], Silva MT[2], Matos TRG[1], Lima JCJS[1], Matos SS[3], Cavalcante MD[3], Grespan R[1], Aragão JMDA[1], Camargo, EA[1] [1]UFS, Lab Pharmacology of the Inflammatory Process, Graduate Program in Physiological Sciences, Brazil [2]UFS, Graduate Program in Natural Sciences, Brazil; [3]UFS, Graduate Program in Pharmaceutical Sciences, Brazil

Introduction: Solanum stipulaceum (commonly known as “jurubeba” or “sacatinga”) is an endemic plant of the Brazilian Caatinga, traditionally used for gastric disorders. Scientific evidence supports its gastroprotective effects, attributed to bioactive compounds with antioxidant and anti-inflammatory properties. Additionally, antioxidant activity has been demonstrated *in vitro* and *in vivo*, along with additional pharmacological effects such as cardiovascular activity and selective cytotoxicity. Thus, investigating its anti-inflammatory and antioxidant potential in the ear edema model may help elucidate its mechanisms and support its therapeutic applications. **Objectives:** This study aimed to evaluate the anti-inflammatory and antioxidant potential of the hydroethanolic extract of Solanum stipulaceum leaves (EHSs) in a mouse ear edema model. **Methods:** Female Swiss mice were subjected to inflammation induction in the right ear by topical application of 12-O-tetradecanoylphorbol-13-acetate (TPA; 1 µg/ear in 20 µL acetone). Five minutes later, animals received topical treatment with EHSs at different doses (0.3, 1.0, and 3.0 mg/ear), vehicle (acetone), or dexamethasone (0.05 mg/ear) as a positive control. The left ears received vehicle only and served as internal controls. Six hours after inflammation induction, animals were euthanized, and ear tissues were collected using an 8 mm punch for edema assessment (mass difference between ears), histological analysis (dermo-epidermal thickness), myeloperoxidase (MPO) activity, total hydroperoxide quantification, and catalase (CAT) activity. Data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey’s post hoc test. **Results:** Compared to the vehicle+TPA group, treatment with all three doses of EHSs significantly reduced inflammatory parameters, including edema ($p < 0.0001$) and MPO activity (0.3 mg/ear, $p = 0.008$; 1.0 mg/ear, $p = 0.016$; 3.0 mg/ear, $p = 0.0008$). Macroscopic anatomical-pathological analysis revealed reduced hyperemia and swelling, which was corroborated by histological findings showing decreased dermo-epidermal thickness (0.3 mg/ear, $p = 0.0006$; 1.0 $p = 0.0043$; 3.0 mg/ear $p = 0.012$). Based on these findings, the 3.0 mg/ear dose was selected for subsequent antioxidant assays as a refinement strategy. At this dose, EHSs reduced total hydroperoxide levels ($p = 0.0104$) and increased CAT activity ($p = 0.0315$) compared to the vehicle+TPA group. **Conclusion:** Taken together, these findings suggest the bioactive potential of S. stipulaceum, indicating that this species may represent a relevant candidate for future investigations aimed at developing therapeutic approaches, particularly as a complementary strategy in the management of skin conditions associated with inflammatory and oxidative stress.

04.034 **Deciphering Calcitoningene-Related Peptide (CGRP)-H_2S Crosstalk in cutaneous wound healing and Nociception**. Jamba MF[1], Tavares YPST[1], Teixeira SA[1], Brain SD[2], Muscará MN[1], Costa SKP[1] [1]ICB-USP, Depto Farmacologia; [2]King's College London-Waterloo, School of Cardiovascular Medicine & Sciences

Introduction: & Aims: The skin, the body's largest sensory organ and a critical protective barrier, has remarkable regenerative capacity. Its disruption triggers a tightly regulated healing process involving immune, vascular, stromal and epithelial cells. Calcitonin gene-related peptide (CGRP), a sensory neuropeptide abundant in sensory nerves, regulates vasodilation, inflammation and early wound healing. Hydrogen sulfide (H_2S), an endogenous gaseous mediator, regulates nociception, inflammation and tissue protection, partly via transient receptor potential (TRP) channels in capsaicin-sensitive sensory neurons. Although both CGRP and H_2S regulate pain and inflammation, whether they interact in inflammatory resolution, nociception and wound healing remains unknown. Using α-CGRP knockout (KO) mice, we investigated endogenous CGRP in cutaneous nociception and wound healing, focusing on potential CGRP–H_2S crosstalk in pain and inflammatory resolution. **Methods:** A 5-mm full-thickness excisional wound was induced in the dorsal skin of 8-week-old male and female C57BL/6 wild-type (WT) and α-CGRP KO mice. Nociception was assessed by primary and secondary mechanical withdrawal thresholds (MWTs) using von Frey filaments and spontaneous pain-related behaviour using the mouse grimace scale. Wound closure was monitored by digital imaging and calliper measurements. Healing responses were assessed on days 2, 4 and 6 post-injury, including myeloperoxidase (MPO) activity, endogenous H_2) production and tissue microvascular perfusion by Laser Doppler flowmetry. Data are presented as mean ± SEM or median ± interquartile range (IQR); $p < 0.05$ was considered significant. **Results:** Wound healing was significantly faster in WT than α-CGRP KO mice, irrespective of sex, with a lower wound-area AUC over 15 days (183.1 ± 14.8 vs. 287.5 ± 3.2, n = 5–6), greater epithelialisation and hair follicle regeneration. α-CGRP KO mice showed higher mechanical withdrawal thresholds at the primary wound site ($AUC_{0–15}$ days: 4.27 ± 1.08 vs. 6.02 ± 0.68, n = 5–6) and lower grimace scores (15.67 ± 3.37 vs. 23.92 ± 5.40, n = 5–6), indicating reduced nociceptive sensitivity, with no difference in secondary hyperalgesia. MPO activity was higher in KO than WT mice on day 2 (26,301 ± 754 vs. 18,178 ± 731, n = 6), whereas cutaneous microvascular perfusion was greater in WT at 1 h (334.0 ± 30.7 vs. 276.9 ± 14.8) and day 2 (219.6 ± 33.5 vs. 154.1 ± 25.0; n = 7). Notably, endogenous H_2S production remained unchanged between genotypes, indicating that CGRP deficiency alters tissue repair, nociception and early inflammatory and vascular responses without affecting H_2S production. **Conclusion:** These findings identify CGRP as a key neuroimmune regulator linking tissue repair and nociception. Preserved endogenous H_2S production despite CGRP deficiency suggests complementary or convergent signalling pathways and supports further investigation of CGRP–H_2S crosstalk in pain and wound resolution.

04.035 **Therapeutic Effects of Oral *Lactiplantibacillus plantarum* 6. 2 Supplementation on Experimental Acute Lung Injury Progression**. Santos ABR[1], Candido JPS[1], Araújo RS[1], Pessoa WFB[2], Alves AF[1,2] [1]UFPB, Program in Natural and Synthetic Products Bioactive, Brazil. [2]UFPB, Biomedical Sciences Dept, Brazil.

Introduction: Acute lung injury (ALI) comprises severe inflammatory pulmonary disorders characterized by disruption of the alveolar–capillary barrier, intense cytokine release, and neutrophilic infiltration. Recent evidence highlights the gut–lung axis as an important modulator of pulmonary inflammation. Microorganisms such as Lactiplantibacillus spp. exhibit anti-inflammatory and immunomodulatory properties, suggesting therapeutic potential in inflammatory lung diseases. In this context, the *Lactiplantibacillus plantarum* 6.2 (Lp62) strain—originally isolated from spontaneous cocoa fermentation in the Ilhéus and Itabuna regions of Bahia, Brazil—has emerged as a promising candidate for modulating inflammatory responses. **Aim:** To assess the therapeutic efficacy of oral Lp62 supplementation as an alternative intervention for mitigating LPS-induced acute lung injury in mice. **Methods:** Fifty Swiss mice were divided into five groups: healthy, ALI, LAC, DEXA, and ALI+LAC. ALI was induced by intranasal LPS administration (10 µg/kg). One hour later, dexamethasone-treated animals received dexamethasone (2 mg/kg) by oral gavage. Lp62 was administered orally for seven days after ALI induction. After euthanasia, bronchoalveolar lavage fluid (BALF) was collected then total and differential cell counts were performed. Lungs were also collected for macroscopic, histological, and histomorphometric analyses using Hematoxylin-Eosin staining. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test, with $p<0.05$ considered statistically significant. **Results:** In BALF, reduced total cellularity and lower neutrophil proportions relative to alveolar macrophages were observed compared to untreated ALI animals, indicating modulation of the acute inflammatory response. Macroscopically, healthy lungs showed preserved architecture without edema or hemorrhage, whereas Ali lungs exhibited diffuse hyperemia, edema, and hemorrhagic areas. Histologically, ALI lungs presented neutrophilic infiltration, septal thickening, alveolar collapse, edema, vascular congestion, and tissue disorganization. Animals treated with Lp62 showed attenuation of pulmonary inflammation and preservation of tissue architecture. Treatment with Lp62 reduced inflammatory infiltrate, preserved alveolar architecture, and attenuated septal thickening and edema. **Conclusion:** Oral supplementation with Lp62 represents a promising therapeutic strategy for ALI due to its anti-inflammatory and immunomodulatory effects, supporting microbiota-targeted therapies focused on the gut-lung axis.

04.036 **Novel Dual-Acting MAO/PDE4 Inhibitors: Pharmacological Characterization of a Potential Multitarget Approach for Inflammatory Lung Diseases**. Ota RSN[1,2], Bezerra LCA[3], Souza LM[1], Ferreira TPT[1], Chavarria DF[4], Borges MFM[4], Kümmerle AE[3], Martins MA[1], Silva PMR[1] [1]IOC-Fiocruz, Lab of Inflammation, Rio de Janeiro, Brazil; [2]UFRJ, PPG Pharmacology and Medicinal Chemistry, Rio de Janeiro, Brazil; [3]UFRRJ, LaDMol-QM, Rio de Janeiro, Brazil; [4]University of Porto, Porto, Portugal.

Introduction: Inflammatory lung diseases remain associated with significant therapeutic limitations, highlighting the need for novel multitarget treatment strategies. Phosphodiesterase-4 (PDE4) is a well-established therapeutic target in inflammatory lung diseases, with clinically demonstrated anti-inflammatory and antifibrotic effects. In parallel, monoamine oxidase (MAO) has emerged as a modulator of oxidative stress and inflammation in multiple tissues, including the lung. In this context, the development of dual PDE4/MAO inhibitors represents an innovative multitarget strategy with the potential to improve the treatment of inflammatory lung diseases. **Objectives:** To assess the pharmacological effect of two investigational compounds (LaDMol-452 and LaDMol-458) as dual MAO/PDE4 inhibitors and to evaluate their anti-inflammatory potential in an *in vitro* system. **Methods:** The compounds were synthesized in the Laboratory of Molecular Diversity and Medicinal Chemistry (LaDMol-QM) at the Federal Rural University of Rio de Janeiro (UFRRJ). MAO inhibitory activity was determined through a collaborative effort with the University of Porto. The PDE4 inhibitory activity was evaluated using the IMAP® PDE Fluorescence Polarization (FP) Assay. Furthermore, the anti-inflammatory potential of the compounds was evaluated *in vitro* by measuring their ability to inhibit LPS-induced TNF-α production in AMJ2-C11 alveolar macrophage cell line. **Results:** The pharmacological evaluation of these compounds revealed their dual inhibitory profile. LaDMol-458 exhibited activity against both MAO-A and MAO-B, with IC_{50} values of 3 μM and 0.3 μM, respectively. In contrast, LaDMol-452 showed selective activity toward MAO-B, with an IC_{50} of 0.22 μM. Both compounds showed potent inhibition on PDE4A4 isoform, with IC_{50} values of approximately 50 nM. For the PDE4B1 isoform, LaDMol-452 exhibited better inhibitory activity (IC_{50} = 443 nM) than LaDMol-458 ($IC_{50} \approx 1$ μM). Additionally, the LaDMol-458 significantly reduced the TNF-α production in the *in vitro* model, providing initial evidence of its anti-inflammatory potential. **Conclusion:** The results demonstrate that these compounds exhibit a dual MAO/PDE4 inhibitory profile and a promising *in vitro* anti-inflammatory activity. Studies are now underway to confirm the benefits of simultaneous modulation of these targets and to evaluate their efficacy in animal models of inflammatory lung diseases, particularly chronic forms.
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04.037 **Biomaterials from Sea-Cucumber Body Wall Promote Bioactive Responses in RAW264. 7 Macrophages**.
Penno SM[1], Cahú TB[1,2], Silva JCA[1], Motta JM[1], Todeschini AR[2], Vilela-Silva ACES[3], Mourão PAS.[1] [1]IBqM-UFRJ, Lab Tecido Conjuntivo-, [2]IBCCF-UFRJ, Lab Glicobiologia Estrutural e Funcional, [3]ICB-UFRJ, Lab Atividade Biológica de Glicoconjugados, Brasil.

Introduction: Echinoderms are marine invertebrates that have mutable connective tissue (MCT) rich in collagen and sulfated polysaccharides. Several pharmacological activities attributed to these compounds have already been described. Furthermore, there are a variety of studies that demonstrate the efficiency of these bioproducts in tissue engineering and regenerative medicine, as they have effects on inflammation and wound healing. **Objective:** Extract and characterize collagen and sulfated polysaccharides (SP) from the sea cucumber *Holothuria grisea*, evaluate their structural characteristics and bioactivity towards RAW 264.7 macrophages. **Methodology:** collagen and SP were extracted from sea cucumber body wall, simultaneously, using alkali-acid treatment, followed by pepsin solubilization. Collagen was characterized by PAGE, hydroxyproline content assay, FT-IR and TEM. Sulfated polysaccharides purification was confirmed by PAGE showing two bands indicating the Sulfated fucan (SF) and Fucosylated chondroitin sulfate (FucCS). Viability of RAW 264.7 was assessed using the MTT assay, while endocytosis was assessed by neutral red uptake assay (NRU). *In vitro* migration ability was assessed by monolayer scratch assay, and NO production was measured using Griess reagent. Macrophage polarization was evaluated by flow cytometry. **Results:** Pepsin Solubilized collagen (PSC) analyzed by SDS-PAGE demonstrated collagen type I-like bands. FT-IR analysis showed peaks related to collagen structure with and without sulfated polysaccharides. TEM demonstrated characteristic bands of collagen. Viability was not affected by SF, FucCS or PSC. Migration was promoted by PSC, while endocytosis increased at high SP concentrations and showed no correlation with cell viability. FucCS and SF inhibited NO production in LPS- stimulated macrophages. Flow cytometry evaluation showed influence of collagen and SP in CD68 and CD206 markers indicating macrophage polarization. **Conclusion:** These preliminary results suggest that biomaterials extracted from the sea cucumber body wall can exert bioactivity on macrophages, with potential beneficial effects on inflammation control and wound healing, demonstrating potential for application as a wound-healing agent. To verify this hypothesis, further complementary experiments will be conducted as this study continues.

04.038 **Anti-Inflammatory Potential and Toxicity of Sulcatone (6-Methyl-5-hepten-2-one) in a *Zophobas morio* Larval Model**. Ferreira CES[1], Acha BT[1], Cunha FCS[2], Soares T[1], Oliveira MP[3], Rêgo AF[4], Macedo JL[1], Alves MMM[3], Oliveira AP[6], Arcanjo DDR[6], Martins MCC[6,7] [1]UFPI, PPG em Biotecnologia (Renorbio), Teresina, PI, Brazil, [2]UFPI, PPG em Tecnologias Aplicadas a Animais de Interesse Regional, Teresina, PI, Brasil, [3]UFDPar, Parnaíba, PI, Brasil, [4]UFPI, PPG em Farmacologia, Teresina, PI, Brasil, [5]UFPI, Depto Morfofisiologia Veterinária, Teresina, PI, Brasil, [6]UFPI, Depto Biofísica e Fisiologia, Teresina, PI, Brasil, [7]UNIFAESF, Centro Universitário

Introduction: Sulcatone (6-methyl-5-hepten-2-one) is a volatile monoterpene found in citrus fruits, animal pheromones, and human sweat. It has demonstrated antioxidant potential. However, its anti-inflammatory properties and toxicity profile have been poorly explored in biological models. Alternative models offer a relevant, low-cost way to assess toxicity and inflammation responses *in vivo*. **Objective:** To evaluate sulcatone's anti-inflammatory effect and toxicity in *Zophobas morio* larvae. **Methods:** We induced inflammation in *Z. morio* larvae with carrageenan. Our groups were a negative control (saline), an inflammatory control (carrageenan 0.5 µg/mL), a positive control (dexamethasone 25 µg/mL), and sulcatone at 3, 30, and 300 mg/kg. Afterward, we collected hemolymph and quantified hemocytes using a Neubauer chamber. We analyzed data by one-way ANOVA, followed by Bonferroni's post hoc test. Significance was set at $p<0.05$. For toxicity, groups of 10 larvae received 10 µL sulcatone solutions by ventral injection (3, 30, 300, and 3000 mg/kg). Dimethyl sulfoxide and saline served as positive and negative controls. We monitored survival for 48 h and expressed mortality as a percentage. The median lethal dose (LD50) was estimated by nonlinear regression. We assessed melanization with densitometry and visual inspection. Nitrite levels were measured using the Griess method. For molecular docking, we tested sulcatone against cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) in AutoDock 4. Interaction analyses were done in UCSF Chimera and Discovery Studio. **Results:** Sulcatone showed low acute toxicity in *Z. morio* larvae, with 30% mortality at the highest dose. The LD50 was not reached within the test range and is considered >3000 mg/kg. Given this low lethality, we tested its anti-inflammatory activity in the carrageenan model. Sulcatone significantly reduced hemocyte counts at 3 mg/kg ($p<0.0001$), 30 mg/kg ($p=0.0090$), and 300 mg/kg ($p=0.0069$). This suggests reduced cellular inflammatory response. Melanization analysis showed dose-response changes in larval pigmentation, suggesting humoral immune involvement. Nitrite levels remained near basal in sulcatone groups. These were significantly lower than after the inflammatory stimulus (LPS), with a 40.4% to 46.9% reduction ($p<0.001$). This suggests decreased nitric oxide signaling. On molecular docking, sulcatone showed favorable interactions with iNOS and COX-2. The binding free energies were -4.81 and -4.64 kcal/mol, respectively. Standard inhibitors were not included for direct comparison. Still, these values suggest moderate predicted affinity. The interaction with iNOS involved hydrogen bonds with GLY101 and SER102. The interaction with COX-2 involved GLY372 and LYS532. This provides preliminary support for nitric oxide and inflammatory mediator modulation. **Conclusion:** Sulcatone showed low toxicity in the larval model. It demonstrated anti-inflammatory and immunomodulatory potential by reducing hemocyte counts and nitrite levels. It also modulated melanization. Molecular docking suggests involvement in nitric oxide and inflammatory mediator pathways.

04.039 **Bosutinib Modulates Microglial Inflammation Induced by Bacterial Insult**. Cunha CMC[1,2,3], Patricio IM[1,2,3], Ferreira-Costa M[1,2,3], Santos FS35, Gomes-Reis GLS[1,2,3], Moraes BPT[3,4], Ferreira AMS[1,2,3], Sayão PGF[1,3,4], Alves-Nunes L[1,3], Ferreira LN[1,3], Bozza PT[1,2], Castro-Faria-Neto HC[1,2], Gonçalves-de-Albuquerque CF[1,2,3,4,5], Silva AR[1,2,5] 1IOC-Fiocruz, Immunopharmacology Lab, Rio de Janeiro, Brazil. [2]IOC-Fiocruz PPG in Cellular and Molecular Biology, Rio de Janeiro, Brazil. [3]Unirio, Immunopharmacology Lab, Rio de Janeiro, Brazil. [4]Unirio, PPG in Molecular and Cellular Biology, Rio de Janeiro, Brazil. [5]UFF, PPG in Neuroscience, Niteroi, Brazil.

Introduction: Microglia are the main defense cells of the central nervous system and have several functions that contribute to the homeostasis of neuronal tissue. In response to bacterial insults, they can acquire a pro-inflammatory cellular phenotype, characterized by the production of TNF-α, IL-6, IL-1β, and nitric oxide (NO), as well as morphological alterations. The main molecular pathway underlying these effects is the TLR4 pathway, a receptor that recognizes LPS from Gram-negative bacteria. The TLR4 pathway involves the activation of several proteins such as MAPKs and the transcription factor NFκB. Src family kinases (SFKs) are protein kinases involved in the regulation of various cellular functions, including the inflammatory response and cytokine secretion. Inhibition of SFK attenuates the exacerbated leukocyte responses in inflammatory reactions. Bosutinib (BOS) is a multi-kinase inhibitor clinically used to treat chronic myeloid leukemia, with potent effects on SFK. **Objectives:** Our objective is to evaluate whether the effect of bosutinib on SFK can modulate the microglia response to bacterial stimulation. **Methods:** Murine microglial cells (BV2) were pretreated with 500 nM BOS 30 minutes before stimulation with LPS (50 or 100 ng/ml) or *E. coli* (MOI 10). 30 minutes after stimulation, cell lysate was collected for evaluation of MAPK p38 and p65 (NFκB subunit) by Western blot. 24 hours after stimulation, a viability assay, Griess assay to quantify NO, and ELISA to evaluate pro-inflammatory cytokines were performed. In addition, immunostaining was performed to evaluate p65 translocation and cell morphology by β-tubulin. Immunohistochemistry was also performed on brain sections from mice induced to polymicrobial sepsis and treated with BOS (3 mg/kg) to evaluate microglial reactivity by IBA-1 staining. Results and **Conclusion:** BOS showed potent immunomodulatory activity on BV2 stimulated with LPS or *E. coli*. It protected against LPS-induced cytotoxicity at 100 ng/ml and significantly reduced TNF-α levels in all stimulated groups. Associated with this, a reduction in p65 phosphorylation and possible modulation in its nuclear translocation were observed. As for NO, BOS seems to control its increase in response to a stronger stimulus (LPS 100ng/ml). Interestingly, BOS maintained high IL-6 concentration and did not reduce p38 phosphorylation. Increased IL-6 with reduced TNF-a may contribute to a pro-resolving profile, cytoskeleton remodeling, and improved phagocytosis. Furthermore, the treatment altered the cellular morphology of microglia in both *in vitro* and *in vivo* settings, apparently contributing to their ramified, vigilant profile. These results corroborate the immunomodulatory potential of BOS in microglia, which may contribute to a more resolving and less pro-inflammatory profile. Funding: FAPERJ, UNIRIO, CNPq, CAPES (Grant 001), COI, FIOCRUZ, BCM. Animal Use Ethics Committee of IOC (L026/2022).

04.040 **Gastroprotective Effects of Isoflavones in Experimental Models of Gastric Ulcer: A Systematic Review**. Santos GJ[1], Couto CM[2], Souza DA[1], Aragão JMDA[1], Ramos LS[1], Grespan R[1], Camargo EA[1] [1]UFS-São Cristóvão, Lab Pharmacology of the Inflammatory Process, Dept Physiology, SE, Brazil; [2]UFS, Dept Pharmacy, Brazil

Introduction: Peptic ulcers affect a significant portion of the global population and are commonly treated with proton pump inhibitors and H2 receptor antagonists, which are often associated with significant adverse effects and high rates of ulcer recurrence. In this context, natural products have emerged as promising sources of bioactive compounds, including isoflavones, which have demonstrated beneficial effects in experimental models of gastric injury. **Objective:** To comprehensively evaluate the scientific evidence regarding the therapeutic potential of isoflavones in preclinical models of gastric ulcer. **Methods:** A systematic review was conducted using Web of Science, ScienceDirect, Scopus, and MEDLINE/PubMed databases. Studies evaluating isolated isoflavones in animal models of gastric ulcer were included, and the risk of bias was assessed using the SYRCLE tool. **Results:** Thirteen studies were included out of 3005 records identified through an extensive search strategy. Overall, isoflavones demonstrated consistent gastroprotective effects when administered prophylactically or therapeutically in rodent models. These effects were associated with increased antioxidant defenses, including catalase and superoxide dismutase activities, elevated levels of reduced glutathione, nitric oxide, and prostaglandin E2, as well as reduced gastric secretion and acidity. In addition, isoflavones decreased pro-inflammatory cytokines, including TNF-α, IL-1β, IL-6, and IL-8, and reduced neutrophil infiltration. Most studies were classified as having low risk of bias for baseline characteristics (91%), incomplete outcome data (100%), and selective outcome reporting (100%). However, across the remaining SYRCLE domains, all studies were classified as presenting unclear risk due to insufficiently detailed methodological descriptions. **Conclusion:** Isoflavones exert protective effects on the gastric mucosa through antioxidant and anti-inflammatory mechanisms, supporting their potential as therapeutic agents for the management of gastric ulcers. However, more well-designed and adequately reported preclinical studies are still needed to strengthen the clinical translation of these findings.

04.041 **Anti-Inflammatory Effect of the Synthetic Alkaloid Tetrahydroisoquinoline 2-(7-Methoxy-1,2,3,4-Tetrahydroisoquinoline-1-YL)Phenol (MTF) In Murine Models of Acute Inflammation**. Oliveira JB[1], Vieira CID[1], Lima LM[1], Moura BVS[1], Laurentino MVS[1], Mota PRV[1], Pordeus GM[1], Ferreira LKDP[2], Silva TG[1], Ferreira LAMP[1], Bernardo LR[1], Gadelha FAAF[3], Dejani NN[1], Piuvezam MR[1] [1]UFPB, Immunopharmacology Lab, Brazil, [2]UFAL, Center for Medical and Nursing Sciences, Brazil, [3]UFPB, Institute for Drug and Medicine Research, Brazil

Introduction: Inflammation is a physiological response of the organism to maintain tissue homeostasis in the face of damaging stimuli. Acute lung injury (ALI), an inflammatory condition that precedes acute respiratory distress syndrome (ARDS), has gained prominence in patients with COVID-19, as respiratory dysfunction occurs due to the accumulation of neutrophils and pro-inflammatory cytokines in the lungs. To date, there is no specific pharmacotherapy for this syndrome, and numerous studies are aimed at elucidating new drugs with anti-inflammatory potential. Thus, the synthetic alkaloid 2-(7-methoxy-1,2,3,4-tetrahydroisoquinoline-1-yl)phenol (MTF) emerges as a promising molecule to add to the therapeutic arsenal of anti-inflammatory drugs. **Objectives:** Therefore, our objective was to evaluate the potential anti-inflammatory effect of MTF in murine models of ALI, paw edema, and peritonitis. **Methods:** In the experimental model of LPA, male BALB/c mice were challenged by nasal instillation with lipopolysaccharide (LPS). One hour later, they were treated orally with MTF (1.25 mg/kg, 2.5 mg/kg, or 5 mg/kg). After 24 hours, bronchoalveolar lavage fluid (BALF), serum, and lungs were collected. For the paw edema model, female Swiss mice were pre-treated with MTF (2.5 mg/kg) and challenged intraplantarly with the phlogistic agents carrageenan, prostaglandin (PGE2), bradykinin (BK), serotonin (5-HT), compound 48/80, or histamine. For the peritonitis model, female Swiss mice were treated orally and challenged intraperitoneally one hour later with carrageenan (1%). Statistical analyses were performed using one-way ANOVA followed by Tukey or Bonferroni post-hoc tests ($p<0.05$), when applicable. **Results:** In the LPA model, treatment with MTF (2.5 mg/kg) reduced lymphocyte- and macrophage-independent neutrophil migration in BALF, and decreased the production of TNF-α, IL-1β, and IL-6 in BALF and serum. Furthermore, MTF reduced vascular permeability in the alveolar region and attenuated histopathological changes such as edema, cellular infiltrate, and hemorrhage. In the other protocols evaluated, pretreatment with MTF reduced paw edema induced by phlogistic agents and, in the peritoneum, there was a decrease in neutrophil and mononuclear cell migration, vascular permeability, and the cytokines TNF-α, IL-1β, and IL-6. In addition, *in silico analyses* showed that MTF has good oral bioavailability, with low theoretical toxicity, and that the anti-inflammatory effects of the molecule may be associated with the inhibition of the TLR4/MAPK-p38 signaling pathway. **Conclusion:** Therefore, the results presented in this work demonstrate the anti-inflammatory potential of MTF, presenting it as a promising molecule for the development of a drug that adds to the anti-inflammatory therapeutic arsenal.

04.042 **Ouabain Improves Pulmonary Function in a Murine Model of Mixed Asthma**. Ribeiro, Martina R[1], Souza-Lima T[1], Siena A[1], Francelino-Alves V[1], Melhado IV[1], Fernandes PH[1], de Sá Lima L[1], Andreotti DZ[1], Oliveira MA[1], Leite J[2], Moriya HT[3], Rodrigues-Mascarenhas S[4], Tavares-de-Lima W[1], Scavone C[1] [1]ICB-USP, Dept. of Pharmacology, SP, Brazil; [2]ICB-UFG, Dept. of Pharmacology, GO, Brazil; [3]EP-USP, Dept. of Telecommunication and Control Engineering, SP Brazil; [4]UFPB, Dept of Cell and Molecular Biology, João Pessoa, PB, Brazil

Mixed asthma is a chronic inflammatory airway disease characterized by the combined involvement of eosinophilic and neutrophilic responses, increased airway hyperresponsiveness, and limited responsiveness to corticosteroid therapy. Ouabain (OUA), a Na+,K+-ATPase ligand, has demonstrated anti- inflammatory effects in experimental models of allergic asthma, but its effects in mixed asthma remain unclear. Here, we investigated the effects of OUA on pulmonary function, lung inflammation, and ATP/Na+,K+-ATPase activity in a murine model of mixed asthma. **Methods:** Female BALB/c mice were sensitized with ovalbumin (OVA) and Complete Freund's Adjuvant and challenged intranasally with OVA on days 21–23 to induce mixed asthma. Mice received ouabain (OUA, 0.56 mg/kg, i.p.), budesonide (BUD), or PBS 1 h before each challenge. Experiments were performed on day 24. Airway hyperresponsiveness was assessed using the FlexiVent system following increasing doses of methacholine (MCh), and respiratory system resistance (R), elastance (H), and compliance were evaluated. Lung inflammation was characterized by eosinoperoxidase (EPO) and myeloperoxidase (MPO) activities and by quantification of TNF-α, IL-1β, IFN-γ, and IL-17A in lung tissue by ELISA. Pulmonary ATP levels were determined by bioluminescence and normalized to total protein content. Na+,K+-ATPase activity was assessed by colorimetric quantification of inorganic phosphate release, including total activity and ouabain-sensitive α1 and α2/α3 isoform activities. Data were analyzed by one- way or two-way ANOVA, as appropriate. **Results:** OVA-challenge increased the R and H values (R:1,2±0,6 cm/H2O.s/mL P=0,0001) (H: 27,7±4 cm/H2O.s/mL P=0,0001). And treatment with ouabain decreases R and H compared to the OVA group (R:0,9±0,3cm/H2O.s/mL)(H: 25,4± 2,7cm/H2O.s/mL). MPO activity increased in OVA vs PBS (3.5± 1.3vs.1.0± 0.6, P=0.015) and was further increased by BUD (6.8± 2.9vs. 3.5±1.3, P=0.007). OUA showed lower MPO activity than BUD (1.4±1.7vs.6.8± 2.9, P=0.0001). EPO activity increased after OVA challenge (4.8±1.9vs.1.00±0.9, P<0.0001) and remained elevated after BUD (5.3±0.4) or OUA (5.4±0.8), with no differences vs OVA. IL-17A levels in lung increased in OVA vs PBS (95.67±33.56vs.61.31±15.06, P=0.0486) and in OVA+OUA vs PBS (106.8±27.63vs.61.3±15.0, P=0.0026), with no difference between OVA and OVA+OUA. Pulmonary ATP levels did not differ between OVA and PBS. OUA significantly reduced ATP levels in both non-asthmatic (105.7±55.7vs.79.6±50.7,P=0.0083) and OVA-challenged mice (151.4±46.3vs.374.1±204.5, P=0.0074). Without detectable changes in total Na+,K+-ATPase or α1 and α2/α3 isoform activities. **Conclusion:** OUA improved pulmonary mechanics in mixed asthma without producing a broad suppression of lung inflammation. The dissociation between improved pulmonary function, persistent inflammatory markers, and reduced ATP levels, with no change in Na+,K+-ATPase activity, suggests that OUA may act through mechanisms beyond conventional anti-inflammatory pathways, potentially involving regulation of pulmonary energy homeostasis and Na+,K+-ATPase-associated signaling.

04.043 **Evaluation of the Anti-Inflammatory Activity Of Novel PPARγ Agonists**. Krepsky LM, Vaz CR, Mello M, Pereira MES, Buzzi FC, Corrêa R, Quintão NL, Benvenutti L, Santin JR Univali, PPG Ciências Farmacêuticas, Brasil

Introduction: Peroxisome proliferator-activated receptor-y (PPARγ) have gained considerable attention as promising therapeutic targets in the modulation of immune and inflammatory responses. Activation of PPARγ has been associated with macrophage polarization, modulation of cytokine production, and attenuation of inflammatory processes, highlighting its potential to treat immune-mediated and inflammatory diseases. **Objective** This study aimed to evaluate the immunomodulatory effects of the partial PPARγ agonists C1, C2, C3, C4, C5, and C6 in RAW 264.7 macrophages using *in vitro* assays of cell viability, macrophage function, and phenotypic modulation. **Methods:** Cytotoxicity was initially assessed through the MTT colorimetric assay using RAW 264.7 in order to determine cell viability following compound exposure. The anti-inflammatory activity of the compounds was subsequently investigated by nitrite production by Griess reaction. Based on the inhibitory effects observed on NO release, the most active compounds were selected for additional evaluation of tumor necrosis factor (TNF) levels and macrophage polarization profiles. Polarization markers, including CD206 and CD80 expression, were analyzed by flow cytometry. **Results:** In the MTT assay, compounds from series C did not show cytotoxic effects in RAW 264.7 macrophages at the tested concentrations. In the analysis of nitrite production induced by lipopolysaccharide (LPS), compounds C3, C5, and C6 (10 μM) significantly reduced NO levels ($p < 0.05$) compared to the control group, suggesting anti-inflammatory activity. The results showed a reduction in TNF production compared to control group for C3 and C6. In addition, all compounds decreased CD80 expression in activated macrophages (M1 phenotype), reinforcing their anti-inflammatory potential. Compound C6 showed the most pronounced effect, with a significant reduction in CD80 expression ($p < 0.05$). For CD206 expression, cells treated with C6 showed increased levels of this marker ($p = 0.06$), indicating a possible shift toward an anti-inflammatory or pro-resolving macrophage phenotype. **Conclusion:** Compounds C3, C5, and C6 presented importante anti-inflammatory activity, including reduction in NO and TNF levels and inducing a M2 macrophage phenotype in cells stimulated wuth LPS, with emphasis for C6, without presenting cytotoxic effect. Collectively, these findings highlight the potential of these compounds as promising agents for the regulation of macrophage-associated inflammatory and immune responses.

04.044 **PPAR-γ Participates in the Anti-Inflammatory and Immunomodulatory Action of Palmitoylethanolamide in Murine Graft-versus-Host Disease**. Tonidandel ZD[1], Linhares AFS[1], Ruggio GMF[1], Rocha ES[1], Sales MA[1], Galvão I[2], Rezende BM[3], Teixeira MM[2], Romero TRL[4], Pinho V[5], Castor MGM[4] [1]UFMG, PPG Pharmacology and Physiology, Brazil. [2]UFMG, Dept. of Biochemistry and Immunology, Brazil. [3]UFMG, Dept. of Pathology, Brazil. [4]UFMG, Dept. of Physiology and Pharmacology, Brazil. [5]UFMG, Dept. of Morphology, Brazil

Introduction: Graft-versus-host disease (GVHD) is a major obstacle to survival following allogeneic hematopoietic stem cell transplantation. Clinical management faces the challenge of glucocorticoid resistance, resulting in a poor prognosis. In this context, endocannabinoids emerge as a therapeutic alternative for restoring immunological homeostasis, with palmitoylethanolamide (PEA) being particularly noteworthy. Although PEA has proven immunomodulatory potential, the nature of its molecular mechanism and the specific receptors involved in controlling inflammation in GVHD have not been fully elucidated. **Objectives:** To investigate the involvement of the Peroxisome Proliferator-Activated Receptor gamma (PPAR-γ) in the mechanisms of PEA in a murine GVHD model. **Methods:** Irradiated BALB/c mice received bone marrow and splenocytes from BALB/c or C57BL/6J donors. Animals were treated with PEA (10 mg/kg) and a PPAR-γ antagonist (GW9662). Mixed lymphocyte reaction (MLR) was performed using responder (C57BL/6J) and stimulator (BALB/c) splenocytes. CD3, CD4, and CD8 markers were evaluated by flow cytometry, and cytokines were measured by ELISA. Data were analyzed by ANOVA/Bonferroni or Kruskal-Wallis/Dunn, according to normality (Shapiro-Wilk), and survival by Log-rank ($p<0.05$). CEUA 203/2021. **Results:** In the *in vivo* experimental model, PEA increased survival and reduced GVHD severity. PPAR-γ participates in this protection, as the effect was reversed by GW9662, which also reversed the PEA-induced reduction of TNF and IFN-γ in the liver and intestine, and the increase of IL-10 in the intestine. *In vitro*, in the MLR, PEA modulated lymphocyte proliferation and activation via PPAR-γ. A reduction in the differentiation and frequency of CD3+CD4+ and CD3+CD8+ effector lineages was observed, alongside the suppression of CD28 in CD3+CD4+ populations. Concurrently, PEA via PPAR-γ favored regulatory differentiation, increasing CD3+CD4+CD25+FOXP3+ lymphocytes, an effect reversed by the antagonist. Furthermore, in the MLR, the activation of this receptor regulated inflammatory mediators, suppressing TNF, IFN-γ, CCL2, CCL3, and CCL5, and increasing IL-10. **Conclusion:** PEA exerts immunomodulatory effects in murine GVHD, and the reversal of these effects by PPAR-γ antagonism confirms the participation of this receptor in the mechanism of action of PEA. **Financial support:** Funding agencies CAPES, CNPq, FAPEMIG, and UFMG.

04.045 **Thiazoquinoline Derivatives Modulate Cytokine Production in PBMCs from Patients with Systemic Sclerosis and in Mouse Splenocytes**. Gonçalves MEO, Ferreira JRS, Cunha EGC, Almeida AR, Pereira MC, Pitta MGR. UFPE, Núcleo de Pesquisa em Inovação Terapêutica - Suely Galdino, PPG em Inovação Terapêutica, Brasil.

Introduction: Systemic sclerosis (SSc) is an autoimmune connective tissue disease characterized by vascular alterations, immune dysregulation (cytokines, chemokines, and autoantibodies), and fibrosis of the skin and internal organs. Current therapeutic approaches aim to minimize disease manifestations; however, there is still no agent capable of targeting the three main pillars of the disease and preventing SSc progression. Thiazoquinoline derivatives (ZKDs) are obtained through the hybridization of thiazolidine-2,4-dione and a quinoline ring. This class comprises potential PPARγ agonists, a nuclear receptor that acts as a transcription factor regulating the expression of genes involved in inflammation and fibrosis. **Objectives:** Therefore, this study aimed to evaluate the *ex vivo* immunomodulatory activity of the derivatives LPSF/ZKD-2 and LPSF/ZKD-4 in cells from patients with SSc and in murine splenocytes. **Methods:** Peripheral blood mononuclear cells (PBMCs) were isolated from heparinized blood samples by Ficoll density gradient centrifugation. Cells were stimulated with 300 ng/mL anti-CD3 and 400 ng/mL anti-CD28 and cultured in the presence or absence of ZKDs (25 μM, 50 μM, and 75 μM). Mouse spleens were mechanically dissociated to obtain splenocytes, which were subsequently stimulated with Concanavalin A (5 μg/mL) and treated or not with ZKDs (1 μM, 10 μM, and 100 μM) to investigate their immunomodulatory potential and support future studies using animal models of SSc. After 48 hours of cell culture, at 37ºC with 5% CO2, culture supernatants were collected for cytokine quantification by ELISA. **Results:** LPSF/ZKD-2, at concentrations of 50 μM and 75 μM, significantly reduced IL-17A secretion ($p<0.0001$), while IFN-γ production was reduced at concentrations of 25 μM, 50 μM, and 75 μM ($p<0.03$) in PBMCs from patients with SSc. In splenocyte supernatants, LPSF/ZKD-2 reduced IL-4 levels at concentrations of 1 μM ($p<0.01$) and 10 μM ($p<0.03$), as well as IL-6 ($p<0.01$) and IL-13 ($p=0.03$) at 1 μM. Furthermore, LPSF/ZKD-4 negatively modulated the production of IL-6 (10 μM and 100 μM, $p<0.0078$) and IL-13 (1 μM and 10 μM, $p<0.0078$). No significant reduction in IL-4 production was observed at the evaluated concentrations of LPSF/ZKD-4 in splenocyte cultures. **Conclusion:** The results suggest that the thiazoquinoline derivatives LPSF/ZKD-2 and LPSF/ZKD-4 exhibit potential immunomodulatory activity by negatively modulating pro-inflammatory and pro-fibrotic cytokines in cells from patients with SSc and in murine splenocytes. The reduction in cytokines occurred at previously evaluated non-cytotoxic concentrations, suggesting an *in vitro* immunomodulatory effect, possibly mediated by PPARγ activation and inhibition of the pro-inflammatory NF-κB pathway. This hypothesis requires mechanistic confirmation. Thus, these compounds demonstrate promise for future preclinical studies, contributing to the development of new strategies for controlling inflammation and fibrosis.

04.046 **Bioactivity-Guided Study of the Anti-Inflammatory Effects of Brazilian Brown Propolis from** *Mimosa tenuiflora* **in LPS-Stimulated RAW 264. 7 Macrophages**. Felício IM[1], Silva TMS[2], Baranger K[3], Picot L[3], Cavalcante FA[1]
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Introduction: Propolis is a natural product produced by *Apis mellifera* bees that exhibits diverse biological activities, including anti-inflammatory effects, which are closely related to its chemical composition. Brazilian brown propolis from *Mimosa tenuiflora* , produced in the Caatinga biome, is rich in pentacyclic triterpenes and flavonoids and has shown promising anti-inflammatory activity. Therefore, this study aimed to investigate through a bioactivity-guided approach the anti-inflammatory activity of the ethanolic extract of brown propolis (BP-EtOH) and its fractions [n-hexane (BP-Hex), ethyl acetate (BP-EtOAc), and methanolic aqueous (BP-MeOH)] in LPS-stimulated RAW 264.7 macrophages. **Methods:** RAW 264.7 macrophages were stimulated with LPS (1µg/mL) in the absence or presence of BP-EtOH, BP-Hex, BP-EtOAc or BP-MeOH (50 and 100 µg/mL). Cell viability was assessed using the MTT assay. Anti-inflammatory activity was evaluated by nitric oxide (NO) production (Griess reaction), TNF-α and IL-6 levels (ELISA), and COX-2, iNOS, and NF-κB expression (Western blot). Based on NO inhibition, subsequent mechanistic analyses were performed at 100 µg/mL. **Results:** None of the samples affected cell viability. LPS increased NO production (45.9 ± 3.2 µM) compared with the control group (8.5 ± 1.2µM). Among the tested samples, only BP-EtOAc significantly reduced NO levels at 100 µg/mL (19.1 ± 2.4 µM). LPS also increased TNF-α (8398.1±7.7pg/mL) and IL-6 production (66.6±1.7pg/mL) compared with the control group (42.6±3.1pg/mL and 12.1±1.2pg/mL, respectively). All samples reduced TNF-α production, with BP-EtOAc showing the greatest inhibitory effect (1621.2±186.1pg/mL). BP-Hex increased IL-6 production (77.0±2.4pg/mL), whereas BP-EtOH (54.9±1.8pg/mL) and BP-MeOH (56.3±1.9pg/mL) partially reduced IL-6 levels. In contrast, BP-EtOAc (14.3±0.4pg/mL) completely prevented the LPS-induced increase, restoring values comparable to those of the control group. LPS increased COX-2 expression (2.8±0.1A.U.) and NF-κB activation (1.26±0.15A.U.) compared with the control group (0.2 ± 0.002 and 0.74±0.05A.U., respectively). BP-EtOAc significantly reduced both markers (0.7±0.04 and 0.90±0.03 A.U., respectively), whereas BP-MeOH reduced only COX-2 expression (1.31±0.09A.U.) and BP-EtOH reduced only NF-κB activation (0.89±0.06A.U.). BP-Hex showed no significant effect. None of the treatments altered iNOS expression. **Conclusion:** Brown propolis exhibited anti-inflammatory activity in LPS-stimulated RAW 264.7 macrophages, and the bioactivity-guided approach identified BP-EtOAc as the fraction responsible for the most pronounced effects, including the inhibition of NO production, TNF-α and IL-6 release, COX-2 expression, and NF-κB activation. These findings suggest that this flavonoid-rich fraction plays a major role in the anti-inflammatory properties of brown propolis.

04.047 **Long-Term Impact of Hormone-Induced Premature Ovulation on Pulmonary Responses to Experimental Asthma: Role of Calcitonin Gene-Related Peptide (CGRP)**. Alves VF[1], Frajblat M[3], Moriya HT[2], Serra CSM[1], Teixeira SA[1], Brain SD[4], Tavares-de-Lima W[1], Muscará NM[1], Costa SKP[1] [1]ICB-USP, Dept. of Pharmacology, São Paulo Brazil; [2]IBCCF-UFRJ, Health Sciences Center; [3]EP-USP, Dept. of Telecommunication and Control Engineering, São Paulo, Brazil; [4]King's College London, School of Cardiovascular Medicine & Sciences, Waterloo Campus.

Introduction: Allergic asthma is a chronic inflammatory airway disease, and its onset has declined in recent decades, raising concerns about the long-term respiratory consequences of early reproductive maturation. However, the impact of hormone-induced premature ovulation (PO) on subsequent pulmonary responses to asthma remains poorly understood. Calcitonin gene-related peptide (CGRP), a neuropeptide involved in neurogenic inflammation, may interact with sex hormones and modulate allergic inflammation. **Aim:** To investigate the role of CGRP in allergic airway inflammation in a murine model of experimental asthma following hormone-induced premature ovulation, using CGRP knockout mice. **Methods:** To induce PO, 21-day-old female C57BL/6 wild-type (WT) and CGRP knockout (KO) mice received 5 IU equine chorionic gonadotrophin (eCG) i.p., followed 48 h later by 5 IU human chorionic gonadotrophin (hCG), for three cycles. Sham groups received PBS. Ovarian response was confirmed by vaginal opening and microscopic evaluation of vaginal lavage cells. For the asthma model, mice were sensitised subcutaneously with ovalbumin (OVA) and challenged intranasally once weekly for three weeks. Controls received PBS. Three hours after the final challenge, respiratory parameters were assessed by enhanced pause (Penh) using the Buxco® system following increasing concentrations of inhaled methacholine (MCh). Groups were: PO + allergic WT; sham + non-allergic WT; PO + allergic CGRP KO and PO + non-allergic CGRP KO. Data are mean ± SEM and were analysed by one- or two-way ANOVA followed by Tukey's post hoc test ($p < 0.05$). **Results:** Control animals that did not undergo premature ovulation (PO) induction exhibited vaginal occlusion during the first cycle and were therefore excluded from the analysis to avoid procedure-induced tissue trauma. Hormonal treatment accelerated vaginal epithelial maturation, enabling successful cytological assessment and identification of oestrus stages. Penh analysis revealed a significant increase in airway reactivity in WT mice subjected to hormone-induced premature ovulation and allergic asthma following MCh challenge at 25 mg/mL ($p = 0.0007$) and 50 mg/mL ($p = 0.0030$), compared with CGRP KO mice subjected to the same PO and allergic asthma protocol, as well as sham-treated non-allergic WT and CGRP KO mice. However, no significant differences were observed between groups in maximum response (Emax) ($p > 0.05$ for all pairs: sham + non-allergic WT (A) vs. PO + allergic WT (B)($p = 0.137$), vs. (C) PO + non-allergic CGRP KO ($p = 0.993$), vs. (D) PO + allergic CGRP KO ($p = 0.949$); B vs. C ($p = 0.181$), vs. D ($p = 0.570$), and C vs. D ($p = 0.345$) or total area under the curve (AUC) ($p > 0.05$ for all pairs: A vs B ($p = 0.762$), vs C ($p = 0.839$), vs D ($p = 0.939$); B vs C ($p = 0.888$), vs D ($p = 0.996$) e C vs D($p = 0.509$). **Conclusion:** Hormone-induced premature ovulation accelerated vaginal maturation and the onset of the estrous cycle. Mice subjected to premature ovulation and allergic asthma exhibited increased airway hyperresponsiveness to MCh, indicating exacerbation of the asthmatic response. The absence of this increase in CGRP KO mice suggests that CGRP contributes to enhanced airway reactivity associated with premature ovulation, without affecting maximal contractile response or overall pulmonary response.

04.048 **Effects of Inactivated *Bifidobacterium animalis* subsp. lactis CCT 7858 on Inflammatory Parameters Induced by Monosodium Glutamate in Wistar Rats**. Comis Neto AA, Arena RV, Batista WT, Luzardo BFS, Gomes, J, Fontoura, EA, Rodrigues, ES, Streb, BL, Rosa SG, Pinton S Unipampa-Uruguaiana, Brazil

Introduction: Obesity is a multifactorial condition associated with metabolic and inflammatory alterations, including hypothalamic neuroinflammation. The experimental model of neonatal monosodium glutamate (MSG)-induced obesity is widely used due to its ability to promote hypothalamic alterations and increase pro-inflammatory markers. In this context, probiotics and their derivatives have demonstrated beneficial effects in the modulation of systemic and central inflammation. Among these derivatives, postbiotics, defined as preparations of inanimate microorganisms and/or their components that confer health benefits to the host, have emerged as an innovative and safer therapeutic strategy, especially due to their greater stability and lower risk associated with the administration of live microorganisms. Although heat inactivation abolishes bacterial viability, structural components such as peptidoglycans, exopolysaccharides, and surface proteins remain preserved and can interact with pattern recognition receptors, thereby modulating immune responses and promoting anti-inflammatory effects. Accordingly, species belonging to the genus Bifidobacterium have demonstrated immunomodulatory and anti-inflammatory properties even after heat inactivation. Therefore, investigating the effects of heat-inactivated Bifidobacterium animalis subsp. lactis on hypothalamic inflammatory parameters in MSG-induced obese animals may contribute to the development of new therapeutic approaches for obesity-associated neuroinflammation. **Objective:** To evaluate the effects of treatment with inactivated Bifidobacterium animalis subsp. lactis CCT 7858 on hypothalamic inflammatory markers in Wistar rats subjected to the neonatal MSG-induced obesity model. Materials and **Methods:** Newborn male Wistar rats received subcutaneous injections of MSG (4 g/kg/day) from the 5th to the 14th postnatal day (PND). Control animals received 0.9% saline during the same period. After weaning (PND 25), animals were divided into four groups: Control, MSG, inactivated Bifidobacterium, and MSG+inactivated Bifidobacterium. Treated groups received 1×10^9 CFU/animal of inactivated Bifidobacterium animalis subsp. lactis CCT 7858 by daily gavage from PND 25 to 53. On PND 54, animals were euthanized and the hypothalamus was collected for western blot analysis of TNF-α and IL-6 proteins. Data were analyzed using one-way ANOVA followed by Tukey's post hoc test ($p<0.05$). CEUA nº 019/2024. **Results:** Animals in the MSG group showed a significant increase in hypothalamic TNF-α and IL-6 expression compared to the control group, indicating the presence of an inflammatory condition associated with neonatal MSG-induced obesity. In contrast, animals treated with inactivated Bifidobacterium animalis subsp. lactis showed a significant reduction in the expression of these pro-inflammatory cytokines compared to the MSG group, demonstrating a potential anti-inflammatory effect of the treatment on hypothalamic tissue. **Conclusion:** Neonatal MSG-induced obesity promotes increased expression of pro-inflammatory markers in the hypothalamus. Treatment with inactivated Bifidobacterium animalis subsp. lactis CCT 7858 significantly reduced TNF-α and IL-6 expression, suggesting a potential anti-inflammatory effect in the central nervous system. Thus, the use of inactivated Bifidobacterium may represent a promising strategy for modulating obesity-associated neuroinflammation. However, further studies are needed to elucidate the underlying mechanisms and better understand the long-term effects of this treatment.

04.049 **Modulation of Pro-inflammatory Cytokines and Oxidative Stress by Isoquercitrin Complexed with γ-Cyclodextrin in a CFA-Induced Arthritis Model**. Moreira FAS, Veloso VL, Oliveira FA UFPI, Center for Research on Medicinal Plants

Rheumatoid arthritis is a chronic inflammatory disease characterized by pain, joint edema, and excessive production of inflammatory mediators and reactive oxygen species. Despite the availability of current therapies, the search for safer and more effective treatment options remains a significant clinical challenge. Isoquercitrin is a natural flavonoid with well-established anti- inflammatory and antioxidant properties; however, its pharmacokinetic limitations may be overcome through complexation with cyclodextrins. In this context, the present study aimed to evaluate the anti-inflammatory and antioxidant effects of isoquercitrin complexed with γ-cyclodextrin (ISO/γ-CD) in a monoarthritis model induced by Complete Freund's Adjuvant (CFA) in rats. Animals were orally treated with ISO/γ-CD (40 mg/kg), vehicle, or diclofenac (10 mg/kg) for 14 days. Joint edema, joint disability, pro-inflammatory cytokines (TNF-α and IL-1β), and oxidative stress markers (nitrite, myeloperoxidase, and reduced glutathione) were evaluated. Treatment with ISO/γ-CD significantly and progressively reduced joint edema throughout the experimental period and decreased joint disability ($p < 0.05$), showing a response profile comparable to that of diclofenac. In addition, significant reductions in TNF-α and IL-1β levels were observed, suggesting modulation of inflammatory pathways associated with arthritis progression. Regarding oxidative stress, ISO/γ-CD reduced nitrite and myeloperoxidase levels, indicating decreased reactive species production and neutrophil activity, while restoring reduced glutathione levels, demonstrating the reestablishment of endogenous antioxidant balance. These findings indicate that ISO/γ-CD exerts anti-inflammatory effects associated with cytokine modulation and oxidative stress control, reinforcing its potential as a promising therapeutic strategy for inflammatory joint diseases. **Keywords:** Rheumatoid arthritis; Isoquercitrin; Inflammation; γ-cyclodextrin; Oxidative stress.

04.050 *In vitro* **Quercetin-Mediated Immunomodulation may act as an Adjuvant Therapy to Amphotericin B in Visceral Leishmaniasis**. Cardoso LL, Fernandes ALM, Thyares DFL, Ferreira RS, Albuquerque YS, Machado GR, Vanderley SER, Comberlang, FC, Almeida, FS, Keesen, TSL. UFPB, Lab Imunologia de Doenças Infecciosas, Depto Biologia Celular e Molecular, João Pessoa, PB, Brazil.

Introduction: Leishmaniasis remains a critical neglected tropical disease worldwide. Conventional treatments such as Amphotericin B (AmB) present high toxicity and severe adverse effects, emphasizing the urgent need for safer alternatives. Quercetin, a well-documented flavonoid, has demonstrated promising anti-leishmanial and immunomodulatory properties, making it a strong candidate for combination therapies. **Objectives:** In this work, we aimed to study the *in vitro* synergistic anti-leishmanial activity of quercetin combined with AmB against L. infantum promastigotes to evaluate the rate of parasite death. Additionally, during monocyte infection, we aimed to evaluate the infection rate, Reactive Oxygen Species (ROS) production, and cytokine modulation (IFN-γ, IL-6, IL-10, IL-12, and IL-17). **Methods:** Promastigotes were treated with quercetin, AmB, or both to evaluate anti-parasitic activity and synergistic interactions (Combination Index) after 72h using the MTT assay. Additionally, PBMCs were infected with L. infantum (1:10) and treated with quercetin, AmB, or both. Flow cytometry was employed to quantify the monocyte infection rate (CFSE+/CD14+) and intracellular ROS production (DHE+) after 3h of treatment. Cytokine levels in culture supernatants were quantified via ELISA after 24h of treatment. The data were analyzed using ANOVA and Tukey's post hoc test ($p \leq 0.05$*). This study was approved by the Ethics Committee for Human Research at Health Science Center/UFPB (CAAE: 90688425.1.0000.5188). **Results:** Quercetin (IC50 = 125.4 µM) and AmB (IC50 = 0.40 µM) combination demonstrated a strong synergistic effect (CI < 1) against L. infantum promastigotes in many combinations, highlighting quercetin 75 µM + AmB 0.15 µM, and quercetin 37.5 µM + AmB 0.15 µM, which showed parasite mortality rates of 59% and 37% respectively, being below the IC50 of both compounds, which is promising when considering a possible reduction in treatment doses for toxic drugs such as AmB. In infected monocytes, quercetin significantly decreased the infection rate and simultaneously increased ROS production, which is important for combating the intracellular parasites. Furthermore, quercetin reduced the production of IL-6, IL-10, and IL-17 during infection, but did not alter IFN-γ, or IL-12 levels. **Conclusion:** Quercetin exhibits immunomodulatory effects by reducing the monocyte infection rate, increasing intracellular ROS levels, and regulating cytokines such as IL-6, IL-10, and IL-17. Moreover, quercetin with AmB presented a synergistic anti-promastigote activity. These findings reinforce quercetin as a highly promising adjuvant therapy for visceral leishmaniasis. **Financial support:** **Fundação Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), and Fundação de Apoio à Pesquisa do Estado da Paraíba (FAPESQ-PB). **Acknowledgments:** CAPES, FAPESQ-PB, Federal University of Paraíba (UFPB), and the LABIDIC research group.

04.051 **Liraglutide Attenuates Fever and Differentially Modulates Oxidative Stress and Thermogenic Markers in Brown Adipose Tissue of Male and Female Rats During Systemic Inflammation**. Cruz EKM, Sousa GLS, Aguiar SCR, Cajado VJ, Amato AA, Souza PEN, Souza FHV. UnB, Faculty of Health Sciences and Technologies, Lab. of Experimental Biomodels, Brazil, UnB, Faculty of Health Sciences, Lab. of Molecular Pharmacology, Brazil, UnB, Institute of Physics, Lab. of Electron Paramagnetic Resonance, Brazil, UnB, PPG Pharmaceutical Sciences, Brazil.

Introduction: Fever is an adaptive response to infection and inflammation that supports host defense, but excessive fever can result in tissue damage and adverse clinical outcomes. Brown adipose tissue (BAT) is central to thermoregulation via non-shivering thermogenesis and is activated during fever, a process linked to increased production of reactive oxygen species (ROS). Liraglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist commonly used to treat type 2 diabetes and obesity, possesses anti- inflammatory and antioxidant properties. Recent evidence demonstrated that liraglutide reduces LPS-induced fever through sex-dependent mechanisms. However, it remains unclear whether BAT oxidative stress and thermogenic pathways contribute to the antipyretic effects of liraglutide. **Objectives:** To investigate the effects of liraglutide on BAT ROS production and thermogenic markers during LPS-induced fever in male and female rats. **Methods:** Male and female Wistar rats (n = 5 per group) were implanted with intra-abdominal temperature transmitters. Fever was induced by lipopolysaccharide (LPS, 50 µg/kg, i.p.), followed 1 hour later by liraglutide (0.3 mg/kg, i.p.). Body temperature (BT) was monitored for 4 hours, and the febrile response was quantified as the delta (Δ) temperature change from baseline to 4 hours post- LPS (ΔT). BAT was collected for quantification of ROS by electron paramagnetic resonance, assessment of thermogenic markers (UCP1 and UCP3) by real-time PCR, and histological analysis. Data were analyzed using ANOVA or Kruskal–Wallis tests with appropriate post hoc comparisons; statistical significance was set at $p < 0.05$. **Results:** LPS induced a significant febrile response in both sexes, increasing BT in males (ΔT: 1.18 vs. 0.17 °C) and females (ΔT: 0.90 vs. -0.19 °C) compared with saline-treated controls. Liraglutide abolished this response and induced hypothermia, reducing BT by about 2.6 °C in males and 2.1 °C in females compared with LPS-treated animals ($p < 0.05$). In male rats, LPS increased BAT ROS levels (290%) and the expression of the thermogenic markers UCP1 (373%) and UCP3 (165%). Liraglutide significantly reduced BAT ROS formation by 86% and UCP3 expression by 62% compared with the LPS group ($p < 0.05$). A reduction in UCP1 expression (66%) was also observed, although this effect did not reach statistical significance ($p = 0.068$). In addition, liraglutide reduced inflammatory infiltrate in BAT from male rats. In contrast, neither ROS production nor UCP1 and UCP3 expression was significantly altered in females, and liraglutide did not affect these BAT parameters. **Conclusion:** Liraglutide reduces LPS-induced fever in both sexes, but modulates BAT oxidative stress, UCP3 expression, and inflammatory infiltrate exclusively in males. These findings support the involvement of BAT in the antipyretic actions of liraglutide in a sex-dependent manner and suggest that alternative mechanisms may underlie its antipyretic effects in females.

04.052 *In vitro* Cytotoxicity and Pharmacokinetic Evaluation of a Novel Green Semisynthetic Acetanilide-Theobromine Hybrid Compound. Sousa M[1], Silva TG[1], Luis LRCS[1], Falcão Mees[1], Gadelha, FAA[1], Dejani NN[1], Fiss GF[2], Luis JAS[2], Vieira GC[1] [1]UFPB, Research Institute for Drugs and Medicines, Lab Immunopharmacology, Brazil, [2]UFPB, Lab Bioenergy and Organic Synthesis Research, Brazil

Introduction: Inflammation is involved in the pathophysiology of several chronic diseases, making the search for new anti-inflammatory agents an area of considerable pharmacological interest. Molecular hybridization consists of combining different bioactive structures into a single molecule in order to enhance their pharmacological properties. In this context, N-phenylacetamide and theobromine derivatives exhibit relevant biological activities, supporting the investigation of new green semisynthetic hybrids regarding their safety profile and pharmacokinetic properties. **Objective:** To investigate the *in vitro* cytotoxicity and predicted pharmacokinetic properties of compound 3D, a green semisynthetic hybrid derived from N-phenylacetamide and theobromine. **Methodology:** Murine RAW 264.7 macrophages were incubated overnight in 96-well plates (1×10^4 cells/well) at 37°C and 5% CO_2, and subsequently exposed to the compounds (25–800 µg/mL) for 24h. Cell viability was assessed using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, based on the reduction of tetrazolium salt into formazan crystals by metabolically active cells. After incubation with MTT for 4h, the crystals were solubilized in dimethyl sulfoxide (DMSO), and absorbance was measured at 570 nm. Data were expressed as mean ± SEM from three independent experiments and analyzed using one-way ANOVA followed by Dunnett's test. IC_{50} values were obtained by nonlinear regression using GraphPad Prism software. Pharmacokinetic properties were predicted using the SwissADME platform. **Results:** Treatment of RAW 264.7 cells promoted a concentration-dependent reduction in cell viability, with approximate viability values of 75% ($p<0.05$), 55% ($p<0.0001$), and 24% ($p<0.0001$) at concentrations of 200, 400, and 800 µg/mL, respectively. The IC_{50} value was estimated at 362 µg/mL. *in silico* pharmacokinetic analysis revealed high gastrointestinal absorption, absence of significant interaction with the major cytochrome P450 isoforms, and no prediction as a P-glycoprotein substrate, suggesting a favorable bioavailability profile. Additionally, the compound exhibited a solubility profile ranging from soluble to moderately soluble in water, moderately lipophilic character (consensus Log P o/w = 1.65), and low skin permeability (Log Kp = -7.42 cm/s). **Conclusion:** Compound 3D, a green semisynthetic hybrid derived from N-phenylacetamide and theobromine, demonstrated low cytotoxicity at concentrations up to 100 µg/mL and favorable predicted pharmacokinetic properties, including high gastrointestinal absorption and reduced potential for metabolic interactions. These findings reinforce its potential as a candidate for future pharmacological investigations aimed at modulating inflammatory processes.

04.053 **Ambroxol Repurposing: Radiographic and Histological Analysis of Joint Degeneration in an Experimental Osteoarthritis Model**. Mesquita MJTA, Cruz ACSN, Teixeira, JTAMMM, Reis ATF, Frota GM, Carvalho TGPM, Carvalho RAF, Teixeira JAM, Andrade, MS, Carvalho RC, Sousa EM, Sousa JCS, Morias SV, Cartágenes MSS, Garcia JBS UFMA PPG in Health sciences, Brazil; CEUMA, Medical School, University, Brazil; UFMA Medical School, Brazil; UFMA College of Pharmacy, Brazil; UFMA, Graduate Program in Biotechnology—Renorbio, Brazil; UFMA, PPG in Adult Health, Brazil; Graduate Program in Applied Biosciences to Health, UFMA Graduate Program in Health sciences, Brazil;

Introduction: Osteoarthritis (OA) is a multifactorial joint disease characterized by progressive cartilage degeneration, subchondral bone remodeling, and structural alterations that compromise joint integrity. Despite the available therapeutic options, current treatment remains mainly focused on symptom control and presents limitations related to efficacy and adverse effects. Ambroxol, widely used as a mucolytic agent, exhibits anti-inflammatory, analgesic, and immunomodulatory properties described in the literature, suggesting potential for therapeutic repurposing in chronic inflammatory diseases. **Objective:** To evaluate the effects of ambroxol on radiographic progression and histopathological alterations in an experimental rat model of osteoarthritis. **Methods:** Adult male Wistar rats (120 days old; 300 ± 50 g) were distributed into six experimental groups (n = 5/group). Osteoarthritis was induced by intra-articular injection of sodium monoiodoacetate (MIA). The experimental groups consisted of: healthy, negative control (CTRL-), meloxicam (2 mg/kg), and ambroxol-treated groups at doses of 10, 50, and 100 mg/kg. Treatments were administered once daily by oral gavage for 28 days. Radiographic evaluation was performed on days 0, 7, 14, 21, and 28 using the Kellgren–Lawrence (KL) classification system. On day 28 (D28), knee joints were collected for histological analysis using hematoxylin and eosin (H&E;) staining, and cartilage degeneration was assessed using the Osteoarthritis Research Society International (OARSI) scoring system. **Results:** Ambroxol treatment reduced the progression of structural joint alterations throughout the experimental period. The group treated with ambroxol at a dose of 100 mg/kg showed a significant reduction in Kellgren–Lawrence radiographic scores from day 14 onward, maintaining this effect until day 28. The 50 mg/kg dose demonstrated a significant reduction in scores on days 21 and 28, exhibiting a profile similar to that observed with meloxicam. Histopathological analysis corroborated the radiographic findings, demonstrating greater preservation of cartilage architecture in the treated groups. While the negative control group exhibited extensive chondral lesions, deep cartilage fissures, tidemark fragmentation, and reduced cellularity, the treated groups showed a lower degree of tissue degeneration and greater structural preservation. OARSI scores were reduced in all treated groups, with the most pronounced effect observed at the 100 mg/kg dose. **Conclusion:** Ambroxol attenuated the progression of structural joint alterations and promoted preservation of cartilage integrity in an experimental osteoarthritis model, demonstrating potential as a promising therapeutic repurposing strategy for osteoarthritis.

04.054 **Role of Estradiol/GPER Signaling in the Sickness Response during Systemic Inflammation**. Costa RA, Schneider RC, Santos MO, Pereira V, Borges AP, Schneider VMM, Alencar ST, Baggio DF, Zampronio AR. UFPR, Inflammation and Fever Lab, Dept Pharmacology, Brazil.

Introduction: Systemic inflammation triggers fever, hyperalgesia and drowsiness, collectively known as the sickness response. The hypothalamus integrates these responses through mediators such as prostaglandins and endothelins. During endotoxemia, sex differences in the febrile response have been reported and appear related to female sex hormones. Previous studies show that ovariectomized (OVX) rats are more responsive to the pyrogenic effect of lipopolysaccharide (LPS) than cycling females, suggesting a role for estrogens. Moreover, males and females differ in hypothalamic serotonin (5-HT) release during endotoxemia, which may influence fever intensity through the inflammatory reflex. **Objective:** To evaluate if female sex hormones also influence other systemic inflammatory responses such as hyperalgesia and hypolocomotion and if female sex-hormones, and particularly estrogen, influence the hypothalamic 5HT levels in females. Additionally, this study evaluated if estrogen modulates the febrile response through G protein-coupled estrogen receptor (GPER) activation. **Methods:** Female Wistar rats were submitted to ovariectomy or sham surgery. Core temperature was monitored using an intraperitoneal temperature logger, and drugs were administered intracerebroventricularly or systemically. Animals received LPS (50 or 100 µg/kg, i.p.), 17β-estradiol (10 µg/kg, s.c., for 5 days), or the GPER antagonist G36 (20 µg, i.c.v.). In independent groups, body temperature and mechanical nociceptive threshold were recorded for 5h. Locomotor activity was then assessed in the open field, and the hypothalamus was collected for HPLC quantification of 5HT and 5-hydroxyindoleacetic acid (5HIAA). All procedures were approved by the institutional animal ethics committee (CEUA/BIO-UFPR,1444/22). **Results:** LPS administration (100µg/kg) induced fever and hyperalgesia in both sham and OVX rats, but OVX rats showed an earlier onset of hyperalgesia (1h) compared to the sham group (3h). In both groups, LPS reduced the number of crossings, speed, and distance traveled in the open field. Regarding hypothalamic 5HT/5HIAA levels, ovariectomy per se increased basal levels of this neurotransmitter. However, while LPS administration increased 5HT/5HIAA levels in sham-operated females as expected, in OVX rats, LPS reduced 5HT/5HIAA levels. E2 administration reduced fever in OVX rats and delayed the onset of hyperalgesia. In the open field, E2 replacement did not modify the reduction in the analyzed parameters in OVX. E2 replacement in OVX rats not only reversed the LPS-induced reduction but also induced a quite pronounced increase in 5HT/5HIAA in the hypothalamus. The i.c.v injection of the GPER antagonist G36 in cycling females significantly increased the febrile response induced by the lower dose of LPS (50ug/kg). **Conclusion:** The febrile response, hyperalgesia and the hypothalamic levels of 5HT during LPS-induced inflammation are modulated by female sex hormones since ovariectomy changes these responses. Estrogen seems to be important in this modulation since the replacement of E2 reverses these changes. The influence of estrogen in the febrile response seems to be mediated by the GPER receptor. **Financial support:** CNPq and UFPR.

04.055 **Differential Effects of Hypothalamic ETB Receptor Blockade in Fever, Hypolocomotion and Serotonin Release During Systemic Inflammation in Male and Female Rats**. Alencar ST, Santos MO, Schneider VMM, Fernandes SMA, Borges AP, Guita GO, Costa RA, Zampronio, AR. UFPR, Inflammation and Fever Lab, PPG Pharmacology, Brazil

Introduction: Systemic inflammation induces sickness syndrome, characterized by fever, hypolocomotion, anorexia, and somnolence. Previous studies demonstrated that during systemic inflammation induced by lipopolysaccharide (LPS), changes in hypothalamic serotonin (5-HT) levels modulate the inflammatory reflex, through the action of endothelin-1 (ET-1) in ETB receptors, differentially in male and female rats. However, it remains unclear whether this modulation occurs directly within the hypothalamus. **Objective:** To determine whether hypothalamic ETB receptor blockade modulates fever, hypolocomotion, and hypothalamic 5-HT levels in male and female rats during systemic inflammation. **Methods:** Male and female Wistar rats were implanted with intraperitoneal temperature sensors. BQ788 or saline was microinjected into the hypothalamus (0,6 pmol in 0.5 µL) before intraperitoneal administration of LPS (100 µg/kg) or vehicle. Body temperature was monitored for 5 h, locomotor activity was assessed in the open field test, and hypothalamic levels of 5-HT and 5-HIAA were quantified by HPLC. To confirm ETB receptor blockade efficacy, female rats also received intracerebroventricular BQ788 (6.0 pmol, 2 µl) before LPS (100 µg/kg) or vehicle administration. Procedures were approved by the Animal Ethics Committee of the Federal University of Paraná (CEUA-BIO/UFPR no. 1601). **Results:** LPS induced fever and reduced locomotor activity in both sexes. In males, hypothalamic BQ788 significantly attenuated fever and reversed hypolocomotion, whereas no effects were observed in females. LPS reduced hypothalamic 5-HT and 5-HIAA levels in males but increased both 5-HT and 5-HIAA in females. Hypothalamic BQ788 reversed these alterations in both sexes. Although hypothalamic BQ788 did not affect fever in females, intracerebroventricular administration attenuated the febrile response. **Conclusion:** ET-1 exerts sex-dependent effects during systemic inflammation. In males, ETB receptor signalling within the hypothalamus contributes to fever, hypolocomotion, and reduced serotonergic activity. In females, ET-1 modulation of fever and sickness behaviour appears to involve additional brain regions beyond the hypothalamus. **Financial support:** CNPq, CAPES and UFPR.

04.056 **Effects of Monoterpenes Linalool, Carvacrol, Gamma-Terpinene and Beta-Myrcene on Cytokine Profile in an Experimental Sepsis Model**. Silva GHO, Previato CFA, Da Rocha EMT, Cuman RKN. Lab Inflammation, State University of Maringá (UEM), Maringá, Paraná, Brazil.

Introduction: Sepsis is a life-threatening syndrome characterized by a dysregulated host response to infection, leading to excessive release of pro- and anti-inflammatory cytokines. Despite advances in clinical management, specific therapies targeting the inflammatory response remain limited. The natural monoterpenes, including linalool (LIN), carvacrol (CAR), gamma- terpinene (GT) and beta-myrcene (MIR), have anti-inflammatory properties in experimental models. **Objectives:** To evaluate the effects of LIN, CAR, GT and MIR on the cytokine profile in septic mices (subjected to polymicrobial sepsis induced by cecal ligation and puncture) (CLP). **Methods:** Male C57BL/6 mice were treated orally with LIN, CAR, GT or MIR (200 mg/kg) by gavage, one hour before CLP. Serum levels of IL-1β, IL-10, TNF-α and IL-6 were determined by ELISA six hours after surgery. Data were analyzed by one-way ANOVA followed by Tukey's test ($p<0.05$). All procedures were approved by the Institutional Animal Ethics Committee (No. 4628291021). **Results:** Levels of cytokines were significantly modulated following treatment with the monoterpenes in an experimental sepsis model. IL-1β, pro-inflammatory cytokine, presented in the early phase of sepsis and perpetuating the systemic cytokine storm, was significantly decreased by all compounds compared to the CLP animals ($p<0.05$), the lower levels were observed for LIN. Regarding to IL-6, only LIN produced a significant reduction ($p<0.05$), suggesting a anti-inflammatory effect for this compound. No significant differences were observed for TNF-α or IL-10 levels among the treated groups. **Conclusion:** These findings indicate that LIN, CAR, GT and MIR modulate the cytokine profile in experimental sepsis, supporting further investigation of these compounds as potential adjuvant strategies in sepsis management. **Financial support:** CAPES and CNPq.

04.057 **Effects of Ispinesib on Parameters Associated with Inflammatory Dynamics in Experimental Cystitis**. Oliveira MM[1], Frota-Gomes TLS[1], Souza ORB[1], Reis-Filho AC[1], Cavalcante DIM[2], Santos RF[1,3], Freitas GBL[1,3]. [1]UFPI, PPG Pharmacology, Brazil. [2]UFC, Dept Pathology and Legal Medicine, Brazil. [3]UFPI, Biochemistry and Pharmacology, Brazil.

Introduction: Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic inflammatory disorder characterized by bladder pain, increased urinary frequency and significant impact on quality of life. Given the limitations of current therapeutic options, drug repositioning strategies combined with structural similarity-based high-throughput screening have emerged as relevant alternatives for identifying new therapeutic leads. Among these, Ispinesib, an antimitotic agent, represents a promising candidate for investigation in IC/BPS. **Objectives:** Investigate the effects of Ispinesib on inflammatory responses in experimental cystitis. **Methods:** Ispinesib was identified through structural similarity screening using CRH receptor antagonists and evaluated by molecular docking against CRHR1 and CRHR2 using Molegro Virtual Docker. The *in vivo* effects of Ispinesib were evaluated in a cyclophosphamide-induced cystitis model in mice. Animals were treated with Ispinesib (0.75, 1.5, or 3 mg/kg, i.p.), followed by hematological evaluation, determination of the neutrophil to-lymphocyte ratio (NLR), histopathological analysis, and CD3 immunostaining. The experimental protocols were approved by the Animal Ethics Committee of UFPI (approval no. 842/2024). **Results:** Molecular docking analysis predicted interaction between Ispinesib and both CRHR1 (MolDock Score = –178.398 and Rerank Score = –120.707) and CRHR2 (MolDock Score = –156.288 and Rerank Score = –91.6104) with higher theoretical affinity for CRHR1. Treatment with Ispinesib at doses of 1.5 and 3 mg/kg significantly reduced total leukocyte counts and the NLR *in vivo* compared with untreated inflammatory animals ($p < 0.05$). Semiquantitative histopathological analysis revealed persistent edema and inflammatory infiltrate of varying severity, although the intermediate dose was associated with predominantly mild histopathological alterations. Furthemore, CD3 immunostaining demonstrated reduced CD3+ cell labeling in groups treated with higher Ispinesib doses. **Conclusion:** Ispinesib modulated leukocytic parameters by reducing leukocyte counts, NLR, and CD3+ cells. Together with the persistence of bladder histological alterations, these findings suggest that the antimitotic activity of Ispinesib may interfere not only with inflammatory pathways but also with mechanisms involved in the resolution of inflammation. Overall, the results indicate a complex biological profile involving leukocytic and tissue alterations associated with inflammatory dynamics.

04.058 **Increased MMP-2 Proteolytic Activity on Cardiac Function During Experimental Sepsis**. Ramos LVR, Cantão MBS, Castro MM FMRP-USP, Pharmacology Dept.

Introduction: Septic cardiac dysfunction is one of the major complications associated with sepsis. Connexin (Cx)43 is the principal gap junction protein in cardiomyocytes and plays a crucial role in electrical impulse propagation and synchronized cardiac contraction. Previous studies have demonstrated that both the expression and function of Cx43 are impaired during septic cardiomyopathy. In addition, increased expression of inducible nitric oxide synthase (iNOS) and elevated nitric oxide (NO) production have been reported in septic cardiac dysfunction. The interaction of NO with reactive oxygen and nitrogen species leads to the formation of peroxynitrite, which is capable of activating metalloproteinases (MMPs), particularly MMP-2, in several cardiovascular disorders, including septic cardiomyopathy. Moreover, MMP-7 has been associated with decreased Cx43 levels in the hearts of rodents after myocardial infarction. However, because MMP-2 and MMP-9 are more abundantly expressed in the heart during sepsis-induced myocardial dysfunction, these enzymes may exert a more pronounced proteolytic effect on Cx43. Therefore, we hypothesize that sepsis increases cardiac MMP-2 and MMP-9 activity, contributing to Cx43 proteolysis and consequently to cardiac dysfunction. **Objective:** To evaluate the activity of MMP-2 and MMP-9 in the hearts of septic mice and investigate their possible proteolytic effects on Cx43 and cardiac function. **Methods:** Sepsis was induced in C57BL/6 mice using the Cecal Ligation and Puncture (CLP) model. The cecum was exposed and punctured twice with a 20G needle to induce severe sepsis. Following surgery, animals received intraperitoneal administration of either doxycycline (Doxy, 20 mg/kg) or vehicle. Twenty-four hours after the procedure, mice were euthanized and the left ventricle was collected for analysis. Echocardiographic assessments were performed before and 24 hours after CLP induction. In addition, gelatin zymography was conducted to determine MMP activity. **Results:** the CLP and CLP+Doxy groups showed 75% mortality rate compared to the 0% in Sham group at the end of 7 days ($p<0.001$). CLP mice also exhibited lower cardiac output, heart rate and left ventricular mass ($p<0.05$). and treatment with Doxy did not alter these parameters. Increased MMP-2 activity was observed in the hearts from CLP mice compared to Sham groups (0.66 ± 0.08 vs. 0.35 ± 0.06 and 0.36 ± 0.04; $p<0.05$) and treatment with Doxy did not change these levels. **Conclusions:** CLP caused cardiac dysfunction and increased activity of MMP-2, while treatment with Doxy did not alter these effects.

04.059 **BD-8, A Novel Digoxin Derivative, Suppresses Inflammatory Responses** *in vitro* **and Ameliorates Acute Lung Injury** *in vivo*. Ferreira DA[1], Medeiros ABA[1], Soares MM[1], Lima EA[1], Cunha TEDH[1], Magalhães DWA[1], Figueiredo ES[1], Silva TG[1], Vieira GC[1], Machado MV[2], Villar JAFP[2], Barbosa LA[2], Carvalho DCM[1,3], Mascarenhas SR[1] [1]UFPB, Lab Immunopharmacology, Biotechnology Center, UFPB, João Pessoa, PB, Brazil-Centro-Oeste Dona Lindú. [2]UFSJ-Lab Organic Synthesis and Nanostructure, UFSJ-Divinópolis, MG, Brazil. [3]ICB-UNIFAL Lab Vaccines, Dept Microbiology and Immunology, Alfenas, MG, Brazil.

Introduction: Acute Lung Injury (ALI) is a severe inflammatory condition caused by infectious or sterile insults. BD-8, a semisynthetic cardiotonic steroid derived from digoxin, emerges as a promising immunomodulatory molecule due to its reduced toxicity and specific targeting of the Na+/K+-ATPase α2 subunit. **Objectives:** This study aimed to evaluate the anti-inflammatory effect of BD-8 molecule. **Methods:** For *in vitro* assays, murine peritoneal macrophages were stimulated with zymosan (ZYM) and/or treated with BD-8 (100/10/1 μM and 100/10/1 nM). Cell viability was assessed by MTT assay, nitric oxide (NO) by Griess reagent, and supernatant IL-1b and IL-10 levels by sandwich ELISA assay. Phagocytic capacity (RedZYM) and intracellular signaling (iNOS, p-p38, p-ERK, p-NF-κB) were evaluated by flow cytometry. For *in vivo* screening, mice were treated with BD-8 (1.12, 0.56, 0.28 mg/kg) before intraplantar carrageenan-induced paw edema, measured via digital caliper and histology. In the ALI model, mice received intranasal LPS (5 mg/kg) and BD-8 (0.56, 0.28 mg/kg; i.p.) at 1, 24, and 48 h post-challenge. BALF was collected for total/differential cell counts, total proteins, and TNF-α levels (Sandwich ELISA assay). Lung sections were evaluated for tissue injury score. **Results:** A reduction in cell viability was observed only at the highest BD-8 concentration tested (100 μM), which was consequently excluded from further analyses. BD-8 (1 and 10 μM) treatment reduced NO levels by 19% and 32%, respectively. Treatment with 10 μM reduced IL-1β levels (12%) and at 100 nM increased IL-10 (39.6%). Treatment with the same concentration reduced the phagocytic activity of RedZYM particles by 36% and iNOS expression by 18.34%, as well as decreased the phosphorylation of p38 by 66.1%, ERK by 32.7%, and NF-κB by 85.8%. Furthermore, BD-8 reduced paw edema and tissue injury at 0.56 (40.5%) and 0.28 mg/kg (76.8%), with the lowest dose showing the strongest anti-inflammatory effect. In the ALI model, BD-8 reduced neutrophil infiltration in BALF at both doses 0.56 (44.8%) and 0.28 mg/kg (50%). Moreover, the lowest dose decreased total cell migration (49%), total protein levels (27%), and TNF-α concentrations in BALF (57.6%), which correlated with attenuated lung injury in the histological analysis (51,5%). **Conclusion:** The results demonstrated that BD-8 exhibits *in vitro* immunomodulatory activity by suppressing macrophage activation via the inhibition of the iNOS, MAPK, and NF-κB signaling pathways. Furthermore, the molecule displays *in vivo* anti-inflammatory efficacy, attenuating carrageenan-induced paw edema and LPS-induced acute lung injury by reducing neutrophil infiltration, protein leakage, and TNF-α levels. Together, these findings highlight the therapeutic potential of BD-8 for the treatment of acute inflammatory diseases.

Keywords: Total proteins. Neutrophils. IL-1β. Paw Edema

04.060 **Graft-Versus-Host Disease Promotes Central Neuroinflammation and Glutamatergic Dysfunction Associated with Anxiety-Like Behavior in Mice**. Linhares AFS[1], Lima ALD[1], Berg BB[1], Rocha ES[2], Ruggio GMF[1], Sales MA[2], Silva MCM[1], Oliveira NFM[3], Campos ZDT[1], Vieira LB[4], Machado FS[5], Pinho V6, Teixeira MM[5], Oliveira ACP[4], Romero MGMC[4]. [1]UFMG, Graduate Program in Pharmacology and Physiology, Brazil; [2]UFMG, Undergraduate student in Biomedical Sciences, Brazil; [3]UFMG Graduate Program in Biochemistry and Immunology, Brazil; [4]UFMG Dept Physiology and Pharmacology, Brazil; [5]UFMG, Dept Biochemistry and Immunology, Brazil; [6]UFMG, Dept Morphology, Brazil.

Introduction: Graft-versus-host disease (GVHD) arises after allogeneic hematopoietic stem cell transplantation due to genetic disparity between donor and recipient. Beyond classical target organs, GVHD may also affect the central nervous system (CNS). Clinical and experimental evidence associates GVHD with anxiety disorders and reduced quality of life. **Objectives:** To investigate anxiety-like behavior in an experimental GVHD model and to identify the involved immune cells, inflammatory mediators, and neurotransmission pathways. **Methods:** Male C57BL/6J and BALB/c mice (8–12 weeks) were used. C57BL/6J mice underwent total body irradiation followed by allogeneic (GVHD group) or syngeneic (control group) bone marrow transplantation. Fifteen days post-transplantation, behavioral tests were performed, followed by euthanasia and inflammatory analyses. To assess glutamatergic involvement, synaptosomal glutamate release was measured, and animals were treated with an NMDA receptor antagonist. For pharmacological evaluation of NMDA receptor involvement, control and GVHD mice were treated with memantine (30 mg/kg/day, intraperitoneally) from the day of transplantation until day 15 post-transplantation. The statistical analysis was selected according to the experimental design and number of groups. Student's t testwas used for comparisons between two groups, whereas one-way ANOVA was applied for experiments involving multiple groups. **Results:** In the open field test, GVHD mice spent more time in the periphery, and in the elevated zero maze they remained longer in closed arms, indicating anxiety-like behavior. Intravital microscopy revealed increased leukocyte adhesion in cerebral venules of GVHD mice. Flow cytometry (FACS) demonstrated CNS infiltration by CD4+ and CD8+ T cells with Th1/Tc1 profiles, regulatory T cells, TNF-α-producing inflammatory monocytes, and IL-10–producing microglia. Synaptosomal assays showed increased glutamate release in cortical and striatal regions of GVHD mice. Treatment with memantine reduced the time spent in closed arms in the elevated zero maze. **Conclusion:** GVHD is associated with anxiety-like behavior and CNS neuroinflammation characterized by infiltration of peripheral pro-inflammatory immune cells. Altered glutamatergic neurotransmission, evidenced by increased glutamate release, was observed. Pharmacological blockade of NMDA receptors suggests involvement of this pathway in the behavioral phenotype. Further studies are required to clarify the role of glutamate in CNS alterations during experimental GVHD. Animal Research Ethical Committee Number: CEUA 106/2024. **Financial support**: CAPES, CNPq, FAPEMIG, and UFMG.

04.061 **Curcumin Modulates Nitric Oxide Production in BV2 Microglial Cells Exposed to** *E. coli*. Barbosa RS[1,2,3], Santos FS[1,2], Castro-Faria-Neto HC[1], Bozza PT[1], Silva AR[1,2], Gonçalves-de-Albuquerque CF[1,2,3] [1]Unirio, Lab Immunopharmacology, Dept Physiological Sciences, Federal, Rio de Janeiro, Brazil. [2]IOC-Fiocruz, Lab Immunopharmacology, Rio de Janeiro, Brazil. [3]Unirio, PPG in Molecular and Cellular Biology, Rio de Janeiro, Brazil.

Introduction: Neuroinflammation is a key component of several neurological disorders and may be triggered by bacterial infections and systemic inflammatory conditions. Microglial cells play a central role in regulating inflammatory responses in the central nervous system, producing cytokines and reactive nitrogen species in response to pathogenic stimuli. Curcumin, a polyphenolic compound extracted from Curcuma longa, has been extensively investigated due to its anti-inflammatory and antioxidant properties. The present study evaluated the effects of free curcumin on inflammatory and viability parameters in BV2 microglial cells challenged with *E. coli*. **Objectives:** To evaluate the effects of free curcumin on nitrite production, IL-6 levels, and cell viability in BV2 microglial cells challenged with *E. coli*. **Methods:** BV2 microglial cells were pretreated with free curcumin at concentrations of 1 μM, 5 μM, and 10 μM for 1 hour prior to bacterial challenge. Subsequently, cells were exposed to *E. coli* at a multiplicity of infection (MOI) of 10 and incubated for 24 hours. After the incubation period, IL-6 levels and nitrite production were determined, and cell viability was evaluated using the resazurin assay. Statistical Analysis: Data were analyzed using one-way ANOVA, followed by an appropriate post hoc multiple-comparison test. Differences were considered statistically significant when $p < 0.05$. **Results:** Incubation with *E. coli* increased nitrite production in BV2 cells. Curcumin treatment significantly reduced nitrite levels compared with the *E. coli* group ($p < 0.05$). Preliminary analyses of IL-6 levels suggest reduced cytokine production in curcumin-treated groups across all tested concentrations; however, these data are still under investigation. Cell viability was maintained across all experimental groups, except for the death control group. **Conclusion:** Curcumin treatment was associated with a significant reduction in nitrite production in BV2 cells challenged with *E. coli*, while cell viability remained preserved. IL-6 analyses indicate reduced cytokine levels in curcumin-treated groups. Further investigations involving additional inflammatory and oxidative stress markers are required to better characterize its effects and underlying mechanisms in this neuroinflammation model.

04.062 **SIRT2 Inhibition Attenuates Neuroinflammation Induced by *Klebsiella pneumoniae* Infection**. Ferreira-Costa M[1], Thiele E[2], Almeida MAP[2], Santos, FS[2], Gomes-Reis, GLS[1], Cunha, CMC[1], Ferreira, A[1], Bozza PT[1], Castro-Faria-Neto HC[1], Gonçalves-de Albuquerque CF[2,3], Silva AR[1] [1]IOC-Fiocruz, Immunopharmacology Lab, PPG in Cellular and Molecular Biology, Rio de Janeiro, Brazil, [2]UFF, PPG in Neuroscience, Rio de Janeiro, Brazil, [3]Unirio, Immunopharmacology Lab, PPG in Molecular and Cellular Biology, Rio de Janeiro, Brazil

Introduction: Sepsis is a life-threatening condition caused by a dysregulated host response to infection and a major cause of morbidity and mortality worldwide. Besides systemic inflammation and organ dysfunction, sepsis affects the central nervous system, leading to sepsis-associated encephalopathy, characterized by neuroinflammation and cognitive impairment. Bacterial infections trigger pro-inflammatory cytokine production and NF-κB activation, contributing to brain dysfunction. *Klebsiella pneumoniae* (KP) is an opportunistic Gram-negative pathogen associated with severe pneumonia and sepsis, recognized as a threat due to the increasing emergence of antimicrobial resistance (AMR). Sirtuins are NAD+-dependent deacetylases involved in inflammation and cellular stress responses. SIRT2 amplifies inflammatory signaling, making its pharmacological inhibition a promising strategy to attenuate infection-induced neuroinflammation. This study investigated the effects of the selective SIRT2 inhibitor AGK-2 on neuroinflammatory responses in a murine model of KP-induced pneumonia.

Objectives: To evaluate the effects of the selective SIRT2 inhibitor AGK-2 on cytokine production and NF-κB signaling in the lung and cerebral cortex in a murine model of KP-induced pneumonia. **Methods:** Procedures were approved by the Animal Ethics Committee of Oswaldo Cruz Foundation (CEUA L0024/18 and L-005/2023 – IOC). Male received an intratracheal instillation of 5×10^8 CFU of KP or saline. AGK-2 (10 mg/kg) or vehicle (DMSO) was administered intraperitoneally 5 and 24 h after infection. At 48 h, animals were euthanized; IL-6 and TNF-α were quantified by ELISA in lung and cerebral cortex, and NF-κB activation was assessed by p65 phosphorylation (p-p65). **Results:** KP infection increased lung IL-6 from 8.4 ± 10.9 to 288.6 ± 142.1 pg/mL ($p<0.0001$) and cortical TNF-α from 20.1 ± 5.2 to 71.7 ± 32.8 pg/mL ($p<0.001$). AGK-2 reduced both to control levels (37.9 ± 57.4 and 21.0 ± 8.6 pg/mL, respectively; $p<0.001$), with no effect in uninfected mice. Lung TNF-α rose from 39.3 ± 35.3 to 184.4 ± 203.3 pg/mL ($p<0.05$), and reduction by AGK-2 was significant (73.9 ± 13.6 pg/mL). Cortical IL-6 did not differ among groups (12.6 ± 7.0, 7.6 ± 2.2, 20.6 ± 9.8 and 14.3 ± 6.1 pg/mL for Ctrl+DMSO, Ctrl+AGK-2, KP+DMSO and KP+AGK-2). NF-κB activation increased from 2.59 ± 0.15 (control) to 4.99 ± 0.51 after infection ($p<0.0001$) and was reduced to 3.00 ± **0.53** by AGK-2 ($p<0.001$), returning to control levels (ns; n=6/group). Cytokine data are mean ± SD (n=7–9/group); one-way ANOVA followed by Bonferroni's test. In addition, AGK-2 modulated systemic leukocyte responses, as evidenced by changes in total and differential cells counts compared with infected untreated animals ($p<0.05$). **Conclusion:** SIRT2 inhibition with AGK-2 attenuated the pulmonary and cortical inflammatory response to KP infection, reducing lung IL-6, cortical TNF-α and NF-κB activation to levels comparable to uninfected controls. The SIRT2 inhibition as a therapeutic strategy for controlling inflammation associated with severe bacterial infections and sepsis-associated encephalopathy.

04.063 **Neutrophil Polarization as an Anti-Tumor Approach**. Amorim NS[1], Amorim CS[2], Valença LS[2], Santos RCM[3], Moraes JA[2]. [1]ICB-UFRJ, Lab Biologia Redox, PPG em Biociências, UERJ, Brazil. [2]ICB-UFRJ, Lab Biologia Redox, Brazil. [3]IBCCF-UFRJ, Instituto de Biofisica Carlos Chagas Filho, Lab Glicobiologia Estrutural e Funcional, Brazil.

Introduction: **and Objectives:** Cancer is a complex disease characterized by the uncontrolled growth of abnormal cells, which invade adjacent tissues and spread throughout the body. Inflammation plays a central role in modulating the tumor microenvironment, and immune cells can both promote and inhibit cancer development. Among these cells, neutrophils can be recruited to the tumor site and are known as tumor-associated neutrophils (TANs), which exhibit high functional plasticity and can polarize into two phenotypes: N1, with antitumor activity, or N2, with a protumor profile. N1 neutrophils have greater cytotoxic capacity against tumor cells, mediated by the production of reactive oxygen species (ROS) with increased levels of pro-inflammatory mediators such as CD95 (FAS), TNF-α, ICAM-1, and NOS2. N1s also exhibit increased NOX activity, leading to the generation of cytotoxic ROS, such as $ONOO^-$ and H_2O_2. In contrast, N2 neutrophils exhibit an anti-inflammatory profile, supporting tumor growth, invasion, and metastasis. In this work, we investigated *in vitro* the polarization of human neutrophils toward an N1-like phenotype using LPS and IFN-γ and their interactions with three tumor cell lines: breast cancer (MDA-MB-231), melanoma (MV3), and glioblastoma (U87-MG). **Methods:** Neutrophils were isolated from the peripheral blood of healthy donors (CAAE 65372522.4.0000.5257) by immunomagnetic negative selection and stimulated with LPS and IFN-γ for 3 h at 37 °C and 5% CO_2. After polarization, we evaluated the production of total ROS (DCF probe), nitric oxide (NO) (DAF probe), peroxynitrite ($ONOO^-$) (APF probe), as well as lipid peroxidation (TBARS assay), extracellular vesicle (EV) release (NanoSight), and tumor cell viability after co-culture with N1-like neutrophils. **Results:** We observed that neutrophils polarized to the N1-like phenotype showed a significant increase in the production of total ROS (MDA-MB-231 +16% vs. N0, p=0.0197; MV3 +32%, p<0.0001; U87-MG +21%, p=0.0075), NO (MDA-MB-231 +54%, p=0.0473; MV3 +35%, p=0.0676; U87-MG +14%, p=0.0293), and $ONOO^-$ (MDA-MB-231 +9%, p=0.0164; MV3 +27%, p=0.0026; U87-MG +34%, p=0.0080) compared with non-activated neutrophils. This was associated with increased lipid peroxidation (MDA-MB-231 +18%, p=0.0306; MV3 +15%, p=0.0390; U87-MG +13%, p=0.0257) and reduced tumor cell viability (MDA-MB-231 -46%, p=0.0442; MV3 -7%, p=0.0008; U87-MG -36%, p=0.0055). N1-like neutrophils also released EVs with higher protein content than N0-EVs (+110%, p=0.0073), and these EVs reduced tumor cell viability (MDA-MB-231 -12%, p=0.0004; MV3 -9%, p=0.0062; U87-MG -14%, p=0.0285). We used fucoidan to confirm the importance of N1-EV communication with tumor cells and observed that this interaction is pivotal for inducing tumor cell death. **Conclusion:** Our results suggest that N1-like polarized neutrophils exert potent antitumor activity *in vitro* through mechanisms dependent on oxidative stress and lipid peroxidation. In addition, extracellular vesicles released by these neutrophils may contribute to this cytotoxic response, highlighting N1-like neutrophils and N1-EVs as promising tools for future antitumor therapeutic strategies.

04.064 **Marine-Derived Collagen and Chondroitin Sulfate Biomaterial Associated With Natural Antioxidants for Experimental Osteoarthritis**. Cahú, TB[1,2,3], Xavier, CHO[1,2], Oliveira, JL[1,3], Penno, SM[1], Freire-de-Lima, CG[4], Todeschini, AR[3], Mourão, PAS[1]IBqM-UFRJ, Lab Tecido Conjuntivo, [2]BioMatrix Inova Simples, [3]IBCCF-UFRJ, Lab Glicobiologia Estrutural e Funcional, [4]IBCCF/UFRJ, Lab Imunomodulação, Rio de Janeiro, Brazil.

Marine biomaterials are promising bioproducts due to their applicability in a range of biomedical approaches, including wound healing, tissue engineering, and joint health and regeneration. Osteoarthritis (OA) is a chronic inflammatory joint disease associated with cartilage degeneration and reduced quality of life, while current treatments often relieve symptoms without promoting tissue regeneration. In this context, the combination of collagen and chondroitin sulfate extracted from fishery by-products is presented as a promising strategy to create a biomaterial capable of supporting cartilage regeneration and modulating the inflammatory response. This study proposed the development of collagen- and chondroitin sulfate-based biomaterial particles containing curcumin (CUR) and mangiferin (MAN) as a novel therapeutic approach for the treatment of osteoarthritis. Collagen extracted from tilapia skin is investigated as a natural and sustainable biomaterial due to its structural, regenerative, and possible immunomodulatory properties, while chondroitin sulfate is included for its anti-inflammatory and chondroprotective effects. Balb/c mice were used in an induced osteoarthritis model involving Freund's adjuvant application in the posterior footpad or carrageenan-induced paw swelling. Animals were treated by gavage with collagen/chondroitin or collagen/chondroitin particles containing CUR or MAN. Results indicated that paw edema could not be distinguished in Freund's adjuvant-induced inflammation, but a clear effect was seen in the carrageenan swelling model, with CUR and MAN significantly reducing the measurements. Histological analysis of the paw and knee joint areas suggested improved architecture compared with the OA-induced group. Collagen/chondroitin treatment improved the histological organization of the cartilage layer, while CUR and MAN further protected the joint tissue. Analysis of local cytokine production showed lower expression of TGF-beta, TNF-alpha, and IL-10 in the CUR and MAN groups compared with the carrageenan group. These results suggest that the incorporation of natural antioxidants such as mangiferin and curcumin into a biomaterial matrix may enhance the beneficial effects in joint inflammation models such as OA. The use of these biomaterials in combination with natural anti-inflammatory compounds supports the development of innovative formulations for tissue regeneration, inflammation control, and translational applications in regenerative medicine.

04.065 **Nanocoumarin as a Leishmanicidal** (*Leishmania braziliensis*) **Strategy: Apoptotic Effects, TNF-α Production, and Molecular Interaction with Matrix Metalloproteinase-9 and Trypanothione Reductase**. Araújo AB[1], Gonçalves IFS[1], Almeida TS[1], Colares NN[1], Lopes AJSB[1], Pereira PIO[1], Rodrigues NLC[2], Teixeira MJ[2], Leal LKAM[1] [1]UFC, Dept Pharmacy, PPG Pharmaceutical Sciences, Brazil [2]UFC, Lab. of Parasitology, Brazil.

Introduction: Cutaneous leishmaniasis is a neglected infectious disease with major global social impact, whose pharmacotherapy still presents important limitations. In Brazil, the main etiological agent of cutaneous leishmaniasis is *Leishmania braziliensis*. In this context, nanocoumarin (NanoCM) has emerged as a promising nanodrug with leishmanicidal activity previously demonstrated by our research group. **Objectives:** To evaluate the role of apoptosis/necrosis and cytokine production in the leishmanicidal effect of NanoCM in macrophages infected with L. braziliensis, as well as to investigate, through molecular docking, possible interactions of coumarin with matrix metalloproteinase-9 (MMP-9) and trypanothione reductase related to this effect. Methods. NanoCM (25, 50, and 100 µg/mL) was added to the suspension of *L. braziliensis* promastigotes for 24 h, and apoptotic/necrotic effects were evaluated by flow cytometry using 7-aminoactinomycin D (7-AAD) and annexin V. To evaluate the effect on J774 macrophages (1×10^5 cells/mL) infected with *L. braziliensis* (amastigote form), increasing concentrations of NanoCM (25, 50, and 100 µg/mL) were added to the culture medium. Cytotoxicity was assessed by MTT assay, TNF-α production by ELISA, and molecular docking analyses were performed against MMP-9 and trypanothione reductase proteins. **Results:** NanoCM significantly reduced the viability of *L. braziliensis* promastigote forms (25 µg/mL: 81.8 ± 0.6%; 50 µg/mL: 70.8 ± 0.5%; 100 µg/mL: 70.3 ± 0.5%) compared to the blank nanoparticle (BN) group (98.1 ± 0.1%), which did not differ from the control group (medium: 98.1 ± 0.1%). In addition, NanoCM increased annexin V labeling, indicating apoptosis, which was greater than with free coumarin, and, to a lesser extent, necrosis. Evaluation of the effect of NanoCM on TNF-α production in infected macrophages revealed an increase in this cytokine (50 µg/mL: 38.6 ± 0.2 pg/mL) compared to the BN group (30.5 ± 1.2 pg/mL), without association with cytotoxicity (MTT). Molecular docking demonstrated binding affinity of coumarin toward trypanothione reductase (-7.842 kcal/mol) and MMP-9 (-7.305 kcal/mol), suggesting possible involvement in mechanisms related to parasite redox imbalance and inflammatory modulation of the host. **Conclusion:** NanoCM exhibited leishmanicidal activity by combining direct antiparasitic action, mainly inducing late apoptosis, superior to free coumarin, and modulation of the host macrophage inflammatory response (M1 phenotype), favoring disease control. **Financial support:** FINEP, CAPES, and CNPq.

04.066 **Nanostructured Lipid Carriers as Topical Delivery Systems for the Hydrogen Sulfide Donor GYY4137 and Psoriasis Treatment**. Passos JS, Lopes LB ICB-USP, Brazil

Introduction: Psoriasis is a chronic inflammatory skin disease that impairs patients' quality of life. Current therapies, especially corticosteroids, are associated with several adverse effects even when topically administered, highlighting the need for safer treatments. Hydrogen sulfide (H_2S) donors, such as GYY4137, have emerged as promising anti-inflammatory agents due to their ability to modulate oxidative stress, inflammation, and cell proliferation, but their instability in aqueous media hinder their therapeutic application. **Objectives:** This study proposed the encapsulation of GYY4137 into nanostructured lipid carriers (NLCs) for topical delivery. The aims were to: (i) develop and characterize GYY4137-loaded NLCs; (ii) evaluate their ability to promote skin localization of the drug; and (iii) investigate their cellular effects. **Methods:** NLCs were obtained using Precirol as solid lipid and oleic acid (OA) or isopropyl myristate (IM) as liquid lipids. Different oil phase proportions (5%-10%) were investigated and GYY4137 was incorporated at 1% (w/w). Formulations were produced by sonication or homogenization at high speed (using UltraTurrax®) and characterized regarding particle size distribution, encapsulation efficiency (EE%), stability, and drug release. Cutaneous availability of GYY4137 was studied using porcine skin. Cellular effects were evaluated in HaCaT keratinocytes using sulforhodamine B (antiproliferative and cytotoxic effects) and H_2DCFDA (production of reactive oxygen species, ROS) assays. **Results:** All formulations displayed nanometric diameter (< 400 nm), but NLC-OA exhibited mean size 1.5-fold larger than NLC-IM. Incorporation of GYY4137 reduced particle size by ~1.5-fold. Increasing the oil phase from 5% to 10% enhanced drug incorporation by 1.5–2.0-fold with EE% values of 94% and 88% for NLC-IM and NLC-OA, respectively. Stability studies demonstrated maintenance of formulation properties for up to 60 days. Both nanocarriers promoted sustained drug release, with approximately only 10% and 7% release after 72h from NLC-OA and NLC-IM, respectively. Skin permeation was time- and formulation-dependent. After 6 h, NLC-IM and NLC-OA increased drug accumulation in the stratum corneum (SC) by 3.9- and 5.2-fold, respectively, compared to control. In the remaining epidermis+dermis (ED), increases of 1.3- and 3.4-fold were observed, while no drug was detected in the receptor phase, suggesting no transdermal delivery. After 24 h, both NLCs increased delivery to the SC and ED by ~3.5- and 3.8-fold, respectively. However, NLC-OA enhanced transdermal permeation by up to 4.1-fold, whereas NLC-IM promoted drug retention within the skin. *In vitro*, the nanocarriers preserved the antiproliferative activity of GYY4137 without inducing ROS formation. **Conclusions:** The NLCs demonstrated high encapsulation efficiency, sustained release ability, and cutaneous penetration-enhancing properties, supporting their application as topical delivery systems for psoriasis treatment.

04.067 **Ouabain Mitigates the Damage of Zika Virus Infection in SH-SY5Y Cells**. Sales-Neto JM[1], Magalhães DWA[2], Carvalho DCM[3], Silva PG[4], Pena LJ[4], Moura MT[5], Rodrigues-Mascarenhas S[1] [1]UFPB, Biotechnology Center, Lab Immunopharmacology, PPG in Biotechnology, João Pessoa, PB. [2]UFPB, Biotechnology Center, Lab Immunopharmacology, Multicenter PPG in Physiological Sciences, João Pessoa, PB. [3]ICB-Unifal, Lab Vaccines, MG, [4]Fiocruz, Aggeu Magalhães Institute, Dept Virology and Experimental Therapy, PPG in Biosciences and Biotechnology in Health, Recife, PE. [5]UFPB, Biotechnology Center, Lab Cellular Reprogramming, Multicenter PPG in Physiological Sciences, João Pessoa, PB

Introduction: With no specific treatments currently available, Zika virus (ZIKV) remains a significant global health threat through its association with severe neurological disorders. Thus, ouabain (OUA) has emerged as a potential approach due to its antiviral and immunomodulatory properties; however, its mechanisms of action against ZIKV in neural cells require further investigation.

Objectives: The objective of this work was to evaluate the effects of OUA on ZIKV-infected SH-SY5Y cells, a model for undifferentiated neurons. **Methods:** SH-SY5Y cells were treated with different concentrations of OUA in the presence and absence of ZIKV to analyze the substance cytotoxicity. Then, after 1 h of ZIKV (multiplicity of infection [MOI]: 0.1), SH-SY5Y cells were treated with OUA (18 nM) and the viral titration by the fifty-percent tissue culture infection dose method using cytopathic effect, flow cytometry analyses and enzyme-linked immunosorbent assay were carried out. **Results:** OUA exhibited potent antiviral activity, reducing ZIKV titers by up to 99.9% without cytotoxicity (selectivity index > 25). Additionally, OUA decreased the ZIKV-induced production of the pro-inflammatory cytokine interleukin-6 (by 25%) and tumour necrosis factor-α (by 50%). Mechanistically, flow cytometry analysis showed that OUA suppressed ZIKV-induced NF-κB phosphorylation (by 75%), providing a basis for its anti-inflammatory effects. Furthermore, OUA treatment restored the phosphorylation mTOR, ERK, and p38, important key neurogenesis-related proteins compromised by ZIKV infection. Moreover, both ZIKV and OUA additively increased SRC phosphorylation, a pathway previously linked to OUA's antiviral activity. **Conclusion:** Our findings demonstrate the potential role of OUA in reverting the deregulated inflammation and neurogenesis impairment caused by ZIKV. These data support OUA as a promising antiviral and neuroimmunomodulatory agent, offering a potential therapeutic strategy for mitigating ZIKV-induced neuropathogenesis. Keywords: Arbovirus. Cardiotonic steroid. Inflammation. Neurogenesis.

04.068 **Extracellular Vesicles from N2-like Neutrophils Enhance Triple-Negative Breast Cancer Aggressiveness through a L-Selectin-Dependent Protumoral Signaling Axis**. Amorim CS[1], Amorim NS[1], Frony AC[2], Miranda BT[3], Pires GS[4], Pinheiro, PSM[4], De-Freitas-Junior JCM[2], Renovato-Martins M[5], Barja-Fidalgo C[2], Moraes JA[1] [1]UFRJ, Redox Biology Lab, Brazil; [2]UERJ, Cellular and Molecular Pharmacology Lab, Brazil; [3]UFRJ, Cellular and Molecular Cardiology Lab, Brazil,[4]UFRJ, Lab for the evaluation and synthesis of bioactive substances, Brazil, [5]UFF, Inflammation and Metabolism Lab, Brazil.

Introduction: **and Objective:** Breast cancer is the second most common type of cancer in the world and the first most common among women. The relationship between cancer and inflammation is well established, and neutrophil infiltration has been described in tumors since 1863. Neutrophils are recruited by the tumor microenvironment and begin to favor tumor growth. Thus, they are called tumor-associated neutrophils (TAN) and can present two different phenotypes: N1 (anti-tumor) or N2 (pro-tumor). In previous work, our research group observed that neutrophils challenged with extracellular vesicles (EVs) derived from melanoma (MV3) or breast tumor cells (MDA-MB-231) were able to adopt an N2-like phenotype. As an *in vitro* polarization strategy for TAN N2, we used extracellular vesicles (EVs) derived from breast tumor cells (MDA-MB-231). We aimed to investigate the role of N2 TAN-derived EVs (N2-EVs) in MDA-MB-231 cells. **Methods:** Neutrophils were isolated using ficoll gradient from the peripheral blood of healthy donors and treated with MDA-EVs for three h at 37°C and 5% CO2. After polarization, we observed some specific markers of neutrophil polarization to a pro-tumor or N2-like phenotype, such as VEGF, IL-8, arginase-1, total intracellular ROS production, CD184, and MMP-9 activity. N2-EVs were collected after two hours of neutrophil polarization and characterized for size (NanoSight) and L-selectin presence by flow cytometry. The effect of N2-EVs on AKT activation, mitochondrial ROS (using MitoSOX probe), invasion capacity (invasion assay with transwell), migratory capacity (wound healing), MMP-9 (gelatin zymography), and NF-κB activity (NF-κB responsive luciferase reporter) of MDA-MB-231 breast tumor cells was observed by treating the cells with the EVs by one h. **Results:** We observed that N2-EVs present L-selectin on their membranes and that fucoidan could block this selectin. Our findings demonstrated that N2-EVs interact with breast tumor cells through L-selectin, and these EVs could also increase mitochondrial ROS production in breast tumor cells via the PI3K/AKT axis. N2-EVs also regulated tumor cells' migratory and invasive capacity, probably through MMP-9 activity and NF-κB upregulation. **Conclusion:** Overall, our results show that N2-EVs can induce tumor cells *in vitro* to a greater migratory and invasive capacity of MDA-MB-231 cells in an L-selectin-dependent manner, increasing their malignancy *in vitro*.

04.069 **Modulation of Bacteria–Host Interactions during Experimental Intestinal Mucositis by a Resveratrol Analog**.
Oliveira LG, Reis ACC, Eufrásio ALL, Souza ILL, Silva AD, Meinel RS, Macedo GC, Avila TV UFJF

Introduction: 5-Fluorouracil (5-FU) is widely used in cancer treatment, but frequently induces intestinal mucositis, a debilitating inflammatory condition associated with epithelial damage and intestinal dysbiosis. Resveratrol (RVT), a natural polyphenol with antioxidant, anti-inflammatory, and immunomodulatory properties, has shown beneficial effects in this context; however, its low bioavailability limits its clinical application. Therefore, the development of analogs with improved pharmacokinetic properties may represent a promising therapeutic strategy. **Objectives:** This study aimed to evaluate the effects of the resveratrol analog AR23 on 5-FU-induced intestinal mucositis in mice and investigate its effects on bacteria–host interactions. **Methods:** Female C57BL/6 mice were treated with 5-FU (75 mg/kg, i.p., for three consecutive days) and concomitantly treated with the resveratrol analog AR23 (50 mg/kg, i.p.). After five days, clinical, hematological, histological, and microbiological parameters were evaluated. *In vitro* assays were performed to evaluate bacterial adhesion to colorectal adenocarcinoma cells (Caco-2), phagocytosis by J774A.1 macrophages, and direct bactericidal activity against *E. coli* isolated from mucositis animals. Statistical analyses were performed using ANOVA test followed by Tukey or T-student when appropriate, considering $p < 0.05$ as statistically significant. **Results:** AR23 significantly attenuated body weight loss induced by 5-FU (-7.5 ± 0.7 vs. -20.3 ± 1.6% in 5-FU-induced mucositis; $p < 0.0009$) and reduced clinical disease scores (1.4 ± 0.4 vs. 6.7 ± 0.3 A.U. in 5-FU-induced mucositis; $p<0.0001$) associated with intestinal mucositis. Importantly, the compound did not interfere with the antitumor-related effects of 5-FU, as demonstrated by the maintenance of bone marrow suppression. Treatment also markedly reduced bacterial translocation to the liver in animals with mucositis ($6 \times 10^3 \pm 3 \times 10^3$ CFU/g in the 5-FU group vs. non-detectable levels in treated animals, p=0.04). Microbiological analyses demonstrated a marked increase in fecal Enterobacteriaceae associated with 5-FU-induced mucositis (145.2 ± 63.9 × 10^6 CFU/g vs. 0.3 ± 0.04 × 106 CFU/g in controls, p=0.028), whereas treatment markedly reduced bacterial counts ($1.3 \pm 1.3 \times 10^5$ CFU/g, p=0.012). *In vitro* assays demonstrated no direct bactericidal effect against *E. coli* (2 x 107 in controls vs 4.6 x107 in AR23 treated group, p=0.51). However, AR23 markedly reduced bacterial adhesion to Caco-2 cells (1x107 vs 2x107 in controls, $p<0.0001$) and increased phagocytosis by J774A.1 macrophages (2x103 vs 1x104 in controls, p=0.05), suggesting modulation of bacteria–host interactions as a mechanism associated with attenuation of intestinal mucositis. **Conclusion:** AR23 showed beneficial effects in 5-FU-induced intestinal mucositis, reducing clinical alterations, bacterial translocation, and microbiological disturbances associated with the disease. These findings suggest that modulation of bacteria–host interactions may contribute to the protective effects of this compound and support its potential as an adjuvant therapeutic strategy during chemotherapy **Acknowledgments:** The authors thank FAPEMIG for **Financial support**.

04.070 **Circulating IL-13 Levels Correlate with Oxidative Imbalance and Impaired Innate Immune Function** *in silica*-**Exposed Workers**. Ferreira TPT[1,2], Ribeiro PC[3], Arantes ACS[1], Guimarães FV[1], Castro-Faria-Neto HC[4], Martins MA[1], Castro HA[3], Silva, PMR[1] [1]IOC-Fiocruz, Lab Inflammation, [2]UFRJ-Duque de Caxias; [3]ENSP-Fiocruz, Occupational Lung Diseases Outpatient Clinic of the Center for Studies on Workers' Health and Human Ecology, [4]IOC-Fiocruz, Lab Immunopharmacology, RJ, Brazil.

Introduction: Occupational exposure to respirable crystalline silica remains a major public health concern worldwide. Silicosis is a progressive, irreversible fibrotic lung disease caused by inhalation of silica particles, leading to chronic inflammation, tissue remodeling, and impaired lung function. Interleukin-13 (IL-13) is a profibrotic cytokine associated with Th2 immune responses and fibrogenic pathways implicated in disease progression. This study investigated inflammatory mediators, with particular emphasis on IL-13, as potential biomarkers of silica exposure and evaluated peripheral blood leukocyte responses *in vitro*. **Methods:** Sixty individuals were enrolled, including 29 workers occupationally exposed to silica dust and 31 unexposed controls. Respiratory symptoms, smoking status, and occupational history were collected using a standardized questionnaire. Plasma cytokines and chemokines were quantified using an antibody-based multiplex immunoassay. Peripheral blood mononuclear cells (PBMCs) and polymorphonuclear neutrophils (PMNs) were isolated and stimulated *in vitro* with PMA (40 µg/mL), LPS (1 µg/mL), or silica particles (300 µg/mL). Cytokine production, reactive oxygen species (ROS) generation, and neutrophil extracellular trap (NET) formation were assessed by ELISA, CM-H_2DCFDA fluorescence probe, and Sytox Green assay, respectively. The study was approved by the Clinical Research Ethics Committee of ENSP/FIOCRUZ (protocol 5.012.171), and all participants provided written informed consent. **Results:** Silica-exposed workers reported a higher frequency of respiratory symptoms, particularly cough and dyspnea. Plasma IL-13 levels were significantly elevated in exposed workers compared with controls (10.43 ± 2.77 vs. 8.97 ± 2.40, mean ± SD; $p = 0.033$). Increased concentrations of IL-7, MIP-1α, IP-10, and eotaxin were also observed. PBMCs from exposed workers exhibited higher spontaneous IL-6 production than controls. LPS, but not silica particles, further increased IL-6 production, although no significant differences were detected between groups after stimulation. PMNs from exposed workers displayed enhanced spontaneous ROS generation and NET release. PMA and LPS, but not silica particles, increased ROS production, with a more pronounced response in cells from exposed workers. In contrast, PMNs from exposed workers exhibited reduced NET formation following PMA and LPS stimulation compared with controls, suggesting altered neutrophil responsiveness. No differences between groups were observed after silica stimulation. **Conclusion:** Occupational exposure to silica is associated with systemic immune dysregulation characterized by elevated circulating IL-13 levels, increased oxidative stress, and altered neutrophil effector functions. These findings support IL-13 as a promising biomarker of silica-induced immune alterations and suggest that combining cytokine profiling with functional innate immune assays may improve the identification of individuals at risk for silica-related disease. Further longitudinal studies are warranted to validate these biomarkers and determine their predictive value for disease progression.

04.071 **Tirzepatide Differentially Modulates Reactive Oxygen Species Production in Brown and White Adipose Tissues During Systemic Inflammation**. Aguiar SCR[1], Vale KBL[1], Cruz EKM[1], Franco GHSP[1], Trindade KP[1], Silva LC[1], Gonçalves LJF[1], Souza PEN[2], Souza FHV[1]. [1]UnB, Lab. of Experimental Biomodels, PPG in Health Sciences and Technologies, Brazil, [2]UnB, Lab. of Electron Paramagnetic Resonance, Brazil.

Introduction: Tirzepatide (TZP) is a dual GLP-1/GIP receptor agonist widely used to treat type 2 diabetes and obesity. Although its metabolic effects are well established, its potential actions on inflammatory responses and oxidative metabolism remain poorly understood, particularly during acute systemic inflammation. Recent evidence demonstrated that liraglutide, a GLP-1 receptor agonist, attenuates lipopolysaccharide (LPS)-induced fever through sex-dependent neuroimmune mechanisms (Sousa, GLS. Pharmaceuticals, 18, 1738, 2025). Whether incretin-based therapies also modulate oxidative stress in thermoregulatory tissues during systemic inflammation remains unknown. **Objectives:** To investigate the effects of TZP on oxidative stress in brown adipose tissue (BAT) and white adipose tissue (WAT) during LPS-induced systemic inflammation. **Methods:** Male Wistar rats received intraperitoneal pretreatment with TZP (100, 300, or 1000 µg/kg) followed by LPS administration one hour later. Body temperature was continuously monitored for 5 h. ROS production was quantified in BAT and WAT using electron paramagnetic resonance (EPR) spectroscopy after incubation with the spin probe CMH. Data were analyzed by one-way ANOVA followed by Tukey's post hoc test. **Results:** LPS increased body temperature by 1.1 ± 0.3 °C compared with saline ($p < 0.05$). Pretreatment with TZP attenuated fever at 1000 µg/kg (0.15 ± 0.10 °C, $p = 0.019$ vs. LPS) and 300 µg/kg (0.22 ± 0.15 °C, $p = 0.032$ vs. LPS), whereas 100 µg/kg had no significant effect ($p = 0.24$). In BAT, ROS production increased from 513.8 ± 36.6 µM (saline) to 1484 ± 275.3 µM after LPS ($p = 0.014$). TZP reduced BAT ROS to 519.4 ± 69.3 µM, 326.5 ± 23.1 µM, and 415.5 ± 37.7 µM at doses of 100, 300, and 1000 µg/kg, respectively ($p <$ 0.05 vs. LPS). No significant differences were observed in gonadal or inguinal WAT (p ˃ 0.05), indicating a tissue-specific antioxidant effect during systemic inflammation. **Conclusion:** TZP markedly reduced ROS production in BAT during LPS-induced systemic inflammation, whereas no significant effects were observed in WAT. These findings demonstrate tissue-specific modulation of oxidative stress by TZP and highlight BAT as a potential site of antioxidant action during systemic inflammation.

04.073 **Hydroethanolic Extract of *Calycophyllum spruceanum* Barks Attenuates Acute Inflammation by Modulation of NO-, TNF-α- and PGE2-Dependent Pathways**. Assreuy AMS[1], Azevedo VGS[1], Silva APAB[2], Nascimento FGS[1], Amorim RMF[1], Peixoto ABS[1], Araujo DF[1], Cunha RM[2] [1]ISCB-UECE, Brazil, [2]UFAC, Lab Fisiofarmacologia, Brazil

Introduction: *Calycophyllum spruceanum*, popularly known as mulateiro, is traditionally used in the Brazilian Amazon to treat inflammatory and painful conditions. The hydroalcoholic bark extract (HECSb) has been shown to reduce carrageenan-induced oxidative stress and suppress inflammatory and nociceptive responses in mice. **Objectives:** To investigate the anti-inflammatory effects of HECSb in mice acute inflammation models and to evaluate the involvement of nitric oxide (NO), tumor necrosis factor-alpha (TNF-α), and prostaglandin E2 (PGE2). **Methods:** Swiss mice were conducted in accordance with the guidelines of the Brazilian National Council for the Control of Animal Experimentation (CONCEA No 73, 2025) and approved by the Institutional Animal Care and Use Committees (CEUA-UFAC No 08/2020; CEUA-UECE No 31032.005059/2024-26). Animals received per oral HECSb (50-150 mg/kg) 1 h before carrageenan to evaluate leukocyte migration, myeloperoxidase activity (MPO), edema, vascular permeability and hypernociception. To investigate the involvement of inflammatory mediators, edema and nociceptive responses were induced by L-arginine, TNF-α and PGE2. Data were analyzed using ANOVA followed by Tukey's test. **Results:** HECSb significantly reduced carrageenan-induced leukocyte migration (47%), neutrophil influx (77%), myeloperoxidase activity (47%), and vascular permeability (18%) in the peritoneal cavity, while increasing the nociceptive threshold by 74%. In the air pouch model, HECSb reduced total leukocyte and neutrophil migration by 59% and 85%, respectively. The extract inhibited carrageenan-induced paw edema during both the early (57%) and late (86%) phases. HECSb also attenuated edema elicited by L-arginine (59%), TNF-α (59%), and PGE_2 (64%). Furthermore, the extract significantly reversed PGE_2-induced hypernociception throughout the evaluation period, increasing nociceptive thresholds by 38–46%. **Conclusion:** The anti-inflammatory effect of HECSb is associated with reduced leukocyte recruitment and modulation of NO-, TNF-α- and PGE_2-dependent inflammatory pathways.

04. Biology and Cardiovascular Diseases

04.001FR **Acute Cardiovascular Response to Resistance Training to Muscular Failure and Progressive Reductions in Training Volume**. Martins AJFM[1], Pires KC[1], Vieira YLM[2], Leite IAH[3], Flora JMG[5] , Santos M[2], Campos AVLL [2], Rodrigues IJS [2], Lacerda LT[2], Brandão CFCCM [2], Andrade MJO[2], Drummond LR [1] [1]UEMG, Dept Physical Education, Brazil, [2]UEMG, Dept Psychology, Brazil

Introduction: Resistance training performed to muscular failure (RTMF) has been widely used to maximize strength and muscle hypertrophy gains, as high levels of fatigue appear to enhance the muscular stimulus. However, this type of training imposes a considerable overload on the cardiovascular system. The rate-pressure product (RPP), calculated as the product of heart rate and systolic blood pressure, is a non-invasive predictor of myocardial oxygen demand. Nevertheless, the influence of different resistance training volumes on RPP remains poorly investigated in the literature. **Objective:** To evaluate the rate-pressure product response to resistance training performed to muscular failure and to protocols with different training volume reductions over an 8-week period. **Methods:** The study was approved by the Research Ethics Committee of the Federal University of Minas Gerais (UFMG) (CAAE: 79108117.5.0000.5149). Eleven healthy male volunteers (18–35 years old), with no resistance training experience within the previous six months, no musculoskeletal injuries, and no use of pharmacological ergogenic aids, were recruited. Participants performed bilateral knee extension exercises to muscular failure and two additional protocols with 10% and 40% fewer repetitions than the muscular failure protocol, with a seven-day interval between sessions over eight weeks. RPP was determined using heart rate measured with a Polar H10 heart rate sensor paired with a Polar M30 watch (Polar®, Oulu, Finland), multiplied by systolic blood pressure measured using a stethoscope and sphygmomanometer (Premium®, China). Measurements were obtained at rest, 1 minute, and 15 minutes after each protocol. Data were analyzed using SigmaPlot 11.0 and are presented as mean ± standard deviation. One-way ANOVA followed by Tukey's post hoc test was used, with statistical significance set at $P \leq 0.05$. **Results:** No significant differences were observed in resting RPP among the different training volume protocols ($P = 0.242$). At 1 minute post-exercise, the muscular failure protocol produced a significantly higher RPP compared with the protocol involving a 40% reduction in training volume ($P < 0.05$). At 15 minutes after exercise, no significant differences were found among the protocols ($P = 0.187$). **Conclusion:** The protocol with the greatest reduction in training volume resulted in a lower cardiovascular demand. Keywords: Cardiovascular, resistance training, myocardial demand. Funding: FAPEMIG, CNPq, and UEMG.

04.002FR **Cardiovascular Responses to Baro-and Chemoreflex Activation in Rat Offspring Exposed to Different Maternal Folic Acid Doses**. Amorim SCB[1], Silva EGS[1], Lima LS[2], Lira MRS[2], Souza JVF[1], Silva JHC[3] [1]UFPE, Centro Acadêmico de Vitória, PPG Multicêntrico em Ciências Fisiológicas, Brasil. [2]UFPE, Centro Acadêmico de Vitória, Brasil. [3]UFPE, Centro Acadêmico de Vitória, Educação Física, Lab Multiusuário de Avaliação Física e Processamento de Sinais, PPG Multicêntrico em Ciênias Fisiológicas, Vitória de Santo Antão, PE, Brasil.

Introduction: Maternal folic acid (FA) intake is essential for fetal development, but both deficient and excessive intake may influence developmental processes involved in cardiovascular regulation. **Objectives:** To investigate whether maternal exposure to different FA doses during gestation and lactation affects cardiac autonomic modulation, baroreflex sensitivity, and chemoreflex responses in 90-day-old male rat offspring. **Methods:** Wistar dams received diets containing 2 mg/kg FA (Control), 0 mg/kg (E0), 20 mg/kg (E10; 10-fold), or 50 mg/kg (E25; 25-fold) during gestation and lactation. Male offspring were evaluated at 90 days of age. Heart rate variability (HRV) was assessed by spectral and time-domain indices, including very-low-frequency (VLF), low-frequency (LF), high-frequency (HF), LF/HF ratio, standard deviation of RR intervals (SDRR), and root mean square of successive differences (RMSSD). Baroreflex sensitivity was evaluated following phenylephrine (1.5 and 2.0 µg/kg) and sodium nitroprusside (7.5 and 10 µg/kg). Chemoreflex responses were assessed following potassium cyanide (KCN; 0.04%, 100 µL/rat), considering changes in heart rate (ΔHR) and arterial pressure (ΔAP). Data were analyzed by one-way ANOVA followed by Tukey's post hoc test, with $p < 0.05$ considered significant. **Results:** No statistically significant differences were observed among groups for any HRV parameter. Although E10 showed numerically higher SDRR (56.67 ± 19.4%) and RMSSD (78.49 ± 27.19 ms) values than Control (36.03 ± 8.69% and 45.17 ± 9.92 ms, respectively), these differences were not significant. Similarly, baroreflex sensitivity responses to phenylephrine and sodium nitroprusside did not differ significantly among groups. Following KCN administration, ΔHR was -205.3, -294.4, -317.3, and -177.3 bpm in Control, E0, E10, and E25, respectively, while ΔAP was 49.36, 39.44, 41.20, and 40.63 mmHg, respectively, with no significant differences among groups. **Conclusion:** Maternal exposure to deficient or excessive FA levels did not significantly modify cardiac autonomic modulation, baroreflex sensitivity, or chemoreflex responses in adult male offspring. These findings suggest that, under the conditions evaluated, maternal FA supplementation did not induce persistent alterations in cardiorespiratory autonomic control.

04.003FR **Association Between Low Heart Rate Variability and Obesity on Blood Pressure and Glucose Metabolism in Women**. Clementino LCRF, Neves TAFV, Moraes RCS, Pereira JKG, Silva JVG, Alves JLB, Martins, VJB. UFPB, PPG in Nutritional Sciences, Brazil.

Introduction: Heart rate variability (HRV) is an important non-invasive marker of autonomic balance. Low HRV is associated with a higher risk of metabolic and cardiovascular diseases. Overweight individuals show lower HRV, associated with impaired glucose metabolism and cardiovascular function. **Objectives:** To evaluate associations among HRV, blood pressure and glucose metabolism in overweight women. **Methods:** This is a cross-sectional study with women aged 20 to 62 years from a non-clinical sample, allocated into three groups according to nutritional status and autonomic function: group normal weight and low Stress Index (4.4-12.35, EBSI, n=10), group obesity and low Stress Index (4.4-12.35, OBSI, n=37), and group obesity and high Stress Index (>12.35-131.00, OASI, n=34). BMI, glucose, glycated hemoglobin, HRV variables (RMSSD, Power LF (ms^2), Power HF (ms^2) and LF/HF ratio), systolic and diastolic blood pressure were measured. Groups were compared by ANOVA and correlations were performed by Pearson or Spearman tests using Statistical Package for the Social Sciences (SPSS). **Results:** Age and glycated hemoglobin did not differ between the groups. BMI (21.51 ± 2.33 vs. 30.59 ± 4.99 vs. 31.41 ± 5.26 kg/m^2, p<0.001, EBSI, OBSI and OASI, respectively), systolic blood pressure (97.92 ± 6.60 vs. 113.46 ± 9.73 vs. 117.01 ± 14.99 mmHg, p<0.001), diastolic blood pressure (62.99 ± 6.21 vs. 71.73 ± 7.27 vs. 74.04 ± 10.87 mmHg, p=0.006) were significantly higher in the OBSI and OASI groups compared to EBSI. Glucose (geometric mean (confidence interval)) (97 (86-108) vs. 82 (77-87) vs. 79 (71-89) mg/dL, p=0.010) and LF/HF ratio (2.41 (1.48-3.93) vs. 1.27 (0.97-1.66) vs. 0.91 (0.51-1.62), p=0.014) were significantly higher in OASI compared to OBSI and EBSI. RMSSD (17 (15-20) vs. 41 (36-47) vs. 71 (38-133), p<0.001), Power LF (203 (165-250) vs. 732 (576-929) vs. 1,002 (569-1,763) ms^2, p<0.001) and Power HF (103 (76-140) vs. 578 (435-768) vs. 1,102 (671-1,810) ms^2, p<0.001) were significantly lower in OASI compared to OBSI and EBSI. Glucose was positively correlated with BMI (r=0.344) and SBP (r=0.218), and negatively correlated with Power LF (r=-0.270), Power HF (r=-0.282), and RMSSD (r=-0.271). BMI was positively correlated with Power VLF (r=0.224), SBP (r=0.461), and DBP (r=0.431). SBP and DBP were negatively correlated with Power HF (r=-0.237; r=-0.211, respectively) and Power VLF (r=-0.266; r=-0.274). **Conclusion:** Women with obesity and low heart rate variability presented higher blood pressure and blood glucose concentrations. This study was funded by CAPES and FAPESQ. Approved by the Ethics Committee with Human Beings of the Health Sciences Center of the Federal University of Paraíba - CCS/UFPB according to the ethical standards for research involving human beings of Resolution 466/2012 (CAAE: 53905321.9.0000.5188).

04.004FR **Influence of Different Resistance Training Volumes on Heart Rate Variability**. Pires KC[1], Vieira YLM[1], Rodrigues IJS[1], Flora JMG[1], Lacerda LT[1], Brandão CFCCM[1], Andrade MJO[2], Drummond LR[1] [1]UEMG, Dept Physical Education, Brazil; [2]UEMG, Dept Psychology, Brazil

Introduction: Resistance training performed to muscular failure (RTF) has been widely used to maximize strength and hypertrophy gains, as high levels of fatigue are thought to enhance the training stimulus. However, this training strategy imposes substantial cardiovascular stress. Heart rate variability (HRV) reflects the fluctuations in consecutive heartbeats and is a noninvasive marker of autonomic nervous system regulation. Although training volume appears to influence HRV responses, its effects require further investigation. **Objective:** To evaluate heart rate variability responses to resistance training performed to muscular failure and to protocols with different reductions in training volume over an 8-week period. **Methods:** This study was approved by the Research Ethics Committee of the Federal University of Minas Gerais (UFMG) (CAAE: 79108117.5.0000.5149). Eleven healthy male volunteers (18–35 years), with no resistance training experience in the previous six months, no musculoskeletal injuries, and no use of pharmacological ergogenic aids, were recruited. Participants performed bilateral knee extension exercises to muscular failure (RTF) and five additional protocols with 10%, 20%, 30%, 40%, and 50% fewer repetitions than the RTF protocol, with a seven-day interval between sessions over an 8-week period. HRV was assessed at rest, 1 minute, and 15 minutes after each protocol. Heart rate variability was recorded using a Polar H10 heart rate sensor paired with a Polar M30 watch (Polar, Oulu, Finland), a validated heart rate monitoring system. Parasympathetic HRV indices were used to assess autonomic recovery. Data were exported from Polar Flow software and analyzed using SigmaPlot 11.0. Results are presented as mean ± standard deviation. One- way ANOVA followed by Tukey's post hoc test was performed, with statistical significance set at $p \leq 0.05$. **Results:** Resting HRV did not differ significantly among the resistance training protocols with different volume reductions ($p = 0.961$). Likewise, no significant differences were observed 1 minute after exercise. However, after 15 minutes of recovery, the protocols with 30% ($p = 0.02$) and 40% ($p = 0.03$) reductions in training volume showed significantly higher HRV values than the resistance training performed to muscular failure. **Conclusion:** Reducing training volume during resistance exercise promotes better cardiac autonomic recovery compared with resistance training performed to muscular failure.

04.005FR **Gut Microbiota and Cardiometabolic, Nutritional, and Redox Markers in Schoolchildren: A Cross-Sectional Study**. Marinho ABGF[12], Pereira JG[12], Nascimento MBESPN[12], Chongo CM[12], Silva RCF[3], Cruz HLA[4], Falcão RM[4], Simões-Alves AC[12], Balbino VQ[4], Morio B[5], Costa-Silva JH[12] [1]Lab Multiusuário de Avaliação Física e Processamento de Sinais, Centro Acadêmico de Vitória, Universidade Federal de Pernambuco, Brasil; [2]NAFPF-CAV-UFPE Lab Multiusuário em Nutrição, Atividade Física e Plasticidade Fenotípica, Brasil; [3]LABMEX-CAV-UFPE Lab Multiusuário de Bioquímica Geral, Molecular e do Exercício, Brasil; [4]Lab Bioinformática e Biologia Evolutiva, Centro de Ciências da Saúde, Universidade Federal de Pernambuco, Brasil; [5]Université Claude Bernard Lyon, França.

Introduction: The gut microbiota may interact with dietary intake, body composition, cardiovascular function, metabolic status, and redox balance during childhood. **Objective:** To investigate associations between gut microbiota composition and dietary intake, body composition, cardiovascular, biochemical, and redox markers in children aged 6–10 years. **Methods:** This quantitative cross-sectional study included 20 children aged 6–10 years enrolled in public schools in Vitória de Santo Antão, Pernambuco, Brazil. Anthropometry, dual-energy X-ray absorptiometry, dietary intake, blood pressure, electrocardiography, heart rate variability, serum glucose, lipid profile, vitamins B9/B12, and oxidative stress markers were assessed. Fecal DNA was extracted, and bacterial 16S rRNA gene sequencing was performed using DNBSEQ-G400. Phylum-level abundances were correlated with study variables using Spearman's correlation ($p \leq 0.05$). No multiple-comparison correction was applied, and the correlation analyses were considered exploratory. The study was approved by the Research Ethics Committee of the Federal University of Pernambuco (CAAE: 80956824.3.0000.9430). **Results:** Desulfobacterota was inversely correlated with total body fat (r = -0.670), android fat (r = -0.638), and dietary lipid intake (r = -0.718). Bacteroidota was inversely correlated with visceral fat (r = -0.526) and positively correlated with systolic (r = 0.466) and diastolic blood pressure (r = 0.448). Firmicutes was positively correlated with subcutaneous fat (r = 0.468) and inversely correlated with carbohydrate intake (r = -0.463) and resting heart rate (r = -0.483). Proteobacteria was positively correlated with subcutaneous fat (r = 0.451) and inversely correlated with systolic (r = -0.529) and diastolic blood pressure (r = -0.448). Actinobacteriota was inversely correlated with HDL-c (r = -0.470) and vitamin B12 (r = -0.529). Firmicutes was positively correlated with TBARS (r = 0.522) and protein carbonyls (r = 0.629), whereas catalase activity was positively correlated with Verrucomicrobiota (r = 0.554) and Desulfobacterota (r = 0.594). GST activity was inversely correlated with Verrucomicrobiota (r = -0.516), Desulfobacterota (r = -0.506), and Cyanobacteria (r = -0.560). **Conclusion:** The relative abundance of gut microbiota phyla was associated with different markers of adiposity, dietary intake, cardiovascular parameters, biochemical profile, and redox status in children. Notably, Desulfobacterota showed inverse correlations with total body fat and dietary lipid intake. Overall, these findings indicate that gut microbiota composition may be related to different components of cardiometabolic health in childhood. Given the cross-sectional design and exploratory nature of the correlation analyses, these findings should be interpreted as correlational associations and not as evidence of causality.

04.006FR **Effects of a Multi-Strain Probiotic on Blood Pressure and Cardiovascular Function in Rats with Renovascular Hypertension**. Freire MOL[1], Souza RMP[2], Andrade JT[2], Fernandes KFD[1], Cruz Neto JPR[1], Flôr AFL[2], França-Falcão MS[2], Souza EL[1], Alves JLB[1] [1]UFPB, Dept Nutrition, Health Sciences Center, PPG Nutrition Sciences, Brazil; [2]UFPB, Dept Biotechnology, Multicenter Graduate Program in Physiological Sciences, Brazil

Introduction: Systemic arterial hypertension (SAH) is a complex disorder associated with gut microbiome impairments, inflammation and endothelial dysfunction. In this context, probiotics emerge as a promising adjunctive treatment strategy for SAH. **Objectives:** To investigate the effects of a multi-strain probiotic on blood pressure and cardiovascular function renovascular hypertensive rats. **Methods:** Male and female Wistar rats were allocated into five groups: Sham (n=9); 2-Kidneys-1-Clip (2K1C) hypertensive rats treated with a placebo (2K1C, n=5–11); 2K1C treated with losartan (Los, n=9–12); 2K1C treated with a probiotic formulation (Prob, n=8–10); and 2K1C treated with a probiotic plus losartan (Prob+Los, n=8–10). Renovascular hypertension was induced by implanting a silver clip in the right renal artery. The rats were treated with a multi-strain containing *Limosilactobacillus fermentum* 139, 263, and 296; *Lactiplantibacillus plantarum* 49, *Lacticaseibacillus casei* 108 and *Lacticaseibacillus paracasei* 98 (1×10^9 CFU) for four weeks. Blood pressure, heart rate, baroreflex and autonomic modulation were recorded in awake rats. In addition, the mesenteric artery was collected for vascular reactivity assays. The data are presented as the standard error of the mean (SEM). One-way and two-way ANOVA with Tukey's post hoc test were used in GraphPad Prism 9 ($p < 0.05$). **Results:** Mult-strain probiotics alone or in combination with losartan reduced systolic (p= <0,0001), diastolic (p=<0,0001), and mean blood pressure (p=<0,0001) levels. Baroreflex sensitivity was improved in groups receiving Los and/or Prob (p= 0,0011). The Prob group showed an increase in parasympathetic tone (p=0.0427), while the Prob+Los group showed a reduction in vasomotor sympathetic drive (p=0.0229). Regarding vascular reactivity, the Prob and Prob+Los groups exhibited a significant decrease in total contractile capacity in response to phenylephrine administration in vessels with functional endothelium (p=0,0054). However, only the Prob+Los group exhibited reduced contraction in endothelium-denuded rings (p=0,0002). The Los, Prob, and Prob+Los groups showed improved vascular sensitivity regarding the vasorelaxant response of vessels pre-contracted with phenylephrine, both with (p=<0,0001) and without endothelium (p=<0,0001) present. Conversely, maximal relaxation was only observed in endothelium-denuded rings in the Prob+Los group (p = 0.0491). No significant changes in the maximum effect were observed in vessels with functional endothelium (p>0.05). **Conclusion:** Treatment with multi-strain probiotics, either alone or in combination with losartan, reduced blood pressure and improved baroreflex sensitivity and autonomic modulation. The intervention also induced changes in vascular function, resulting in reduced contractility and increased vasorelaxation.

04.007FR **Intake of NaCl and $NaHCO_3$ during the Development of 2-Kidney-1-Clip Hypertension in Rats**. Pereira MS, Lima RVS, Cavalcante ABL, Cunha SMP, Figueiredo EVS, Roncari CF, David RB. UFC (UFC), School of Medicine, Dept Physiology and Pharmacology, Fortaleza, CE, Brazil.

Introduction: In rats, NaCl intake follows an inverted U-shaped concentration–response curve (CRC), with a peak near isotonicity. The renin–angiotensin–aldosterone system (RAAS) participates in the regulation of sodium intake, in part through the action of angiotensin II (Ang II) on type 1 receptors (AT1), mainly located in the subfornical organ. Central administration of Ang II induces greater intake of 0.15 M $NaHCO_3$ compared to other solutions, including NaCl. Rats with 2-kidney, 1-clip (2K1C) hypertension exhibit chronic activation of the RAAS and increased intake of hypertonic NaCl, either spontaneously or induced by central Ang II injections, suggesting modulation of the CRC for different salts during the development of hypertension. **Objective:** The aim of this study was to determine the CRC for NaCl and $NaHCO_3$ in 2K1C rats. **Methods:** Protocols were approved by CEUA-UFC (#2706070721). Male Wistar rats (≈150 g) were subjected to unilateral renal stenosis or sham surgery (SHAM). Between the 4th–5th and 8th–9th post-surgical weeks (PSW), rats were housed in individual metabolic cages with food, one bottle containing water and another containing NaCl or $NaHCO_3$ dissolved in distilled water at concentrations of 0, 0.08, 0.15, 0.23, or 0.3 M, for 3 days each. Daily fluid intake was calculated as the average of the last 2 days. Urinary volume was recorded during the metabolic cage sessions, and body weight was monitored weekly throughout the experimental period. At the end of the protocol, mean arterial pressure (MAP) and heart rate (HR) were measured, and animals were euthanized. Rats with MAP > 129 mmHg were classified as hypertensive (2K1C-H), while those not meeting this criterion were classified as normotensive (2K1C-N). **Results:** Between the 4th–5th PSW, the mean daily intake of 0.23 M NaCl (ml/100 g body weight ± SEM) was higher in H-2K1C rats (14 ± 3; n = 6) compared to N-2K1C (5 ± 2; n = 8) and SHAM (4 ± 2; n = 6) groups ($p < 0.05$). No differences between groups were observed for other NaCl concentrations or PSWs. $NaHCO_3$ intake, water intake, urinary volume, and body weight did not differ among groups under any condition. MAP in H-2K1C rats (147 ± 6 mmHg; n = 6) was significantly higher than in N-2K1C (113 ± 3 mmHg; n = 8) and SHAM (103 ± 4 mmHg) groups ($p < 0.05$). **Conclusion:** These results suggest a transient rightward shift in the CRC for NaCl (i.e., increased palatability specifically for hypertonic NaCl) and selectivity for NaCl in sodium intake in 2K1C rats.

05. Pain and Nociception Pharmacology

05.001 **α-Terpineol-Loaded Nanosystems for the Treatment of Pain Induced by Sarcoma 180 Cells**. Poderoso VM[1], Amorim JCG[1], Araujo DS[1], Fagundes LS[1], Sá MEB[1], Silva VGO[1], Barreto MS[2], Gonçalves VSS[2], Lisboa JS[2], Pacheco PGS[2], Silva AS[2], Souza JB[2], Araújo ZS[3], Guimarães AG[4]. [1]LAFACE-UFS, Dept Pharmacy, Lab Clinical and Experimental Pharmacology, Brazil, [2]UFS, Graduate Program in Pharmaceutical Sciences, Brazil, [3]UFS-Lagarto, Graduate Program in Health Sciences, Brazil, [4]UFS, Dept Pharmacy, Brazil.

Introduction: Cancer pain is one of the most prevalent symptoms in individuals with advanced-stage disease. α-Terpineol stands out as a potential agent for the management of cancer pain. However, its physicochemical limitation may hinder its therapeutic application. Thus, nanotechnology emerges as a promising strategy for optimizing these properties, improving bioavailability, and enhancing systemic biological effects. **Objectives:** To develop α-terpineol- loaded nanocapsules (NCs) and investigate their therapeutic potential against cancer-induced pain in mice Sarcoma 180 tumor cells. **Methods:** α-Terpineol- loaded nanocapsules were developed using the preformed polymer interfacial deposition method and characterized in terms zeta potential, differential scanning calorimetry (DSC), and scanning electron microscopy (SEM). Cancer- related pain was evaluated in a mouse model of cancer-related pain induced by Sarcoma 180, through the analysis of spontaneous nociception and the simulation of cancer-associated allodynia. Statistical analyses were performed using GraphPad Prism® 8.0. The Shapiro-Wilk test and ANOVA with Tukey's post- hoc test were applied (statistical significance at $p < 0.05$). **Results:** The α -terpineol-loaded nanocapsules exhibited zeta potential (± 10 to ± 20 mV) within the ranges considered appropriate. DSC analysis indicated the effective incorporation of the monoterpene into the nanosystem. Scanning electron microscopy images confirmed the formation of spherical nanoparticles with a homogeneous distribution. Animals treated with nanocapsules containing α-terpineol showed a significant reduction in withdrawal reflexes associated with spontaneous nociception. Treatment at a dose of 25 mg/kg resulted in a marked decrease in nociceptive behavior ($p < 0.0055$ and $p < 0.0001$), while the 50 mg/kg dose exerted an even more pronounced antinociceptive effect, with high statistical significance in both comparisons ($p < 0.0001$). Similarly, nociception induced by non-noxious palpation was also attenuated by treatment with α-terpineol. The 25 mg/kg dose significantly reduced the number of withdrawal reflexes starting from the second assessment ($p < 0.001$) compared to the vehicle group. In turn, the 50 mg/kg dose produced a more intense and sustained analgesic effect throughout the entire experimental period, maintaining a consistent reduction in the nociceptive response compared to the vehicle group ($p < 0.0001$). **Conclusion:** The proposed method was effective in developing stable nanocapsules with suitable physicochemical properties loaded with α-terpineol. The resulting nanocapsule demonstrated robust and prolonged antinociceptive effects, reducing both spontaneous and palpation-induced nociception, with greater duration and magnitude compared to the free compound. **Acknowledgments:** We are grateful for the financial support from the National Council for Scientific and Technological Development (CNPq/Brazil) and the Coordination for the Improvement of Higher Education Personnel (CAPES/Brazil).

05.002 **Correlation Between Antinociceptive Effects Previously Observed** *in vivo* **and Opioid Receptor Interactions of α-Phellandrene: Insights From Molecular Docking And Dynamics**. Dias WA[1], Martins RYC[1], Sales SCS[1], Santos ALS[1],Gomes JGF[1], Barbosa BDS, Sousa DP[2], Almeida FRC[1] [1]UFPI, CCS, PPGFARM, Lab Pain Pharmacology, [2]UFPB, Dept Pharmacy, Federal University of Paraíba, Brazil.

Introduction: Cancer pain is one of the most debilitating symptoms associated with tumor progression and remains a major therapeutic challenge. Previous studies demonstrated that α-phellandrene, a naturally occurring monoterpene found in essential oils, exerts significant antinociceptive effects in experimental models of cancer pain. However, the molecular mechanisms underlying these effects remain poorly understood. **Objectives:** To investigate the interactions of α-phellandrene with μ, κ and δ opioid receptors through molecular docking and molecular dynamics simulations, aiming to provide mechanistic support for previously reported antinociceptive effects in a mouse model of cancer pain induced by Sarcoma 180. **Methods:** Previously reported pharmacological data demonstrated the antinociceptive activity of α-phellandrene in Sarcoma 180-bearing mice using Von Frey, spontaneous paw-licking, open-field and rota-rod tests. To investigate the molecular basis of these effects, molecular docking studies were performed using crystallographic structures of μ, κ and δ opioid receptors. Subsequently, 100 ns molecular dynamics simulations were carried out for α-phellandrene-receptor complexes, using morphine as a reference ligand. Structural stability was evaluated through root mean square deviation (RMSD), root mean square fluctuation (RMSF), secondary structure conservation and protein-ligand interaction analyses. **Results:** Previous *in vivo* studies demonstrated that α-phellandrene significantly reduced nociceptive responses at doses of 6.25, 12.5 and 25 mg/kg ($p<0.05$), without relevant motor impairment or signs of toxicity. Molecular docking predicted favorable binding of α-phellandrene to μ, κ and δ opioid receptors. Molecular dynamics simulations revealed stable accommodation of the monoterpene within the receptor binding pockets throughout the 100 ns simulations. RMSD and RMSF analyses indicated maintenance of complex stability and receptor structural integrity. Persistent hydrophobic interactions were observed with conserved residues, including Tyr, Phe, Ile, Met, Trp, His and Asn. The interaction profile showed similarities to that of morphine, supporting the participation of opioid signaling pathways in the antinociceptive effects previously observed experimentally. **Conclusion:** Molecular docking and molecular dynamics analyses provided mechanistic evidence supporting the interaction of α-phellandrene with μ, κ and δ opioid receptors. These findings offer a molecular explanation for previously reported antinociceptive effects and reinforce the potential of α-phellandrene as a promising scaffold for the development of novel analgesic agents for cancer-associated pain.

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05.004 **Study of the Cutaneous Safety and Antinociceptive Potential of Canabigerol-Based Creams**. Bazilio YS[1], Rezende B[1], Macario VSG[1], Guedes GN[1], Maia EP[1], Romana B[1], Oliveira L[2], Maluf D[2], Antunes F[3], Fontes FL[1], Montes GC[1] [1]IBRAG-UERJ, Roberto Alcântara Gomes Institute of Biology, Brazil, [2]UFPR, Dept Pharmacy, Brazil, [3]UENF-Darcy Ribeiro, Center for Agricultural Sciences and Technology, Brazil

Introduction: RDC No. 1.015/2026 of Anvisa expanded the use of dermatological formulations containing *Cannabis sativa* L. derivatives, increasing interest in studies investigating the safety and therapeutic potential of cannabinoids such as cannabigerol (CBG). **Objective:** To evaluate the cutaneous safety and antinociceptive activity of creams containing CBG in preclinical models of acute and chronic pain. **Methodology:** Experiments approved by CEUA/IBRAG/UERJ (No. 030/2023) were conducted in Wistar rats, while those approved by CEP (85230324.8.0000.5259) were performed in human tissue treated with creams containing CBG (0.3; 1 and 3%). As controls, cream without active ingredient (negative control), methyl salicylate 3%, and hydrocortisone 1% (positive controls) were used. The cutaneous irritative potential was evaluated in human ear skin cells using the MTT cell viability assay and histopathological analysis. Antinociceptive activity was investigated in two different experimental models: (i) Formalin test (n=9/group), in which 0.6 g of cream was applied to the animals' right hind paw before injection of 2.5% formalin (60 µL), with evaluation of the neurogenic (0–5 min) and inflammatory (15–45 min) phases; and (ii) neuropathic pain model induced by spinal nerve ligation (SNL), in which the surgical procedure induced mechanical and thermal hyperalgesia in animals after 7 days. Animals received daily treatment with vehicle cream or CBG (1 and 3%) for 14 days, and thermal and mechanical hyperalgesia were evaluated. At the end of treatment, spinal cord and brain tissues were collected for molecular biology analyses. **Results:** The MTT assay in human skin cells demonstrated absence of cutaneous irritability for the tested formulations. In the formalin test, CBG reduced reactivity in the neurogenic phase to 22.9 ± 4.5 s (1%) and 28.5 ± 7.1 s (3%) versus vehicle (60.4 ± 7.9 s). In the inflammatory phase, vehicle group values (187.4 ± 20.5 s) were reduced to 51.0 ± 7.1 s (0.3%), 109.4 ± 14.7 s (1%), and 111.4 ± 7.9 s (3%), comparable to positive controls (hydrocortisone: 55.4 ± 4.8 s; salicylate: 62.9 ± 12.8 s). In the chronic pain model, CBG 1% significantly increased thermal latency to 5.5 ± 1.3 s compared to 1.8 ± 0.2 s in the control group, demonstrating a consistent antinociceptive effect in different pain models. In mechanical hyperalgesia, from day 10 onward, the CBG 1% group showed progressive recovery, reaching 121.5 ± 13.5 g at day 21, whereas the control group reached only 100.7 ± 9.0 g at the same time point. **Conclusion:** Creams containing CBG showed no irritative potential in human skin cells and demonstrated significant antinociceptive effects in experimental models of acute and chronic pain.

05.005 **Synthetic Flavonoid Presents Antinociceptive Effects in a Diabetic Peripheral Neuropathy Model**. Dambros LV[1], Silva RD[1], Atuati SF[1,2], Oliveira SM[1,2] [1]UFSM-Santa Maria, Lab Neurobiology of Pain – Pain Research Group, Brazil; [2]USFM-Santa Maria, PPG Biological Sciences: Toxicological Biochemistry, Brazil

Introduction: Diabetic peripheral neuropathy (DPN) is one of the most prevalent chronic complications of diabetes mellitus, affecting sensory neurons and significantly impairing patients' quality of life through persistent pain and sensory dysfunction. Hyperglycemia-induced oxidative stress and neuroinflammation play central roles in the development and progression of DPN. Current pharmacological approaches are often limited by incomplete efficacy and adverse effects, reinforcing the need for safer and more effective therapeutic alternatives. Diosmetin, a flavonoid with recognised antinociceptive, anti-inflammatory, and antioxidant activities, has shown beneficial effects in experimental pain models. **Objective:** Evaluate the effect of diosmetin on nociceptive symptoms in an experimental model of streptozotocin-induced peripheral diabetic neuropathy in mice. **Methods:** Male Swiss mice (25–30g; Ethical approval #1834131025) received a single intraperitoneal administration of streptozotocin (STZ) (200 mg/kg) to induce type 1 diabetes mellitus, confirmed by elevated glucose levels. Body weight, food intake, and water consumption were monitored throughout the experimental period. On day 8 after streptozotocin injection, following the establishment of diabetic peripheral neuropathy, animals were treated with diosmetin (0.15 mg/kg; p.o.) and were subjected to a time-response curve analysis to evaluate its antinociceptive effect. Mechanical and cold allodynia were evaluated throughout the experimental period. Statistical analyses were performed using one or two-way ANOVA followed by appropriate post hoc tests. **Results:** STZ increased glucose levels on the 4th day after injection and induced mechanical and cold allodynia on the 8th day, characterising diabetic peripheral neuropathy. STZ-treated animals exhibited reduced body weight gain and increased food and water intake compared to baseline and vehicle-treated groups. Diosmetin (0.15 mg/kg, p.o) attenuated mechanical and cold allodynia throughout the evaluation period, suggesting protective effects against diabetic neuropathic pain, possibly related to antioxidant and anti-inflammatory mechanisms. **Conclusions:** Diosmetin reduced nociceptive manifestations in experimental diabetic peripheral neuropathy and may represent a promising pharmacological strategy for the management of painful diabetic neuropathy. **Financial support:** Coordenação de Aperfeiçoamento de Pessoal de Nível Superior — Brasil (CAPES), Finance Code: 001; Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul-FAPERGS; Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). We thank CNPq, PROBIC/FAPERGS-UFSM, CAPES/PROEX and PIBIC/CNPq-UFSM for their fellowship support.

05.006 **Evaluation of the Antinociceptive Activity of** *Cereus jamacaru* **DC.** (**Cactaceae**) **Roots**. Deus GO[1], Santos EE[2], Costa WK[3], Correia MTS[3], Souza TA[4], Abreu LS[5], Oliveira AM[2], Cibulski SP[2], Alves HS[1,2] [1]UEPB, CCBS, Dept. of Pharmacy, Brazil, [2]UEPB, PPG in Pharmaceutical Sciences (PPGCF), Brazil, [3]UFPE, CB, Dept. of Biochemistry, Lab Natural Products, Brazil, [4]IPeFarM-UFPB, Institute of Research in Drugs and Medicines, Brazil, [5]UFF, Institute of Chemistry, Brazil

Introduction: In the Brazilian semi-arid region, roots from *Cereus jamacaru* are used in folk medicine to treat inflammation, respiratory, and digestive disorders. Although the species is rich in secondary metabolites, biological records for components such as saponins remain scarce. **Objectives:** This study evaluated the phytochemistry profile and *in vivo* antinociceptive activity of a fraction of the roots from *C. jamacaru*. **Methods:** Roots were dried, pulverized, and macerated (ethanol:water 7:3) to obtain the crude hydroethanolic extract. The methanol-water fraction (MWF) was obtained through vacuum liquid chromatography and subjected to analysis by mass spectrometry (MS). Swiss mice received oral treatment with MWF (50, 100, or 200 mg/kg), saline, morphine, or indomethacin as positive control. Antinociceptive activity was assessed using acetic acid-induced abdominal writhing, formalin, and tail immersion tests. Data were analyzed using one-way ANOVA followed by Dunnett's test (neurogenic and inflammatory phases), ($p < 0.001$). **Results:** MS analysis of MWF fraction showed the presence of saponins. Oral treatment with MWF at the doses of 50, 100, and 200 mg/kg significantly reduced writhing by 27%, 35.3%, and 74.7%, respectively. In the formalin test, all doses reduced licking time in the first phase (38.6% to 62.7%), while the doses of 100 and 200 mg/kg were effective in the second phase (56.5% and 90% reduction). In the tail immersion test, the dose of 200 mg/kg increased tail-flick latency, comparable to that observed for morphine after 60 min. The antinociceptive effect of MWF was reversed by naloxone, but not by atropine, suggesting opioid system involvement. **Conclusion:** The methanol-water fraction of *C. jamacaru* roots exhibits potent central and peripheral antinociceptive activity mediated by the opioid system. These findings corroborate the traditional use of the species for pain relief and suggesting that saponins may contribute substantially to the observed activity, highlighting this species as a promising source for new analgesic agents.

05.007 **Cannabinoid Receptor 2 as a Potential Therapeutic Target in an Experimental Model of Nociplastic Pain**. Lopes JPV, Atuati SF, Assis ACP, Oliveira SM. UFSM, Pain Neurobiology Lab, Graduate Program in Biological Sciences: Toxicological Biochemistry, Brazil.

Introduction: Fibromyalgia is a chronic pain syndrome that affects 2–3% of the world's population. Fibromyalgia pain is accompanied by comorbidities such as anxiety, depression, and migraine, which negatively affect patients' quality of life, as it impacts daily activities and social interactions. Pregabalin, duloxetine, milnacipran and cyclobenzaprine are approved by the Food and Drug Administration for fibromyalgia treatment, but these therapies present limited efficacy and cause adverse effects that limit their use. Thus, to improve fibromyalgia management, it is necessary to develop new analgesic agents that are consistently effective and have fewer adverse effects. β-Caryophyllene is a sesquiterpene present in various plants such as cannabis (*Cannabis sativa*), black pepper (Piper nigrum), clove (Syzygium aromaticum), and hops (Humulus lupulus). It has demonstrated antinociceptive effects across various models of pathological pain. Since the cannabinoid β-Caryophyllene modulates pain, we evaluated its effects on nociceptive behaviours and comorbidities in a fibromyalgia-like nociplastic pain model in mice. **Methods:** To induce the fibromyalgia-like nociplastic pain model, reserpine (1 mg/kg) was injected subcutaneously once daily into the back of Swiss mice for three consecutive days. Plantar mechanical allodynia (von Frey test), muscle strength (grip strength test), and cold allodynia (acetone drops) were evaluated before reserpine administration (baseline) and on the fourth day after the first reserpine administration (baseline 2). After baseline 2, animals were orally treated with either vehicle (10 mL/kg), β-caryophyllene (100 mg/kg) or pregabalin (30 mg/kg; reference drug). Nociceptive behaviours were assessed from 0.5 to 6 hours after the treatments.The depressive-like behaviour was evaluated by the forced swimming test. The involvement of cannabinoid receptor 2 (CB2R) was evaluated using a CB2R inverse agonist (AM630, 1 mg/kg, intraperitoneal). **Results:** Reserpine-treated mice developed plantar mechanical allodynia, loss of muscle strength, cold allodynia, and depressive-like behaviour. β-caryophyllene reduced mechanical and cold allodynia from 0.5 to 2 hours and from 1 to 4 hours after its administration, with inhibitions of 100% and 89 ± 4%, respectively. β-caryophyllene also reduced the loss of muscle strength of mice at 1 and 2 hours after treatment, with an inhibition of 97 ± 7%, as well as the depressive-like behaviour by 90 ± 7%. AM630 (1 mg/kg, i.p.), a selective CB2 receptor inverse agonist, abrogated the antinociceptive effects of β-caryophyllene. **Conclusions:** β-caryophyllene has shown pharmacological potential to alleviate nociceptive symptoms and comorbidities in the fibromyalgia-like nociplastic pain model, possibly through modulation of the CB2R. It has the potential for developing new analgesic drugs, particularly for treating pain and depressive-like symptoms, as those observed in fibromyalgia.

05.008 **Evaluation of the Antinociceptive Effect of Hydroalcoholic Extracts from the Leaves and Fruits of** *Libidibia ferrea* (**Mart. ex Tul.) L. P. Queiroz 2009 in a Formalin-Induced Pain Model**. Oliveira, JLS[1]; Barros, AG[1], Menezes, DP[2]; Almeida, FRC[1], Dittz, D[2] [1]UFPI, Pain Pharmacology Lab, Brazil; [2]UFPI, Antineoplastic Pharmacology Lab, Brazil.

Introduction: Pain is a major public health issue, and current treatments present limitations and adverse effects, encouraging the search for natural therapeutic alternatives. Libidibia ferrea, native to the Brazilian Caatinga and Cerrado, is traditionally used to treat inflammatory and painful conditions. This study evaluated the acute and subchronic antinociceptive effects of hydroalcoholic extracts from the leaves (EHFL) and fruits (EHFR) of L. ferrea in a murine nociception model, as well as hematological alterations after subchronic treatment. **Methodology:** Extracts were provided by Phytobios Pesquisa, Desenvolvimento e Inovação LTDA, obtained by exhaustive maceration in 96% ethanol and concentrated at 45 °C (SisGen A8B0495). Female Swiss mice (20–40 g) received intraplantar injection of 2% formalin. Mechanical nociceptive thresholds were assessed using the Von Frey test at 10, 60, 120, and 180 min. Animals (n=6/group) received EHFL or EHFR (100, 200, or 300 mg/kg, p.o.), morphine (10 mg/kg, s.c.), pregabalin (10 mg/kg, p.o.), or vehicle. In the subchronic protocol, treatments were administered daily for 14 days. Naloxone (2 mg/kg, i.p) was used to evaluate opioid pathway involvement. Hematological analyses were performed at the time of euthanasia. On the 14th day of the subchronic treatment, blood samples were collected via cardiac puncture from anesthetized animals (CEUA/UFPI 736/22). Data were analyzed by ANOVA, followed by Tukey's test ($p<0.05$). **Results:** EHFL and EHFR significantly increased nociceptive thresholds from 60 to 180 min in the acute protocol ($p<0.05$). The 200 and 300 mg/kg doses showed the strongest effects, similar to morphine and pregabalin. In the subchronic protocol, all extracts promoted sustained antinociceptive effects compared with the negative control ($p<0.05$). Naloxone did not significantly reverse the effects of the extracts, unlike morphine, suggesting no relevant opioid pathway involvement. Hematological analysis showed a significant increase only in platelet count (25.17%, $p<0.05$) in the EHFR 200 mg/kg group compared with Sham. **Conclusion:** L. ferrea extracts demonstrated acute and subchronic antinociceptive effects without significant opioid pathway involvement or hematological alterations in erythrocytic and leukocytic lineages.

05.009 **Antinociceptive Effects of MSCs and MSC-EVs are Associated with CXCR2 Pathway in Neuropathic Pain Mice Model**. Velozo ACL[1], Opretzka LC[2], Jesus MVAC[1], Cruz ABO[1], Santos MGS[3], Santos GC[3], Soares MBP[3], Villarreal CF[1]. [1]UFBA, School of Pharmacy, Salvador, Brazil; [2]SENAI-CIMATEC, Salvador, Brazil; [3]Fiocruz-BA, Salvador, Brazil

Introduction: Neuropathic pain is a chronic disorder related to central sensitization and neuroimmune mechanisms. Cytokines and chemokines signaling plays a key role in the development and resolution of this condition. Mesenchymal stem cells (MSCs) and their extracellular vesicles (MSC-EVs) are known to regulate inflammatory and neuroimmune responses, however the mechanisms underlying their effects on some chemokine-mediated mechanisms in neuropathic pain remain unknown. This study investigated the effects of MSC and MSC-EVs on mechanical and thermal hypersensitivity, motor impairment and physical performance in neuropathic mice, and examined the involvement of the CXCL1/CXCR2 pathway to their antinociceptive effects.. **Methods:** Neuropathic pain was induced in C57BL/6 mice (CEUA IGM/FIOCRUZ 020/2022) by partial sciatic nerve ligation. On day 7, the animals received a single intravenous administration of MSCs (1×10^6 cells) or MSC-EVs produced by 1x106 cells (CEP HUCFF/UFRJ 519.235). Mechanical and thermal sensitivity were evaluated using the von Frey and Hargreaves tests, respectively. Motor impairment was assessed with rota-rod test, while functional and physical performance were analyzed by treadmill testing based on running distance and duration. To explore the mechanisms involved, SB225002 (a CXCR2 antagonist), 1 mg/kg, i.p. was administered at the time of maximal antinociceptive effect, followed by reassessment of nociceptive thresholds. Serum CXCL1 concentrations were measured on days 21 and 60 using ELISA. **Results:** Neuropathic were established by the development of persistent mechanical and thermal hypersensitivity. A single administration of MSC or MSC-EVs was able to induce a progressive and sustained of attenuation mechanical and thermal hypersensitivity ($p<0.05$). Neuropathy-induced loss in treadmill performance was reversed by both treatments ($p<0.05$), without motor impairment. Pharmacological blockade of CXCR2 with SB225002 partially reduced the antinociceptive effects of MSC and MSC-EVs ($p<0.05$), indicating that CXCR2 pathway contributes to their antinociceptive mechanism. At 21 days post-neuropathy, serum CXCL1 levels did not differ among groups. At 60 days, only neuropathic mice showed elevated CXCL1 levels ($p<0.05$), possibly driven by persistent nerve injury and chronic inflammation. **Conclusion:** Both MSCs and MSC-EVs effectively reversed sensory hypersensitivity and functional impairment in an experimental neuropathic pain without causing motor deficits. Improved physical performance supports their translational potential. The partial loss of analgesia after CXCR2 antagonism suggests that chemokine signaling contributes to their mechanism of action. CXCR2 activation may also involve other ligands, including CXCL2/3 or IL-8, as well as local paracrine signaling in pain pathways. Together, these findings expand the understanding of MSC and MSC-EV mechanisms and support MSC-EVs as a promising cell-free therapy for neuropathic pain.

05.010 **Antihyperalgesic and Antinociceptive Effects of Delta-3-carene on Persistent Inflammation Induced by Complete Freund's Adjuvant in Mice Models**. Venâncio GSO, Lossavaro PKMB, Machado LL, Diniz FS, Toffoli-Kadri MC, Silva-Filho SE. UFMS, Faculty of Pharmaceutical Sciences, Food and Nutrition, Lab Pharmacology and Inflammation, PPG in Pharmaceutical Sciences, Brazil.

Introduction: Delta-3-carene (CAR) is a monoterpene, one of the main components of pine essential oil, which has demonstrated promising anti- inflammatory activity. Inflammation is a complex biological response of the body to harmful stimuli, such as infections, injuries, or chemical agents. Classic signs of inflammation include heat, redness, edema, and pain, with potential loss of function, mainly in chronic inflammation. In this context, non-steroidal anti-inflammatory drugs remain the mainstay of the pharmacological therapy of inflammatory diseases. However, these drugs have a high incidence of adverse effects, such as gastrointestinal lesions and cardiovascular effects, limiting this therapeutic approach. **Objectives:** The present study aimed to investigate the effects of CAR on edema formation and mechanical hyperalgesia in the Complete Freund's Adjuvant (CFA)-induced persistent inflammation in mice. **Methods:** The experimental procedures were approved by the Animal Ethics Committee of UFMS (protocol number 1.288/2023). Male Swiss mice were utilized in this study. At time zero, 20 µL of CFA was injected into the mice's right hind paw (intraplantar). The animals were orally treated with CAR (50 mg/kg), dexamethasone (reference drug), or vehicle (control) (n=6 animals/group) 24 h after the injection of CFA, and once a day, for 21 days. Mechanical hyperalgesia and paw edema were measured 6, 11, 16, and 21 days after CFA injection. The evaluation of mechanical hyperalgesia was performed using a digital analgesimeter (Von Frey), and the edema formation was measured with a plethysmometer, expressed as the percentage of reduction in edema in treated mice compared to that in the control mice ($p < 0.05$, ANOVA, Tukey's test). **Results:** CAR treatment at a dose of 50 mg/kg reduced mechanical hyperalgesia and edema formation at all evaluated time points. As expected, dexamethasone reduced both of the analyzed parameters at all evaluated time points. **Conclusion:** In conclusion, CAR presented anti- inflammatory activity, reducing the edema formation and mechanical hyperalgesia. CAR is a promising candidate for treating chronic inflammation. However, further studies are needed to clarify its molecular targets and enable its clinical application. **Financial support:** CAPES, CNPq, FUNDECT.

05.011 **Antinociceptive Potential and Skin Irritation Profile of Ointments Containing Cannabis Extract**. Guedes GN[1], Macario VSG[1], Rezende B[1], Bazilio YS[1], Maia EP[1], Cunha LG[1], Romana B[2], Montes GC[1] [1]IBRAG-UERJ Lab Pharmacology and Psychology; [2]UERJ Dept Histology and Embryology; [3]UFPR, Dept Pharmacy, Brazil.

Introduction: RDC No. 1,015/2026 from Anvisa increased interest in developing topical formulations containing *Cannabis sativa* L. derivatives due to the therapeutic potential of cannabinoids (CBD and CBG) and root compounds. **Objective:** To evaluate the skin safety and antinociceptive activity of ointments containing CBD, CBG, or Cannabis root extracts in acute and chronic pain models. **Methods:** Approved by CEUA/IBRAG/UERJ (030/2023) and CEP (85230324.8.0000.5259). Wistar rats (n=10/group) received 2.5% formalin (60 µL, intraplantar) in the right hind paw, and neurogenic (0–5 min) and inflammatory (15–45 min) phases were recorded. Thirty minutes before, 0.6 g of CBD (1 and 1.67%), CBG (1%), Cannabis root (1%), hydrocortisone 2% (positive control), or vehicle ointments were topically applied. For carrageenan-induced mechanical/thermal hyperalgesia (1%; 100 µL, intraplantar), hyperalgesia was confirmed after 2 h, followed by treatment with CBD (1 and 1.67%), CBG 1%, hydrocortisone 2%, or vehicle, with evaluations up to 180 min (mechanical: Randall–Selitto; thermal: paw immersion in water at 46 °C). Skin irritability was evaluated in human skin treated with formulations containing CBD 1.67%, placebo, methyl salicylate, and hydrocortisone, using PBS and 5% SDS as negative and positive controls, respectively. Cell viability was determined by MTT assay. **Results:** In the formalin test, CBD reduced neurogenic-phase reactivity from 59.7 ± 5.7 s (vehicle) to 21.4 ± 3.7 s (1%) and 28.0 ± 5.8 s (1.67%). CBG (1%) reduced reactivity to 18.6 ± 4.5 s, and Cannabis root (1%) to 23.4 ± 5.0 s. In the inflammatory phase, vehicle reactivity (131.7 ± 22.7 s) decreased to 61.4 ± 19.3 s (CBD 1%), 5.7 ± 3.1 s (1.67%), 78.5 ± 13.0 s (CBG 1%), and 51.4 ± 3.8 s (Cannabis root 1%). In the carrageenan model, CBG 1% increased the mechanical threshold from 135 min onward, without relevant thermal effects, whereas Cannabis root showed significance from 240 min in thermal evaluation. CBD (1 and 1.67%) showed no consistent effect versus vehicle. In the irritability test, CBD 1.67% significantly increased cell viability versus PBS, indicating low skin irritability. **Conclusion:** Topical formulations containing Cannabis derivatives showed antinociceptive potential without inducing skin irritation.

05.012 **Reserpine-Induced Fibromyalgia Model in Swiss Mice: Behavioral Characterization and Sex-Related Difference**. Rech KS, Camargo KGA, Brito MSC, Werner MFP UFPR, Gastrointestinal and Pain Lab., Dept Pharmacology, Brazil

Introduction: Fibromyalgia is a complex chronic pain syndrome characterized by widespread musculoskeletal pain, fatigue, sleep disturbances, and mood disorders. Its pathophysiology is associated with central sensitization and an imbalance of monoaminergic neurotransmitters. Given the limited efficacy of currently available pharmacological treatments, reliable experimental models are essential for investigating novel therapeutic approaches. The reserpine-induced fibromyalgia model reproduces key clinical features of the disease by inducing central monoamine depletion. **Objectives:** To standardize the reserpine-induced fibromyalgia model in male and female Swiss mice by characterizing the development and persistence of mechanical and cold allodynia, heat hyperalgesia, muscle strength impairment, anhedonia-like behavior, and by determining whether these outcomes differ between sexes. **Methods:** Male and female Swiss mice received reserpine (1 mg/kg, s.c.) once daily for three consecutive days. Mechanical allodynia was assessed using the von Frey test on days 4, 9, and 14, cold allodynia using the acetone test on days 4 and 14, and heat hyperalgesia using the hot plate test on days 6 and 12. Muscle strength was evaluated using the Kondziela inverted screen and weight-lifting tests on days 6 and 12, respectively. Motivational behavior and self-care were assessed using the sucrose splash test on day 9. Parametric data were analyzed using one-way repeated-measures ANOVA followed by Bonferroni's post hoc test, whereas nonparametric data were analyzed using the Mann–Whitney test. **Results:** Reserpine administration produced a significant and persistent reduction in mechanical withdrawal thresholds and cold nociceptive latency in both sexes. On day 14, the von Frey test revealed a 90.36% reduction in mechanical threshold in females (basal: 1.017 ± 0.095; reserpine day 14: 0.098 ± 0.048) and a 70.61% reduction in males (basal: 1.516 ± 0.178; reserpine day 14: 0.446 ± 0.104) compared with baseline values. In the acetone test, reserpine-treated animals exhibited increased in the percentage of response to acetone, which was more pronounced in females (control day 14: 0%; reserpine day 14: 90%) than in males (control day 14: 0%; reserpine day 14: 66.66%). No statistically significant differences were observed in muscle strength (Females – control: 5.00 (3.00-5.00), reserpine: 5.00 (3.33-5.00); Males – control: 2.00 (1.66-2.33), reserpine: 3.67 (2.33-5.00) or grooming time on the sucrose splash test (Females – control: 120.09 ± 15.39 s, reserpine: 104.91 ± 15.39 s; Males – control: 99.44 ± 8.13 s; reserpine: 118.03 ± 14.94 s). **Conclusion:** The reserpine-induced monoamine depletion model in Swiss mice proved to be a robust and reproducible model of fibromyalgia-like pain. Although no changes in muscle strength or self-care behavior were detected under the present experimental conditions, the model induced persistent nociceptive hypersensitivity. Moreover, female mice exhibited greater pain sensitivity than males, reinforcing the translational relevance of sex-dependent differences in fibromyalgia. **Human or Animal Research Ethical Committee Number**: Animal Ethics Committee of the Federal University of Paraná (CEUA/UFPR), Protocol No. 1638. **Financial support:** Coordination for the Improvement of Higher Education Personnel (CAPES).

05.013 **Comparative Study of Monoterpenes in the Treatment of Fibromyalgia in Murine Models: A Literature Review**. Araújo RBC[1], Oliveira, JLS[1], Jorge SAS[2]. [1]UFPI, Pain Pharmacology Lab, Brazil. [2]UFPI, Organic Geochemistry Lab, Brazil.

Introduction: Fibromyalgia is a nociplastic pain syndrome characterized by widespread musculoskeletal pain, fatigue, sleep disturbances, and cognitive impairment. Because conventional therapies often provide limited symptom relief, monoterpenes have emerged as promising compounds due to their analgesic, anti-inflammatory, antioxidant, and neuroprotective properties. **Objectives:** To compare the pharmacological evidence on the main monoterpenes investigated in murine models of fibromyalgia and experimental models of chronic pain related to its pathophysiology. **Methods:** A narrative literature review was conducted using PubMed, Scopus, ScienceDirect, Frontiers, and Google Scholar. Publications from January 2021 to December 2025 were retrieved using the descriptors *fibromyalgia*, *monoterpenes*, *linalool*, *geraniol*, *citronellol*, *limonene*, *menthol*, *chronic pain*, *nociception*, *mice*, *and murine model*, combined with the Boolean operators AND and OR. A total of 487 records were identified. After removal of 119 duplicates, 368 studies were screened by title and abstract; 321 were excluded for not meeting the eligibility criteria. The remaining 47 full-text articles were assessed, and 28 studies were included in the qualitative analysis. Eligible studies comprised original investigations in murine models of fibromyalgia and preclinical studies evaluating the pharmacological effects of monoterpenes in chronic pain models. **Results:** The selected studies showed that reserpine-, repeated acidic saline-, and repeated cold stress-induced murine models are the most frequently used for preclinical fibromyalgia research. Among the evaluated compounds, **linalool** and **geraniol** presented the strongest evidence in murine fibromyalgia models, reducing mechanical hyperalgesia and pain-related behavioral alterations. In complementary chronic pain models, **citronellol, menthol**, and **limonene** exhibited antinociceptive and anti-inflammatory effects associated with modulation of TNF-α, IL-1β, IL-6, oxidative stress, and TRP channels. Collectively, these findings indicate that monoterpenes target mechanisms involved in central sensitization and neuroinflammation. **Conclusion:** Current preclinical evidence supports the pharmacological potential of monoterpenes as promising therapeutic candidates for fibromyalgia. Linalool and geraniol showed the most consistent evidence in murine models, while citronellol, menthol, and limonene demonstrated relevant effects in experimental chronic pain models. Further preclinical and clinical studies are required to confirm their efficacy, safety, and mechanisms of action. **Financial support:** Institutional Scientific Initiation Program of the Federal University of Piauí (ICV/UFPI).

05.014 **Synthetic Flavonoid as a Therapeutic Alternative for the Treatment of Chemotherapy-Induced Neuropathic Pain**. Dias R, Serafini PT, Atuati SF, Oliveira SM UFSM Pain Neurobiology Lab Graduate Program in Biological Sciences: Toxicological Biochemistry, Brazil.

Introduction: Patients with cancer may experience pain from multiple factors, including tumour progression, surgical procedures, or adverse effects of antineoplastic therapies. Pain from these treatments can lead to discontinuation of therapy and adversely affect patients' overall health and quality of life. Cisplatin is a chemotherapeutic agent widely used to treat metastatic solid tumours. Despite its antitumour efficacy, cisplatin can induce neurotoxicity, resulting in peripheral neuropathy, characterised by burning pain, spontaneous/continuous pain, and hypersensitivity to mechanical and thermal stimuli, which compromises patients' quality of life. In clinical practice, Duloxetine is prescribed to alleviate chemotherapy-induced peripheral neuropathy. However, its therapeutic benefits remain limited, justifying the need to investigate new treatment strategies. Natural products represent an important source of potential therapeutic agents. Diosmetin is a flavonoid found in natural plant products and is also chemically synthesised. **Objectives:** Since systemic diosmetin has been shown to attenuate neuropathic pain in experimental models, we investigated its effects in cisplatin-induced neuropathy in mice. **Methodology:** We used male C57BL/6 mice (approved by the Institutional Animal Care and Use Committee; ethical approval #7706310124) that received cisplatin (0.23 mg/kg, intraperitoneal) every 48 hours for 10 days. On the 11th day, mice were treated with diosmetin (0.15 mg/kg, orally by gavage) or duloxetine (30 mg/kg, orally by gavage). The nociceptive parameters evaluated were mechanical allodynia, muscle strength, and thermal hyperalgesia. In addition, we assessed potential adverse effects, including alterations in hepatic (AST and ALT) and renal (urea and creatinine) biomarkers. **Results:** Cisplatin induced mechanical allodynia, heat hyperalgesia, and muscle strength loss on day 11 after the first cisplatin administration. Diosmetin reduced mechanical allodynia from 0.5 to 4 h after treatment, with inhibition of 93.17 ± 8.29%, reduced heat hyperalgesia at 1 and 2 h after treatment, reaching 100% inhibition, and attenuated muscle strength loss from 1 to 4 h, when compared with the cisplatin + vehicle group. Duloxetine, the reference drug, also reduced the mechanical allodynia from 1 to 4 hours after treatment. Diosmetin did not cause alterations in the measured hepatic and renal biomarkers, indicating a safe profile for diosmetin (Serafini et al., Mol. Neurobiol., v. 63, p. 519, 2026; https://doi.org/10.1007/s12035-026-05785-0). **Conclusion:** The flavonoid diosmetin was effective in reducing cisplatin-induced pain behaviours in mice, suggesting a potential alternative for treating cisplatin-induced neuropathic pain. **Acknowledgements:** FAPERGS, CAPES, CAPES/PROEX, CNPq; Molecular Neurobiology (<https://doi.org/10.1007/s12035-026-05785-0>). PIBIC/CNPq-UFSM.

05.015 **Effects of the PPARγ Agonist TZD-D3 on Joint Degeneration and Pain in a Monoiodoacetate (MIA)-Induced Osteoarthritis Model**. Goldoni RC[1], Goldoni FC[1], Eisendecker HI[1], Malburg CC[2], Antunes AT[2], Pereira MES[1], de Campos-Buzzi F[1], Santin JRS[1], da Costa R[3], Quintão NLM[1] [1]Univali, PPG in Pharmaceutical Sciences, [2]Univali, Dentist Course, Santa Catarina, Brazil, [3]UFRJ, School of Pharmacy, RJ, Brazil.

Introduction: Osteoarthritis (OA) is a chronic progressive joint disease characterized by cartilage degeneration, subchondral bone remodeling, synovitis and persistent pain. Current treatments are mainly symptomatic and may cause adverse effects during prolonged use. PPARγ, a nuclear receptor involved in inflammatory and immune regulation, has emerged as a potential therapeutic target. **Objective** This study aimed to evaluate the effects of the PPARγ partial-agonist TZD-D3 in a murine model of OA. **Methods:** C57BL/6 mice (8-12 weeks) were used (CEUA approval: 01/26). OA was induced by a single 10 µL intra-articular injection of monoiodoacetate (MIA; 0.1 mg/mL) into either the left or right knee joint according to a randomized design. Mechanical sensitivity was assessed in both hind paws, from days 0 to 25 after MIA injection to establish baseline responses and also characterize the development of mechanical hypersensitivity. Treatment was started [TZD-D3 (0.1-1 mg/kg, i.p.); Diclofenac (30 mg/kg, p.o.) or vehicle (10 mL/kg, i.p.)], once a day for 21 consecutive days. The mice behaviors were assessed using the von Frey filaments and automated analysis performed by Blackbox One (BB). **Results:** Mechanical hypersensitivity became evident from day 15 after MIA injection. In the last von Frey assessment, the control group showed significantly reduced paw withdrawal threshold compared with the vehicle group ($p<0.0001$). Diclofenac, used as a positive control, did not significantly change the mechanical withdrawal threshold compared with the control group ($p=0.50$). However, TZD-D3 (1.0 mg/kg) reduced the mechanical hypersensitivity compared with the control group ($p=0.048$). Paw pressure and luminance parameters obtained using the BB, reflecting the force exerted on the animal's supporting surface, did not differ significantly among groups. Ethogram-based behavioral analysis revealed that the TZD-D3 (1 mg/kg) showed qualitative preservation of locomotor activity and rearing behavior compared with the control group. **Conclusion:** MIA induced mechanical hypersensitivity and behavioral alterations. TZD-D3 reduced the mechanical hypersensitivity and also changed the locomotor activity and rearing, suggesting preservation of locomotor function and exploratory behavior. Further experiments are needed to investigate the mechanisms underlying TZD-D3 activity, but these findings suggest that the PPARγ agonist may represent a potential therapeutic alternative for OA. **Acknowledgments:** UNIVALI, CAPES, CNPq, FAPESC, CIEnP-INOVAMED.

05.016 **Network Pharmacology: Potential Therapeutic Targets of Melittin in Chronic Neuropathic Pain**. Teixeira RMS[1], Boaventura de Oliveira AM[1], Almeida TC[1], Sant'Anna MB[1], De Franco M[2], Picolo G[1]. [1]IBu, Lab Pain and Signaling, São Paulo, Brazil; [2]Pasteur Institute, Diagnostic Section, São Paulo, Brazil

Introduction: Chronic neuropathic pain affects approximately 30% of adults worldwide. Current treatments show limited efficacy and significant adverse effects, highlighting the need for novel therapeutic targets. Melittin, the principal peptide of honeybee venom, has shown potential in chronic pain modulation, although its molecular mechanisms remain poorly understood. Network pharmacology offers an integrative computational strategy to identify drug targets, protein interactions, and signaling pathways associated with complex diseases. **Objectives:** The aim of this work was to identify molecular targets, hub genes, and signaling pathways involved in melittin-mediated modulation of chronic neuropathic pain as a broad disease category, without stratification according to specific etiology or anatomical origin through integrated network pharmacology and functional enrichment analyses. **Methods:** Melittin-associated targets were obtained from PubChem and predicted using PharmMapper, followed by human gene annotation through UniProt. Chronic neuropathic pain-related genes were retrieved from GeneCards and Cortellis. Shared targets were identified using Venn analysis. Protein–protein interaction (PPI) networks were generated with STRING and visualized in Cytoscape, while CytoHubba was used to determine hub genes based on node degree. GO and KEGG enrichment analyses were performed using PANTHER and ShinyGO 0.85 ($p < 0.05$). **Results:** A total of 81 overlapping genes associated with melittin and chronic neuropathic pain were identified. GO enrichment analysis revealed significant biological processes related to cell death, responses to external and chemical stimuli, programmed cell death, and regulation of cell migration, the most significant term had an 1.0×10^{-21}. Enriched cellular components included the extracellular space, extracellular region, vesicles, and secretory granules, with FDR values as low as 9.0×10^{-12}. Molecular function analysis showed enrichment in protein kinase activity, phosphotransferase activity, enzyme binding, and protein tyrosine kinase activity, with FDR values as low as 8.0×10^{-12}. **Conclusion:** This study identified genes and enriched pathways potentially involved in melittin-mediated modulation of chronic neuropathic pain. The findings suggest convergence on kinase signaling, immune activation, apoptosis, and neuronal survival pathways, supporting melittin as a multi-target therapeutic candidate capable of modulating inflammatory and nociceptive mechanisms in chronic neuropathic pain. **Financial Support**: Fapesp 2013/07467-1 (CETICS PROGRAM), CAPES, Butantan Foundation and CNPq.

05.017 **Protease Activated Receptor 2 Mediates the Migraine-Like Pain in a Nociplastic Pain Model**. Mendes, TO[1], Perazzio, ACA[1], Becker, G[1], Fialho, MFP[2], Brum, ES[3], Lopes, JPV[1], Oliveira, SM[1] [1]UFSM, Pain Neurobiology Lab, Graduate Program in Biological Sciences: Toxicological Biochemistry, Centre of Natural and Exact Sciences, Brazil; [2]New York University, College of Dentistry, Dept Molecular Pathobiology, Pain Research Center, United States of America; [3]UFRGS, NeuPain, Dept Biochemistry, Institute of Basic Health Sciences, Brazil,

Introduction: Fibromyalgia is a complex clinical condition that affects approximately 2 to 3% of the world's population and is characterised by chronic widespread pain of nociplastic origin, as well as symptoms such as loss of muscle strength and allodynia upon touch; patients also report a high prevalence of migraines, which significantly compromise the life quality of patients. Despite its clinical impact, the underlying mechanisms remain poorly understood and underexplored. Mast cells are increasingly recognised as neuroimmune modulators that promote nociception by releasing mediators such as tryptase, which activate the protease-activated receptor 2 (PAR2) in sensory neurons. **Objectives:** This study investigated the involvement of mast cell tryptase and PAR2 activation in the migraine-like pain in a nociplastic pain model in mice. **Methods:** Periorbital mechanical allodynia (PMA), an experimental correlate of migraine-like pain, was induced in male C57BL/6 mice (ethics protocol #1472311023) using reserpine (1 mg/kg, subcutaneously, once daily for 3 days) and assessed using Von Frey filaments. The involvement of mast cell tryptase and PAR2 was investigated using pharmacological approaches. Mast cells were depleted using an escalating-dose protocol of compound 48/80 (0.5–4 mg/kg, i.p., twice daily for 4 days). Tryptase was inhibited with nafamostat (10 mg/kg, p.o.), and PAR2 was antagonised with AZ3451 (60 µg/kg, i.p., PAR2 negative allosteric modulator). **Results:** PMA was observed in mice on day 4 following the first reserpine administration. The mast cell depletion with compound 48/80 prevented the development of reserpine-induced PMA by 92.8 ± 18.5% (*$p < 0.05$). Consistently, inhibition of mast cell tryptase with nafamostat, as well as PAR2 antagonism with AZ3451, significantly attenuated reserpine-induced PMA Nafamostat reduced allodynia from 1 to 3 h after its administration, with an inhibition of 71.0 ± 5.7% at 2 h (*$p < 0.05$), whereas AZ3451 reduced allodynia by 27.4 ± 8.0% at 2 h (*$p < 0.05$). **Conclusions:** Our pharmacological findings suggest that migraine-like pain in a reserpine-induced nociplastic pain model involves mast cell mobilisation and tryptase release, leading to PAR2 activation. Thus, PAR2 signalling seems to be a promising therapeutic target, opening new avenues for developing treatments aimed at managing migraine-related symptoms in fibromyalgia. Acknowledgements: UFSM, CNPq, FAPERGS, CAPES/PROEX. **Financial support**s: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior — Brasil (CAPES/PROEX, process #88881.171656/2025-01; Grant AUXPE #3119/2025) – Finance Code 001; Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul – (FAPERGS #25/2551-0000849-2; E. S. Brum); Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq; Grant #309404/2023–1, S.M.O.; Grant #152071/2024-5, G.B.). We thank CAPES (Grant #88887.280173/2026-00, Oliveira, T.M.; Grant #88887.015792/2024-00, Perazzio A.C.) and CNPq for their fellowship support.

05.018 **Nanosystems Containing α-Terpineol in the Treatment of Tumor-Induced Cancer Pain**. Silva AS[1], Gonçalves VSS[1], Souza JB1, Pacheco PGS[1], Barreto MS[1], Lisboa JS[1], Araújo ZS[2], Poderoso VM[3], Silva VGO[3], Sá MEB[3], Fagundes LS[3], Araujo DS[3], Amorim JCG[3], Guimarães AG[4]. [1]UFS, Graduate Program in Pharmaceutical Sciences, Brazil, [2]UFS, Graduate Program in Health Sciences, Lagarto Campus, Brazil, [3]LAFACE-UFS, Dept Pharmacy, Lab Clinical and Experimental Pharmacology, Brazil, [4]UFS, Dept Pharmacy, Brazil.

Introduction: Cancer pain is a complex and debilitating condition, often associated with tumor progression and a reduced quality of life for patients. In this context, α-terpineol has demonstrated antinociceptive potential in experimental models, making it a promising alternative for the development of new therapeutic strategies in the management of cancer-related pain. **Objective:** To develop nanocapsules (NCs) loaded with α-terpineol and evaluate their effects on cancer-related pain induced by Sarcoma 180 tumor cells in mice. Method: Nanocapsules loaded with α-terpineol were developed using the interfacial deposition method in a preformed polymer and characterized in terms of particle size, pH, polydispersity index (PDI), content, and encapsulation efficiency. Antinociceptive activity was evaluated in a Sarcoma 180 cell-induced cancer pain model by measuring mechanical hyperalgesia with an electronic analgesimeter, performed before induction (day 0), on day 8 to confirm hyperalgesia, and subsequently every other day starting on day 9 through day 14. Data were analyzed using GraphPad Prism® 8.0 and expressed as mean ± standard error of the mean; an ANOVA test with Tukey's post-hoc test was applied, and statistical significance was set at $p < 0.05$. **Results:** The unloaded nanocapsules (162.06 ± 183.93 nm) and the nanocapsules loaded with α-terpineol (160.70 ± 170.20 nm) exhibited appropriate mean particle sizes and physicochemical parameters consistent with stable nanoscale systems. pH values for NC with α-terpineol (6.41 and 6.93) were within the ranges considered appropriate. In the PDI analysis, after 90 days, a higher degree of particle coalescence was observed, indicating time-dependent variations in the system's stability. The α-terpineol content and encapsulation efficiency were 70.9% and 96.6%, respectively. The nanocapsules containing α-terpineol at doses of 25 and 50 mg/kg significantly reduced mechanical hyperalgesia by 50.3% and 63.5%, respectively. Notably, the 50 mg/kg dose exhibited the greatest antinociceptive efficacy, maintaining reductions in hyperalgesia throughout the 6-hour evaluation period. **Conclusion:** The proposed method was effective in producing stable nanocapsules containing α-terpineol with suitable physicochemical properties. The nanostructured system exhibited a significant and prolonged antinociceptive effect, reducing both spontaneous and evoked nociception, and demonstrated greater intensity and duration of action compared to free α-terpineol.

05.019 **Mitochondrial Aldehyde Dehydrogenase-2 and 4-Hydroxynonenal Mediates Morphine Analgesic Tolerance and Hyperalgesia via TRPA1 Activation**. Pennachioni NP[1,2], Hosch NG[1], Martins BB[1], Silva GSA[1], Troitiño VC[1,2], Dallazen JL[1,3], Kiataki LGS[1,3], Andersson D[4], Bevan S[4], Zambelli VO[1,3]. [1]IBu. Pain and Signaling Lab, IBu, São Paulo. [2]University of Sao Paulo, Interunits Biotechnology Postgraduate Program. [3]Kings College London, Wolfson Sensory, Pain and Regeneration Centre, [4]IBu, Centre of Excellence in New Target Discovery, São Paulo.

Introduction: Long-term morphine treatment is limited by opioid-induced hyperalgesia (OIH) and tolerance. Evidence suggests that opioid-induced oxidative stress leads to reactive aldehyde 4-hydroxynonenal (4-HNE) accumulation which can activate the transient receptor potential ankyrin 1 (TRPA1) ion channel. Aldehyde dehydrogenase-2 (ALDH2), a mitochondrial enzyme that detoxifies 4-HNE, regulates inflammatory and neuropathic pain states. Here we investigated if ALDH2-4-HNE-TRPA1 axis contributes to morphine-induced adverse effects using genetic, pharmacological and cellular gain and loss of function approaches. **Methods:** Wild-type (WT), ALDH2 inactivating point mutation (ALDH2*2), and Trpa1 knockout (Trpa1-/-) mice received morphine (10 mg/kg/day, subcutaneously, s.c.) for 5 or 10 days, with or without Alda-1, an ALDH2 positive allosteric modulator (16 mg/kg/day, s.c., osmotic pump), or HC-030031, TRPA1 antagonist (1, 3, 10µg, intrathecally), 30min before morphine. OIH was assessed using von Frey filaments, and analgesic tolerance was evaluated using hot plate and tail immersion tests. Dorsal Root Ganglia (DRG) were analyzed by Western blot for 4-HNE adducts and calcium-related signaling proteins. Ca^2+ imaging was performed in naive WT DRG primary neurons after prolonged morphine exposure. HEK293 cells engine expressing TRPA1, mu-opioid receptor (MOR), and the cAMP biosensor G-Flamp2 was used to assess acute and chronic morphine-induced signaling changes. **Results:** Compared with WT, ALDH2*2 mice developed mechanical OIH (mean diff -0.50 p<0005). and analgesic tolerance (mean diff -0.35 p<0,01) 2 days earlier after chronic morphine administration. Interestingly, Alda-1 completely prevented these effects in WT, and partially in ALDH2*2 mice (mean diff 0.4 p<0,05, comparing ALDH2*2 morphine-vehicle vs ALDH2*2 morphine-Alda-1). Chronic morphine increased 4-HNE accumulation in DRG, while Alda-1 reduced 4-HNE adducts in ALDH2*2 mice. HC-030031 dose-dependently reduced mechanical OIH (0.4 and 0.5, p<0,05, 3µg and 10µg treated groups, respectively) and thermal tolerance in WT mice, while reducing Ca^2+/calmodulin-dependent protein kinase II activation without changing 4-HNE levels, supporting TRPA1 activation downstream 4-HNE accumulation. In Trpa1-/- mice, morphine-induced OIH was completely prevented for up to 10 days, whereas analgesic tolerance was delayed by 5 days, indicating partial dissociation between these effects. In DRG cultures, prolonged morphine exposure increased neuronal responsiveness to veratridine, a sodium channel activator. HEK293 cells co-expressing TRPA1-MOR-G-Flamp2, acute morphine inhibited cAMP production, while this effect was lost after prolonged exposure, consistent with cellular tolerance and functional loss of Gi signaling. **Conclusion:** These findings identify TRPA1 as a key effector of chronic morphine-induced OIH and an important contributor to analgesic tolerance downstream of ALDH2 dysfunction and 4-HNE accumulation. Integrating pharmacological, biochemical, and genetic approaches, these data support ALDH2-4-HNE-TRPA1 pathway as a promising target to reduce opioid-induced OIH analgesic tolerance, preserving morphine analgesia. **Financial support:** CAPES, FAPESP 2023/14271-8, 2025/05902-0

05.020 **Targeting Drp1-Mediated Mitochondrial Fission to Mitigate Paclitaxel-Induced Neurotoxicity in Dorsal Root Ganglion Sensory Neurons**. Troitiño VC[1,2], Hosch NG[1], Behr BB[1], Schiess, MC[1], Pennachioni NP, Santos LGK[1], Silva GSA[1], de Ocesano CP[3], Buri MV[3], Chudzinski-Tavassi AM[3], Zambelli VO[1,3]. [1]IBu, Pain and Signaling Lab, São Paulo. [2]USP, Interunits Biotechnology Postgraduate Program, São Paulo. [3]IBu, Centre of Excellence in New Target Discovery, IBu, São Paulo.

Introduction: Paclitaxel (PTX)-induced peripheral neuropathy (CIPN) is a major dose-limiting adverse effect of chemotherapy and has been associated with mitochondrial dysfunction. Excessive mitochondrial fission mediated by dynamin-related protein 1 (Drp1) may contribute to neuronal damage. This study investigated PTX-induced neurotoxicity in primary dorsal root ganglion (DRG) neurons and evaluated the effect of the Drp1 inhibitor SC9 on mitochondrial oxidative stress. **Methods:** Primary DRG neurons from male C57BL/6 mice (CEUAIB 1065301023) were treated with PTX (0.1–10 μM), with or without SC9 (2 μM), for 24 or 48 h. Cell viability was assessed by MTT and LDH assays. Neuritogenesis and CGRP expression were analyzed by High-Content Screening. Mitochondrial morphology and superoxide production were evaluated using MitoTracker and MitoSOX fluorescence imaging. Experiments were performed with n = 3–4 independent cultures. Statistical significance was set at $p < 0.05$. **Results:** PTX (10 μM, 48 h) reduced neuronal viability by 31.5% in the MTT assay and increased LDH release by 32.4%, confirming cytotoxicity. PTX disrupted neurite organization, reducing total neurite length by 88.2%, average neurite length by 84.7%, and the number of neurite processes connected to the cell body by 41.5%. PTX also increased CGRP expression by 44.9% (5 μM) and 52.8% (10 μM), reduced mitochondrial area by 44.7% and perimeter by 36%, and increased mitochondrial superoxide production by 21.5%. SC9 significantly attenuated PTX-induced superoxide accumulation (34.2%). **Conclusion:** PTX induced neuronal damage characterized by reduced viability, neurite degeneration, increased CGRP expression, mitochondrial fragmentation, and oxidative stress in primary DRG neurons. The attenuation of mitochondrial superoxide production by SC9 suggests that excessive mitochondrial fission may contribute to PTX-induced neurotoxicity. These findings support further investigation of Drp1-mediated mitochondrial dynamics as a potential therapeutic target for chemotherapy-induced peripheral neuropathy.

05.021 **Involvement of Transient Receptor Potential Ankyrin 1 in Nociplastic Pain-Associated Behaviours in Mice**.
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Fibromyalgia is a potentially disabling idiopathic disorder characterised by chronic and spontaneous widespread pain and comorbidities, including fatigue. Emerging evidence implicates transient receptor potential ankyrin 1 (TRPA1) in fibromyalgia; however, whether these mechanisms contribute to spontaneous nociception and fatigue remains unclear. Here, we investigated the role of TRPA1 in these outcomes using a reserpine-induced model in male mice (approximately 25 g). To induce this model, mice received a subcutaneous (s.c.) injection of reserpine (1 mg/kg) or vehicle (10 ml/kg) once a day for 3 consecutive days. On the 4th day, the mice received by oral gavage (p.o.) the selective TRPA1 antagonist A967079 (100 mg/kg) or vehicle (10 mL/kg). Mice were allocated to treatment groups using a randomisation procedure (http://www.randomizer.org/). Behavioural assessments included hind paw-licking behaviour evoked by a sub- nociceptive dose of H2O2 (0.2 µmol/paw), thigmotaxic behaviour (indirect evaluation of spontaneous nociception), and muscle strength (fatigue). Following testing, animals were euthanised, and hind paw tissue was collected for H_2O_2 quantification using a horseradish peroxidase (HRP)-based assay. Results were analysed by one-way ANOVA followed by Bonferroni post hoc test and expressed as mean ± standard error of the mean (SEM)(n = 6/group). Differences were considered statistically significant at $P < 0.05$. The sub- nociceptive dose of H2O2 (a TRPA1 agonist) induced nociceptive behaviour in reserpine-treated animals ($P < 0.05$), which A967079 attenuated ($P < 0.05$). The fibromyalgia model induced thigmotaxic behaviour ($P < 0.05$) and reduced the mice's muscle strength ($P < 0.05$), which A967079 alleviated ($P < 0.05$). Reserpinized mice presented increased H_2O_2 levels in paw homogenates ($P < 0.05$), which A967079 reduced ($P < 0.05$). Our findings demonstrate that TRPA1 contributes to the developmente of spontaneous pain, as the TRPA1 antagonist reduced the thigmotaxic behaviour, nociception potentiation induced by a subniciceptive dose of H_2O_2, and fatigue-like behaviour in this rodent model, supporting its relevance to fibromyalgia pathophysiology and associated symptoms. Acknowledgements: CNPq, FAPERGS, CAPES/PROEX.

05.022 **Aldehyde Dehydrogenase-2 Modulates Ethanol-Induced Neuropathy and Neuroinflammation**. Souza, DF[1]; Hösch, NG[1]; Troitiño, VC[1]; Pennachioni, NP[1]; Dallazen, JL[2]; Santos, LG[2]; Martins DO[3]; Campos, ACP[3]; Pagano, RL[3]; Zambelli, VO[1] [1]IBu, Lab Pain and Signaling, São Paulo, Brazil; [2]IBu, Centre of Excellence in New Target Discovery (CENTD), , São Paulo, Brazil. [3]HSL, Lab Neuroscience, , São Paulo, Brazil.

Introduction: Ethanol is widely used around the world, and its excessive consumption leads to physical, psychological, and social problems, becoming a public health issue. Alcoholic neuropathy is a chronic condition characterized by the degeneration of autonomic, sensory, and motor nerve fibers, leading to chronic hypernociception. Aldehyde dehydrogenase-2 (ALDH2) is the main enzyme responsible for the clearance of toxic aldehydes that accumulate after ethanol metabolism (i.e., acetaldehyde). Loss-of-function mutations in the ALDH2 gene, specifically the ALDH2*2 allele, have been strongly correlated with an increased prevalence of neuropathic pain. Interestingly, AD6626, an ALDH2-positive allosteric modulator, restored enzyme activity and reversed ethanol-induced neuropathy. Aims: Investigate the participation of ALDH2 in ethanol-induced neuroinflammation. Materials and **Methods:** Male wild-type (WT) C57BL/6 and ALDH2*2 mice were subjected to oral administration of ethanol (1 g/kg) or water (control) for 6 weeks. The animals were orally treated with AD6626 (40 mg/kg/day) or its vehicle immediately before ethanol administration (CEUAIB: 7634280225). Mechanical (von Frey test) and thermal (tail immersion test) nociceptive testswere performed weekly. At the end of the protocol, the spinal cord was collected for immunohistochemical analysis of astrocyte and microglial activation, targeting glial fibrillary acidic protein (GFAP) and ionized calcium-binding adaptor molecule 1 (IBA-1), respectively. **Results:** Ethanol administration reduced the mechanical nociceptive threshold in WT mice from the third week compared to controls (decreases the threshold by 0,3g). ALDH2*2 mice developed mechanical hypernociception earlier, in the second week (38.4% vs controls), and exhibited lower mechanical thresholds than ethanol- treated WT mice throughout the six-week experimental period (13.5%). AD6626 partially prevented ethanol-induced mechanical hypernociception in both strains compared with their respective ethanol-treated groups (WT 38.6% and ALDH2*2 38.9%). Similarly, ethanol exposure decreased the thermal nociceptive latency in both WT and ALDH2*2 mice by the second week compared to controls (WT 3,7s and ALDH2*2 3,5s), indicating the development of thermal hypernociception. AD6626 attenuated this effect in both groups (WT 0,4s and ALDH2*2 0,7s). Furthermore, ethanol increased astrocyte activation in the spinal cord of WT and ALDH2*2 mice compared with control animals (WT 43.4% and ALDH2*2 49.8%). AD6626 reversed astrocyte activation, restored ALDH2 activity (31.2%), and produced similar effects on microglial expression. **Conclusion:** ALDH2 activity is linked to alcoholic neuropathy. Neuronal activation in the periphery, such as microglia and astrocytes, contributes to the onset of this neuropathy. ALDH2 activators, such as AD6626, may be promising analgesics and may help with pain caused by chronic alcohol consumption.

05.023 **Repetitive Transcranial Magnetic Stimulation Prevents the pro-Oxidative Effect of a Very Low Dose of Naltrexone and Modulates Nociception in Rats Subjected to a Model of Fibromyalgia**. Roland S[1,2], Dal Bosco T[1,3], Steimetz LC[1], da Silva BP[1], Chagas MC[1], Caumo W[1,3], Stein DJ[1,3], Torres ILS[1,2,3] [1]HCPA, Lab Pain Pharmacology and Neuromodulation: Preclinical Investigations, Brazil; [2]UFRGS, Institute of Basic Health Sciences, PPG in Biological Sciences: Pharmacology and Therapeutics, Brazil; [3]UFRGS, School of Medicine, PPG in Medicine: Medical Sciences, Brazil

Introduction: Fibromyalgia (FM) is a complex disorder characterized by central sensitization and amplification of nociceptive stimuli. Due to its multifactorial nature, combined therapeutic approaches may enhance treatment efficacy and improve symptom management. **Objective:** To evaluate the effects of a very low dose of naltrexone (VLDN) and/or repetitive transcranial magnetic stimulation (rTMS) on nociceptive response, neuroinflammation, neuroplasticity, and oxidative stress biomarkers in a rat model of FM. **Methods:** Ninety six female Wistar rats were allocated to 3 groups: control (CT, n=12), acetic acid (AA, n=12), and FM (n=72). The FM model was induced by 1 injection daily of reserpine in 0.5% AA (1 ml/kg, s.c./3 days). Mechanical allodynia was evaluated by von Frey (VF) test at baseline (D0), D8, and D19. After the establishment of the model (D8), the FM group was subdivided into 6 groups (n=12/group): FMS (FM+saline); FMSh (FM+sham rTMS); FMShVLDN (FM+sham rTMS+VLDN); FMrTMS (FM+active rTMS); FMVLDN; FMrTMSVLDN (FM+active rTMS+VLDN). Treatment consisted of 10 days with active (200 mT, 1 Hz, 5 minutes) or sham rTMS and/or VLDN (0.5 mg/kg, p.o.). The levels of IL-1β, BDNF, and IL-4 were quantified by ELISA in the hippocampus (HC), brainstem (BS), and cerebellum (CB). The oxidative stress markers total ROS, sulfhydryls (SH), nitrites $(NO)_2$, and catalase (CAT) were assessed in the cervical spinal cord (CSC). Data were analyzed by one-way ANOVA/Duncan, with a significance level of $P<0.05$. **Results:** At baseline, no significant differences were observed across groups in mechanical nociceptive threshold ($F(2,21)=0.192$; $P=0.827$). The pain model establishment was detected at D8, indexed by a lower threshold of the FM group compared to both the CT and AA groups ($F(2,32)=8.767$; $P=0.001$), indicating mechanical allodynia. After treatment (D19), the allodynia was partially reversed in the FMSh and FMShVLDN groups ($P<0.05$), being similar to the CT ($P>0.05$). The FM model also induced an increase in IL-1β levels in the BS ($P=0.05$) compared to the AA group, which was similar to the CT. No significant differences were observed among groups for the other biomarkers analyzed in all central structures ($P>0.05$, for all). The animals treated with VLDN (FMVLDN group) showed higher ROS levels ($P<0.05$) compared to other groups, an effect that was prevented by rTMS (rTMS+VLDN group) ($P<0.05$). The FMShVLDN group exhibited higher levels of NO_2. There were no significant differences between groups in the other neurochemical markers analyzed ($P>0.05$). **Conclusions:** The experimental FM model reproduced sensorimotor changes similar to those observed in human FM, inducing neuroinflammation. VLDN and rTMS promoted partial modulation of these parameters, with an antioxidant effect of the rTMS, suggesting therapeutic potential in the multidimensional management of chronic pain. Keywords: Fibromyalgia; Chronic pain; Neuroinflammation; Very low dose naltrexone; Repetitive transcranial magnetic stimulation; Female rats.

05.024 **Assessment of Cognitive Deficits and Emotional Symptoms in a Model of Complex Regional Pain Syndrome Type I and the Effect of Pregabalin in Mice**. Morais RIF[1], Antoniazzi CTD[1], Fim YV[2], Brito HA[2], Dalmolin L[3], Trevisan G[1]. [1]UFSM, PPG in Pharmacology, Brazil, [2]UFSM, Undergraduate Program in Pharmacy, Brazil, [3]UFSM, Undergraduate Program in Medicine, Brazil.

Introduction: Complex regional pain syndrome type I (CRPS-I) is a chronic pain condition often associated with depression, anxiety, or cognitive impairment. These symptoms indicate changes in the central nervous system. Memory deficits remain poorly understood in clinical practice and have yet to be investigated in animal models, specifically regarding the chronic post-ischemic pain (CPIP) model. **Objectives:** The study sought to investigate the relationship between chronic nociception and the development of cognitive alterations (working memory and object recognition) in an animal model of CRPS-I. **Methodology?** C57BL/6J mice (males and females) were used to induce the chronic post-ischemic pain (CPIP) model by placing a tourniquet on their left ankle for 2 hours (CEUA UFSM #2190110723). The development of nociception was monitored on days 1, 5, 10, and 15 post-induction using the von Frey test (mechanical allodynia) and the acetone drop test (thermal allodynia). On day 15, after confirmation of the chronic phase, the animals were treated with pregabalin (60 mg/kg, intragastric route) or vehicle. One hour after treatment, behavioral tests were performed, including the open-field test (exploratory activity), Y-maze test (working memory), and novel object recognition test (recognition memory). The gene expression of cholinergic system markers (AChE, ChAT, and M1R) and neurotrophic factors (Gfap and Nrf2) was analyzed using quantitative real-time PCR (RT-qPCR). Furthermore, oxidative stress markers (DCF, SOD, and H_2O_2) and pro-inflammatory cytokines (TNF-α and IL-1β) were quantified using specific commercially available assay kits. **Results: Results:** Animals subjected to the CPIP model developed mechanical allodynia (females 0.10±0.06 and males 0.13±0.08) and persistent cold hyperalgesia (females 15.14±0.8 and males 14.71±0.78) from day 1 to 15, with no significant differences between sexes. Although they did not exhibit impairments in locomotor activity, animals with chronic pain showed reduced exploratory behavior and impairments in working memory (lower alternation percentage in the Y-maze – females: 49.77%±2.68 and males: 53.11%±2.56) and recognition memory (lower discrimination index in the novel object recognition test; females: 0.40±0.02 and males: 0.27±0.02). Treatment with pregabalin reversed allodynia and attenuated or restored memory deficits in both males and females (Y-maze – females: 86.61%±0.47 and males: 87.92%±0.76 and novel object recognition test – females: 0.70±0.02 and males: 0.75±0.02). A marked upregulation was observed for GFAP (5.0±0.34), Nrf2 (3.98±0.99), and AChE (4.92±0.54). Conversely, the transcriptional levels of the cholinergic markers ChAT (0.73±0.08) and M1R (0.74±0.06) were significantly downregulated. The model successfully induced a robust neuroinflammatory response and widespread oxidative stress across the prefrontal cortex, hippocampus, spinal cord, and plasma, as evidenced by elevated TNF-α (7.24±0.76, 10.24±1.36, 19.32±2.03), IL-1β (3.66±0.54, 3.59±0.48, 4.64±0.66), H_2O_2 (8.71±1.45, 13.89±2.16, 13.58±3.29, 31.40±3.49), and DCF (75.93±6.42, 86.04±7.86, 103.3±11.40) levels. Notably, therapeutic intervention with pregabalin significantly attenuated both the pro-inflammatory and pro-oxidant states, restoring these molecular and biochemical parameters toward baseline levels. **Conclusion:** These findings underscore the need for therapies addressing both pain and neurocognitive comorbidities.

05.025 **Sexual Dimorphism in Musculoskeletal Orofacial Pain Induced by Sleep Deprivation and Emotional Stress in Rats**. Alves BWF[1,2], Moura MNS[1.3], Menezes KLS[1], Nascimento RR[1.3], Magalhães FJP[1.3], Pereira LS[1], Alves MP[1], Ribeiro MVS[1], Cajado AG[1.3], Pereira AF[1.3], Vale ML[1.3] [1]NPDM-UFC, Lab Inflammation and Cancer Pharmacology, Drug Research and Development Center, Brazil; [2]UFC, Dpt of Morphology. [3]UFC, Dpt of Physiology and Pharmacology.

Introduction: Orofacial pain (OP), particularly temporomandibular dysfunction (TMD) of muscular origin, affects 27–34% of the world population, with higher prevalence among women. Emotional stress (ES) and sleep deprivation (SD) are recognized contributors to pain exacerbation. Painful TMDs are increasingly understood as conditions associated with nociplastic pain, characterized by alterations in nociceptive processing and central sensitization mechanisms, even in the absence of evident tissue damage or inflammation proportional to reported pain intensity, which justifies the investigation of psychosocial and behavioral factors in their pathophysiology. **Objectives:** To investigate sexual dimorphism in musculoskeletal OP induced by paradoxical SD, ES, and their combination, as well as their effects on anxiety-like behavior, working memory, and morphological changes in the adrenal gland. **Methods:** Eighty male and female Wistar rats were subjected to the communication box ES model and paradoxical SD using the modified multiple platform method, and divided into eight groups (n=8/group): control (CONTM/CONTF), emotional stress (ESM/ESF), sleep deprivation (SDM/SDF), and their combination (ESSDM/ESSDF). Mechanical nociceptive tests in the masseter and temporal muscles (Von Frey test), open field test, Y-maze, and morphological analysis of the adrenal glands were performed, with the zona fasciculata of the adrenal cortex evaluated for cytoplasmic vacuole area quantification. Statistical differences in the Von Frey behavioral test were assessed by two-way ANOVA, while the remaining parametric assays were analyzed by one-way ANOVA, both followed by Tukey's post hoc test. **Results:** ES and SD induced mechanical hypersensitivity in the masticatory muscles in both sexes, with significant effects of group, day, and their interaction ($P<0.0001$), and greater intensity in females. In the open field test, all experimental groups showed increased locomotor and exploratory activity relative to controls, with crossings increasing by up to 66.6% in males and 51.2% in females, and rearing by up to 66.2% in males and 49.1% in females ($P<0.05$), with a more pronounced effect of SD in males only. In the Y-maze, incorrect alternations increased by up to 254.6% in males and 160.2% in females ($P<0.05$ vs. respective controls), indicating working memory impairment in both sexes. SD was the most impactful stimulus, producing sustained hyperalgesia, anxiety-like behavior, and working memory deficits in males, along with greater adrenal morphological alterations. **Conclusion:** ES and SD, alone or in combination, induce musculoskeletal OP with evident sexual dimorphism and cognitive and behavioral impairments, while adrenal morphological changes suggest HPA axis activation, reinforcing the relevance of these factors in TMD pathophysiology. Ethics approval: Approved by the Animal Ethics Committee (CEUA/NPDM/UFC), protocol nº 18290921-0. Financial support: FUNCAP; CNPq; CAPES. Keywords: Sleep Deprivation; Psychological Stress; Facial Pain; Sex Differences;

05.026 **Evaluation of the Effects of the Monoterpene Isopulegol on Locomotor Activity and Nociception in a Murine Model of Fibromyalgia**. Oliveira, JLS[1], Reis Filho, AC[1], Martins, RYC[1], Barros, AG, Araujo, RBC[1], Sousa, RCL[2], Almeida, FRC[1] [1]UFPI, Pain Pharmacology Lab, PPG Pharmacology, Brazil [2]UFPI, Cancerology Lab, PPG Pharmacology, Brazil.

Introduction: Fibromyalgia (FM) is a chronic widespread pain syndrome associated with neurotransmitter alterations and functional impairment, predominantly affecting women. Current treatments have limited efficacy and are often associated with adverse effects, highlighting the need for novel therapeutic approaches. Isopulegol (ISO), a naturally occurring monoterpene, has demonstrated antinociceptive activity in experimental pain models; however, its effects in FM remain unknown. **Objective:** To evaluate the antinociceptive potential of ISO in a murine model of fibromyalgia. **Methods:** ISO was dissolved in 0.9% NaCl containing 2% Tween 80 for oral administration. Female Swiss mice (25–35 g) were maintained under controlled conditions. FM was induced by intramuscular injections of 20 µL acidic saline (pH 4.0) into the gastrocnemius muscle on days 1 and 5. Control groups received neutral saline (pH 7.4) or vehicle. Mechanical and cold thermal nociception were assessed using the von Frey and acetone tests, respectively. In the acute protocol, animals (n=6) received ISO (25 or 50 mg/kg, p.o.) or morphine (10 mg/kg, s.c.), and evaluations were performed from 0 to 6 h after administration. In the subacute protocol, animals received daily treatment with ISO, vehicle, or pregabalin (5 mg/kg, p.o.) until day 18, with assessments every two days. Locomotor activity was evaluated in the open-field test on day 4. All procedures were approved by the CEUA-UFPI (740/2022). **Results:** In the open-field test, SHAM, neutral saline, pregabalin, and ISO-treated groups (25 and 50 mg/kg) showed locomotor activity values of 68.5 ± 5.0, 64.6 ± 4.7, 72.8 ± 8.9, 63.5 ± 3.5, and 57.3 ± 4.3, respectively, compared with the negative control group (34.1 ± 3.9), indicating increased locomotion ($p<0.05$). In the acute protocol, ISO did not significantly alter mechanical nociceptive thresholds, whereas morphine significantly increased the threshold for up to 4 h, reaching 3.2 ± 0.9, 4.2 ± 0.8, 8.7 ± 2.4, and 8.8 ± 3.8 g ($p<0.05$). In the acute thermal assessment, ISO and morphine significantly reduced response time between the 1st and 5th hours ($p<0.05$). In the subacute protocol, pregabalin significantly increased the mechanical nociceptive threshold from day 9 (3.23 ± 0.4 g), whereas ISO 50 mg/kg produced a significant effect from day 7 (3.3 ± 0.4 g; $p<0.05$). Thermal nociception showed a significant reduction in response time in nearly all treated groups from the first day of treatment ($p<0.05$). **Conclusion:** These findings suggest that ISO exerts antinociceptive effects in a murine model of FM, improving thermal nociception and locomotor activity, while also reducing mechanical hypersensitivity following subacute treatment.

05.027 **Antinociceptive Effects of *Oxandra martiana* Extract in Acute and Neuropathic Pain Models**. Macario V[1,2], Rezende B[1,2], Santos YB[1], Guedes GN[1], Maia EP[1], Antunes F4, Abreu L[5], Fontes-Dantas FL[2,3], Montes GC[1,2] [1]UERJ, Neurobiology Lab, Brazil, [2]FISCLINEX/UERJ – PPG in Clinical and Experimental Physiopathology, Brazil, [3]UERJ, Neuropharmacogenetics Lab, Brazil, 4UENF, Animal Clinical and Surgical Lab, Brazil, [5]UFF, Chemistry and Natural Products Lab, Brazil.

Introduction: Pain represents a major therapeutic challenge due to the limitations of currently available analgesics, including reduced efficacy and adverse effects. In this context, natural products represent an important source of bioactive compounds with pharmacological potential. Although species of the Oxandra genus have demonstrated several pharmacological activities, the antinociceptive potential of *Oxandra martiana* has not yet been investigated. **Objectives:** To evaluate the antinociceptive activity of the ethanolic extract from the leaves of *Oxandra martiana* (OM[2]FE) in experimental models of acute and neuropathic pain, as well as to investigate the involvement of opioid mechanisms in its pharmacological effects. Methods: All procedures were approved by the Animal Use Ethics Committee of the State University of Rio de Janeiro (CEUA/UERJ, protocol no. 051/2024). In the acute pain model, dose-response studies were performed using the formalin test following intraperitoneal administration of OM(2)FE (30 and 100 mg/kg, i.p.) and oral administration (173 and 300 mg/kg, p.o.). Locomotor activity was evaluated using the open field test, and central antinociceptive activity was assessed using the hot plate test (55 ± 0.5 °C). The involvement of opioid pathways was investigated by pretreatment with naloxone and CTOP prior to extract administration. In the neuropathic pain model, animals underwent spinal nerve ligation (SNL) and were orally treated with OM(2)FE (300 mg/kg) for 14 days, starting on the 7th day after surgery. Mechanical hyperalgesia was evaluated using the Randall-Selitto test, and thermal hyperalgesia was assessed by paw withdrawal latency in a 46 °C water bath. **Results:** In the formalin test, OM(2)FE (100 mg/kg, i.p.) reduced nociceptive behavior by approximately 45% and 61% during the neurogenic and inflammatory phases, respectively. After oral administration (300 mg/kg, p.o.), the extract reduced nociceptive behavior by approximately 44% and 54% during the neurogenic and inflammatory phases, respectively. In the hot plate test, OM(2)FE (100 mg/kg, i.p.) significantly increased thermal latency, with a maximal effect observed at 60 minutes, producing an antinociceptive activity of approximately 30% at this time point. In the open field test, the extract did not induce significant locomotor alterations, suggesting the absence of nonspecific motor effects. Pretreatment with naloxone and CTOP reduced the antinociceptive effect of the extract, suggesting the participation of opioid mechanisms, particularly involving μ-opioid receptors. In the neuropathic pain model, OM(2)FE (300 mg/kg, p.o.) increased the mechanical pressure response threshold by approximately 114% and thermal latency by 88% compared with SNL animals treated with vehicle. **Conclusion:** *Oxandra martiana* exhibits antinociceptive activity in experimental models of acute and neuropathic pain, with pharmacological evidence of opioid pathway involvement and absence of nonspecific motor alterations. These findings highlight the potential of this species as a source of bioactive compounds for the development of new therapeutic approaches for pain management.

05.028 **Sex Differences in Thermal Analgesia Induced by Pharmacoacupuncture with Melittin in Male and Female Rats**. Leonor MGR[1], Boaventura de Oliveira AM[1], Teixeira RMS[1], Almeida TC[1], Sant'anna MB[1], Marques-Porto R[2], Picolo G[1]. [1]IBu, Lab Pain and Signaling, São Paulo, Brazil; [2]IBu, Lab Development and Innovation, São Paulo, Brazil.

Introduction: Sex-related differences in pain sensibility and analgesic efficacy of drugs are widely reported. Furthermore, most basic searches, preclinical assays, and clinical trials are still conducted primarily in male rats and men. This contributes to the limited understanding of pain mechanisms, hormonal influence, and the effectiveness of new compounds in females. Additionally, thermal pain - which involves recovering from burn injuries or treating chronic conditions that are hypersensitive to temperature changes - can be incredibly difficult to treat. Considering that, the search for new analgesic compounds and therapeutic approaches effective in both sexes is essential. In this context, melittin stands out due to its prolonged antinociceptive effects in association with pharmacoacupuncture. Then, this study aimed to compare the analgesic effects of melittin, the main compound of the bee venom, on thermal pain models, investigating nociceptive and analgesic differences in male and female rats in neuropathic pain models. **Methods:** Neuropathy was induced in Wistar female and male rats (CEUA 2959281125) (3-6 weeks, 180– 200g), by the chronic constriction of the sciatic nerve (CCI). The treatment protocols begin on the 15th day after CCI induction. Apitoxin can develop analgesia in both sexes at a concentration of 1mg/kg. Based on that, melittin was used in a correspondence dose (60%, 0.6mg/kg), since it represents this percentage of apitoxin contend. Melittin (0,6mg/kg) was applied as pharmacoacupuncture in Suzanli (ST36) acupoint. Pain nociceptive behavior was assessed by using the stimulus-evoked test (Acetone test and Hargreaves). **Results:** Evaluating basal sensitivity between sexes, females exhibited longer thermal withdrawal latencies than males (17 vs. 12 s, $p < 0.05$, t-test) to heat (Hargreaves). When comparing chronic conditions, females presented less nociceptive behavior (4 vs 6 s, $p < 0.05$, t-test) in the cold thermal test (Acetone Test). Melittin induced analgesia in the Hargreaves test (45% CCI + Mel vs. CCI + Vehicle 6 hours after treatment, 2way ANOVA) and in the acetone test in males (76% of analgesia CCI + Mel vs. CCI + Vehicle 3 hours after treatment, 2way ANOVA), while females just presented analgesia in the acetone test (73,3% of analgesia CCI + Mel vs. CCI + Vehicle 3 hours after treatment, 2way ANOVA). **Conclusion:** In conclusion, melittin demonstrated potential analgesic effects on thermal sensitivity in male rats. In contrast, female rats exhibited analgesia only in the cold thermal test under chronic neuropathic pain conditions. These findings reinforce the importance of investigating sex-related differences in pain mechanisms and analgesic responses. Keywords: Sex difference, Melittin, Analgesia.

05.029 **Cannabidiol-Loaded Microemulsion Enhances Antinociceptive Efficacy and Modulates Neuroinflammatory and Oxidative Stress Pathways in Neuropathic Pain**. Santana TCM[1], Cruz ABO[2], Oliveira LGS[3], Lauria PSS[4], Nunes VLC[5], Brustolim, D[2], Egito EST[3], Viana MDM[2], Villarreal CF[1,2] [1]Fiocruz-BA, Gonçalo Moniz Institute, Brazil; [2]UFBA, School of Pharmacy, Brazil, [3]UFRN, Federal University of Rio Grande do Norte, Pharmacy Dept, Brazil; [4]Dept Cell Biology and Human Anatomy, University of California Davis, Sacramento, United States; 5UFBA, School of Medicine, Brazil

Introduction: Neuropathic pain (NP) is a debilitating chronic condition often refractory to current therapies. Although cannabidiol (CBD) shows therapeutic potential in NP, its use is limited by poor biopharmaceutical properties. **Objectives:** To investigate whether a lipid-based CBD formulation (LS–CBD) potentiates the antinociceptive effects of free CBD in a NP model, also evaluating the underlying mechanisms, and signs of systemic toxicity. Methods: LS–CBD was obtained by ultrasonication of a phospholipid-based microemulsion, followed by CBD incorporation under magnetic stirring and was physiochemically characterized. Male C57BL/6 mice (CEUA approval no. 118/2023) subjected to partial sciatic nerve ligation were orally treated with CBD or LS–CBD (25, 50, and 75 mg/kg) under acute or repeated (7 days) treatment. Sham-operated mice were untreated. Mechanical (von Frey), thermal (Hargreaves), and motor coordination (rota-rod) tests were performed. Antinociceptive efficacy, duration, and magnitude of antinociception (AUC) were compared. qRT-PCR in dorsal root ganglion evaluated NRF2, CAT, SOD-1, NOS2, GFAP, IL-6, and IL-10 expressions. Additionally, toxicity-related parameters (hematological, biochemical, body weight monitoring, and histopathological analysis of organs) were evaluated. **Results:** LS–CBD demonstrated suitable stability, pH, and encapsulation efficiency profiles. For mechanical stimuli, LS-CBD showed greater antinociceptive efficacy (53.72% vs. 26.51%, $p<0.05$), higher global antinociception (AUC: 0.59 vs. 0.44, $p<0.05$), and longer duration of effect (6 h vs. 4 h) than CBD. For thermal stimuli, both treatments showed high efficacy, slightly higher for LS-CBD (88.79% vs. 88.25%, $p>0.05$), with similar AUCs (19.97 vs. 19.91, $p>0.05$). However, LS-CBD prolonged antinociception (8 h vs. 4 h, $p<0.05$) and remained effective at all doses tested (25–75 mg/kg), unlike CBD. Under repeated treatment, at doses that did not induce motor impairment or tolerance development, LS-CBD showed greater antinociceptive efficacy than CBD at both time points, with a more pronounced increase over time (16.10–27.80% vs. 15.74–17.83%, $p<0.05$) and higher global antinociception (AUC: 0.85 vs. 0.67, $p<0.05$), for mechanical nociception. For thermal nociception, both treatments exhibited high efficacy with similar AUC values. qRT-PCR analysis demonstrated reduced expression of neuroinflammatory and glial activation markers, accompanied by increased expression of antioxidant enzymes. Repeated oral administration of CBD or LS-CBD did not induce hematological, biochemical, macroscopic, histopathological, or body weight alterations in mice. In addition, renal and hepatic functions remained preserved, reinforcing the favorable systemic safety profile of both treatments. **Conclusion:** LS–CBD enhanced antinociceptive efficacy of free CBD, without inducing toxicity, highlighting this lipid-based formulation as a promising therapeutic strategy for managing NP.

05.030 **Advanced Glycation End-Products Promote Neuronal Dysfunction and Neurodegeneration in Sensory-Like Neurons and Sensorimotor Organoids**. Silva GSA[1], Bufalo MC[3,4], Chudzinski-Tavassi AM[3,4], Pereira JD[2], Zambelli VO[1,3]. [1]IBu, Lab Pain and Signaling, Brazil. [2]University of ALABAMA at Birmingham, Dept Neurology, USA. [2]IBu, Center of Excellence in New Target Discovery, Brazil. [4]IBu, Innovation and Development Center, Brazil.

Advanced glycation end-products (AGEs) are formed by the irreversible binding of sugar molecules to proteins, such as collagen. Elevated AGEs have been associated with peripheral neuropathy and pain. We previously demonstrated that AGEs induce mitochondrial dysfunction, which is reversed by the RAGE antagonist FPS-ZM1. However, the mechanisms by which AGEs contribute to neuronal hypersensitization and axonal degeneration remain unclear. Here, we sought to investigate the mechanisms underlying AGE-induced neuronal degeneration and sensitization. First, sensory-like neurons differentiated from the SH-SY5Y cell line were incubated with glycated collagen (GC), and the following parameters were assessed: (a) cytoskeletal proteins (actin filaments and βIII-tubulin) by High Content Screening, (b) pro-nociceptive signaling pathways through calcium influx, and (c) ATF3 and phospho-p38/p38 MAPK proteins by Western blot. Assays were performed ± FPS-ZM1. Next, we expanded our investigation to sensorimotor organoids derived from human induced pluripotent stem cells, which better mimic the organization and cellular heterogeneity of neuromuscular junctions. To characterize neuronal differentiation in sensorimotor organoids, βIII-tubulin and BRN3A were evaluated by immunostaining to confirm neuronal and sensory neuron differentiation, respectively. Then, we evaluated whether AGEs hypersensitize sensorimotor organoids. For that, AGE-induced sensitization was assessed by ATF3 and c-Fos mRNA expression (RT-qPCR) and calcium flux imaging. Additionally, the loss of myelin basic protein (MBP) and the mitochondrial marker TOMM20 was quantified by Western blot. Normal collagen (NC) was used as a control. Our results showed that GC reduced actin filament immunostaining by 30.69% and βIII-tubulin immunostaining by 25.21% compared with NC, indicating that AGEs disrupt the cytoskeleton, leading to impaired neuritogenesis, which may be associated with axonal degeneration. GC also increased capsaicin-induced calcium influx by 52.13% compared to NC, indicating neuronal hypersensitization, which was blocked by FPS-ZM1. Western blot analyses revealed that GC increased phospho-p38/p38 (104.72%) and ATF3 (69.24%) vs NC. Interestingly, the RAGE antagonist reversed the phospho-p38/p38 ratio, suggesting that RAGE regulates this pathway. To further validate these mechanisms in a more complex model, in sensorimotor organoids, BRN3A and βIII-tubulin confirmed the sensory neuron phenotype. GC increased c-Fos and ATF3 mRNA expression by 288.5% and 79.7%, respectively, as well as increased calcium flux, compared to NC. Furthermore, GC decreased MBP levels compared to NC, suggesting demyelination. In parallel, at 24 h, GC reduced TOMM20 levels, indicating mitochondrial loss. In conclusion, these findings contribute to understanding the role of AGEs/RAGE signaling in neurodegeneration and may support the development of experimental platforms for investigating neurodegenerative diseases.

05.031 **Therapeutic Effects of Botulinum Neurotoxin-A Formulations in a Model of Temporomandibular Joint Dysfunction**. Couto ACG[1], Silva TM[1], Costa ARG[2], Santos DO[2], Faria PR[2], Crosara TA[3], Januzzi E[3], Silva CR[1] [1]UFU, GPANI, PPGGB, Brazil; [2]UFU, Dep. Oral and Maxillofacial Pathology, Brazil; [3]NEON, MG, Brazil.

Introduction: Temporomandibular disorder (TMD) is a debilitating condition affecting the temporomandibular joint (TMJ) and associated structures, often comorbid with anxiety and depression. Given that many patients are refractory to conventional therapies, botulinum neurotoxin type A (BoNT-A) has emerged as a viable intervention. However, different commercial formulations exist, and their efficacy may differ. This study evaluated the effects of two distinct BoNT-A brands in a mouse model of TMD induced by Complete Freund's Adjuvant (CFA). **Methods:** To induce TMD, adult C57BL6/J male mice (20-25 g, n=5/group; CEUA: 23117.011633/2022-55) were anesthetized with 2% isoflurane and received 20 µL of CFA (1 mg/mL) into the right TMJ. Experimental groups were: Naïve, CFA, CFA + Botox (0.06U), and CFA + Xeomin (0.06U). Fourteen days post-induction, animals were treated subcutaneously with Botox or Xeomin in the perinasal area. Pain behavior was assessed 7, 14, 18, 22, and 28 days post-induction: mechanical allodynia was evaluated via the "Up and Down" method with Von Frey filaments, and spontaneous pain by observing face rubbing for 30 min. Anxiety-like behavior was assessed on day 19 using the elevated plus maze (EPM), and depressive-like behavior on day 20 via the forced swim test (FST). Histological analysis of the TMJ was conducted on day 21 using a synovitis scoring system to determine the inflammatory index and synovial hyperplasia. Data normality was determined by the Kolmogorov-Smirnov test and followed by ANOVA and Tukey's post hoc.**Results:** Treatment with Botox and Xeomin reduced mechanical allodynia by 90% and 74%, respectively, 7 days post-injection ($p<0.001$), and decreased spontaneous pain at 4, 7, and 14 days post-treatment ($p<0.001$) compared to the CFA group. Neither treatment reduced anxiety-like behavior. However, they significantly decreased immobility time in the FST, 34% for Botox; 29% for Xeomin, indicating an improvement in depressive-like behavior. There are no significant differences between the two treatments. Histological analysis showed that neither treatment reduced the inflammatory index nor synovial hyperplasia induced by CFA. **Conclusion:** Both BoNT-A formulations reduced pain and depressive-like behavior associated with TMJ dysfunction, but failed to improve soft tissue inflammation, including synovial hyperplasia and inflammatory cell infiltration. These results indicate that the analgesic effects of BoNT-A are independent of structural recovery of the TMJ. **References:** 1 - T.C. Abrahão Cunha, A.C. Gontijo Couto, E. Januzzi, R.T. Rosa Ferraz Gonçalves, G. Silva, C.R. Silva, Toxicon X 12 (2021) 100083. 2 - S. Jariyasakulroj, Y. Shu, Z. Lin, J. Chen, Q. Chang, P.-F. Ko, J.-F. Chen, (2025). 3 - M.F. Brin, M. Nelson, N. Ashourian, A. Brideau-Andersen, J. Maltman,Toxins (Basel). 16 (2024). Animal Research Ethical Committee Number: CEUA: 23117.011633/2022-55 **Financial support:** FAPEMIG, CAPES and CNPq (311281/2022-2)

05.032 **Anti-Inflammatory and Chondroprotective Potential of *Hibiscus sabdariffa* L. in Experimental Osteoarthritis: Phytochemical Analysis and Histopathological Evaluation**. Cruz ACSN[1], Mesquita MJTAM[1], Miranda AJA[2], Lima VAS[2], Xavier JKAM[2], Ataides GC[2], Rocha CQ[2], Teixeira JTAMMM[3], Sousa JCS[4], Carvalho RC[5], Fernandes SCSS[7], França CPC[8] Andrade MS[6], Cartagenes MSS[1]. [1]LEED-UFMA, Experimental Lab for Pain Studies, Brazil; [2]LQPN, UFMA, Natural Products Chemistry Lab, Brazil; [3]CEUMA, Medical School, Brazil; [4]UFMA, Dept Morphology, Brazil; [5]UFMA, Graduate Program in Health Sciences, Brazil; [6]UFMA, Graduate Program in Adult Health, Brazil; [7]CEUMA, Nursing, Brazil; [8]UniRV-Formosa, Brazil.

Introduction: Osteoarthritis (OA) is an inflammatory disease associated with cartilage degradation and joint pain. In this context, *Hibiscus sabdariffa* L. (Hs) stands out due to the presence of flavonoids, anthocyanins, and phenolic compounds with anti-inflammatory and antioxidant potential. **Objective:** To evaluate the pharmacological potential of Hs in experimental OA through phytochemical analysis and preclinical evaluation. **Methods:** The study was approved by the Animal Ethics Committee (CIAP: 02.0341.2019) and supported by CAPES (N°: 88887.893418/2023-00). Hs leaves were subjected to drying, hydroalcoholic extraction, and lyophilization to obtain the hydroethanolic extract. Phytochemical analysis was performed using liquid chromatography coupled with mass spectrometry (LC-MS/MS), which employed retention time analysis and fragmentation patterns (MS^2 and MS^3) to identify the bioactive compounds present in the extract. The 28-day experimental study used male Wistar rats with OA induced by sodium monoiodoacetate (MIA), distributed into control, meloxicam (MLX), Hs extract (45 and 90 mg/kg), and ethyl acetate fraction (EAF) (1 mg/kg) groups. Treatments were administered by oral gavage. Histological analysis was performed using optical microscopy, with the Mankin histopathological criteria and the OARSI classification grades (0–6) for assessing OA. **Results:** Phytochemical analysis of Hs identified phenolic compounds and flavonoids, including caffeic acid 3-glucoside, fraxetin, caffeoylquinic acid, rutin, quercetin 3-O-hexoside, kaempferol-3-O-hexoside, apigenin-O-acetylxyloside, as well as the anthocyanins cyanidin-3-O-rhamnoside and cyanidin-O-rutinoside. Histological evaluation showed that the MLX-treated group partially reduced OA-induced histological alterations. The groups treated with Hs exhibited cartilage preservation and reduction of the inflammatory process, with the best response observed at the dose of 90 mg/kg, which demonstrated greater tissue integrity and chondroprotective action. The EAF (1 mg/kg) also showed a protective effect, even at a low dose. OARSI classification demonstrated high scores in the saline group, indicating greater cartilage degeneration. The groups treated with Hs showed reduced scores, particularly the EAF (1 mg/kg), which exhibited a significant reduction ($p<0.05$). MLX produced the greatest reduction in histopathological scores ($p<0.01$), demonstrating superior protection against OA-induced lesions. **Conclusion:** Hs extract showed a protective effect in experimental OA, promoting a reduction in inflammatory alterations and preservation of articular cartilage. These effects may be related to the presence of phenolic compounds and flavonoids identified in the phytochemical analysis, highlighting the therapeutic potential of this plant in the management of osteoarthritis.
Keywords: *Hibiscus sabdariffa* ; osteoarthritis; phytochemistry; bioactive compounds.

05.033 **CBD- and CBG-Loaded Nanoemulsions in Experimental Models of Acute and Neuropathic Pain**. Rezende B[1,2], Macario VMS[1,2], Santos YB[1], Nascimento GG[1], Audízio LR[4], Antunes F[4], Maluf DF[5], Oliveira L[5], Lopes BA[6], Döll-Boscardin PM[6], Nadal JM[6], Farago PV[6], Fontes-Dantas FL[2,3], Montes GC[1,2,3] [1]UERJ, Neurobiology Lab, Brazil, [2]FISCLINEX-UERJ, PPG in Clinical and Experimental Physiopathology, Brazil, [3]UERJ, Neuropharmacogenetics Lab, Brazil, [4]UENF PPG Veterinary Medicine, Brazil, [5]UFPR, Brazil, 6UEPG, Brazil

Introduction: Pain management remains a major therapeutic challenge, especially in chronic and neuropathic conditions. In this context, phytocannabinoids such as cannabidiol (CBD) and cannabigerol (CBG) have attracted considerable interest due to their antinociceptive and anti- inflammatory properties. Nanoemulsion-based systems may represent a promising approach to improve the pharmacological efficacy of these lipophilic compounds. **Objectives:** The present study aimed to investigate the antinociceptive potential of CBD- and CBG-loaded nanoemulsions in experimental models of acute and neuropathic pain. **Methods:** All procedures were approved by the Animal Ethics Committee of the Universidade do Estado do Rio de Janeiro (CEUA/UERJ, protocol no. 030-2023). Pharmacological screening was performed using the formalin, hot plate (55 ± 0.5 °C), and open field tests. Animals received oral administration of CBD- or CBG-loaded nanoemulsions (50 µL). To evaluate cannabinoid receptor involvement, animals were pretreated intraperitoneally (i.p.) with the CB1 antagonist AM281 (1 mg/kg) or the CB2 antagonist SR144528 (10 mg/kg) before formalin administration. Neuropathic pain was induced by spinal nerve ligation (SNL), followed by the evaluation of thermal hyperalgesia and mechanical hypersensitivity. In the chronic protocol, animals received oral treatment with nanoemulsions (100 µL). Statistical analyses were performed using GraphPad Prism. Formalin data were analyzed by one-way ANOVA followed by Dunnett's test, hot plate and SNL data by two-way ANOVA followed by Sidak's test, and open field data by unpaired Student's t-test. Differences were considered significant at $p < 0.05$. **Results:** Oral treatment with CBD- and CBG-loaded nanoemulsions significantly reduced nociceptive behavior in both neurogenic and inflammatory phases of the formalin test. Pretreatment with AM281 and SR144528 attenuated the antinociceptive effects of both formulations, suggesting the involvement of cannabinoid receptors. In the hot plate test, both nanoemulsions increased latency to thermal stimulus, indicating central antinociceptive activity. No significant locomotor alterations were observed in the open field test. In the SNL model, chronic oral treatment significantly reduced thermal hyperalgesia and mechanical hypersensitivity in animals that developed neuropathic pain. **Conclusion:** CBD- and CBG-loaded nanoemulsions demonstrated significant antinociceptive effects in experimental models of acute and neuropathic pain. The involvement of cannabinoid receptors, together with the absence of locomotor impairment, highlights the therapeutic potential of these cannabinoid-based nanoformulations for pain management.

05.034 **Flavones Modulate Nociception and Neuroinflammation in Preclinical Models of Neuropathic Pain: A Systematic Review and Meta-Analysis**. Batista TSC, Nascimento ACS, Palmeira DN, Mota CMD, Camargo EA [1]UFS, PPG Health Sciences, Brazil, [2]UFS, PPG Physiological Sciences, [3]UECE, Facisc

Introduction: Neuropathic pain (NP), caused by lesions or functional abnormalities in the somatosensory system, affects approximately 10% of the world's population and continues to pose a significant therapeutic challenge, primarily due to the limited efficacy and frequent adverse effects associated with available treatments.In this context, natural products containing flavonoids—especially flavones—have garnered attention for their previously reported antinociceptive, anti-inflammatory, and neuroprotective properties. **Objective:** To synthesize preclinical evidence on the effects of flavones in animal models of NP.Methods: Four databases (PubMed/MEDLINE, Embase, LILACS, and Web of Science) were searched through June 2024. The outcomes assessed included mechanical and thermal nociceptive responses, as well as neuroinflammatory changes in peripheral and central tissues. Methodological consistency was assessed using the SYRCLE risk of bias tool, and Review Manager 5.4.1 software was used to perform the statistical analysis. **Results:** A total of 21 studies were included, of which 17 contributed to the meta-analyses. A subgroup analysis of the pooled data compared the control groups with the groups of animals treated with flavones and showed that flavones significantly reduced the mechanical nociceptive threshold ($p<0.0001$; heterogeneity [I2]= 80%; effect size [ES]= 3.66; 95% confidence interval [CI]; 2.37-4.95), measured by von Frey apparatusand thermalnociceptive responses ($p<0.0001$; I2= 80%; ES= 3.79; 95% CI; 2.70-4.88) measured by the hot plate or Hargreave's tests. These effects were observed in models of NP induced by different types of surgery and chemotherapy.These behavioral responses were followed by a suppression of pro-inflammatory cytokine production and glial stimulation, particularly in the spinal cord. Mechanistically, flavones have been linked to the regulation of key pathways, including NF-κB and NLRP3, as well as the GABAA, opioid, 5-HT1A, α2-adrenergic, and TRPV1 receptors. Despite these consistent findings, most studies were associated with a considerable proportion of uncertain risk-of-bias classifications, mainly due to insufficient methodological description. **Conclusion:** The available preclinical evidence indicates that flavones consistently reduce NP behaviors and neuroinflammation, potentially through modulation of glial activity, cytokine production, and key signaling pathways. However, the high risk of bias and methodological limitations highlight the need for well-designed studies to improve translational validity.

05.035 **Repeated Low-Dose Dual FAAH/MAGL Inhibition Produces Central Behavioral Effects without Antiallodynic Efficacy in Experimental Neuropathic Pain**. Morais ITS[2,3], Marçal MM1, Silva BP[1], Chagas MC[2], Stein DJ[2,3], Caumo W, Torres ILS[1,2,3] [1]UFRGS, Institute of Basic Health Sciences, PPG in Biological Sciences: Pharmacology and Therapeutics, Brazil. [2]HCPA, Lab Pain Pharmacology and Neuromodulation: Preclinical Investigations, Brazil. [3]UFRGS, School of Medicine, PPG in Medicine: Medical Sciences, Brazil.

Introduction: Neuropathic pain (NP) is difficult to manage and does not respond adequately to conventional treatments. Modulating the endocannabinoid system (ECS) by inhibiting the enzymes fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MAGL) raises levels of anandamide (AEA) and 2-arachidonoylglycerol (2-AG), which may help treat NP. **Objectives:** To evaluate the effects of repeated low doses of the dual FAAH/MAGL inhibitor JZL195 on nociceptive response, locomotor and exploratory activities, and central levels of BDNF in rats subjected to the sciatic nerve chronic constriction injury (CCI) model. **Methodology:** Fifty adult male Wistar rats were randomly assigned to five groups (n = 10/group): (1) Control (CT); (2) SHAM: surgery without nerve constriction; (3) NP: submitted to CCI surgery; (4) NPvh: CCI + vehicle treatment; and (5) NPJZL: CCI + JZL195 treatment. This study was approved by CEUA/HCPA (#2023.0141). On day 0 (D0), the animals underwent SHAM or CCI surgery. On D14, mechanical allodynia was assessed by the von Frey (VF) test to confirm the establishment of the NP model. On D15, treatments were initiated and consisted of five days (D15–D19) with vehicle (Tween 80/propylene glycol/saline solution, 2 ml/kg, i.p.) or JZL195 (3 mg/kg/day, i.p.). On D17, locomotor and exploratory activities were assessed using the open field test. The VF test was repeated at the end of the treatment (D19). On D20, the animals were euthanized, and the hippocampus (HC), brainstem (BS), and lumbar spinal cord (LSC) were dissected for analysis of the levels of BDNF by ELISA. Data were analyzed using GEE and one-way ANOVA, with results expressed as mean ± SEM at a significance level of $P < 0.05$. **Results:** The NP groups exhibited mechanical allodynia, confirming the effectiveness of the NP model (GEE/Bonferroni, $P < 0.01$). There was no effect of JZL195 treatment on the mechanical nociceptive threshold. In the open field test, the one-way ANOVA indicated a difference between groups in grooming time ($P = 0.032$); the SHAM and NPJZL groups showed higher grooming times than the CT group (Duncan, $P < 0.05$); NP and NPvh were similar to the other groups (Duncan, $P > 0.05$). No significant differences were observed between groups in BDNF levels in the BS ($P = 0.076$), HC ($P = 0.672$), and LSC ($P = 0.235$). **Conclusion:** The CCI model was effective in generating mechanical allodynia. The FAAH/MAGL inhibition by repeated low doses of JZL195 did not affect mechanical allodynia. On the other hand, it increased grooming behavior, which may act as an "arousal-inhibitory system," aiding the animal in restoring equilibrium, indicating a potential central effect of JZL195. The dissociation between behavioral and nociceptive outcomes highlights the complexity of ECS modulation and emphasizes the importance of establishing effective dosing protocols for the translation of cannabinoid-based therapies.

05.036 **Antinociceptive Activity of Antidepressant Drugs**. Oliveira MMF[1], Batista CB[1], Rodrigues DCN[1], Sousa RWR[1], Almeida ML[1], Freitas MM[1], Silva CLA[1], Feitoza LLS[1], Ferreira PMP[1,2] [1]UFPI, Lab Experimental Cancerology (LabCancer), Dept Biophysics and Physiology, PPG Pharmacology, Brazil; [2]UFC, Lab Experimental Oncology (LOE), Dept Physiology and Pharmacology, Brazil

Introduction: Nociceptive pain remains an important therapeutic challenge, highlighting the need for new pharmacological alternatives. Drug repositioning represents a promising strategy to accelerate therapy development while reducing costs and research time. In this context, antidepressants have attracted attention due to their ability to modulate pathways involved in nociception. **Objective:** To evaluate the preclinical antinociceptive potential of antidepressants currently used in clinical practice and to investigate the pharmacological mechanisms of selegiline as a promising candidate for drug repositioning. **Methods:** Initially, female Swiss mice (CEUA/UFPI #0885/2025) were pretreated with antidepressants amitriptyline, bupropion, desvenlafaxine, fluoxetine, mirtazapine, selegiline, trazodone (20 mg/kg, p.o.) and received an injection of acetic acid 1% for screening of antinociceptive activity based on the number of abdominal contortions and latency to the first writhing. Selegiline, showing the most pronounced effects, was subsequently evaluated in the formalin test (2.5%, intraplantar) to analyze neurogenic and inflammatory phases of nociception through paw licking time (in seconds). To investigate the underlying pharmacological mechanisms, animals were pretreated with naloxone (5 mg/kg, i.p.), atropine (2 mg/kg, i.p.), L-NAME (20 mg/kg, i.p.), glibenclamide (10 mg/kg, i.p.), or cimetidine (25 mg/kg, i.p.) before selegiline administration (20 mg/kg, p.o.). Data were assessed by one-way ANOVA followed by Dunnett ($p < 0.05$). **Results:** With exception for desvenlafaxine, all drugs (amitriptyline, bupropion, fluoxetine, mirtazapine, selegiline, and trazodone) diminished number of contortions, but selegiline stood out, with 74% reduction (29.82 ± 3.92) and similar to that for morphine- treated animals (12.46 ± 5.65) when compared with the negative control (112.8 ± 10.7, $p < 0.05$). Selegiline and fluoxetine significantly increased the latency to the first writhing (454.4 ± 41.11 and 537.7 ± 100.9 s, respectively; negative control: 177.6 ± 24.1 s). Selegiline reduced nociceptive behavior during the neurogenic step (1st phase: 41.9 ± 18.5 s) and completely suppressed paw licking behavior during the inflammatory phase when compared to the negative control (100.0 ± 16.2 and 111.9 ± 31.2 s, respectively, $p < 0.05$). Antinociception-related selegiline effects were not blocked that by the pretreatment with cimetidine, atropine, L-NAME, and glibenclamide ($p < 0.05$). Meanwhile, naloxone attenuated but not reversed the antinociceptive action of selegiline (66.0 ± 34.3 s). **Conclusion:** Among all antidepressants evaluated, selegiline exhibits strong antinociceptive action in experimental *in vivo* pain models. particularly against inflammatory nociception. **Financial support:** CNPq and CAPES

05.037 **Transcranial Direct Current Stimulation Attenuates Mechanical Hypernociception in Collagen-Induced Arthritis Mice without Modifying Disease Severity**. Santos, NG[1,2,3], Leite, ADD[2], Freitas, VS[2], Gaia, R[2], Flor, B[2,3], Vieira, MLG[2], Chapacais, GF[2], Pilotti, S[1,2,3], Stein, DJ[1,3], Torres, ILS[1,3], Xavier, RM[1,2]1UFRGS, School of Medicine, PPG in Medical Sciences, Porto Alegre, Brazil; [2]Hospital de Clínicas de Porto Alegre (HCPA), Division of Rheumatology, Lab Autoimmune, Porto Alegre, Brazil; [3]Hospital de Clínicas de Porto Alegre (HCPA), Lab Pain Pharmacology and Neuromodulation: Preclinical Investigations, Porto Alegre, Brazil

Introduction: Rheumatoid arthritis (RA) patients frequently experience persistent pain despite adequate inflammatory control, suggesting the involvement of central sensitization and dysfunction of descending inhibitory pathways. Transcranial direct current stimulation (tDCS) is a non-invasive neuromodulation technique capable of modulating nociceptive and neuroinflammatory mechanisms. **Objective:** To evaluate the effects of tDCS on nociceptive and inflammatory outcomes in mice with collagen-induced arthritis (CIA). **Methods:** Thirty male DBA/1J mice were allocated into four groups (n=6–8): healthy control (CO) and arthritis treatment groups: CIA+sham tDCS (CIAS), CIA+active tDCS (CIAT), and CIA+anesthesia (CIAA). Arthritis was induced by the injection of bovine type II collagen (CII) diluted in Complete Freund's Adjuvant (CFA) on day zero (D0), followed by a booster dose 18 days later using CII diluted in Incomplete Freund's Adjuvant (IFA). Active or sham tDCS (0.5 mA, 1 Hz) was applied daily from day 30 to day 40 post-induction for 15 minutes, under 2% isoflurane anesthesia. Body weight, arthritis clinical score, locomotor and exploratory behavior, evaluated by Open Field Test, and mechanical allodynia, evaluated by von Frey test, VFT, were assessed throughout 45 days. Data were analyzed using repeated-measures ANOVA, Tukey's post hoc test, and Spearman correlation ($p<0.05$). Approved by the Institutional Ethics Committee on the Use of Animals (nº2023.0484). **Results:** CIAS animals showed reduced body weight at D40 from CO ($p=0.018$). Arthritis scores remained elevated in CIAT and CIAS at D40 ($p=0.026$ and $p=0.030$, respectively) and in CIAS at D45 ($p=0.025$) compared with CO. The mechanical allodynia progressively increase during disease progression, with higher allodynia observed in CIAA animals at D35 ($p=0.012$) and D42 ($p=0.010$), and in CIAS at D42 ($p=0.010$), compared with CO. No difference in the mechanical allodynia was detected between CO and CIAT from D35. A negative correlation was observed between arthritis clinical scores and the mechanical nociceptive threshold assessed by the von Frey test (VFT) at different experimental time points: arthritis score at D25 and VFT at D21 (rho=-0.481; $p=0.008$), arthritis score at D30 and VFT at D28 (rho=-0.457; $p=0.013$), arthritis score at D35 and VFT at D35 (rho=-0.513; $p=0.009$), arthritis score at D40 and VFT at D35 (rho=-0.473; $p=0.017$) and D42 (rho=-0.628; $p=0.001$), as well as arthritis score at D45 and VFT at D42 (rho=-0.641; $p=0.001$). **Conclusion:** Repeated tDCS applied during the course of CIA diminished mechanical allodynia without affecting the clinical severity of arthritis, indicating a modulatory influence on pain processing pathways rather than peripheral inflammatory pathways. These findings reinforce the potential of tDCS as an adjunct neuromodulatory approach for pain management in rheumatoid arthritis.

05.038 **Central Sensitization in a Viral Infection Model Facilitates Migraine-like Responses in Female Rats**. Baggio DF., Borges AP., Schneider VMM., Costa RA., Alencar TS., Malheiros MB., Pereira V., Zampronio ARUFPR – Inflammation and Fever Lab, PPG Pharmacology, Brazil

Introduction: Viral infections can trigger persistent inflammatory changes and neurological symptoms, including fatigue, headache, and migraine, which have been reported more frequently in women. Migraine is a complex neurological disorder associated with trigeminovascular system sensitization and neuroinflammation. In the pathophysiology of migraine, inflammatory mediators such as endothelin-1 (ET-1) may contribute to the amplification and maintenance of nociceptive signaling. However, the impact of previous viral-like systemic inflammation on subsequent ET-1-induced migraine-like responses remains unclear. **Objectives:** This study aimed to evaluate whether previous viral-like systemic inflammation promotes central sensitization and facilitates ET-1-induced migraine-like responses in female rats. **Methods:**. Experiments were conducted in 60-day-old female Wistar rats. Systemic inflammation was induced by intraperitoneal injection of polyinosinic:polycytidylic acid (Poly I:C; 600 µg/kg), a synthetic double-stranded RNA that mimics viral infection. To characterize the acute effects of Poly I:C administration, mechanical hind paw hyperalgesia, spontaneous locomotor activity, and periorbital allodynia were assessed. Three days after the resolution of periorbital allodynia, migraine-like responses were induced by intraganglionic injection of ET-1 (1 or 10 pmol/10 µL) into the trigeminal ganglion, and periorbital mechanical allodynia and photosensitivity were evaluated. **Results:** Female rats subjected to Poly I:C injection exhibited paw hyperalgesia as early as the first hour after administration, which persisted until the second day after stimulation, whereas periorbital allodynia persisted longer, until the seventh day. No statistical differences were observed in locomotor activity throughout the evaluation period. Notably, the lower dose of ET-1 evoked migraine-like responses exclusively in Poly I:C-treated rats, whereas the higher dose induced comparable responses in both vehicle- and Poly I:C-treated groups. **Conclusion:** Previous viral-like systemic inflammation promotes central sensitization, thereby facilitating ET-1-induced migraine-like responses in female rats. Approval by the Animal Research Ethics Committee: The experimental protocols were submitted for evaluation by the Animal Use Ethics Committee (CEUA – BIOUFPR) with approval number 1675/2025. **Financial support:** CAPES and CNPq.

05.039 **L-Malic Acid in a Mouse Model of Neuropathy: Pharmacodynamic and Pharmacokinetic Aspects**. Calazans MO[1], Viana GB[1], Machado DPD[1], Pires LO[2], Reis ISFS[2], Fernandes SOA[2], Cardoso VN[2], Romero TRL[1], Duarte IDG[1], Perez AC[1] [1]UFMG, Lab Pain and Analgesia, Dept Pharmacology, Institute of Biological Sciences, [2]UFMG, Lab Radioisotopes, Dept Clinical and Toxicological Analysis, Faculty of Pharmacy

Pain is defined as an unpleasant sensory and emotional experience, and its chronicity can affect an individual's well-being; chronic neuropathic pain results from lesions in the nervous system. Its treatment is multifactorial, and the pharmacological approach is not always entirely effective. In this context, the search for new therapeutic alternatives is essential. Malic acid is a natural compound abundant in nature, with low toxicity, and is used in the food and pharmaceutical industries. Preliminary studies from our group indicate that L-malic acid has a significant antinociceptive effect in neuropathic pain models, reversing hypernociception upon acute treatment (800 µg/paw), through the recruitment of the endocannabinoid system and the PI3Ky/NO/cGMP/K+ channels. Nitric oxide (NO) is an important intracellular signalling molecule and exhibits dual effects on pain, depending on its concentration. Therefore, one of the objectives of the present study was to quantify NO levels in the method employed. Furthermore, the effects of repeated-dose treatment with malic acid on dose tolerance in neuropathic animals, as well as its biodistribution to identify target organs in healthy animals, were investigated. Male and female Swiss mice, approximately eight weeks old, were used (CEUA: 238/2024). NO levels were quantified using the Griess method, which measures nitrite concentration, a stable metabolite of NO, by spectrophotometry. For the tolerance assay, animals underwent sciatic nerve constriction surgery, and hypernociception was measured using the paw compression test. Assessments were performed daily, and from day 11 onwards, L-malic acid was administered (at doses of 20, 40 e 60 mg/kg, intraperitoneally) to construct the time-effect X dose-response curve. For the distribution profile assay, L-malic acid was labelled with technetium-99m (^{99}ᵐTc), and the ^{99}ᵐTc-L-malic acid complex was administered intraperitoneally to healthy animals. Analyses were performed using *in vivo* scintigraphic imaging (Nucline® gamma camera – Mediso) and ex vivo gamma counting of organs (Wizard2® 2470 gamma counter – Revvity) at 1 hour and 24 hours. The results showed an increase in NO release at a dose of 800 µg/paw in naïve animals, whereas this increase was smaller in neuropathic animals. Regarding tolerance, the doses of 40 60 mg/kg reversed 50% and 100% of the hypernociception, respectively, in a sustained and unchanged manner over the 10 days of treatment; and the biodistribution profile identified the spleen and liver as target organs, while other organs exhibited reduced uptake of the complex. In conclusion, based on the **Results:** L-malic acid 800 µg/paw induces local NO release; no tolerance to the doses was developed during repeated-dose treatment; and in the case of prolonged therapy with L-malic acid, hepatosplenic function requires attention and monitoring. The suggestion is that L-malic acid is an innovative therapeutic candidate for neuropathic pain.

05.040 **Treatment with Repeated Low Doses of JZL195, a Dual Inhibitor of Endocannabinoid-Metabolizing Enzymes, Fails to Reverse Thermal Hyperalgesia in Rats Subjected to a Neuropathic Pain Model**. Stein DJ[1,2], Marçal MM[1,3], Moreira ERAS1, Chagas MC1, Caumo W[1,2], Torres ILS[1,2,3] 1HCPA, Lab Pain Pharmacology and Neuromodulation: Preclinical Investigations, Brazil; [2]UFRGS, School of Medicine, PPG in Medicine: Medical Sciences, Brazil; [3]UFRGS, Institute of Basic Health Sciences, PPG in Biological Sciences: Pharmacology and Therapeutics, Brazil

Introduction: Neuropathic pain (NP) affects 7–10% of the human population. Currently available treatments are often ineffective or cause significant adverse effects, highlighting the need for novel therapeutic strategies. In this sense, modulation of the endocannabinoid system, which is comprised of the endocannabinoids anandamide (AEA) and 2-arachidonoylglycerol (2-AG), their degrading enzymes, fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MAGL), respectively, and cannabinoid receptors CB1 and CB2, has emerged as a promising approach for NP management. **Objectives:** To evaluate the effects of repeated administration of low doses of JZL195, a dual FAAH/MAGL inhibitor, on nociceptive behavior and neuroinflammatory markers in rats submitted to the chronic constriction injury (CCI) model. **Methods:** Fifty adult male Wistar rats were randomly assigned to five groups (n = 10/group): (1) Control (CT); (2) SHAM: surgery without nerve constriction; (3) NP: submitted to CCI surgery; (4) NPvh: CCI + vehicle treatment; and (5) NPJZL: CCI + JZL195 treatment. On day 0 (D0), animals underwent CCI surgery. Thermal hyperalgesia was assessed on D14 using the hot plate test to confirm the establishment of NP. Treatment consisted of five days (D15–D19) with vehicle (Tween 80/propylene glycol/saline solution, 2 ml/kg, i.p.) or JZL195 (3 mg/kg/day, i.p.). After euthanasia, the levels of TNF-α in the hippocampus (HC), brainstem (BS), and lumbar spinal cord (LSC), as well as the levels of IL-10 in the LSC, were quantified by ELISA. Data were analyzed using one-way ANOVA / Duncan, with a significance level of $P < 0.05$. **Results:** The CCI model successfully induced thermal hyperalgesia in NP groups ($F(4,45) = 3,415$; $P = 0.016$). However, JZL195 treatment did not reverse this nociceptive response. Post hoc comparisons indicated that the NP, NPvh, and NPJZL groups were similar to each other ($P > 0.05$, for all), yet exhibited lower thermal thresholds than the CT group ($P < 0.05$, for all). No significant differences were observed from the SHAM group ($P > 0.05$, for all). TNF-α levels in the LSC exhibited significant differences among groups ($F(4,45) = 2,931$; $P = 0.031$), with reduced levels in the NPvh group relative to the NP and SHAM groups ($P < 0.05$, for both). No differences were detected among the other groups ($P > 0.05$, for all). JZL195 seems to have partially prevented a reduction in TNF-α levels in the LSC induced by its vehicle. No significant differences were observed across groups for TNF-α levels in the HC ($F(4,45) = 0,852$; $P = 0.500$) and BS ($F(4,45) = 1,078$; $P = 0.379$). **Conclusion:** Repeated administration of low-dose JZL195 did not reverse thermal hyperalgesia in rats with NP. However, JZL195 modulated spinal TNF-α levels, suggesting a possible effect on neuroinflammatory pathways. These findings support a likely dose-dependent response and highlight the importance of dose optimization in the development of endocannabinoid-based therapies for pain management.
Keywords: Chronic neuropathic pain; Fatty acid amide hydrolase (FAAH); Monoacylglycerol lipase (MAGL), TNF-α, IL-10

05.041 **Microcirculatory and Antinociceptive Effects of Photobiomodulation in Chronic Constriction Injury**. Baptista FBO[1], Bonifácio RP[1], Santos MER[1], Elias MLC[2], Santos TCS[2], Gonçalves LRC[2], Zychar BC[2],Chacur M[1] [1]ICB-USP, Dept Anatomy, Functional Neuroanatomy of Pain Lab, Sao Paulo, Brazil. [2]IBu, Pathophysiology Lab, Sao Paulo, Brazil.

Introduction: Neuropathic pain is associated with persistent neuroimmune activation and inflammatory responses, including alterations in microvascular dynamics and leukocyte recruitment. These vascular events contribute to the maintenance and amplification of pain states. Photobiomodulation therapy (PBMT) has emerged as a promising non-pharmacological approach due to its anti-inflammatory and analgesic properties; however, its effects on inflammatory alterations in the microcirculation associated with neuropathic pain remain poorly understood. **Objectives:** This study investigated the effects of PBMT on nociceptive behavior and mesenteric microcirculatory alterations induced by chronic constriction injury (CCI). **Methods:** Male Wistar rats (CEUA 1955290825) underwent CCI surgery and received PBMT treatment (904 nm, 7 J/session). Mechanical sensitivity was evaluated throughout the experimental period.Two therapeutic approaches were analyzed: a preventive protocol, in which PBMT was initiated 5 days before CCI and maintained for 7 days after surgery, and a reversal protocol, initiated 14 days after CCI induction and performed for 10 consecutive days. Inflammatory responses were assessed by intravital microscopy through the quantification of rolling, adherent, and migrated leukocytes in mesenteric post-capillary venules. **Results:** CCI promoted marked mechanical hypersensitivity accompanied by increased leukocyte–endothelium interactions and leukocyte migration, indicating inflammatory alterations in mesenteric microcirculation. PBMT significantly reduced nociceptive hypersensitivity and attenuated leukocyte recruitment, particularly leukocyte migration, demonstrating modulation of inflammatory cell trafficking.Preventive PBMT limited the establishment of inflammatory responses, whereas the reversal protocol improved established microvascular dysfunction and persistent pain behavior. **Conclusion:** These findings suggest that PBMT exerts both protective and therapeutic effects on neuropathic pain through the modulation of leukocyte–endothelium interactions and inflammatory alterations in mesenteric microcirculation. The results further support the potential of PBMT as a strategy capable of targeting different stages of neuropathic pain progression.

05.042 **Ketamine Reduces Formalin-Induced Inflammatory Nociception in Male Mice: Preliminary Dose-Response Evidence**. Silva AJM, Mascarenhas DC UEM, Dept Pharmacology and Therapeutics, Brazil Graduate Program in Pharmaceutical Sciences, Brazil

Introduction: Pain is a complex sensory and emotional experience involving peripheral and central mechanisms of modulation, with glutamatergic neurotransmission playing a key role in nociceptive processing. Ketamine, a noncompetitive NMDA receptor antagonist traditionally used as a dissociative anesthetic, has gained attention at subanesthetic doses due to its potential antinociceptive and neuroplastic effects. **Objective:** This study aimed at determining an analgesic dose of ketamine in male mice submitted to an inflammatory pain model induced by formalin injection into the paw. **Methods:** Male mice were first evaluated in the hot plate test to exclude intrinsic differences in basal nociceptive sensitivity among experimental groups. Subsequently, animals (n=5-8) received vehicle or ketamine at 10, 25, or 50 mg/kg and were submitted to the formalin test. Nociceptive behavior was quantified as the time spent licking the formalin-injected paw. Data were analyzed by one-way ANOVA followed by Duncan's post hoc test. **Results:** The hot plate test indicated no relevant baseline nociceptive bias ($p > 0.05$) among groups before pharmacological treatment. In the formalin test, ketamine produced a dose-related reduction in paw-licking time, with the highest dose showing the most pronounced antinociceptive effect. Although one-way ANOVA indicated a strong trend toward significance among groups ($F_{3,19} = 2.51$; $p = 0.0896$), Duncan's post hoc analysis revealed a significant reduction in nociceptive behavior in animals treated with ketamine 50 mg/kg compared with vehicle-treated controls ($p = 0.0319$). These preliminary findings suggest that 50 mg/kg ketamine may represent an effective analgesic dose under the present experimental conditions. **Conclusions** : Despite the limited sample size, especially in the treated groups, the observed dose-dependent profile supports the continuation of the study with an increased number of animals. This dose will be used in subsequent experiments investigating whether ketamine can reverse susceptibility-induced hypernociception in mice exposed to social stress, a model designed to distinguish resilient and susceptible phenotypes. Thus, these data provide an initial pharmacological basis for exploring ketamine as a glutamatergic modulator of inflammatory pain and stress-related vulnerability to enhanced nociception. **Acknowledgments:** All tests were approved by the local Animal Research Ethical Committee (CEUA nº 2134170325). This study was supported by UEM, Fundação Araucária, and CNPq.

05.043 **Antinociceptive and Anti-Inflammatory Effects of Different Full Spectrum Oils of Phytocannabinoids in Mice Models of Pain and CFA Induced Inflammation**. Junger MG, Matheus ME, Oliveira DR, Miranda ALP. UFRJ, Faculty of Pharmacy, PPG Pharmaceutical Sciences, Brazil

Introduction: Pain significantly impacts global quality of life and generates high healthcare costs. Phytocannabinoids offer therapeutic potential by modulating the endocannabinoid system (ECS) which regulates pain and inflammation through CB1 and CB2 receptors (Johnson, BW. Biomedicines, v. 13, p. 530, 2025). **Objectives:** To evaluated the antinociceptive and anti-inflammatory profile of five phytocannabinoids full-spectrum oils: Extract 1 (CBG), Extract 2 (THC), Extract 3 (CBD/THC), Extract 4 (CBD) and Extract 5 (THCV/THC) using Swiss mice in hot plate, capsaicin, formalin, CFA-induced inflammation and open field tests. **Methods:** Eight-week-old adult mice of both sexes were treated orally with extracts at doses of 10 mg/kg, 20 mg/kg, or 30 mg/kg one hour before nociceptive stimuli. In the CFA model, the animals received an intraplantar injection of CFA (20 µL) and pain and inflammation parameters were monitored for 15 days: mechanical allodynia/hyperalgesia (von Frey filaments), edema (paw thickness) and locomotor activity (open field test). **Results:** At 10 mg/kg, Extract 4 (CBD) was the most effective, inhibiting capsaicin-induced licking by 54% and increasing hot plate latency by 40%, comparable to morphine. While Extracts 1, 2, 3, and 5 showed no significant effect at 10 mg/kg, higher doses yielded different outcomes. In the 30 mg/kg capsaicin model, four of the five extracts (Extracts 2, 3, 4, and 5) significantly reduced nociceptive behavior by 40–50% compared to control ($p < 0.05$). No significant effect was observed in formalin test at doses of 10 and 20 mg/kg. Open field tests confirmed that these effects were not associated with sedation. In the CFA model (10 mg/kg), hyperalgesia is significantly inhibited by THC, CBD and CBD/THC in both sexes, with greater effect in females. CBD/THC was less effective compared to unique treatment. **Conclusion:** Results confirm the antinociceptive efficacy of CBD and demonstrate that higher doses (30 mg/kg) of other phytocannabinoids compositions (Extracts 2, 3, 4, and 5) also presents potential in modulating acute and chronic pain. Dimorphism observed in CFA model may result from estradiol potentiation and CB1/CB2 recruitment; males rely mainly on CB1, yielding greater therapeutic efficacy in females during persistent inflammatory pain (Blanton, HL. Pharmacol. Biochem. Behavior, v. 202, p. 173107, 2021). Future studies with different doses may reveal distinct responses. **Financial Support**: CAPES. CEUA/UFRJ 044/26. **Acknowledgments:**: APEPI, CAPES.

05.045 **Development of Murine Platform for Investigating Neuroinflammatory Targets in Post-COVID Pain Induced by the Spike Protein**. Trefilio LM[1,2], Guimenes BD[1,3], Fernandes GG[1,4], Mesquita IA[1], Rezende B[1,3], Gonçalves VMS[1,3], Montes GC[1,2,4], Fontes-Dantas FL[1,2,4] [1]UERJ, Roberto Alcantara Gomes Biology Institute, Dept Pharmacology and Psychobiology, NeuroPharmacoGenetics Lab, Brazil. [2]UERJ, Roberto Alcantara Gomes Biology Institute, Dept Pharmacology and Psychobiology, PPG Biosciences, Brazil. [3]UERJ, Roberto Alcantara Gomes Biology Institute, Dept Pharmacology and Psychobiology, PPG Clinical and Experimental Pathophysiology, Brazil. [4]UFJF, Dept Biophysics and Physiology, Brazil.

Introduction: The SARS-CoV-2 pandemic has highlighted significant chronic neurological challenges known as Long COVID, which may manifest as fatigue, "brain fog" and debilitating painful symptoms such as myalgia and neuropathic pain. A proposed mechanism for these sequelae is Autoimmune Encephalitis, an immune-mediated inflammatory CNS disorder. Corroborating this hypothesis, previous studies have shown that Spike protein (SP) possesses structural similarities with Myelin Oligodendrocyte Glycoprotein (MOG), a well-known peptide related with deflagration of multiple sclerosis and widely used in experimental autoimmune encephalomyelitis (EAE). Our hypothesis is that SP induces persistent hyperalgesia in rats in a similar fashion as EAE. **Objectives:** Develop and clarify the role of immune response in an animal model of long COVID associated with persistent pain. **Methods:** Male Wistar rats (Committee approval N°029/2024) were immunized via subcutaneous injection with MOG35-55, Total SP, SP fragment 249-278 or a vehicle. Nociceptive tests for thermal and mechanical hyperalgesia were conducted between the 0 and 21st days post-immunization. Spinal cord analysis involved metabolomic, and immunohistochemistry for GFAP, IBA1, TNF, MBP, FluoroMyelin (FM), SYP and PSD95. Systemic immune responses were characterized in serum via ELISA (anti-MOG and anti-SP) and in the spleen through gene expression targeted for IFN, IL6, TNF, CTLA4 and PDCD1. **Results:** Rats immunized with MOG, SPT or 249-278 displayed significant hyperalgesia ($p<0,0001$, either), without the classic paralysis scores seen in standard EAE. Immunofluorescence revealed a robust gliosis in dorsal horn, with microglial ($p<0,0001$) and astrocytes ($p<0,0076$) increased density associated with altered morphology ($p=0,0008$). Also, an increased immunoreactivity for TNF was observed ($p=0,008$). Regarding myelin integrity, FM ($p=0,0659$) and MBP ($p=0,0108$) analysis showed a slight reduction in MBP stain without whole myelin reduction. Metabolomic analysis revealed perturbation in the excitatory synapses of all immunized rats, which was further corroborated by augmented colocalization of synaptic markers PSD95 and SYP in layers I/II of dorsal horn ($p=0,0127$). ELISA showed that anti-MOG antibodies were not altered in SP groups. Gene expression indicates an increase in the cellular immune response, with elevated mRNA levels of TNF ($p=0,0179$), IL6 ($p=0,0009$), IFN ($p<0,0001$), PDCD1 ($p=0,0103$), and CTLA4 ($p=0,0017$) confirming a T-cell-mediated environment. **Conclusion:** The SP triggers an EAE-like neuroinflammatory state where pain sensitization is driven by central neuroinflammatory and synaptic mechanisms rather than direct demyelination. These findings support the use of this platform for the investigation of pharmacological strategies targeting neuroinflammation and maladaptive synaptic plasticity associated with persistent pain in Long COVID. **Acknowledgments:** The study was supported by FAPERJ and CAPES.

05.046 **Sex and Environmental Factors Influence FFA1 Receptor and BDNF Expression in a Mouse Model of Inflammatory Pain**. Estrázulas M[1,2], Neculqueo GW[1,2], Farias ABS[1,2], Campos MM[1,2] [1]PUCRS, PPG em Medicina e Ciências da Saúde, Porto Alegre, RS, Brazil, [2]FADIC, Escola de Ciências da Saúde e da Vida, Porto Alegre, RS, Brazil.

Introduction: Every year, 20% of the global population experiences chronic pain (Presto P. Int. J. Mol. Sci., v. 24, 11944, 2023), with females significantly outnumbering males among patients. Pre-clinical research continues to explore how animal models can better replicate the complexity of human pain. Environmental enrichment (EE) is a paradigm that promotes species- specific behaviors, reducing stress and improving well-being. These behavioural changes trigger morphological modifications, such as brain-derived neurotrophic factor (BDNF) expression, favoring neuronal survival (Murakami S. Neurosci. Res., v. 53, p. 129, 2023). Studies have shown a link between the Free Fatty Acid Receptor 1 (FFA1) and neurogenesis in the hypothalamus, ameliorating pain sensitivity (Engel DF. Sci. Rep., v.6, 1107, 2020). **Objectives:** Few animal studies examine sex dimorphism and environmental enrichment (EE) when evaluating pharmacological strategies for inflammatory pain. We explored the interaction between EE, sex, BDNF, and FFA1 receptor modulation in a mouse model of inflammatory pain. **Methods:** C57BL/6J mice received complete Freund's adjuvant (CFA; 50 ml) intraplantarly, and brain slices were assessed for neuromodulation after 21 days. They received the FFA1 partial agonist GW9508 (2 and 8 mg kg^{-1}) or the selective antagonist GW1100 (4 mg kg^{-1}) from days 7 to 14 under standard or EE conditions (under rotation using cotton balls, wood blocks, plastic tunnels, Lego® blocks, and cardboard paper). Cortical levels of BDNF and FFA1 receptors were assessed by immunohistochemistry in the whole cortex and the anterior cingulate cortex (ACC). This project was approved by the ethics committee (CEUA PUCRS 11019). **Results:** GW9508 increased cortical BDNF counts in females under both SE (8 and 2 mg kg^{-1}; $p = 0.0028$ and $p = 0.0056$) and EE (2 mg kg^{-1}; $p = 0.047$). In males, cortical BDNF increased only with 8 mg kg^{-1} under SE ($p = 0.0136$) and EE ($p = 0.0348$). GW1100 reduced cortical BDNF in females from both environments (SE $p = 0.0098$; EE $p = 0.0127$), whereas in males this reduction occurred only under EE ($p = 0.0065$). In the ACC, BDNF increased only in EE females treated with GW9508 2 mg kg^{-1} ($p = 0.0172$). Cortical FFA1 expression decreased in females treated with GW1100 under SE ($p = 0.0012$) and EE ($p = 0.0392$). In males, GW9508 (8 mg kg^{-1}) increased cortical FFA1 under SE ($p = 0.0301$), while GW1100 reduced expression under EE ($p = 0.0047$). In the female ACC, FFA1 immunopositivity increased with GW9508 in SE (8 mg kg^{-1} $p = 0.0302$; 2 mg kg^{-1} $p = 0.0227$) and EE (8 mg kg^{-1}; $p = 0.0008$). In males, ACC FFA1 increased under SE only with GW9508 8 mg kg^{-1} ($p = 0.0002$), whereas EE responded to both 8 mg kg^{-1} ($p = 0.0005$) and 2 mg kg^{-1} ($p = 0.0165$). **Conclusion:** and Implications: These findings highlight the interaction between EE, BDNF, and FFA1 receptors, emphasizing sex differences in responses to chronic inflammatory pain.

05.047 **Structure–Property Relationship of Alkyl 4-Phenylbenzoates: ADMET profiling and Antinociceptive Activity of Pentyl 4-Phenylbenzoate in Experimental Neuropathic Pain**. Oliveira JLS[1], Prado FM[1], Reis Filho AC[1], Gomes JGF[2], Barbosa BS[2], Santos ALS[3], Sousa DP[4], Almeida FRC[1]. [1]UFPI, LAFDOR, PPGFARM, Brazil; [2]UFPI, LPNNEX, PPGFARM, Brazil; [3]UFPI, LPNNEX, PPGQ, Brazil; [4]UFPB, Dept Pharmacy, Brazil

Introduction: Neuropathic pain is a chronic condition associated with sensory dysfunction and limited therapeutic options. Structural modification of bioactive molecules is an important strategy in drug discovery to optimize pharmacokinetic and pharmacodynamic properties. Alkyl 4-phenylbenzoates represent a promising class of compounds whose biological activity may be influenced by changes in lipophilicity, molecular flexibility, and absorption-related properties. **Objectives:** To investigate the structure–property relationship of alkyl 4-phenylbenzoate derivatives through *in silico* ADMET analysis and correlate these properties with the antinociceptive activity of pentyl 4-phenylbenzoate in an experimental model of neuropathic pain. **Methods:** A series of structurally related compounds, including 4-phenylbenzoic acid and its methyl, ethyl, propyl, butyl, and pentyl esters, were evaluated using the ADMETlab 3.0 platform. Physicochemical and medicinal chemistry parameters, including molecular weight, lipophilicity (logP), aqueous solubility (logS), topological polar surface area (TPSA), molecular flexibility, and quantitative estimate of drug-likeness (QED) were analyzed. The antinociceptive activity of pentyl 4-phenylbenzoate was evaluated in mice subjected to paclitaxel-induced neuropathic pain following oral administration at doses of 50, 100 and 200 mg/kg for 10 consecutive days, with behavioral assessments performed every two days using the acetone and von Frey tests. Statistical significance was considered at $p < 0.05$. **Results:** ADMET analysis demonstrated that increasing the alkyl chain length progressively enhanced molecular flexibility and lipophilicity, with logP values ranging from 3.61 for 4-phenylbenzoic acid to 5.38 for pentyl 4-phenylbenzoate, while aqueous solubility decreased accordingly. Despite these changes, all derivatives maintained favorable molecular weight, TPSA, and drug-likeness profiles according to Lipinski's rule of five. In the *in vivo* assays, pentyl 4-phenylbenzoate exhibited a dose-dependent antinociceptive effect, with the 200 mg/kg dose producing a significant reduction in nociceptive responses throughout the experimental period in both the acetone and von Frey tests. The observed pharmacological effect may be associated with improved membrane permeability and tissue distribution resulting from increased hydrophobicity, suggesting a positive relationship between structural modification and biological activity. These findings indicate that alkyl chain elongation may contribute to the optimization of pharmacologically relevant properties within this chemical series. **Conclusion:** The integration of experimental and computational data suggests that structural modifications of alkyl 4-phenylbenzoates directly influence their physicochemical and pharmacokinetic properties. The superior antinociceptive activity observed for pentyl 4-phenylbenzoate, particularly at the 200 mg/kg oral dose, may be related to its increased lipophilicity and molecular flexibility, highlighting this derivative as a promising scaffold for the development of new therapeutic agents for the treatment of neuropathic pain.

05.048 **Effect Level Dependent Antinociceptive Interaction between Cannabidiol and Cannabigerol in a Rat Model of Streptozotocin-Induced Diabetic Neuropathy: an Isobolographic Analysis**. Rauchbach L[1], Ferreira MV[1], Rampim LR[1], Wolaniu L[1], Castro-Junior CJ[2]; Crippa JA[3]; Zanoveli JM[1], Cunha JM[1]. [1]UFPR, Dept Pharmacology, Curitiba, PR, Brazil; [2] IEP SCBH, Núcleo de Pós-Graduação, Belo Horizonte, MG, Brazil; [3]FMRP-USP, National Institute for Translational Medicine (INCT-TM, CNPq); Dept Neuroscience and Behavior, University of São Paulo, Ribeirão Preto, SP, Brazil.

Introduction: Neuropathic pain is a prevalent and debilitating complication of diabetes, for which current treatments offer limited efficacy and significant side effects. Cannabidiol (CBD) and cannabigerol (CBG) are non-psychotomimetic phytocannabinoids with documented antinociceptive activity, but their pharmacological interaction in diabetic neuropathic pain remains uncharacterized. **Objectives:** This study used isobolographic analysis to classify the CBD+CBG interaction in a rat model of streptozotocin (STZ)-induced diabetes. **Methods:** Diabetes was induced in male Wistar rats by a single intraperitoneal injection of STZ (60 mg/kg). Mechanical allodynia was assessed using the electronic von Frey test before and after treatment with CBD (0.1, 0.3, or 3 mg/kg, i.p.), CBG (0.1, 0.3, 1, or 3 mg/kg, i.p.), or fixed-ratio CBD+CBG combinations based on individual ED20 and ED40 values. Dose-response relationships were obtained by linear regression, and the experimentally determined combined dose (Zmix) was compared with the theoretical additive dose (Zadd) by Student's t-test. The interaction index (α) was obtained by dividing the experimentally obtained ED of the drug pair by the theoretical additive ED. Experiments were approved by the ethics committee (CEUA-BIO UFPR #1584). **Results:** STZ-induced diabetes significantly reduced mechanical thresholds in DBT rats compared to NGL animals by day 14 after diabetes induction. When compared to DBT+VEH group, both compounds attenuated mechanical allodynia, with peak effects at 60 min post-injection: 1) CBD produced significant antinociception at 0.3 mg/kg ($\Delta = 9.37$ g, $p = 0.05$) and 3 mg/kg ($\Delta = 16.60$ g, $p < 0.05$), with %MPE of AUC confirming significant effect at 3 mg/kg (32.04%; $p < 0.05$); 2) CBG produced significant antinociception at 1 mg/kg ($\Delta = 8.04$ g, $p = 0.0028$) and 3 mg/kg ($\Delta = 8.65$ g, $p = 0.0007$), with %MPE of AUC confirming significant effect at 3 mg/kg (28.98%, $p = 0.0217$). Linear regression yielded ED20 of 0.701 mg/kg (CBD) and 1.087 mg/kg (CBG), and ED40 of 8.642 mg/kg (CBD) and 8.830 mg/kg (CBG). All fixed-ratio combinations produced significant antinociception when compared to the DBT+VEH group (all $p < 0.0001$ at 60 minutes). Isobolographic analysis revealed an interaction: at ED20, Zmix (0.187 mg/kg) was significantly lower than Zadd (0.936 mg/kg; $p = 0.006$; $\alpha = 0.20$), indicating synergism; at ED40, Zmix (60.978 mg/kg) significantly exceeded Zadd (8.760 mg/kg; $p = 0.010$; $\alpha = 6.96$), indicating subadditivity. **Conclusion:** CBD and CBG produce effect-level-dependent interactions in STZ-induced diabetes, with synergism at ED20 and subadditivity at ED40, reinforcing that isobolographic analysis at multiple effect levels is necessary for accurate characterization of cannabinoid combinations.

05. Biology and Gastrointestinal Diseases

05.001FR **Gut Microbiota Profiles Across Insulin Resistance Levels in Children**. Neves TAFV[1], Moraes RCS[1], Clementino LCRF[1], Silva JVG[1], Alves JLB[1], Martins VJB[2] [1]UFPB Dept Nutrition, Brazil; [2]UFPB Dept Biomedical Sciences, Brazil

Introduction: Insulin resistance (IR) is a metabolic condition associated with overweight and obesity, related to the development of type 2 diabetes mellitus, metabolic syndrome, and other relevant aspects of cardiovascular risks. The gut microbiota has been increasingly recognized as an important regulator of host physiology and pathophysiology. Studies suggest gut microbiota plays a role in human health with the potential to affect glucose metabolism. **Objectives:** The aim of this study was to investigate the gut microbiota of children across different levels of HOMA-IR. **Methods:** A total of 72 children aged 7-12 years, of both sexes, enrolled in public primary schools in João Pessoa, Brazil, were included in the study and stratified into three groups (T1, T2 and T3) according HOMA-IR tertiles. Anthropometric parameters, biochemical tests, and gut microbiota were assessed. Gut microbiota was assessed through 16S rRNA gene sequencing. Statistical analyses were performed using one-way ANOVA with Tukey's post hoc test (SPSS v. 26.0). Gut microbiota sequencing data were processed in R, including LEfSe analysis and Spearman correlation ($\alpha < 0.05$). **Results:** Compared to the T1 and T2 groups, the T3 group had significantly higher weight (38.31 ± 12.08 vs 44.45 ± 14.69 vs 54.46 ± 10.44 kg, $p < 0.001$ respectively), BMI-for-age (BMI/Z) (1.02 ± 1.63 vs 1.87 ± 1.67 vs 3.16 ± 0.95, $p < 0.001$, respectively) and body fat percentage (26.56 ± 8.51 vs 31.53 ± 11.15 vs 42.26 ± 8.44 %, $p < 0.001$, respectively), waist circumference (WC) (64.63 ± 8.76 vs 72.94 ± 12.55 vs 82.80 ± 8.93 cm, $p < 0.001$, respectively) and hip circumference (78.67 ± 9.51 vs 84.85 ± 12.35 vs 92.90 ± 7.99 cm, $p < 0.001$, respectively). Insulin and HOMA-IR concentrations were significantly higher in T3 compared to both groups (56.24 [49.88–62.78] vs 117.86 [106.65–131.56] vs 228.02 [200.23–262.28] pmol/L, $p < 0.001$; and 1.00 [0.89–1.12] vs 2.12 [1.92–2.34] vs 3.93 [3.49–4.44], $p < 0.001$, respectively). LEfSe analysis identified Lachnospiraceae UCG-004 as enriched in T3 (LDA score > 3.5, $p < 0.05$), and its relative abundance was positively correlated with BMI/Z ($p < 0.01$) and WC ($p < 0.05$). In contrast, the Christensenellaceae R-7 group were negatively correlated with both BMI/Z and WC ($p < 0.01$). **Conclusion:** These findings indicate that children with higher IR levels showed a progressive increase in adiposity markers. The identification of specific microbial taxa across HOMA-IR tertiles highlights the potential association between gut microbiota and early metabolic alterations in childhood. This study was funded by CAPES and FAPESQ (grant no. 009/2021, Term 3.044/2021). Approved by the Ethics Committee with Human Beings of the Health Sciences Center of the Federal University of Paraíba - CCS/UFPB according to the ethical standards for research involving human beings of Resolution 466/2012 (CAAE: 53905321.9.0000.5188).

06. Cardiovascular and Renal Pharmacology

06.001 **Effects of Long-Acting Testosterone (Nebido®) on the Renal Function of Isolated Kidneys from Hypertensive and Normotensive Rats**. Portacio LFS, Sousa BMS, Santiago RO, Paz IA, Santos CF, Nascimento NRF. UFC

As the primary androgen hormone, testosterone plays diverse roles in the human body, influencing metabolism, the cardiovascular system, and psychological function. Therefore, when properly indicated, testosterone replacement is essential to maintaining an individual's balance and quality of life. However, evidence suggests that when this hormone is supplemented without proper indication, renal function can be adversely affected. Furthermore, studies demonstrate that testosterone can exacerbate arterial hypertension in hypertensive animals (RECKELHOFF, J. L. et al., 1998). This study aims to understand the changes induced by long-acting testosterone (Nebido®) in the isolated kidneys of both hypertensive and non-hypertensive rats. Methods: Following approval by CEUA/UECE No. 00333395/2020, normotensive animals were randomly assigned to 6 groups: control (n=5); Nebido 10ng, 10ng, and 100ng per mL (n=6 per group); Nebido 100ng combined with its antagonist, flutamide 10^{-5}\text{ M} (n=5); and flutamide 10^{-5}\text{ M} alone. The hypertensive animals followed the exact same group distribution. After anesthesia, the animals' right renal arteries were cannulated for perfusion with Krebs- Henseleit solution supplemented with 6% bovine albumin and inulin. Perfusate and urine samples were collected every 10 minutes for a total of 120 minutes. **Results:** In the Wistar rat groups, all Nebido concentrations increased RVR by 300%, GFR and UF by 0.4%, and excreted Na and K by 9% and 3%, respectively, compared to the control group. When Nebido was combined with Flutamide, these increases were inhibited; however, PP and UF remained lower than in the control group. Regarding the SHR animals, a significant increase was also observed in RVR and GFR (both by 0.4%) and PP by 28% compared to the control group, while Na and K excretion showed only a discrete increase (0.6% and 0.75%, respectively). In contrast, Nebido was found to cause fluid retention in SHR kidneys, which may be linked to the worsening of hypertension following hormone replacement reported in this strain. DISCUSSION: In this study, we observed that Nebido causes a diffuse increase in renal functions alongside fluid retention. This presentation may lead to renal overload, potential kidney damage, and the worsening of AH through a volume overload mechanism.

06.002 **Positive Inotropic Effect of Iochroma arborescens Extract in an Isolated Organ Bath Model**. Sousa BMS[1], Portácio LFS[1], Martins RES[1], Silva ALM[1], Paz IA[1], Rocha KAD[2], Pessoa ODL[2] Santos CF[1] Nascimento NRF[1] [1]UECE, Instituto Superior de Ciências Biomédicas, Lab Fisiofarmacologia Cardiovascular e Renal. [2]ISCB-UFC, Lab Análise Fitoquímica de Plantas Medicinais II

Introduction: Iochroma arborescens, formerly Acnistus arborescens, belongs to the Solanaceae family, popularly known as fruto do sabiá, marianeira, or false rooster spur. It is a small-sized plant that grows in elevated areas, occurring throughout the Atlantic Forest from Northeastern to Southern Brazil and also found in the Ceará Caatinga (SANTOS; PESSOA, 2017). It is traditionally used in folk medicine as a diuretic, among other applications. This study aimed to investigate the cardiotonic and vasodilatory effects of Iochroma arborescens extract in guinea pigs (Cavia porcellus) using an isolated organ bath model. **Methodology:** Approved by the Animal Ethics Committee for Animal Use of UECE under protocol 02639769/2022 and SisGen A86B918. 4 guinea pigs (Cavia porcellus) were anesthetized with 5% isoflurane and euthanized by cervical dislocation. Surgery was performed to remove the right and left atria and the aorta. The tissues were mounted in 10 mL organ baths containing Krebs-Henseleit solution. The effects of cumulative concentrations of the hexane extract from Iochroma arborescens leaves (EHIa- 1µg/mL, 3µg/mL, 10µg/mL, 30µg/mL, 100µg/mL, 300µg/mL, and 1000µg/mL) were studied on spontaneous contractions of the right atrium, on the contraction amplitude of electrically stimulated left atrium (supramaximal, 5ms, 2Hz), and on aortic rings (5mm) pre-contracted with phenylephrine (1 µM). **Results:** EHIa produced a positive inotropic effect in electrically stimulated left atrium, increasing from a control value of 1.8±0.2 mN to 3.5±0.3 mN at 100µg/mL ($p<0.001$), to 6.3±0.7 mN at 300µg/mL ($p<0.001$), and to 8.9±0.09mN at 1000µg/mL ($p<0.001$). The positive control isoproterenol (1µM) increased the values to 12.7± mN. No changes in end-diastolic tension were observed in either right or left atrium at any concentration tested. Within this concentration range, EHIa did not significantly alter spontaneous contraction frequency of the right atrium, from a control value of 172±15.7bpm to 179.1±21.9bpm at 300µg/mL and to 156±29.8bpm at 1000µg/mL. EHIa relaxed phenylephrine-precontracted aortic rings up to 114.8±3% of maximal contraction, with an EC50 of 52µg/mL and a 95% confidence interval ranging from 40.3 to 68.05µg/mL. **Conclusion:** EHIa exhibits positive inotropic properties without inducing positive chronotropism and without altering cardiac relaxation capacity, in addition to presenting a potent vasorelaxant effect, thus characterizing an inodilatory effect. These effects may have important hemodynamic impacts *in vivo*, which will be evaluated in future studies. This inodilatory effect may be useful in the treatment of cardiopathies since, in addition to increasing cardiac performance, it may potentially improve coronary perfusion and reduce afterload. References: SANTOS, S. M.; PESSOA, O. D. L. Acnistus arborescens: estudo químico/farmacológico das espécies silvestre e cultivada. In: XXXVI ENCONTRO DE INICIAÇÃO CIENTÍFICA, 2017, Fortaleza. Revista Encontros Universitários da UFC, v. 2, n. 1, Fortaleza: UFC, 2017.

06.003 **Testosterone Enhances Stress-Induced Tachycardia without Altering Autonomic Modulation in Female Rats**. Martins SCA[1], Belem IJA[1], Suzuki GMF[1], Lautherbach N[2], Kettelhut IC[2], Correa FMA[1], Tostes RC[1], Santos JD[1]
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Introduction: Female sex hormones exert cardioprotective actions, whereas androgens are associated with pro-hypertensive effects. Transmasculine individuals undergoing gender-affirming hormone therapy with testosterone (GAHT-T) often reach high levels of testosterone and are frequently exposed to psychosocial stressors. Nevertheless, the interaction between testosterone therapy and cardiovascular regulation during stress remains unknown. **Objectives:** To investigate whether testosterone, in an experimental model of GAHT-T, enhances cardiovascular responses during acute restraint stress. **Methods:** Eight-week-old female Sprague-Dawley rats received testosterone cypionate (24 mg/kg/week, s.c.) or vehicle for eight weeks. A group of vehicle-treated male rats was included for assessment of the "male phenotype". Mean arterial pressure (MAP) and heart rate (HR) were recorded through femoral artery catheterization during baseline (10 min), restraint stress (60 min), and recovery (30 min) periods. Heart rate variability (HRV) and spontaneous baroreflex sensitivity analyses were performed to evaluate autonomic modulation. **Results:** Testosterone treatment increased body mass, reduced abdominal and retroperitoneal adipose tissue mass, and elevated tibialis anterior and *Extensor digitorum longus* (EDL) muscle mass. Histological evaluation showed enlarged cross-sectional area of tibialis anterior and EDL muscle fibers in testosterone-treated females, similar to those observed in male rats, consistent with a "masculinizing" phenotype. The hormonal treatment also increased serum testosterone levels in female rats. Regarding cardiovascular responses, testosterone amplified restraint stress-induced tachycardia without altering MAP or the reduction in caudal cutaneous temperature. HRV analyses indicated that testosterone did not modify LF/HF ratio or spontaneous baroreflex sensitivity during stress or recovery periods. **Conclusion:** Testosterone promotes "masculinizing" effects in female rats. Under stressful conditions, testosterone enhances tachycardic responses without altering autonomic modulation or spontaneous baroreflex sensitivity. Collectively, these findings suggest potential mechanisms through which GAHT-T may influence cardiovascular function during acute stress.

06.004 **Closantel Attenuates Arterial Hypertension and Improves Renal Redox Profile in Spontaneously Hypertensive Rats**. Silva JK, Silva JWA, Farias TSP, Santana DC, Carvalho JM, Santos VBS, Cerqueira ACL, Calzerra NTM, Vieira LD. UFPE, Lab Vascular and Renal Physiology and Pharmacology, Brazil.

Introduction: Arterial hypertension is a highly prevalent disease with a high mortality risk, whose limitations in conventional therapy drive the search for new therapeutic targets. In this context, the SPAK/OSR1 signaling pathway stands out for positively regulating renal (NKCC2 and NCC) and vascular (NKCC1) cation-chloride cotransporters, which are fundamental for blood pressure control. Furthermore, the modulation of this pathway is associated with the control of cellular redox status. The antihelminthic closantel has the capacity to inhibit the SPAK/OSR1 pathway and associated cotransporters, making it relevant to investigate its effects on cardiovascular and oxidative parameters in spontaneously hypertensive rats (SHR). **Objectives:** To evaluate the effects of early treatment with closantel on blood pressure and renal oxidative stress in SHR. **Methods:** Starting at the 5th week of life, oral treatment of SHR was initiated with vehicle (water 1 mL/kg/day; n=5), closantel (5 or 10 mg/kg/week; n=7 and 6, respectively), or furosemide (20 mg/kg/day; positive control; n=6). After 8 weeks, hemodynamic parameters (mean, systolic, and diastolic blood pressure — MBP, SBP, and DBP; and heart rate — HR) and markers of redox balance in the renal cortex were evaluated, including lipid peroxidation (MDA levels), non-protein thiol levels (npSH), reactive oxygen species (ROS) production, and NADPH oxidase activity. **Results:** The SHR group presented a mean blood pressure (MBP) of 184 ± 8 mmHg. Treatment with closantel (10 mg/kg) significantly reduced MBP to 150 ± 11 mmHg ($p<0.05$), whereas treatment with furosemide reduced MBP to 164 ± 4 mmHg ($p<0.05$). Closantel treatment also reduced SBP and DBP, but did not alter HR. Lipid peroxidation and ROS production in the renal cortex were about 35% lower ($p<0.05$) in the SHR group treated with closantel (5 or 10 mg/kg) compared to the untreated SHR group, and NADPH oxidase activity was reduced by more than 60% ($p<0.05$). Treatment with closantel (10 mg/kg) elevated npSH levels by 60% ($p<0.05$) in the renal cortex, whereas no effect was observed in the group receiving the lower dose (5 mg/kg). The SHR group treated with furosemide showed a pattern of protective effects similar to that of the group treated with closantel (10 mg/kg). **Conclusion:** Early treatment with closantel exerts an antihypertensive effect in SHR, paralleled by an improvement in renal redox balance. Future studies are needed to confirm whether modulation of the SPAK/OSR1 pathway and cation-chloride cotransporters is associated with the drug's effect, as well as the safety of prolonged treatment.

06.005 **Long-Acting Testosterone (Nebido®) Increases Albumin Endocytosis in Renal Epithelial Cells**. Martins, RES; Portacio, LFS; Santiago, RO; Paz, IA; Neves, CC; Santos, CF; Nascimento, NRF. UECE, UFC

Albumin, the most abundant macromolecule in blood plasma, is responsible for several physiological functions, such as maintaining oncotic pressure and volume, and transporting ions, drugs, vitamins, and hormones. Due to its size and negative charge, the passage of albumin through the renal glomeruli is limited. However, a small fraction manages to be filtered and is reabsorbed in the renal proximal tubule epithelium via megalin-mediated endocytosis. Evidence suggests that this endocytic process is modulated by sex hormones, such as estrogen (EL-LATEEF et al, 2019). This study aims to analyze how long- acting testosterone (Nebido®) alters albumin endocytosis in a porcine renal epithelial cell line. **Methods:** A cell line derived from the renal proximal tubule epithelium of pigs (LLC- PK1) was cultured in tissue culture plates containing sterile glass coverslips. The cells were incubated in a CO2 incubator at 37°C until they reached confluence. Afterward, the cells were washed with Ringer's solution and incubated with the compounds of interest for 2 hours (Nebido 10^{-14}M to 10^{-7}M, Flutamide 10^{-6}M, or both). The cells were then washed, and a medium containing fluorescein-isothiocyanate-labeled bovine serum albumin (BSA-FITC) was added for 30 minutes. Following this, the cells were properly lysed and prepared for immunofluorescence. The remaining homogenate was analyzed using a fluorometer. **Results:** It was observed that Nebido, whether combined or not with its inhibitor (Flutamide 10^{-6}M), increased the endocytosis of fluorescein-labeled albumin compared to the control group and the group that received flutamide alone. The experiment also showed that the PKB inhibitor MK-2206 (10^{-6}M) is capable of reversing the enhancement of albumin endocytosis induced by Nebido, whereas a specific inhibitor of the MAPK/ERK pathway (U0126) failed to produce this effect. A complementary assay was performed using fluorescein-isothiocyanate- labeled dextran—a key marker for fluid-phase endocytosis—to evaluate whether Nebido's effects are specific to albumin endocytosis receptors. Consequently, it was found that Nebido does not influence fluid-phase endocytosis, demonstrating that its action is linked to receptor-mediated albumin endocytosis.

06.006 **Metabolic State-Dependent Catecholamine Release and Vascular Responses in Fasting and Digesting Snakes**. Dal Pozzo CFS[1,2], Oliveira MG[1], Vicentini NCS[1], Castro SA [1], de Nucci G[1], Wang T[2] [1]Unicamp, Dept Pharmacology, Brazil [2]Aarhus University, Section for Zoophysiology, Denmark

Introduction: During digestion, snakes experience large cardiovascular changes to meet increased metabolic demands, including tachycardia driven by vagal tone withdrawal and non-adrenergic, non-cholinergic factors. Stroke volume doubles without cardiac growth, while blood pressure remains stable, likely due to reduced peripheral resistance. However, specific transitions in arterial resistance from fasting to digestion remain unclear. Endothelial-derived catecholamines, 6-cyanodopamine (6-CYD) and 6-nitrodopamine (6-ND), are potent endogenous positive chronotropic factors. 6-ND is also released by the corn snake aorta and promotes vasodilation, whereas the vascular effects of 6-CYD in snakes remain unknown. **Objectives:** This study aimed to investigate whether the release of adrenaline (ADR), noradrenaline (NA), 6-CYD, and 6-ND differs between fasting and digesting pythons and whether adrenergic regulation of mesenteric arteries varies with metabolic state. **Methods:** ADR, NA, 6-CYD, and 6-ND release from mesenteric vessels and small intestine was quantified by tandem mass spectrometry in 4 fasting (2–3 weeks) and 4 digesting (24–48 h after meal) pythons. Tyrosine hydroxylase (TH) immunohistochemistry was performed in mesenteric arteries and small intestine. Second-order mesenteric arteries from 12 snakes (6 per group) were mounted in a wire myograph, and concentration-response curves to ADR and NA were performed with or without 100 nM 6-CYD. The effect of 100 nM 6-ND on ADR responses was also evaluated in 4 digesting snakes. Data were analyzed using paired Student's t-test ($p < 0.05$). **Results:** 6-ND was the predominant catecholamine released by mesenteric vessels and small intestine, with increased levels in the small intestine of digesting snakes. TH immunolabeling was detected in endothelial cells of mesenteric arteries and epithelial cells of the small intestine. The maximal response (Emax) to ADR was significantly reduced in digesting compared with fasting snakes, whereas the response to NA was unchanged. 6-CYD enhanced the NA Emax exclusively in fasting snakes, an effect absent during digestion. Neither 6-CYD nor 6-ND altered the vascular response to ADR in digesting snakes. **Conclusion:** For the first time, we demonstrate that 6-ND is the predominant catecholamine released by mesenteric vessels and small intestine in pythons, with increased intestinal release during digestion. Vascular responses to catecholamines also differ according to metabolic state, with reduced ADR responsiveness during digestion and 6-CYD potentiation of NA responses only during fasting. These findings suggest metabolic state-dependent regulation of catecholamine release and vascular responsiveness.

06.007 **Cardiovascular Effects of Nerolidol in Hypertensive Animals**. Reis GS, Santana IR, Santana AS, Silva EAP, Barreto AS. UFS, Graduate Program in Health Sciences, Brazil.

Introduction: Systemic arterial hypertension (SAH) is one of the major risk factors for the development of cardiovascular diseases (CVDs), which are associated with high morbidity and mortality rates worldwide. Studies have highlighted that the use of natural products may positively contribute to the treatment of hypertension, including terpenes, whose therapeutic properties exert effects on the cardiovascular system. Nerolidol (NRD) is a sesquiterpene with anti-inflammatory, antioxidant, and cardioprotective properties. However, due to its low solubility and high volatility, incorporation into a formulation capable of enhancing its bioavailability and oral absorption is required. **Objectives:** To evaluate the cardiovascular effects of pure nerolidol and nerolidol complexed with hydroxypropyl β-cyclodextrin in hypertensive rats. **Methods:** Thirty male hypertensive Wistar rats were used (hypertension induced by L-NAME, 20 mg/kg/day, for 7 days). Mean arterial pressure (MAP) and heart rate (HR) were measured before and after a single oral administration (200 mg/kg and 100 mg/kg, by gavage) of nerolidol in its pure form (NP) or complexed with hydroxypropyl β-cyclodextrin (NHCD). Hemodynamic effects were monitored for 48 hours after treatment. Since hypotensive and bradycardic responses may be related to direct activation of muscarinic (M2 and M3) and nicotinic receptors, molecular docking analysis was performed to evaluate the potential binding affinities of NRD. **Results:** The predicted binding energies obtained through molecular docking were -7.4, -7.2, and -6.7 kcal/mol, respectively. Oral administration of both NRD and NHCD induced antihypertensive responses, with the greatest effects observed in the NHCD-treated group. **Conclusion:** NRD induces hypotension accompanied by bradycardia and, when administered orally in both its pure and complexed forms, demonstrated promising antihypertensive effects. **Acknowledgments:** The authors acknowledge the Graduate Program in Health Sciences (PPGCS) and CAPES for technical collaboration and institutional support.

06.008 **Sodium Nitrite Attenuates Increased Circulating Asymmetric Dimethylarginine Induced by Reduced Uterine Perfusion Pressure in Preeclamptic Rats**. da Costa LC, Silva MLS, Toghi CJ, Doreto AH, Kushima H, Colenci FBC, Dias-Junior CA, da Costa LC IBB-Unesp, Dept Biophysics and Pharmacology, Brazil

Preeclampsia (PE) is a pregnancy-specific hypertensive disorder characterized by hypertension, proteinuria, maternal organ dysfunction, and fetal growth restriction after the 20th week of gestation. PE affects approximately 2–8% of pregnancies worldwide and remains a major cause of maternal and fetal morbidity and mortality. Its pathophysiology is strongly associated with placental ischemia, oxidative stress, and systemic endothelial dysfunction. Reduced nitric oxide (NO) bioavailability plays a central role in this process, contributing to vasoconstriction and impaired vascular function. Increased circulating levels of asymmetric dimethylarginine (ADMA), an endogenous inhibitor of endothelial nitric oxide synthase (eNOS), have been consistently associated with PE and may contribute to decrease NO production and endothelial dysfunction. Additionally, nitrite (NO_2^-) has emerged as an important alternative source of NO under hypoxic conditions, although its role in PE remains incompletely understood. Therefore, this study investigated whether sodium nitrite treatment could attenuate circulating ADMA levels and improve vascular dysfunction in pregnant rats subjected to reduced uteroplacental perfusion pressure (RUPP), an experimental model of placental ischemia. Pregnant Wistar rats were divided into Sham, RUPP, Sham-Nitrite, and RUPP-Nitrite groups. Sodium nitrite (15 mg/kg/day) was administered orally from gestational day 14 to 21. RUPP rats developed hypertension, reduced fetal and placental weights, impaired acetylcholine-induced relaxation, increased phenylephrine-induced vasoconstriction, reduced NO metabolites, and elevated plasma ADMA levels. Sodium nitrite treatment attenuated hypertension, improved fetal and placental parameters, partially restored endothelial function, reduced vascular hyper- reactivity, and normalized NO metabolite levels in RUPP rats. Importantly, sodium nitrite markedly reduced circulating ADMA levels in the RUPP-Nitrite group, highlighting a potential modulatory effect of nitrite-derived NO on the ADMA-NO pathway. Since elevated ADMA contributes directly to reduce NO bioavailability and endothelial dysfunction, the attenuation of ADMA by sodium nitrite may represent an important mechanism underlying the vascular protective effects observed in treated animals. Overall, these findings demonstrate that sodium nitrite improves endothelial dysfunction and vascular impairment associated with placental ischemia while significantly decreasing circulating ADMA levels in experimental preeclampsia, supporting sodium nitrite as a promising therapeutic strategy for PE.

06.009 **Therapeutic Potential of *Spondias tuberosa* Against Age-Related Vascular Dysfunction: Evidence from EPC Modulation and Vascular Reactivity**. Gonçalves TAF[1,2], Sousa JRO[2], Silva LLM[2], Silva VO[2], Lima VS[1], Soares EMC[1], Oliveira JCPL[1], Fernandes GFS[3], Silva CCN[3], Cavalcante RV[1], Medeiros IA[1] [1]UFPB, Dept Pharmaceutical Sciences, Brazil, [2]UFPB, Dept Biomedical Sciences, Brazil, [3]UFPB, Dept Biotechnology

Introduction: Endothelial progenitor cells (EPCs) originate in the bone marrow and migrate to ischemic sites, where they differentiate into endothelial cells and contribute to vasculogenesis and angiogenesis. Aging impairs this reparative capacity by reducing EPC migration, proliferation, and secretion of pro-angiogenic factors, largely due to increased oxidative stress and apoptosis. In this context, antioxidant compounds have emerged as promising therapeutic alternatives. *Spondias tuberosa* Arruda, a fruit native to the Brazilian semi-arid region, has been recognized for its antioxidant properties. **Objectives:** This study evaluated the effects of the freeze-dried hydroalcoholic extract of *Spondias tuberosa* Arruda bark (LEHST) on vascular function and EPC biology in a rat model of D-galactose-induced aging. Methods: Experimental protocols were approved by the CEUA-UFPB (No. 2834150324). Rats were allocated into three groups: young control (CTL), aged control (D-GAL), and aged rats treated with LEHST (100 mg/kg) for eight weeks. Physical parameters and vascular reactivity to phenylephrine (Phe), acetylcholine (ACh), and sodium nitroprusside (SNP) were evaluated in isolated superior mesenteric arteries. EPCs were quantified and characterized by flow cytometry using CD34, CD133, and VEGFR2 markers. EPC functionality was assessed through colony-forming unit (CFU), adhesion, and migration assays using cells obtained from bone marrow (BM) and peripheral blood (PB). **Results:** LEHST improved external signs of aging, including hair loss and coat dullness, without affecting body weight. In mesenteric arteries, LEHST reduced senescence- associated β-galactosidase (SA-β-gal) labeling, suggesting an anti-senescent effect. Treatment also prevented age-induced vascular hypercontractility (Emax: D-GAL = 102.8% ± 12.1% vs. LEHST = 57.0% ± 6.2%) and fully restored endothelium-dependent relaxation to ACh (Emax: D-GAL = 74.5% ± 7.6%; LEHST = 120.2% ± 5.6%; CTL = 100%). These vascular effects were associated with increased EPC mobilization into circulation (LEHST: 2.2% ± 0.2 vs. D-GAL: 1.4% ± 0.1) and recovery of EPC function. Aging markedly impaired EPC proliferative capacity (CFU) in both BM and PB samples (BM: CTL = 13.3 ± 1.4 vs. D-GAL = 6.0 ± 0.5; PB: CTL = 8.3 ± 0.3 vs. D-GAL = 5.5 ± 0.5), whereas LEHST restored colony formation (BM = 10.3 ± 0.8; PB = 8.6 ± 0.6). Cell adhesion, reduced in the D-GAL group (101.3 ± 6.4 vs. CTL = 118.5 ± 1.2), was significantly increased by LEHST treatment (157.0 ± 5.8). In migration assays, the wound gap after 24 h was significantly reduced in both CTL and LEHST groups, indicating preserved migratory capacity. **Conclusion:** Treatment with LEHST (100 mg/kg) attenuated vascular senescence, improved endothelial function, and prevented age-related vascular hypercontractility in D-galactose-induced aging. These effects were associated with enhanced EPC mobilization and preservation of EPC functional properties, including proliferation, adhesion, and migration. Together, these findings suggest that LEHST may represent a promising strategy for mitigating vascular dysfunction associated with aging.

06.010 **Perivascular Adipose Tissue Dysfunction Induced by Acute Exposure to Cisplatin in male and female rats**. Almeida ACR, Jesus BR, Akamine EH ICB-USP, Dept. Pharmacology, Brazil. USP, Graduate Program in Functional and Molecular Biology, Brazil.

Introduction: Cardiovascular diseases and cancer are leading causes of mortality and morbidity worldwide. Although anticancer therapies improve cancer prognosis, they may induce cardiovascular toxicity by affecting endothelial and vascular smooth muscle cells. In this way, some anticancer drugs lead to cardiovascular diseases, including arterial hypertension. Perivascular adipose tissue (PVAT), which surrounds blood vessels, regulates vascular function by releasing relaxing and contractile factors and may also be affected by anticancer therapies. Dysfunction of PVAT alters its secretome, increasing vasoconstriction. However, there is no data about the effects of anticancer drugs on PVAT. Cisplatin, an alkylating-like agent, is one of the most widely used anticancer drugs for the treatment of solid tumors, particularly germ cell tumors. This drug induces DNA damage, impairing replication and transcription processes, thereby exerting cytotoxic effects. **Objectives:** This study aimed to evaluate whether acute exposure to cisplatin induces PVAT dysfunction by altering its anti-contractile properties in both male and female Wistar rats. **Methods:** Thoracic aortas from 16-week-old male and female Wistar rats were cut in 3 mm rings, in which PVAT was either preserved (PVAT+) or dissected (PVAT-). Thoracic aorta rings were mounted in an organ bath system for vascular reactivity assays. PVAT+ and PVAT- rings from both sexes were exposed to cisplatin (10 µM, 100 µM and 200 µM) for 2h. Control rings were exposed to vehicle (0.9% NaCl). Concentration–response curves to noradrenaline (NA, 10-11 \- 3x10-5 M) were obtained. Male groups included 5–7 animals/group and female groups 4–7 animals/group. Statistical analysis was performed using one-way ANOVA, followed by Dunnett's multiple comparisons test. **Results:** In control rings of male rats, PVAT+ rings presented a reduction of the NA-induced contractile response in comparison to PVAT- rings (41%, $p < 0.05$), showing the anticontractile action of PVAT. Cisplatin-treated PVAT+ rings, at concentrations of 10 µM and 100 µM, showed NA-induced contraction higher than control PVAT+ rings (66% and 80%, respectively, $p < 0.05$), indicating an impairment of the anticontractile function of PVAT. In PVAT-, 10 µM and 100 µM cisplatin did not change the response to NA. At 200 µM, cisplatin reduced the NA-induced contractile response in both PVAT- and PVAT+ rings. In contrast, in female rats, the anti-contractile action of PVAT was also observed. Exposure to cisplatin at 10, 100 and 200 µM did not significantly alter NA-induced contractile responses in either PVAT- or PVAT+ rings compared with their respective controls. **Conclusion:** These findings suggest that acute exposure to cisplatin induces PVAT dysfunction in a sex-dependent manner, impairing its anticontractile function in male rats. In contrast, female rats appear to be resistant to these effects, indicating potential sex-related differences in vascular responses to cisplatin.

06.011 **Cardiovascular Effects of Sesquiterpenes in Animal Models: A Systematic Review**. Reis GS, Reis-Sobrinho G, Santana IR, Santana AS, Silva EAP, Barreto AS. LAFAC-UFS, Dept Physiology, Lab. of Cardiovascular Pharmacology, PPG in Health and Science, Brazil.

Introduction: Cardiovascular diseases (CVDs), including Systemic Arterial Hypertension (SAH), Acute Myocardial Infarction (AMI), Diabetic Cardiomyopathy (DC), and Heart Failure (HF), represent the greatest burden of morbidity and mortality in the world today. Given the complexity of these pathologies, the search for new therapeutic strategies has turned toward natural compounds with cardioprotective potential. In this context, sesquiterpenes (SQs) emerge as promising candidates due to their ability to interact with specific biological targets of the circulatory system. These compounds are synthesized from three isoprene units (C15) and exhibit a broad spectrum of bioactivity, notably their anti-inflammatory, analgesic, and antitumor properties. Due to the lipophilicity and versatility of their carbon chain, sesquiterpenes facilitate molecular interactions that directly modulate myocardial physiology and vascular integrity. **Objectives:** To analyze the cardiovascular effects of SQs in murine models, focusing on hemodynamic and functional parameters, oxidative stress, and inflammation. **Methods:** This systematic review followed PRISMA guidelines and searched PubMed, Embase, Web of Science, and Scopus databases without period or language restrictions. Inclusion criteria comprised randomized *in vivo* experimental studies using murine CVDs models treated with SQs compared to concurrent control groups. *In vitro*, ex vivo, or studies lacking quantitative data were excluded. Two independent, blinded reviewers performed screening and data extraction via Rayyan software, with conflicts resolved by a third reviewer. Methodological quality and risk of bias were assessed using SYRCLE's Risk of Bias tool. Analyzed outcomes included hemodynamic parameters, cardiac function and structure, and biochemical markers of oxidative stress and inflammation (PROSPERO: CRD420261400755). **Results:** From 992 records, 24 studies were included, analyzing 756 rodents subjected to CVDs models. Regarding the SQs pharmacological intervention protocols, the identified routes of administration were: oral (n=9), subcutaneous (n=4), intraperitoneal (n=7), intravenous (n=1), intragastric (n=2), and intramyocardial (n=1). This variation demonstrates the methodological heterogeneity in the literature regarding the cardiovascular effects of this class of compounds. In SAH, SQs attenuated hypertension via calcium channels, MLC2, NO, and cGMP. In MI, they reduced fibrosis, oxidative stress, and cytokines, improving HR, MAP, and ejection fraction. In CD, they exerted anti-hypertrophic, anti-apoptotic, and anti-inflammatory actions via MAPK and ATF6. In HF, they mitigated hypertrophy and remodeling, preserving myocardial function. **Conclusion:** SQs possess robust cardioprotective potential through inflammatory and oxidative stress modulation, effectively attenuating CVDs outcomes. Therefore, they consolidate as promising pharmacological candidates, demanding translational investigations to validate their clinical efficacy and safety. **Acknowledgments:**: to PPGCS and CAPES for the technical collaboration and institutional support.

06.012 **Sympathetic Neurogenic and Protein Kinase-Dependent Vasoconstriction Induced by Cardiotonic Steroids in Isolated Human and Animal Vessels**. Paiva JGM[1], Vieira EP1, Silva ALM[1], Oliveira IMB[1], Paz IA[1], Paulino FWV[1], Rocha MRS[1], Campos R[1], Lima CC2, Santos CF[1], Nascimento NRF[1] [1]ISCB-UECE, Lab Fisiofarmacologia Cardiovascular e Renal, PPG em Ciências Fisiológicas, Brasil. [2]ISCB-UECE, Lab Fisiologia Pulmonar, PPG em Ciências Fisiológicas, Brasil.

Introduction: Cardiotonic steroids (CTS), such as ouabain, digoxin, and bufalin, play an important role in blood pressure regulation and the development of hypertension. Although direct inhibition of Na+/K+-ATPase (NKA) in vascular smooth muscle is the classical mechanism proposed for vasoconstriction, evidence suggests the involvement of central and sympathetic pathways, as well as cellular signaling pathways mediated by Src kinases. Elevated levels of endogenous CTS are associated with salt-sensitive hypertension and preeclampsia. **Objectives:** To investigate the vascular effects of ouabain, digoxin, and bufalin in different species and vascular segments, testing the hypothesis that CTS-induced vasoconstriction results from norepinephrine release by sympathetic neurons rather than from a direct contractile effect on vascular smooth muscle. **Methods:** Segments of the thoracic aorta, mesenteric artery, and renal artery from rats, guinea pigs, rabbits, and humans were mounted in organ baths for isometric tension recording. Concentration–response curves (0.1–100 μM) were generated in the absence or presence of inhibitors/blockers classified as follows: prazosin (a selective α_1-adrenoceptor antagonist), guanethidine (a peripherally acting sympatholytic agent), PP2 (a Src kinase inhibitor), staurosporine (a nonspecific protein kinase/PKC inhibitor), and tezosentan (an endothelin receptor antagonist). Tyrosine hydroxylase expression and ERK1/2 phosphorylation were assessed by Western blotting. **Results:** CTS induced vasoconstriction only at high concentrations and with a delayed onset, with species-dependent sensitivity. In relation to the maximal contraction induced by phenylephrine (Phe), ouabain and digoxin elicited no response in the rat aorta, whereas bufalin reached 20.6%. In the guinea pig aorta, ouabain reached 71.55%, bufalin 94.05%, and digoxin 79.68%; in the second branch of the mesenteric artery, ouabain reached 58.96% and bufalin 12.4%. In rabbits, the aorta exhibited responses of 101.24% to ouabain and 55.03% to bufalin (with no response to digoxin) whereas in the mesenteric artery, the values were 76.77% for bufalin, 33.64% for ouabain, and 16.20% for digoxin. In the rabbit renal artery, bufalin reached 68.84%, ouabain 51.56%, and digoxin 30.06%. In all responsive models, vasoconstriction was abolished by prazosin and guanethidine, demonstrating dependence on sympathetic neurotransmission. PKC blockade with staurosporine significantly reduced contraction; in the rabbit aorta, the ouabain-induced response decreased to 13.83%, whereas PP2 and tezosentan had no relevant effects. Tyrosine hydroxylase expression was four to five times higher in guinea pig vessels than in rat vessels. **Conclusion:** Vasoconstriction induced by high concentrations of CTS *in vitro* does not result from direct activation of vascular smooth muscle, but rather from an indirect neurogenic mechanism mediated by norepinephrine release and the activation of protein kinase-dependent pathways, most likely PKC. These findings reinforce the role of the sympathetic nervous system in the vascular effects of CTS and suggest adrenergic blockade as a potential therapeutic strategy for hypertension associated with these compounds. **Financial support**: Funcap - Fundação Cearense de Apoio ao Desenvolvimento Científico e Tecnológico.

06.013 **Topical Treatment with a Lyophilized Hydroalcoholic Extract of *Spondias tuberosa* Fruit Peel Improves Erectile Function and Endothelial Reactivity in D-Galactose-Induced Aged Rats**. Cordeiro AIF, Soares EC, Gonçalves IGA, Veras RC, Medeiros IA UFPB, Lab Cardiovascular Pharmacology, PPG in Bioactive Natural and Synthetic Products / CCS, Brazil

Introduction: Erectile dysfunction (ED) is associated with aging and endothelial dysfunction, leading to impaired nitric oxide signaling and reduced corpus cavernosum relaxation. Oxidative stress also contributes to vascular involved in ED pathophysiology. Natural products with antioxidant properties have emerged as promising therapeutic alternatives. *Spondias tuberosa* Arruda, a plant endemic to the Brazilian Caatinga biome, contains bioactive compounds with recognized antioxidant potential. Therefore, this study investigated the effects of topical treatment with a lyophilized hydroalcoholic extract of *Spondias tuberosa* Arruda (LEHST) fruit peel on erectile function in aged rats. **Objectives:** To evaluate the effects of topical application of lyophilized hydroalcoholic extract of *Spondias tuberosa* fruit peel (LEHST) on erectile function in D -galactose-induced aged rats, with emphasis on intracavernosal pressure/mean arterial pressure (ICP/MAP) ratio and corpus cavernosum vascular reactivity. **Methods:** Male Wistar rats (8 weeks old) were randomly assigned to four groups: Control (CTL), D-galactose (D-GAL), LEHST90, and LEHST300. Accelerated aging was induced by intraperitoneal administration of D-galactose (150 mg/kg) for eight weeks. Simultaneously, animals received topical treatment on the penis with vehicle or a lyophilized hydroalcoholic extract of *Spondias tuberosa* Arruda fruit peel incorporated into a gel formulation (90 or 300 mg/g). Erectile function was assessed by the ICP/MAP ratio. Corpus cavernosum reactivity was evaluated in isolated organ baths through concentration-response curves to acetylcholine (ACh) and sodium nitroprusside (SNP). Data were expressed as mean ± SEM and analyzed by Student's ±T-test or one-way ANOVA followed by Tukey's post hoc test, considering $P < 0.05$ as statistically significant. **Results:** D-galactose-induced aging significantly reduced the ICP/MAP ratio and impaired acetylcholine-induced relaxation of the corpus cavernosum compared with the control group. Topical treatment with the lyophilized hydroalcoholic extract of *Spondias tuberosa* Arruda peel restored erectile responses, with the 90 mg/g and 300 mg/g gel increasing the ICP/MAP ratio to values comparable to controls. Both treatment groups (90 mg/g and 300 mg/g) improved endothelium-dependent relaxation induced by acetylcholine (10^{-9}M to 10^{-3}M), whereas no significant changes were observed in sodium nitroprusside-induced relaxation (10^{-10}M to $3x10^{-4}$M). These findings suggest that the extract improves erectile function primarily through endothelial protection. **Conclusion:** Topical treatment with the lyophilized hydroalcoholic extract of *Spondias tuberosa* Arruda In addition to improving the ICP/MAP relationship and the response to ACh, peel improved erectile function in D-galactose-induced aged rats. These findings suggest that the extract may exert protective effects on endothelial function and represents a promising therapeutic strategy for age-related erectile dysfunction.

06.014 **Standardization of a Neointimal Hyperplasia Model in Rat Carotid Artery: Full Lumen Occlusion and Elevated Oxidative Stress Four Weeks After Partial Carotid Ligation**. Fernandes GFS[1], Oliveira JCPL[2], Evangelista IP[1], Medeiros IA[3], Veras RC[3]. [1]UFPB, Biotechnology Center, Lab Cardiovascular Pharmacology, Brazil. [2]UFPB, Lab Cardiovascular Pharmacology, PPG in Bioactive Natural and Synthetic Products, Brazil. [3]UFPB, Dept Pharmaceutic Sciences, Health Sciences Center, Lab Cardiovascular Pharmacology, PPG in Bioactive Natural and Synthetic Products, Brazil.

Introduction: Cardiovascular diseases remain the leading cause of global morbidity and mortality, driven partially by pathological vascular remodeling where neointimal hyperplasia (NIH) stands out as a hallmark feature of restenosis following clinical interventions. To develop effective therapeutic strategies, there is a critical need for reproducible, standardized animal models that precisely replicate this complex pathophysiological process. **Objectives:** In this study, we proposed a standardized partial carotid artery ligation (PCL) model to evaluate neointimal formation in rats. **Methods:** Histological stains were used to assess the development of neointima layer and media layer integrity, reactive oxygen species (ROS) immunofluorescent probes were utilized to evaluate oxidative stress in this model. A comprehensive comparative analysis was implemented between PCL arteries and non-ligated (non-PCL) contralateral arteries four weeks post-surgery. The study was approved by Comissão de Ética no Uso de Animais of Universidade Federal da Paraíba, under the protocol 5365080524. **Results:** Histomorphometric assessment revealed a complete occlusion of carotid lumen in PCL arteries compared to the non-PCL. Crucially, a longitudinal analysis allowed us to map the NIH development along the vessel axis, successfully establishing a profile of neointimal thickness as a function of distance from the ligation site. This morphological remodeling was accompanied by a markedly elevated oxidative stress profile within the vascular wall which confirmed intense ROS and O2·- accumulation in the remodeled layers when compared to the contralateral arteries (11202 ± 1171 a.u. *vs* 5448 ± 705 a.u. and 9820 ± 1436 a.u. *vs* 4667 ± 437 a.u., respectively). **Conclusion:** Taken together, our findings demonstrate that this standardized model successfully drives robust neointimal hyperplasia characterized by precise spatial progression and high oxidative stress, providing a reliable platform for investigating vascular remodeling and its potential therapeutic interventions.

06.015 **Attenuation of Angiotensin II-Induced Vasoconstriction by Novel Thiazolidinedione Derivatives in Isolated Aorta from Wistar Rats**. Silva KT[1], Ferreira JG[1], Arrospide TM[2], Alves SML[1], Aires RS[1], Santos RCA[1], Ferreira LFL[2], Dos Anjos JV[2], Silva MCC[1], Araújo AV[1] [1]UFPE, Centro Acadêmico da Vitória, Brasil, [2]UFPE, Lab Síntese Orgânica, CCEN, Brasil

Introduction: Systemic Arterial Hypertension (SAH) is a multifactorial clinical condition characterized by persistently elevated blood pressure levels. Angiotensin II AT1 receptor antagonists are among the main drugs used in its treatment. In this context, compounds with the potential to antagonize these receptors have been investigated as candidates for new antihypertensive agents. Thiazolidinediones constitute a class of heterocycles with diverse biological properties and, being described as bioisosteres of carboxylic acids, may exhibit affinity for AT1 receptors. **Objective:** To evaluate the effects of the new thiazolidinedione derivatives (CTZPAPh, CTZPAPCl, and CTZDApF) on the contractile responses induced by angiotensin II (Ang II) in aortic rings of Wistar rats, investigating their potential as AT1 receptor antagonists. **Methods:** Two-month-old male Wistar rats were used. After euthanasia, the thoracic aorta was isolated and segmented into rings, which were mounted in a bath system for isolated organs. After the stabilization period and verification of tissue viability, cumulative concentration-effect curves for angiotensin II (Ang II) were obtained, in the absence or in the presence of the compounds CTZPAPh, CTZPAPCl, and CTZDApF (100 µmol/L), in preparations without functional endothelium. From the generated curves, the maximum effect (Emax) and potency (pCE50) were determined. Data are expressed as mean ± standard error mean. Statistical difference was considered when $p < 0.05$. **Results:** In the presence of the evaluated compounds, a marked reduction in Ang II-induced contraction was observed. CTZPAPh substantially reduced the maximum effect of the contractile response of Ang II (Emax: control = 1.45 ± 0.20 g; CTZPAPh = 0.19 ± 0.12 g), while CTZPAPCl and CTZDApF compounds practically abolished the Ang II-induced contraction (Emax = 0.08 ± 0.03 g and 0.06 ± 0.005 g, respectively). **Conclusion:** The thiazolidinedione derivatives evaluated promoted a significant reduction in the contractile responses induced by angiotensin II in rat aorta, suggesting a possible antagonistic interaction with AT1 receptors. These findings reinforce the pharmacological potential of these molecules as prototypes for the development of new antihypertensive agents, although further studies are needed to confirm the mechanism of action involved.

06.016 **Vascular Effects Induced by Supplementation with Fermented Mangaba** (*Hancornia Speciosa*) **Pulp in Animals with Renovascular Hypertension**. Duarte MOAS, Galvão AC, Gadelha DDA, Fernandes GFS, Costa WKA, Magnani M, Medeiros IA, Falcão MSFUFPB, CBiotec, Brasil; UFPB, CCS, Brasil; UFPB, CCS, Brasil; UFPB, CBiotec, Brasil; UFPB, CT, Brasil; UFPB, CT, Brasil; UFPB, CCS, Brasil; UFPB, CBiotec, Brasil

Arterial hypertension is a multifactorial condition and one of the major risk factors for the development of cardiovascular diseases, being associated with oxidative stress and endothelial dysfunction. Renovascular hypertension, an angiotensin II-dependent model, is widely used to investigate the pathophysiological mechanisms underlying this disease. In this context, phenolic compounds present in fruits such as mangaba (Hancornia speciosa) exhibit well-recognized antioxidant activity; however, their bioavailability may be limited. Fermentation with lactic acid bacteria, such as Lactobacillus acidophilus (LA-5) and Lactobacillus casei (LC-1), has been shown to enhance the bioaccessibility of these compounds, thereby potentiating their biological effects. The present study aimed to evaluate the vascular effects of orally administered fermented mangaba pulp supplementation in normotensive and renovascular hypertensive rats. The animals were divided into four groups: two receiving only the vehicle by oral administration (SHAM and 2R1C) and two supplemented with the fermented pulp (2R1C+PULP and SHAM+PULP). The 2R1C groups underwent placement of a clip on the renal artery to induce renovascular hypertension, whereas the SHAM groups underwent a sham surgical procedure. Vascular reactivity parameters were evaluated in isolated mesenteric arteries. All data were expressed as mean ± standard error of the mean and analyzed using one-way ANOVA followed by Tukey's post hoc test. A value of $p < 0.05$ was considered statistically significant. The results demonstrated that 2R1C animals exhibited greater contractile reactivity to phenylephrine compared with the SHAM group (131.16 ± 6.39% vs. 95.65 ± 2.93%). Notably, supplementation with fermented mangaba pulp attenuated this hyperreactivity (96.36 ± 5.53% vs. 131.16 ± 6.39%). Endothelium-dependent relaxation induced by acetylcholine was significantly reduced in the 2R1C group compared with the SHAM group (82.11 ± 2.27% vs. 101.88 ± 3.89%), whereas supplementation restored the maximal relaxation response (110.00 ± 1.55% vs. 82.11 ± 2.27%), suggesting an improvement in endothelial function. No significant differences were observed among the groups regarding sodium nitroprusside-induced relaxation. These findings suggest that fermented mangaba pulp exerts beneficial effects on vascular reactivity, which may be primarily associated with endothelial modulation, highlighting its potential as a complementary strategy for the prevention or attenuation of vascular alterations associated with hypertension.

06.017 **SC1, an Improved-Solubility Oxadiazolinone, Displays AT1 Antagonist-Like Vascular and Renal Effects in 5/6 Nephrectomy-Induced Chronic Kidney Disease**. Aires RS[1], Santana DC[2], Barbosa FM[1], Barbosa AMM[1], Monteidro VHS[1], Ferrreira LFL[3], Vieira LD[2], Calzerra NTM[2], Anjos JV[3], Araujo AV[1] [1]UFPE Centro Acadêmico de Vitória, Brasil; [2]UFPE, Lab Fisiologia e Farmacologia Cardiorrenal, Brasil; [3]UFPE, Lab Síntese Orgânica Medicinal, Centro de Ciências Exatas e da Natureza, Brasil

Introduction: Angiotensin II type 1 receptor (AT1R) antagonists are widely used in chronic kidney disease (CKD) for their cardiorenal benefits. However, residual risk and treatment-limiting adverse effects remain. These limitations support the search for novel AT1R-targeting compounds. SC1 is an oxadiazolinone with improved aqueous solubility and potential AT1R antagonist- like activity. **Objectives:** To investigate the predicted interaction of SC1 with AT1R and compare its vascular, antihypertensive, and renal redox effects with losartan in 5/6-nephrectomized (Nx) rats. **Methods:** Molecular docking was performed in AT1R structures 4YAY and 4ZUD using GOLD Suite 5.3/CHEMPLP. Ang II concentration-response curves were obtained in thoracic aortic rings with intact or removed endothelium from sham and Nx Wistar rats before incubation with SC1 or losartan. Nx rats received vehicle, SC1 (10 mg/kg), or losartan (10 mg/kg) by gavage. Systolic blood pressure (SBP) was measured by tail-cuff after a single dose and after 14 days. Renal redox status was assessed by ROS production and NADPH oxidase, SOD, and catalase activities. Data are mean±SEM and were analyzed by one-way ANOVA/Tukey or two-way repeated-measures ANOVA/Holm–Sidak ($p<0.05$). **Results:** SC1 yielded docking scores of 75.51 and 74.53 in the 4YAY and 4ZUD AT1R structures, respectively, with three predicted hydrogen bonds with Arg167 in both structures, a key anchoring residue for AT1R antagonists within the orthosteric binding site. In endothelium-intact aortas, SC1 reduced the Emax of Ang II-induced contraction from 1.04±0.07 to 0.41 ± 0.10 g in sham rats and from 0.63±0.13 to 0.14±0.04 g in Nx rats. No significant inhibition of Ang II-induced contraction was observed after endothelial removal, whereas losartan abolished the response in rings with or without endothelium. In Nx rats, SC1 significantly reduced SBP as early as 1 h after oral administration (170±3 vs. 188 ± 2 mmHg), and the effect persisted for up to 4 h (159±4 vs. 185 ± 2 mmHg). In contrast, losartan significantly reduced SBP only at 4 h (165±11 vs. 185±2 mmHg). After 14 days, both treatments reduced SBP compared with Nx+vehicle (SC1: 161±6 and losartan: 160±2 vs. 188±3 mmHg), with no significant difference between the treatments. Nx increased renal NADPH oxidase activity (2.2 ± 0.4 vs. 1.2±0.35 A.U. in sham); while SC1 (1.6±0.5 A.U.) and losartan (1.1±0.1 A.U.) restored values toward sham. Both treatments increased SOD activity, while only losartan reduced ROS production and neither treatment affected catalase activity. **Conclusion:** Docking predicts an SC1 binding mode compatible with AT1R antagonism. SC1 also inhibits Ang II-induced vascular contraction through an endothelium-dependent mechanism, lowers SBP, and partially improves renal redox balance, supporting further pharmacokinetic, mechanistic, and preclinical investigation in CKD.

06.018 **Resistance Exercise Restores Cardiac Mechanical Function and Reduces Arrhythmogenic Susceptibility in Experimental Hypothyroidism**. Matos LFS[1]; Durço AO[2]; Bazilio JES [1]; Santos Júnior SA[1]; Miranda CM[1]; Gomes JVS[1]; Santana MNS[1]; Almeida MMSF[1]; Santo D[1] [1]UFS-São Cristovao, Heart Biophysics Lab, Dept, Brasil; [2]Unifesp, Cardiobiology Lab, Dept Biophysics, São Paulo, Brasil

Introduction: Hypothyroidism (Hypo) is a prevalent endocrine disorder associated with cardiovascular dysfunction, including reduced cardiac contractility, oxidative stress, arrhythmias, and mitochondrial impairment. Resistance exercise (RE) has emerged as a potential non-pharmacological cardioprotective strategy. This study investigated whether moderate-intensity RE could prevent or reverse cardiac dysfunction and arrhythmias in experimental hypothyroidism. **Methods:** Wistar rats (8–9 weeks old; CEUA UFS nº 1143200525) were divided into six groups: Control, Hypo (0.02% methimazole for 30 days), Exe (resistance training using a squat apparatus from day 11), Exe+Hypo, Hypo+Levo (levothyroxine 20 µg/kg), and Exe+Hypo+Levo. ECG and echocardiography were performed on days 10 and 31 under anesthesia (10% ketamine + 2% xylazine). On day 31, animals were euthanized for blood, histological, and western blot analyses. **Results:** The Hypo group showed significant electrocardiographic alterations, including bradycardia and prolonged PR, QT, and QTc intervals. Exe+Hypo improved only QTc, while the remaining ECG parameters remained altered compared with Control. Echocardiography demonstrated reduced fractional shortening (FS) and ejection fraction (EF) in Hypo animals, which were restored in Exe and Exe+Levo groups. Histological analyses revealed reduced cardiomyocyte area, increased mononuclear infiltration, and enlarged intercellular spaces in Hypo hearts. These alterations were attenuated by exercise and/or levothyroxine treatment, indicating preservation of myocardial structure. After arrhythmia induction with caffeine (120 mg/kg, i.p.) and dobutamine (1 mg/kg, i.p.), Hypo animals developed ventricular tachycardia, whereas exercise-, levothyroxine-, and combined-treated groups showed marked reductions in ventricular arrhythmias. Analysis of calcium-handling proteins demonstrated reduced phospholamban, total and phosphorylated CaMKII, Orai1, and calsequestrin expression in the Hypo group, accompanied by increased oxidized CaMKII. Exercise restored Orai1, phospholamban, and CaMKII levels and partially recovered calsequestrin expression. Together, these findings indicate that exercise partially improves electrical remodeling, reduces arrhythmogenic susceptibility, and restores cardiac mechanical function in experimental hypothyroidism. **Conclusion:** Moderate-intensity resistance exercise attenuated major cardiac alterations induced by experimental hypothyroidism, restoring systolic function, preserving myocardial architecture, and reducing stress-induced ventricular arrhythmias. These benefits were associated with modulation of calcium- handling proteins and attenuation of oxidative stress-related pathways, supporting resistance exercise as a promising complementary strategy for preventing cardiovascular complications associated with hypothyroidism.

06.019 **Basal Release of 6-Cyanodopamine and 6-Nitrodopamine from Rat Isolated Aorta and Their Role in Vascular Relaxation**. Cisota FNX[1], Said G[1], Lima AT[1], Junior JB[1,2], Souza VB[1], Schenka AA[1], Peterson LW[3], Ferro A[2], Antunes E[1], Nucci G[1,4] [1]FCM-Unicamp, Dept Pharmacology, Campinas, SP, Brazil; [2]King's College London, Faculty of Life Sciences and Medicine, London, UK; [3]Dept Chemistry, Rhodes College, Memphis, TN, USA; [4]ICB-USP, São Paulo, SP, Brazil

Introduction: 6-Cyanodopamine (6-CYD) and 6-nitrodopamine (6-ND) are recently described endogenous catecholamines with cardiovascular activity (1,2). Although 6-ND has been identified as an endothelium-derived vascular modulator, the presence of 6-CYD in rat aorta and the mechanisms underlying the vascular actions of both compounds remain unclear. Since the endothelium is a major regulator of vascular tone (3), we investigated whether rat isolated thoracic aorta basally releases 6-CYD and 6-ND and compared their vasorelaxant mechanisms. **Methods:** Thoracic aortas were obtained from male Wistar rats. Basal release of 6-CYD and 6-ND was quantified by LC–MS/MS after incubation of aortic segments in Krebs–Henseleit solution. Vascular reactivity was assessed in isolated thoracic aortic rings pre-contracted with U-46619. Concentration–response curves to 6-CYD and 6-ND were performed in endothelium- intact and endothelium-denuded rings, and after incubation with L-NAME, ODQ, indomethacin, SQ-22536, SCH-23390 or haloperidol. Tyrosine hydroxylase expression was evaluated by immunohistochemistry and fluorescence in situ hybridization. **Results**: Rat thoracic aorta basally released both 6-CYD and 6-ND, with 6-ND levels significantly higher than 6-CYD. Both catecholamines induced potent concentration-dependent relaxation in U-46619-precontracted aortic rings. 6-ND was slightly more potent than 6-CYD, with pEC_{50} values of 8.9±0.5 and 8.5±0.6, respectively; Emax values were 79.1±4.1% for 6-ND and 88.9±2.8% for 6-CYD. Endothelium removal abolished 6-CYD-induced relaxation and markedly reduced the response to 6-ND. L-NAME, ODQ, indomethacin and SQ-22536 significantly inhibited 6-CYD-induced relaxation, but did not affect 6-ND responses, suggesting that 6-CYD involves NO/sGC, prostanoid and adenylyl cyclase-dependent pathways, whereas 6-ND acts through a distinct mechanism. SCH-23390 did not modify responses to either catecholamine. Haloperidol inhibited 6-CYD-induced relaxation but not 6-ND-induced relaxation, indicating involvement of D_2-like receptors in the 6-CYD response. Tyrosine hydroxylase protein and mRNA were detected in endothelial cells and adventitial neural structures. **Conclusion**: Rat isolated thoracic aorta basally releases 6-CYD and 6-ND, which are among the most potent endogenous vasodilator mediators described in this tissue. Although both catecholamines depend on endothelial integrity, they relax rat aorta through distinct mechanisms. 6-CYD appears to involve NO/sGC, prostanoid, adenylyl cyclase and D_2-like receptor pathways, whereas 6-ND-induced relaxation is largely independent of these mechanisms. These findings reveal new catecholaminergic pathways by which the vascular endothelium may regulate vascular tone. **References**: 1. Zatz R, De Nucci G. Physiology. 2024;39:44–59. 2. Britto-Júnior J, et al. Life Sciences. 2025;366–367:123504. 3. Furchgott RF, Zawadzki JV. Nature. 1980;288:373–376.

06.020 **Gentisic Acid Induces Vasorelaxation in the Superior Mesenteric Artery of SHR Through Activation of the NO/cGMP Pathway and Modulation of Calcium Influx**. Costa LFO[1], Santana DC[1], Oliveira KA2, Santos KMO2, Cerqueira ACL2, Santos VBS1, Vieira LD[1], Calzerra NTM[1] [1]UFPE, Depto Fisiologia e Farmacologia, Recife, Brazil; [2]UFPE, Depto Ciências Farmacêuticas, Recife, Brazil

Introduction: Hypertension is a chronic non-communicable disease associated with increased peripheral vascular resistance, partly due to reduced nitric oxide bioavailability and alterations in the regulation of vascular calcium influx. Phenolic compounds with antioxidant properties have been investigated for their vascular effects. Among these compounds, gentisic acid (GA) has shown hypotensive and bradycardic effects following acute administration (bolus injection) in spontaneously hypertensive rats (SHR) in previous studies conducted by our research group. However, its vascular mechanisms remain unclear. **Objectives:** To evaluate the vasorelaxant effect of GA in the superior mesenteric artery of SHR and to investigate the mechanisms underlying this vascular response. **Methods:** Adult male SHR (4 months old) were used. Superior mesenteric artery rings were mounted in organ baths, and concentration–response curves to GA were obtained in preparations with and without endothelium. Mechanisms were investigated using pharmacological blockers and extracellular calcium concentration–response curves. Experimental protocols were approved by the Animal Research Ethics Committee (CEUA-UFPE n. 0078/2025). Data are expressed as mean ± SEM; comparisons were performed using an unpaired Student's t-test ($p < 0.05$). **Results:** GA induced concentration- dependent vasorelaxation in phenylephrine-precontracted superior mesenteric artery rings in the presence (Emax = 107.8 ± 4.4; pD_2 = 4.7 ± 0.1; n = 7) and absence of endothelium (Emax = 67.1 ± 8.9; pD_2 = 4.4 ± 0.1; n = 7), although the response was more pronounced in vessels with intact endothelium. In endothelium-intact preparations, GA-induced vasorelaxation involved the NO/cGMP pathway, as evidenced by the attenuation of its effect following pretreatment with L-NAME (Emax = 90.2 ± 4.6; pD_2 = 4.0 ± 0.1; n = 6) and ODQ (Emax = 91.3 ± 3.8; pD_2 = 4.0 ± 0.1; n = 6) vs. control. In contrast, pretreatment with indomethacin did not modify the vasorelaxant response to GA (Emax = 104.5 ± 12.8; pD_2 = 5.3 ± 0.2; n = 5), suggesting that cyclooxygenase- derived metabolites are not involved in this effect. In endothelium-denuded preparations, blockade of potassium channels with TEA (Emax = 75.5 ± 6.4; pD_2 = 4.5 ± 0.1; n = 6) and 4-AP (Emax = 59.8 ± 6.7; pD_2 = 4.4 ± 0.1; n = 6) did not significantly affect GA-induced relaxation. However, the endothelium- independent vasorelaxant effect is partly associated with inhibition of calcium influx, since pretreatment with GA attenuated the contractile response induced by $CaCl_2$ (Emax = 63.2 ± 9.7; pD_2 = 3.0 ± 0.1; n = 4) compared with the response in the absence of GA (Emax = 100.0 ± 0.0; pD_2 = 3.4 ± 0.04; n = 4). **Conclusion:** GA induces concentration-dependent vasorelaxation in the superior mesenteric artery of SHR. This effect is mediated, at least in part, by activation of the NO/cGMP signaling pathway and inhibition of calcium influx, mechanisms that may contribute to the hypotensive effects of GA previously observed *in vivo*. Keywords: Gentisic acid; Vasorelaxation; NO/cGMP pathway; Calcium influx; Mesenteric artery; Hypertension.

06.021 **SATICl as an α1-Adrenergic Antagonist and Possibly a Potassium-Channel Opener**. Silva MEF1, Silva MCC1, Alves SML1, Feitosa SG2, dos Anjos JV2, Araújo AV1 1UFPE, Centro Acadêmico de Vitória, Brasil; 2CCEN-UFPE, Depto Química Fundamental, Brasil

Introduction: α1-adrenergic receptors (α1-AR) are responsible for the regulation of several responses, and new studies aim to overcome limiting factors that restrict the recurrent use of α1-AR antagonists. In previous studies conducted by our group, SATICl reduced the contractile efficacy of phenylephrine (FEN), suggesting antagonism of α1-AR, and potassium chloride (KCl), indicating that another signaling pathway besides α1-AR was likely also at play. **Objectives:** evaluate SATICl's mechanism of action on rat thoracic aorta. **Methods:** Wistar male rats (250-350 g) were anesthetized with isoflurane and euthanized by guillotine. Their thoracic aortas were isolated, cut into 4 mm rings, and suspended in isolated organ bath chambers. Cumulative concentration-effect curves for SATICl were performed on rings pre-contracted with FEN (0.1 μmol/L) or an isomolar solution of KCl (20 or 80 mmol/L). Differences between groups were verified by Student's t test, by using GraphPad Prism 9.0. The significance level for rejecting the null hypothesis was 5%. **Results:** SATICl induced relaxation of aortic rings pre-contracted with FEN (Emax = 91.2 ± 7.8%, n = 5) and KCl 20 (Emax = 92.65 ± 0.77%; pEC50 = 4.21 ± 0.48, n = 2) or 80 mmol/L (Emax = 60.98 ± 9.48%; pEC50 = 4.07 ± 0.16, n = 6). However, the relaxation was more efficient in rings pre-contracted with KCl 20 mmol/L when compared to KCl 80 mmol/L. **Conclusion:** The data suggests that SATICl may be a potassium channel opener and a α1-AR antagonist. More studies are needed to further assess its mechanism of action.

06.022 (-)-Borneol Inclusion Complex in β-Cyclodextrin Attenuates Isoproterenol-Induced Myocardial Inflammation in Rats Through Regulation of Cytokine Expression. Souza, FM[1], Albuquerque, BA[2,3,4], Rego, AF[2,3,4], Rocha, VA[2,3,4], Portela, EP[2,3,4], Silva, ND[2,3,4], Oliveira, AP[2,3,4,5]. [1]UFPI, Northeast Biotechnology Network; [2]UFPI, PPG in Pharmacology; [3]NPPM-UFPI, Cardiovascular Pharmacology Lab; [4]UFPI, Medicinal Plant Research Center; [5]UFPI, Dept Biophysics and Physiology

Introduction: The biomolecule (-)-borneol [(-)-BOR] is present in the essential oils of numerous medicinal plants. Studies indicate (-)-BOR as a compound with broad pharmacological activity on the cardiovascular system. OBJECTIVES: To evaluate the effect of the (-)-BOR/β-cyclodextrin (βCD) inclusion complex on isoproterenol (ISO)-induced myocardial necrosis. Methods: Male Wistar rats (200–250 g) were used. The animals were divided into three groups: one received saline solution (orally for 7 days, and subcutaneously on days 8 and 9); another received ISO (85 mg/kg, subcutaneously, on days 8 and 9); and a third was pre-treated with (-)-BOR/βCD (100 mg/kg, orally) for 7 days, followed by ISO (85 mg/kg, subcutaneously, on days 8 and 9). After euthanasia, blood was collected for biochemical analysis, and the heart was removed to obtain histological sections stained with hematoxylin and eosin (H&E;), which were evaluated and photomicrographed for semi-quantitative scoring of tissue damage. An *in silico* study (AutoDock 4.2) was conducted to evaluate the interaction of (-)-BOR with the transcription factor NF-κB and TNF-α. Subsequently, pro-inflammatory cytokines potentially involved in the effect of the inclusion complex were investigated. All experimental procedures were approved by the Ethics Committee on Animal Use of UFPI (CEUA/UFPI no. 822/2024). Results: Assessment of pro-inflammatory cytokines in cardiac tissue demonstrated that the ISO-treated group showed a significant increase in TNF-α (360 pg/mL), IL-1β (360 pg/mL), and IL-6 (380 pg/mL) levels compared to the saline group (160 pg/mL, 170 pg/mL, and 90 pg/mL, respectively). Pre-treatment with the (-)-BOR/βCD inclusion complex significantly reduced these inflammatory mediators, with values of approximately 100 pg/mL for TNF-α and IL-1β and around 50 pg/mL for IL-6, approaching the levels observed in the control group. Significant differences were observed between the Saline and ISO groups ($p < 0.05$) and between the ISO and ISO+(-)-BOR/βCD groups ($p < 0.05$). Conclusion: Pre-treatment with the (-)-BOR/βCD inclusion complex was effective in attenuating myocardial injury induced by ISO, likely due to the anti-inflammatory properties of the complex.

06.023 **Effect of Cisplatin on the Perivascular Adipose Tissue Function: The Cellular Senescence Role**. Jesus BR, Almeida ACR, Da Silva GH, Akamine EH. USP, PPG Functional and Molecular Biology, Brazil.

Introduction: Adverse effects of anticancer remain a persistent challenge, and vascular toxicity is one of the most relevant, since it increases the risk of cardiovascular diseases. The mechanisms involved are not yet fully elucidated, but endothelial dysfunction may play a role. Perivascular adipose tissue (PVAT), alongside the endothelium, also regulates vascular function. However, the effects of antineoplastic drugs on PVAT are not yet known. Anticancer therapies, including alkylating agents such as cisplatin, induce senescence in both tumor and non-tumor cells. Cellular senescence is characterized by cell cycle arrest and prevents tumor growth; however, by acquiring a pro- inflammatory phenotype, it can also favor the development of tumor cells and lead to dysfunction in non-tumor tissues. The present project hypothesizes that cisplatin induces senescence and alterations in PVAT playing a role in the antineoplastic drugs-induced cardiovascular toxicity. **Objectives:** In order to understand cardiovascular toxicity induced by antineoplastic drugs, we aim to evaluate whether treatment with cisplatin promotes senescence and PVAT dysfunction. **Methods:** Wistar male and female rats were subjected to 5 weeks of treatment with cisplatin (3 mg/kg) or vehicle. All animals received 2 mL of saline solution subcutaneously to avoid dehydration. Metabolic and hemodynamic parameters were assessed before and after treatment. Then, animals were euthanized and thoracic aorta was used in vascular reactivity. Noradrenaline, acetylcholine and sodium nitroprusside curves were performed. Data were submitted to normality tests and analyzed by t-Student test, one-way ANOVA or two-way ANOVA. **Results:** Cisplatin treatment in male rats did not alter systolic blood pressure or heart rate, but caused a significant reduction in body weight at the end of treatment. This is consistent with the trend for reduced food consumption observed in these animals. In addition, rats treated with cisplatin showed a significant increase in renal weight and a non- significant increase in water consumption and urinary volume. Cisplatin treatment did not significantly alter the concentration-response curves to noradrenaline, acetylcholine, or sodium nitroprusside from male and female Wistar rats. However, cisplatin treatment tended to reduce noradrenaline- induced contraction, without impairment of PVAT anticontractile effect. In females, cisplatin treatment did not alter systolic blood pressure, heart rate, body weight, food consumption, water consumption, and urinary volume. However, a significant increase in renal weight and an apparent increase in liver weight were observed. Cellular senescence will be assessed in further analysis. **Conclusion:** Cisplatin treatment does not alter hemodynamic parameters but provokes signs consistent to renal and hepatic toxicity. The lack of influence in PVAT's anticontractile effect might signal a preservation of this tissue in spite of treatment. **Acknowledgments:** The authors thank Sônia Maria Rodrigues Leite for technical support during animal handling and experimental procedures Animal Research Ethical Committee CEUA/ICB-USP Protocol Number 2437170225. **Financial support** provided by CAPES Academic Master's scholarship process number 88887.193961/2025-00.

06.024 **Grape Pomace Attenuates Arterial Hypertension and Cardiac Remodeling in Spontaneously Hypertensive Rats**. Guimarães CS, Schiavinato TA, Costa KCM, Giachini FR UFMT, Graduate Program in Basic and Applied Immunology and Parasitology, Brazil.

Introduction: Systemic arterial hypertension is a chronic multifactorial disease associated with persistent inflammation and pathological cardiac remodeling. Although antihypertensive therapies effectively control blood pressure, inflammatory and fibrotic processes are not always adequately managed. Grape pomace (Vitis vinifera), an agro-industrial by-product rich in polyphenols, exhibits antioxidant, anti-inflammatory, and antifibrotic properties, suggesting potential cardioprotective effects. **Objectives:** To evaluate the phytochemical composition of grape pomace and investigate its effects on blood pressure and cardiac remodeling in spontaneously hypertensive rats (SHR) and normotensive Wistar rats. **Methods:** Total flavonoids, phenolic acids, and antioxidant capacity were assessed in fresh grapes and grape pomace. Male SHR and Wistar rats were randomly assigned to four groups (n=7/group): SHR Control, SHR Treated, Wistar Control, and Wistar Treated. Treated groups received a grape pomace-enriched diet (300 mg/kg/day) for 14 days. Blood pressure was measured by non-invasive tail-cuff plethysmography on days 0 and 14. After euthanasia, hearts were collected for morphometric analyses, including cardiomyocyte diameter and interstitial collagen deposition. Statistical analyses were performed using one-way ANOVA followed by Tukey's post hoc test. **Results:** Grape pomace showed a higher total flavonoid content than fresh grapes (237.32 ± 6.44 vs. 150.58 ± 4.26 mg/100 g). No significant differences in water intake were observed among groups. Body weight increased in treated animals compared with their respective controls. Grape pomace supplementation significantly reduced systolic blood pressure in SHR rats (165 ± 0.8 vs. 144 ± 1.1 mmHg, $p<0.05$). Relative heart weight normalized to tibial length was higher in treated SHR animals than in controls (0.6 ± 0.02 vs. 0.5 ± 0.01 g/cm, $p<0.05$). Morphological analyses demonstrated attenuation of cardiac hypertrophy, evidenced by a reduction in cardiomyocyte diameter (10.9 ± 0.02 vs. 9.4 ± 0.18 µm, $p<0.05$) and interstitial collagen deposition (33.6 ± 1.8 vs. 30.2 ± 0.5%, $p<0.05$). These findings suggest a shift toward adaptive rather than pathological cardiac remodeling. **Conclusion:** Grape pomace supplementation reduced arterial blood pressure and attenuated hypertension-induced cardiac remodeling in spontaneously hypertensive rats. These findings support the antihypertensive and cardioprotective potential of grape pomace and reinforce the value of agro-industrial residues as sustainable sources of bioactive compounds for the prevention and management of cardiovascular damage associated with hypertension. **Acknowledgements**: Laboratory of Vascular Biology and Histopathology - Federal University of Mato Grosso.

06.025 **Evaluation of the Molecular Mechanisms Involved in the Antiplatelet Effect of Inosine**. Alves DS, Brazão SC, Lima GF, Brito FCF UFF, Lab. of Experimental Pharmacology, PPG Biomedical Sciences (Physiology and Pharmacology), Brazil

Introduction: Among cardiovascular diseases, atherothrombotic disorders are particularly significant, as rupture of an atherosclerotic plaque triggers platelet activation and the coagulation cascade. Inosine, a nucleoside derived from adenosine, acts through A1, A2A, A2B, and A3 receptors, modulating adenylate cyclase and intracellular cAMP levels (Fredholm, B.B. Pharmacol. Rev., v. 63, p. 1, 2011). Previous studies demonstrated anti-inflammatory, hypolipidemic, and antiplatelet effects of inosine (Lima, G.F. Eur. J. Pharmacol., v. 882, p. 173289, 2020). **Objectives:** To investigate the mechanisms underlying the *in vitro* antiplatelet effects of inosine. **Methods:** Antiplatelet activity was evaluated *in vitro* by the Born and Cross (1963) method using human platelet-rich plasma (PRP) in a Chrono-Log 560-CA aggregometer. Aggregation was monitored by light transmittance, calibrated with PRP at 0% and platelet-poor plasma (PPP) at 100%. ADP (5 µM) and collagen (1 µg/mL) were used as agonists. Inosine was pre-incubated at different concentrations in the presence or absence of guanylate cyclase inhibitor (ODQ 10 µM), adenylate cyclase inhibitor (SQ22536 100 µM), or endothelial nitric oxide synthase inhibitor (L-NAME 100 µM). Results were analyzed by one-way ANOVA followed by Bonferroni post-test ($p<0.05$). **Results:** Inosine reduced ADP-induced (DMSO: 84.75 ± 1.52% x INO: 65.67 ± 4.70%) and collagen-induced platelet aggregation (DMSO: 84.63 ± 2.71% x INO: 71.25 ± 1.93%) in human PRP. SQ22536 reversed the antiplatelet effect of inosine against ADP (DMSO: 84,75 ± 1,52% x INO: 65,67 ± 4,70% x INO+SQ22536: 81,67 ± 3,25%) and collagen (DMSO: 84,63 ± 2,71% x INO: 71,25 ± 1,93% x INO+SQ22536: 77,88 ± 2,31%), demonstrating a cAMP-dependent mechanism. ODQ and L-NAME potentiated the antiplatelet effect of inosine against ADP (INO: 65,67 ± 4,70% x INO+ODQ: 34,00 ± 4,03% x INO+L-NAME: 46,83 ± 4,98%) and collagen (INO: 71,25 ± 1,93% x INO+ODQ: 12,25 ± 6,07% x INO+L-NAME: 32,86 ± 5,92%). **Conclusion:** Inosine exerted *in vitro* antiplatelet effects in human PRP by reducing ADP- and collagen-induced platelet aggregation. This effect was dependent on the cAMP signaling pathway, as it was abolished by adenylate cyclase inhibition. Reduced cGMP levels potentiated the antiplatelet response, suggesting an interaction between cyclic nucleotide pathways. Lower cGMP concentrations may decrease PDE2 and PDE5 activation, thereby favoring intracellular cAMP maintenance and enhancing platelet inhibition. Collectively, these findings suggest that inosine modulates platelet function by increasing intraplatelet cAMP levels, possibly through reduced PDE2 activity.

06.026 **Investigation of the Vasorelaxant Effect of Octyl Gallate Microemulsion in Isolated Rat Aorta**. Alves HF, Oliveira JCPL, Fernandes GFS, Veras RC, Medeiros IA UFPB, Dept Pharmaceutical Sciences, Cardiovascular Pharmacology Lab, Institute of Drug and Medicine Research, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil.

Introduction: Vascular tone depends on the balance between vasoconstrictor and vasodilator mechanisms, with nitric oxide (NO) and intracellular Ca^{2}+ signaling playing key roles. Disruption of this balance contributes to vascular dysfunction and cardiovascular disease. Octyl gallate, a gallic acid derivative, has antioxidant and anti-inflammatory properties and may interfere with Ca^{2}+-dependent mechanisms. However, its vascular effects remain poorly explored. **Objective:** To evaluate the vasorelaxant effect of octyl gallate loaded in a microemulsion (OGME) and the involvement of the NO/sGC pathway in rat aorta. **Methods:** Male Wistar rats (12 weeks; 250–350 g) were used under CEUA/UFPB approval (No. 4129280422; ID 001638). Thoracic aortas were isolated, cut into 3-mm rings, and mounted in organ baths containing Krebs solution at 37.4 °C under 2 g basal tension. Vascular viability was assessed with KCl 60 mmol/L and endothelial function with phenylephrine (PHE; 10^{-6} mol/L) followed by acetylcholine (ACh; 10^{-6} mol/L). Cumulative OGME concentration-response curves (10^{-7};– 3×10^{-4} mol/L) were performed in rings with or without endothelium, under basal tone or after PHE contraction. The NO/sGC pathway was investigated using L-NAME (100 µmol/L), PTIO (100 µmol/L), or ODQ (10 µmol/L), incubated for 30 min. Data were expressed as mean ± standard error and analyzed by ANOVA ($p<0.05$). **Results:** OGME did not alter basal tone. In PHE-contracted rings, OGME induced concentration-dependent relaxation, with Emax of 98.84 ± 1.4% and EC50 of 20.99 ± 1.13 µmol/L without endothelium, and Emax of 100.1 ± 3.6% and EC50 of 0.99 ± 0.08 µmol/L with endothelium, indicating greater potency in the presence of endothelium. The vehicle had no effect. In endothelium-denuded rings contracted with KCl, OGME also produced concentration-dependent relaxation (Emax = 99.72 ± 1.45%; EC50 = 19.65 ± 0.86 µmol/L). L-NAME, PTIO, and ODQ did not change Emax, but reduced potency, increasing EC50 to 20.88 ± 0.97, 26.46 ± 3.91, and 13.12 ± 1.17 µmol/L, respectively. **Conclusion:** OGME produced potent concentration-dependent vasorelaxation with high efficacy in rat aorta. The greater potency in endothelium-intact rings and its reduction after interference with the NO/sGC pathway suggest participation of this mechanism, while relaxation in denuded rings indicates additional endothelium-independent mechanisms. These findings support OGME as a promising candidate for further investigation in vascular pharmacology. **Acknowledgments:** CAPES/CNPq, Laboratory of Cardiovascular Pharmacology, Federal University of Paraíba, and collaborators.

06.027 **Vascular Effects Screening of Propafenone Analogs in Isolated Aortas in Wistar Rats**. Souza, RM, Lima NCB, Silva FAO, Rocha DG, Mesquita JLF, Soares JJF, Franco VMF, Lima GC, de Mattos MC, Lima RF, Jamacaru FVF, Jorge RJB, Monteiro HSA. UFC

Introduction: According to the WHO, hypertension (HTN) is one of the main causes of mortality worldwide. With approximately 1.4 billion people affected, only one in five treated patients has the disease under control, and thousands of people around the world face the risks associated with hypertension. In this context it is necessary to investigate new therapeutic aproches. Pharmacological repurposing is an innovative strategy capable of optimizing established therapeutic options. Thus, propafenone, a β-blocker, has demonstrated a vasodilatory effect through its analogs, indicating that its repurposing can be explored in the treatment of HTN. **OBJECTIVES:** This study aims to evaluate the vasodilatory activity of propafenone analogs RAC-5a, RAC- 5b, RAC-5c and RAC-5d through screening. **Methods:** Adult male Wistar rats, weighing between 280 and 320g, from the animal facility of the Drug Research and Development Center (NPDM/UFC) (CEUA No 27060722-0), were used in this study. The animals were anesthetized using ketamine (80mg/kg) and xylazine (10mg/kg) for dissection of the thoracic aorta. Then, the vessels were sectioned into aorta rings, preserving the endothelium, and placed in an isolated organ bath system. Stabilization in the system was performed for one hour, followed by dose-response curves of the analogs (10^{-7}; to $3x10^{-4}$M). **Results:** The synthesized analogs were first analyzed using molecular docking, which identified better binding affinity and stronger interactions between the amino acid residues of the β-receptors in RAC-5b and RAC-5c. Regarding the vasoactive activity screening, 6 aorta rings were used per experimental group (n = 6). In pre-contracted ring preparations with phenylephrine (PHE) (1 µmol/L), analogs were compared with 1% dimethyl sulfoxide (DMSO) as a control, identifying Emax and EC50 respectively, RAC–5a (130.48±12.03%; 54.742 [35.025-92.313]), RAC–5b (106.6±7.33%; 10.842 [4.488-26.407]), RAC–5c (55.5±6.292%; 3.061 [0.397-28.079]) and RAC-5d (108.5±24.50%; 39.260 [8.639-564.702]), evidencing a vasodilatory response greater than 50% compared to the control (13.6±2.44%; 6.697 [0.751-77.244]). Therefore, it is noteworthy that RAC-5b and RAC-5c showed greater efficacy. Thus, the most promising, RAC- 5b, was chosen to proceed with viability tests, and to evaluate whether the action of the RAC-5b analog surpasses propafenone. Hence, a methodology similar to the screening was followed, yet comparing RAC-5b to propafenone: the rings pre-contracted with PHE (1 µM) in intact endothelium, showed no statistically significant difference in relation to EC50 and Emax. In aortas pre-contracted with KCl in intact endothelium, Emax was lower (35.16±9.26%), with no significant difference in EC50 values in relation to PHE. **Conclusion:** These results reinforce the importance of pharmacological repurposing, demonstrating that propafenone analogs exert a vasodilatory effect, especially RAC-5b, compared to propafenone.

06.028 **Effects of** *Arthrospira platensis* **Supplementation on Cardiovascular Parameters in Asthmatic Rats**. Oliveira, GNM, Vieira, MM, Gadelha, DDA, Oliveira TA, Cavalcanti CO, Cruz, JC, Vasconcelos, LHC UFPB, Lab Farmacologia Funcional Prof. George Thomas, Instituto de Pesquisa em Fármacos e Medicamentos, Brazil; UFPB, PPG em Produtos Naturais e Sintéticos Bioativos, Brazil; UFPB, Programa Multicêntrico de Pós-graduação em Ciências Fisiológicas, Brazil; UFPB, Depto Biotecnologia, Brazil, UFPB, Depto Ciências Biomédicas, Brazil.

Introduction: Asthma can cause cardiovascular impairment beyond the respiratory system. *Arthrospira platensis* (AP), a dietary supplement approved for human consumption in Brazil, has emerged as a promising alternative treatment due to its antihypertensive, anti-inflammatory, and antispasmodic properties. **Objective:** This study investigated the effects of AP supplementation on cardiovascular parameters in asthmatic rats. **Methods:** Male Wistar rats were randomly assigned to control group (CG), asthmatic group (AG), and asthmatic group supplemented with AP (AP100; 100 mg/kg/day). Asthma was induced using an ovalbumin (OVA) sensitization and challenge protocol over 21 days. Powdered AP was suspended in saline (0.9% NaCl) and administered daily by gavage throughout the experimental period. CG and AG animals received saline only. One day after the final OVA challenge, the femoral artery and vein were catheterized for cardiovascular recordings. Baseline mean arterial pressure (MAP) and heart rate (HR) were measured. Baroreflex sensitivity (BRS) was assessed by intravenous administration of L-(-)-phenylephrine (8 µg/kg) and sodium nitroprusside (25 µg/kg), while peripheral chemoreflex was evaluated by intravenous injection of potassium cyanide (40 µg/kg). Data were expressed as mean ± SEM. Data comparison was performed using ANOVA one-way followed by Tukey's post-hoc test. **Results:** No differences in baseline MAP were observed among CG, AG, and AP100 (111.4 ± 2.6, 116.0 ± 6.3, and 111.3 ± 3.3 mmHg, respectively; n = 6-7). Similarly, HR did not differ among groups (345.1 ± 13.5, 382.3 ± 15.6, and 382.4 ± 11.1 bpm, respectively; n = 7). However, BRG was significantly reduced in AG (-2.331 ± 0.4031 bpm·mmHg^{-1}) compared with CG (-4.565 ± 0.5464 bpm·mmHg^{-1}), and AP supplementation did not prevent this impairment (-2.723 ± 0.4698 bpm·mmHg^{-1}). In addition, no differences were observed in chemoreflex responses among the groups for either ΔMAP (63.3 ± 21.3, 78.7 ± 18.3, and 65.3 ± 4.1 mmHg, respectively; n = 3) or ΔHR (-371.7 ± 42.4, -369.3 ± 56.7, and -332.7 ± 22.8 bpm, respectively; n = 3). **Conclusion:** Experimental asthma impaired baroreflex sensitivity without affecting baseline cardiovascular parameters or peripheral chemoreflex responses. Furthermore, *Arthrospira platensis* supplementation did not improve the cardiovascular alterations observed in asthmatic rats under the conditions evaluated in this study.

06.029 **Resveratrol Attenuates Vascular Dysfunction in Rats in a High Sugar Diet by Reducing Oxidative Stress, Visfatin and MMP-2 Activity**. Manoel LB[1], Blascke de Melo MM[1], Dourado TMH[1], Assis VO[1], Bueno EKP[1], Fazan Jr R[2], Tirapelli CR[1], Castro MM[1] [1]FMRP-USP, Dept Pharmacology, Brazil; [2]FMRP-USP, Dept Physiology, Brazil

Metabolic syndrome is a highly prevalent condition associated with obesity and characterized by a cluster of metabolic abnormalities that increase cardiovascular risk. In this context, adipose tissue expansion promotes the release of pro-inflammatory adipokines and reactive oxygen species (ROS), contributing to endothelial dysfunction, vascular remodeling, and hypertension. Among these adipokines, visfatin has attracted increasing interest due to its ability to sustain inflammation and redox imbalance through activation of molecular pathways associated with vascular dysfunction. These pathways include increased ROS production and activation of the transcription factor NF-κB, which stimulates the expression of inflammatory mediators and matrix metalloproteinase (MMP)-2. Elevated MMP-2 activity contributes to extracellular matrix degradation and maladaptive cardiovascular remodeling, a phenomenon frequently observed in metabolic syndrome, even before the establishment of overt hypertension. Resveratrol, a polyphenol with antioxidant and anti-inflammatory properties, has been investigated for its cardioprotective effects in different experimental models. Therefore, we hypothesized that resveratrol reduces visfatin expression, oxidative stress, NF-κB activation, and MMP-2 activity, thereby preventing vascular dysfunction in rats with metabolic syndrome. **Objectives:** Elucidate the signaling pathway involved in arterial remodeling associated with metabolic syndrome and hypertension. **Methods:** Sprague Dawley rats received a standard or high-sugar diet (HSD) ad libitum for 16 weeks. During the last 6 weeks, animals were treated with vehicle or resveratrol (10 mg/kg/day, gavage). Systolic blood pressure (SBP) was measured invasively. Aortas were collected for in situ zymography, DHE and Picrosirius Red staining, NF-κB fluorescence, Western blotting for visfatin, and vascular reactivity to phenylephrine in the presence or absence of perivascular adipose tissue (PVAT). Plasma glucose, triglycerides, malondialdehyde, and nitrite were also evaluated. Statistical analysis was performed using two-way ANOVA followed by Tukey's post-test (CEUA: 180/2022). **Results:** HSD-fed rats showed increased body weight, adiposity, food intake, plasma glucose, and triglycerides ($p<0.05$ vs. control), without changes in SBP. Resveratrol did not modify metabolic parameters. However, HSD markedly increased oxidative stress in the aortic wall, as demonstrated by enhanced DHE fluorescence and elevated plasma malondialdehyde levels, both reduced by resveratrol ($p<0.05$). In parallel, plasma nitrite bioavailability was increased after resveratrol treatment ($p<0.05$). HSD also increased aortic visfatin expression, NF-κB nuclear intensity, MMP-2 activity, collagen deposition, and vascular hypercontractility to phenylephrine, all of which were attenuated by resveratrol ($p<0.05$). **Conclusion:** Six weeks of resveratrol treatment reduced visfatin expression, oxidative stress, NF-κB activation, MMP-2 activity, and collagen deposition in the aorta, while increasing nitric oxide bioavailability and improving vascular reactivity in rats with metabolic syndrome induced by chronic HSD consumption.

06.030 **Inosine-Induced Vasodilation Is Partially Mediated by Endothelial NMDA Receptor Activation**. Stein AT[1,2], Brazão SC[1,2], Autran LJ[1,2], Pereira NCA[1,2], Mendes ABA[1,2], Motta NAV[1,3], Lima GF[1,2], Brito FCF[1,2]. [1]UFF, Lab. of Experimental Pharmacology, Brazil, [2]UFF, PPG Biomedical Sciences (Physiology and Pharmacology), Brazil, [3]UFF, PPG Cardiovascular Sciences, Brazil.

Introduction: Atherosclerosis is a chronic inflammatory disease driven by endothelial dysfunction and oxidative stress and is the leading cause of cardiovascular disease. N-methyl-D-aspartate (NMDA) receptors are expressed in endothelial cells and may regulate vascular function. Inosine, a purinergic metabolite with antioxidant and anti-inflammatory properties, has emerged as a potential vasoprotective agent, but its mechanisms remain unclear. **Objectives:** To investigate the role of NMDA receptor signaling in early atherosclerotic vascular dysfunction and the protective effects of inosine. **Methods:** Adult male Wistar rats (250–300 g) were randomized into Control (C), Control + inosine (C+I), Hypercholesterolemic (HC), and HC + inosine (HC+I) groups. HC groups received a hypercholesterolemic diet, and inosine (10 mg/kg/day/gavage) was administered during the last 15 days. Vascular reactivity, biochemical, and molecular analyses were performed in aortic tissue after euthanasia under ketamine/xylazine anesthesia. Data were analyzed by one-way ANOVA with Bonferroni post hoc test ($p<0.05$). **Results:** Animals subjected to a high- cholesterol diet showed increased total cholesterol (1193 ± 57.34 vs. 97.51 ± 3.58 mg/dL), triglycerides (234.30 ± 9.72 vs. 139.0 ± 9.91 mg/dL), LDL (1118 ± 58.92 vs. 31.06 ± 2.56 mg/dL) and reduced HDL (36.82 ± 1.05 vs. 41.93 ± 1.25 mg/dL). Treatment with inosine, reduced cholesterol levels (1008 ± 52.01 mg/dL), triglycerides (206.5 ± 4.24 mg/dL), VLDL (41.31 ± 0.84 mg/dL), and LDL (917.20 ± 56.45 mg/dL). Hypercholesterolemia induced endothelial dysfunction, with impaired acetylcholine-mediated relaxation (94.95 ± 2.86% vs. 104.60 ± 3.61%), increased phenylephrine-induced contraction (-LogEC50: 7.49 ± 0.17 vs. 7.07 ± 0.09), reduced eNOS and NMDAR1 expression, and dysregulation of antioxidant enzyme expression (SOD, catalase, and GPx). Inosine treatment improved endothelial function, increasing acetylcholine-induced relaxation (112.20 ± 3.55%) and reducing the contractile response to phenylephrine (-LogEC50: 6.77 ± 0.11), in addition to restoring eNOS and NMDAR1 expression, as well as the antioxidant profile in hypercholesterolemic rats. *In vitro* analysis showed that NMDA receptor activation induced vasodilation (34.69 ± 2.70%), potentiated by glycine (61.50 ± 4.15%) and abolished by MK-801 (8.30 ± 2.32% and 11.27 ± 2.19%) in aortic rings. Notably, inosine-induced vasodilation (83.42%) was reduced by 26.68% in the presence of MK-801, indicating that its vasodilatory effects are partially mediated by NMDA receptor activation. **Conclusions:** Hypercholesterolemia induces early vascular dysfunction associated with impaired endothelial NMDA receptor expression. Inosine exerts vasoprotective effects by improving endothelial function and modulating NMDAR1 expression, while NMDAR activation contributes to inosine- induced vascular relaxation, highlighting a novel interaction between purinergic and NMDA signaling in early atherogenesis.

06.031 **Influence of Estrogen Deficiency on Platelet Aggregation and Vascular Response in Rats**. Meneses CES[2], Azevedo PSS[2], Rego AMF[1], Santos MJ[1], Rocha KF[2], Albuquerque BA[2], Rêgo AF[2], Sena EP[2], Rocha VA[2], Oliveira AP[2,3]
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Introduction: Menopause is associated with an increased incidence of cardiovascular diseases, and estrogen deficiency is one of the factors involved in this process. Estrogen participates in the regulation of vascular and platelet function, and its reduction may contribute to alterations related to cardiovascular homeostasis. Therefore, the present study evaluated the influence of estrogen deficiency on platelet aggregation and vascular response in rats. **Objectives:** To evaluate the influence of estrogen deficiency on platelet aggregation and vascular response in normal, obese and ovariectomized rats. **Methods:** Platelet aggregation was evaluated in platelet-rich plasma (PRP) using adenosine diphosphate (ADP) as agonist. Initially, the participation of calcium was investigated by adding different concentrations of $CaCl_2$ to PRP. Subsequently, the aggregatory responses of normal, obese and ovariectomized (OVX) rats were compared. In addition, vasorelaxant activity was evaluated in endothelium-denuded aortic rings pre-contracted with phenylephrine. In another experimental protocol, rats received oral treatment for seven days, after which ADP-induced platelet aggregation and vascular reactivity to phenylephrine were evaluated. **Results:** ADP promoted concentration-dependent platelet aggregation, and the concentration of 20 µM was selected for subsequent protocols. $CaCl_2$ also increased platelet aggregation, showing the highest response at 20 µM. In OVX rats, ADP-induced platelet aggregation was lower than that observed in normal rats (8.50 ± 2.07% versus 43.81 ± 2.86%). Similarly, obese rats showed lower platelet aggregation (7.83 ± 2.14%) compared with normal rats, with no statistical difference being observed between OVX and obese groups. In endothelium-denuded aortic rings, concentration-dependent vasorelaxation was observed in both normal (pD_2 = 5.61 ± 0.12) and OVX rats (pD_2 = 4.65 ± 0.21). After seven days of oral treatment, a reduction in ADP-induced platelet aggregation was observed when compared with the control group, as well as changes in vascular response to phenylephrine. **Conclusion:** The results demonstrate that estrogen deficiency influenced ADP-induced platelet aggregation. In addition, differences in aggregatory responses were observed among normal, obese and ovariectomized rats. In endothelium-denuded aortic rings, concentration-dependent vasorelaxation was observed in both normal and ovariectomized rats. Furthermore, seven days of treatment reduced ADP-induced platelet aggregation and altered vascular response to phenylephrine. Keywords: platelet aggregation; ovariectomy; vascular reactivity; estrogen deficiency.

06.032 **Enhanced Platelet Response Induced by ·OH-Oxidized Collagen**. Cantuária NM[1], Toledo TA[1], Gibbins JM[2], Gaspar RS[1]. [1]FCM-Unicamp, Dept Pharmacology, Brazil, [2]University of Reading School of Biological Sciences, Reading, UK.

Introduction: Excessive production of reactive oxygen species (ROS) resulting from oxidative imbalance contributes in several ways to the pathophysiology of cardiovascular diseases (CVDs). Platelet adhesion and thrombus formation depend on endothelial injury, which exposes the extracellular matrix (ECM) of the sub endothelium. This endothelial ECM is rich in type I collagen, a long-lived protein. Although the prothrombotic effects of ROS are well established, it remains unclear whether collagen oxidation contributes to platelet dysfunction. **Objectives:** To investigate the effects of collagen oxidation on the function of cardiovascular cells and to identify biophysical alterations that may explain these effects. **Methods:** Collagen was oxidized using five collagen:$CuCl_2$ molar ratios (1:1, 1:3, 1:10, 1:30, and 1:100) in the presence of H_2O_2 at a collagen:H_2O_2 ratio of 1:200 and incubated for at least 30 minutes. A total of 28 donors were used, distributed across the different experiments. Platelet aggregation assays were performed by turbidimetry using platelet-rich plasma (PRP) (n=7) and washed platelets (WP) (n=8). Different inhibitors were employed to identify the signalling pathways involved in platelet aggregation (n=5). Platelet adhesion was assessed in PRP (n=8), platelets were stained with phalloidin and visualized using a Leica STELLARIS 5 confocal microscope. A fluorescence assay using DCF was performed to determine ROS production during the reaction between H_2O_2 and $CuCl_2$ (n=5). Circular dichroism (CD) analysis was performed to evaluate the structure of control and oxidized collagen. Endothelial cell (HUVEC) viability (n=6) and migration assays were assessed (n=5). **Results:** Collagen oxidized by hydroxyl radicals (•OH) increased platelet aggregation in both PRP and WP preparations. Sulfosuccinimidyl oleate (SSO) and Dasatinib did not show any difference between the control and oxidized collagen; only Acetylsalicylic acid (ASA) showed reduced aggregation with oxidized collagen. Platelet adhesion was also enhanced on oxidized collagen. In addition, MTT assays suggested increased endothelial cell proliferation; however, oxidized collagen did not appear to affect endothelial cell migration. Increased fluorescence was observed in the DCF assay, indicating that the reaction between H_2O_2 and $CuCl_2$ generates ROS. The CD analysis showed that oxidation does not affect the collagen triple-helix structure or its thermal stability, however, it leads to destabilization of the helical domains. **Conclusions:** Collagen oxidized by •OH can enhance platelet function and HUVEC proliferation. These findings provide evidence for a potential mechanism underlying the development of CVDs and may contribute to the identification of novel therapeutic strategies.

06.033 **Cardiovascular and Metabolic Effects Induced by *Cannabis sativa*-Based Oils in Spontaneously Hypertensive Rats**. Silva MC, Aires RS, Queiroz TM UFPE, Academic Center of Vitória, Multicenter Graduate Program in Physiological Sciences, Brazil

Introduction: *Cannabis sativa* phytocannabinoids, such as cannabidiol (CBD) and tetrahydrocannabinol (THC), interact with the endocannabinoid system, modulating cardiovascular function and energy homeostasis. Preclinical evidence suggests these compounds influence vascular tone and metabolic parameters, but their chronic effects on hypertension require further elucidation . **Objective:** Therefore, this study aimed to investigate the effects induced by chronic treatment with oil rich in the cannabinoids isolated CBD and CBD+THC on cardiovascular and metabolic parameters in SHR rats. **Methods:** Twelve-week-old male SHR were divided into: CONTROL, CBD, and CBD+THC groups. Oils were administered via oral gavage for 28 days. Body weight, food, and water intake were monitored, and systolic (SBP) and diastolic (DBP) blood pressure were measured indirectly. After euthanasia, thoracic aorta reactivity to phenylephrine (Phe), acetylcholine (ACh), and sodium nitroprusside (NPS) was assessed in rings with and without endothelium. Differences were considered significant when $p<0.05$. The statistical program used was GraphPad Prism® 11.0. **Results:** Treatment did not alter water or food intake. However, both treated groups prevented the weight gain observed in controls from day 1 to 28 (CBD: Δ -3g and CBD+THC: Δ -3g vs CONTROL: Δ +5.75g). After 28 days, SBP was significantly reduced in the CBD+THC group (186.8 ± 2.13 mmHg, n= 5) compared to CONTROL (200 ± 2.34 mmHg, n= 4) and CBD groups (198.6 ± 1.72 mmHg, n= 5). A similar reduction was observed for DBP in the CBD+THC group (101.4 ± 1.05 mmHg, n=5) compared to the CBD group (105.4 ± 1.72 mmHg, n=5Regarding aortic reactivity, no differences were found in the maximum contractile response to Phe or in the vasodilatory responses to ACh and NPS among groups. **Conclusion:** It is concluded that treatment with oils rich in phytocannabinoids promoted weight gain and a reduction in systolic and diastolic blood pressure, but did not alter vascular parameters, nor food and water consumption. We would like to thank FACEPE, CNPq, and CAPES for their fungind.

06.034 **Effects of γ-Terpinene on Hematological Parameters and Platelet Aggregation in Spontaneously Hypertensive Rats** (**SHR**). Rêgo AF[1,2], Rocha VA[1,2], Sena EP[1,2], Albuquerque BA[1,2], Silva ND[1,2], Acha BT[3], Soares HS[2], Silva FAHV[2], Costa MRS[2], Rêgo AMF[2], Nascimento BN[2], Barbosa SLM[4], Ferreira PMP[4,5], Oliveira AP[1,2,6]. [1]UFPI, Health Sciences Center, Graduate Program in Pharmacology, Brazil. [3]Renorbio-UFPI, Northeast Biotechnology Network, Brazil. [4]UFPI, Health Sciences Center, Graduate Program in Pharmaceutical Sciences, Brazil. [5]LOE-UFC, Lab Experimental Oncology, Dept Physiology and Pharmacology, Brazil. [6]UFPI, Health Sciences Center, Dept Biophysics and Physiology, Brazil.

Introduction: γ-Terpinene is a monoterpene found in essential oils with potential cardiovascular activity and effects on hemostasis and inflammatory processes. **Objective:** To investigate the effects of γ-terpinene on hematological parameters and platelet aggregation in male spontaneously hypertensive rats (SHR). **Methods:** Experimental protocols were approved by the Ethics Committee on Animal Use of UFPI (CEUA/UFPI No. 854/2025). Animals were orally treated for 15 days with vehicle or γ-terpinene at doses of 50 and 100 mg/kg. Platelet aggregation was induced by ADP (20 μM), and the involvement of the Ca^2+/calmodulin pathway was evaluated using calmidazolium, while the nitric oxide pathway was investigated using sodium nitroprusside (SNP). Hematological analyses were also performed. **Results:** γ-Terpinene significantly reduced ADP-induced platelet aggregation (44.8 ± 1.7%), yielding aggregation values of 5.0 ± 0.4% and 6.3 ± 0.3% at doses of 50 and 100 mg/kg, respectively. Calmidazolium reduced platelet aggregation to 11.5 ± 0.9%; however, its association with γ-terpinene did not produce an additional significant reduction, suggesting that the antiplatelet effect is not dependent on the Ca^2+/calmodulin pathway. SNP reduced aggregation to 26.5 ± 1.5%, and its association with γ-terpinene potentiated the antiplatelet effect, particularly at the dose of 50 mg/kg (3.0 ± 1.0%), indicating the involvement of the nitric oxide pathway. Hematological analyses revealed a significant reduction in absolute neutrophil counts in γ-terpinene-treated groups, with no relevant changes observed in the other evaluated parameters. **Conclusion:** γ-Terpinene exhibited significant antiplatelet activity in spontaneously hypertensive rats, predominantly involving the nitric oxide pathway. Furthermore, it demonstrated a favorable hematological safety profile at the studied doses. **Financial support:** CAPES, UFPI, and CNPq.

06.035 **Sodium Nitrate Treatment Attenuates Cardiac Dysfunction in an Experimental Model of Preeclampsia**. Toghi CJ[1,2], da Silva A[3], Palei AC[2], Dias-Junior CA[1] [1]IBB-Unesp, Dept Biophysics and Pharmacology, Botucatu, SP, Brazil, PPG Biomolecular and Pharmacological Sciences, Brazil; [2]University of Mississippi Medical Center, Dept Surgery, School of Medicine (SOM), Jackson, Mississippi, United States of America (USA); [3]University of Mississippi Medical Center, Dept Physiology and Biophysics, Jackson, USA Hypertensive disorders of pregnancy are among the leading causes of maternal morbidity and mortality worldwide, and preeclampsia stands out due to its important cardiovascular complications. The disease is characterized by the onset of hypertension after the twentieth week of gestation and is associated with inadequate remodeling of the uterine arteries, leading to placental hypoxia, increased oxidative stress, and systemic endothelial dysfunction. In addition to vascular alterations, recent evidence shows that preeclampsia also impairs maternal cardiac function, causing ventricular hypertrophy, diastolic dysfunction, and persistent alterations in cardiac mechanics. In this context, nitric oxide (NO) plays a fundamental role in maintaining vascular and cardiovascular function. However, preeclampsia is associated with reduced NO bioavailability, which aggravates endothelial and cardiac dysfunction. An interesting alternative is the nitrate–nitrite–NO pathway, which allows NO formation even under hypoxic conditions. Therefore, nitrate has been investigated as a potential therapeutic strategy in preeclampsia. Thus, the aim of this study was to evaluate the cardiovascular impact of experimental preeclampsia using the Reduced Uterine Perfusion Pressure (RUPP) model in Wistar rats, as well as to investigate the potential therapeutic effects of sodium nitrate treatment. For this purpose, pregnant Wistar rats were allocated into four groups: Sham+Placebo (n=8), Sham+Nitrate (n=9), RUPP+Placebo (n=9), and RUPP+Nitrate (n=8). On gestational day 14, the rats underwent uterine and placental blood flow restriction using silver clips (RUPP) or a sham procedure. Between gestational days 14 and 20, the animals were treated with sodium nitrate (140 mg/mL/kg/day, by gavage). On gestational day 21, blood pressure measurements and echocardiographic assessments were performed. The RUPP+Placebo group exhibited higher mean arterial pressure compared to the Sham+Placebo group (103.1±2.3 vs. 89.1±2.6 mmHg; $P<0.05$). Fractional shortening and global longitudinal strain were significantly reduced in the RUPP+Placebo group compared to the other groups (18.6±1.6, 35.6±2.5, 36.4±1.4, and 26.8±2.8 %; -14.8±1.1, -20.5±1.3, -19.8±1.6, and -19.9±1.7 %, respectively; $P<0.05$). Late diastolic velocity was lower in the RUPP+Placebo group compared to the RUPP+Nitrate group (501.4±105.1 vs. 773.3±56.5 cm/s; $P<0.05$). Left ventricular mass was greater in the RUPP+Placebo group than in the Sham+Nitrate group (547.4±30.9 vs. 453.4±19.6 mg; $P<0.05$), and left ventricular anterior wall thickness during systole was greater in the RUPP+Placebo group compared to the RUPP+Nitrate group (3.1±0.1 vs. 2.7±0.1 mm; $P<0.05$). These findings indicate that the RUPP model of preeclampsia induces adverse maternal cardiac dysfunction, whereas sodium nitrate treatment partially attenuates structural and functional alterations. Keywords: Preeclampsia, nitric oxide, nitrate, cardiac function

06.036 **Cardioprotective Effects of Naringenin Against Doxorubicin- and Isoproterenol-Induced Cardiotoxicity in Hypertensive Rats**. Dada A, Silva RCMVAF, Zanovello M, Macarini AF, Moser JC, Panizzi EA, Brandão LG, Boeing T, Cechinel Filho V, Souza P Univali, PPG em Ciências Farmacêuticas, Itajaí, Santa Catarina, Brazil

Introduction: Naringenin (NAR), a citrus flavanone with antioxidant, anti-inflammatory, and cardiometabolic properties, has been associated with the attenuation of oxidative stress, inflammation, and myocardial remodeling, which are key mechanisms involved in doxorubicin (DOX)-induced cardiotoxicity. Because hypertension is a major risk factor for DOX-induced cardiac dysfunction, and hypertensive cancer patients are more susceptible to developing cardiotoxicity, spontaneously hypertensive rats (SHR) were selected as a clinically relevant model of cardiovascular comorbidity. To further exacerbate myocardial injury and reproduce an acute cardiac insult superimposed on chronic DOX cardiotoxicity, isoproterenol (ISO) was administered following DOX treatment. **Objective:** To evaluate the cardioprotective potential of NAR in SHR subjected to combined DOX- and ISO-induced cardiotoxicity. **Methods:** SHR (n = 6–8/each group) were allocated into the following groups: vehicle, NAR, DOX+ISO, and NAR+DOX+ISO. NAR (100 mg/kg, orally) was administered for 15 days; DOX (2.5 mg/kg, i.p., six doses on alternate days) and ISO (85 mg/kg, i.p., during the last two days) were used to induce cardiotoxicity. Hemodynamic parameters (tail-cuff plethysmography), biochemical, inflammatory (MPO, NAG, TNF, IL-1β, IL-10), oxidative stress (LPO, GSH, SOD, GST), and histological parameters (eight microscopic fields per sample, blinded analysis) were evaluated. Statistical analysis was performed using one- or two-way ANOVA followed by Bonferroni's post hoc test, with $p < 0.05$ considered statistically significant. **Results:** DOX+ISO reduced systolic (Δ -30.91 mmHg) and mean arterial pressure (Δ -16.14 mmHg) compared with the vehicle group, accompanied by cardiac hypertrophy (increased heart weight by 22.17% compared with the vehicle), elevated markers of myocardial injury (lactic acid: +115.3% and CK-MB: +47.3% vs. the vehicle group), increased clot formation (≅88% higher compared to the vehicle), and dyslipidemia (total cholesterol, LDL-C, HDL-C, and triglyceride levels increased by 145.49%, 184.52%, 87.13%, and 143.44%, respectively, compared with the vehicle group). By attenuating the marked reduction in blood pressure induced by DOX+ISO, NAR preserved hemodynamic stability, which may contribute to maintaining coronary and systemic perfusion during cardiac injury. NAR reduced aortic weight (34.83% lower than DOX+ISO), decreased cardiac injury markers (lactic acid, LDH, and CK-MB decreased by 43.12%, 39.64%, and 32.85%, respectively, compared with the DOX+ISO group), lipid peroxidation, and cardiac TNF levels, with a trend toward reduced MPO activity. NAG, SOD, GST, GSH, IL-1β, and IL-10 did not differ among groups. NAR also improved renal parameters (urea and uric acid) and the lipid profile and reduced myocardial fiber separation on histological analysis without affecting collagen deposition. **Conclusion:** Under the conditions of this study, NAR attenuated hemodynamic, biochemical, and histological alterations associated with DOX+ISO-induced cardiotoxicity in SHR. Further studies are warranted to elucidate the mechanisms and confirm the therapeutic potential of NAR.

06.037 **Propafenone Analogs Promote Vasorelaxant Effects Involving Potassium and L-Type Calcium Channels**. Lima NCB, Rocha DG. Silva FAO. Mesquita JLF. de Souza ARL, de Mattos MC, Lima GC, Lima RF, Jamacaru FVF, Monteiro HSA, Jorge RJB LAFAVET-UFC-Porangabuçu, Depto Fisiologia e Farmacologia, Lab Farmacologia de Venenos e Toxinas, PPG em Farmacologia, Brasil

Introduction: Cardiovascular diseases remain among the leading causes of mortality worldwide, underscoring the urgent need for the development of novel therapeutic strategies. Previous molecular docking studies demonstrated that four synthesized propafenone analogs (RAC-5A, RAC-5B, RAC-5C, and RAC-5D), developed by the Laboratory of Biotechnology and Organic Synthesis (LABS), exhibited greater selectivity for β1- and β2-adrenergic receptors, as well as sodium channels, compared to conventional propafenone, suggesting their potential applicability in the treatment of cardiovascular disorders. **OBJECTIVES:** This study aimed to investigate the vasorelaxant effects of propafenone analogs in isolated rat arteries. **Methods:** Male Wistar rats obtained from the animal facility of the Drug Research and Development Center (NPDM) were used in this study. Animals were anesthetized with ketamine and xylazine (80 and 10 mg/kg, respectively) for thoracic aorta excision. The experimental protocol was approved by the Animal Ethics Committee of NPDM (CEUA No. 27060722-0). Thoracic aortas were dissected into rings with intact endothelium and mounted in isolated organ baths containing Krebs solution under continuous carbogenation. Following a 60-minute stabilization period, cumulative concentration–response curves for the propafenone analogs (10^{-7}; to 3×10^{-4} M) were constructed. Among the compounds evaluated, RAC-5A and RAC-5B exhibited the most pronounced vasorelaxant effects, with RAC-5B selected for further pharmacological investigation due to its greater efficacy and potency (Emax = 106.60 ± 7.33%; EC50 = 10.842 [4.488–26.407]; pEC50 = 4.96 ± 0.15). Additional experiments were performed using phenylephrine- or KCl-induced contractions, as well as pharmacological blockers to investigate the involvement of potassium channels, using tetraethylammonium (TEA), 4-aminopyridine (4-AP), and glibenclamide, and L-type calcium channels, using nifedipine, in the mechanisms underlying the observed vascular responses. Six rings were used per experimental group (n = 6), obtained from two animals (N = 2). Statistical analyses were conducted using GraphPad Prism® software, applying normality tests followed by Student's t-test with Tukey's post hoc test for parametric data, or Kruskal–Wallis test followed by Dunn's post hoc test for non-parametric data. **Results:** The findings demonstrated that RAC-5B induces significant vasorelaxant effects in isolated rat arteries through mechanisms involving K+ channels and L-type Ca^{2}+ channels, suggesting its potential pharmacological application in cardiovascular diseases. **Conclusion:** These results reinforce the therapeutic potential of pharmacological repurposing of propafenone analogs, particularly RAC-5B, as promising candidates for the development of novel strategies targeting cardiovascular diseases.

06.038 **Distinct Glycation Modifications of Type I Collagen Differentially Regulate Platelet Reactivity**. Fróes RBL, Silva BS, Gaspar RS FCM-Unicamp, PPG Farmacologia, Lab Matriz Extracelular, Brasil.

Introduction: Type 2 diabetes mellitus (T2DM) is associated with chronic hyperglycemia and increased atherothrombotic risk, characterized by platelet hyperreactivity. Advanced glycation end products (AGEs) may accumulate in long-lived extracellular matrix proteins, including subendothelial collagen, potentially altering platelet-collagen interactions and contributing to the prothrombotic state observed in diabetes. **Objective:** To investigate the effects of type I collagen glycation on platelet function and to evaluate the involvement of the receptor for AGEs (RAGE) in this process. **Methods:** Bovine type I collagen was glycated with methylglyoxal (MGO), glucose or ribose for 7 days at 36°C. AGE formation was evaluated by immunofluorescence and collagen organization was assessed by differential interference contrast microscopy. Platelet aggregation was assessed by optical aggregometry using platelet-rich plasma (PRP) and washed platelets (WP) from healthy volunteers. Platelet adhesion assays were performed using PRP or WP incubated onto control or glycated collagens. The involvement of RAGE was investigated using azeliragon and RAGE antagonist peptide (RAP). Platelet viability was evaluated after treatment with RAGE antagonists. **Results:** Glycation by MGO increased AGE incorporation while preserving collagen fibrillar organization (n=1). MGO-glycated collagen increased platelet aggregation in PRP by 38.63% (n=7), whereas glucose-glycated collagen increased aggregation by 57.68% (n=7) at higher molar ratios. In washed platelets (WP), MGO-glycated collagen increased aggregation by 260.5% compared with control collagen (n=12). Similarly, ribose-glycated collagen increased aggregation by 130.12% and 160.24 % at the 1:100 and 1:1000 molar ratios, respectively, accompanied by marked increases in slope and maximal aggregation (n=5). Furthermore, MGO-glycated collagen increased platelet adhesion, doubling platelet-covered area (CTR = 7.81 ± 0.88%; MGO 1:30 = 15.55 ± 2.73, n=5). Pharmacological RAGE blockade showed similar inhibitory effects on platelet aggregation induced by glycated and non-glycated collagens (n=5), and no changes in platelet viability were observed following antagonist treatment (n=4). **Conclusion:** Type I collagen glycation increases platelet reactivity and promotes a prothrombotic extracellular matrix phenotype without disrupting collagen fibrillar organization. The similar effects observed with MGO- and ribose-glycated collagens in WP suggest that different glycation crosslinks are sufficient to enhance platelet responses independently of plasma components. These effects were independent of RAGE. The glycation of subendothelial collagen may represent a mechanistic link between chronic hyperglycemia and increased thrombotic risk, while receptors other than RAGE may be implicated.

06.039 **Effect of Thiazolidinedione Derivatives, Possible AT1 Antagonists, on Vascular Reactivity in Isolated Wistar Rat Aorta**. Ferreira JG[1], Silva KT[1], Arrospide TM[2], Alves SML[1], Santos RCA[1], Ferreira LFL[2], Aires RS[1], Silva MCC[1], Dos Anjos JV[2], Araújo AV[1] [1]UFPE, Centro Acadêmico da Vitória, Brasil, [2]UFPE, Lab Síntese Orgânica, CCEN, Brasil

Introduction: One of the first-line classes of antihypertensive drugs used in clinical practice are angiotensin II AT1 receptor antagonists. Thiazolidinediones are heterocycles explored in medicinal chemistry due to their various bioactive properties. Structurally, these compounds are described as bioisosteres of carboxylic acids, but with a tendency to be more lipophilic. Carboxylic acid bioisosteres can act as AT1 receptor antagonists. **Objective:** to evaluate the effect of new thiazolidinedione compounds (CTZPA- BipH, CTZPApBr and CTZPAmTol) with potential antagonistic activity on AT1 receptors in rat aorta. **Methods:** Two-month-old Wistar rats were used. They were anesthetized with isoflurane, euthanized by guillotine decapitation. Their aortas were isolated and sectioned into rings, the functional endothelium was removed, and the rings were suspended in organ baths in aerated Krebs solution with carbogenic solution. After stabilization and viability tests, concentration-effect curves were peeformed for Angiotensin II (Ang II) in the absence or in the presence of CTZPA-BipH, CTZPApBr, or CTZPAmTol (100 µmol/L). The maximum effect and pharmacological potency were calculated from the results obtained. Data are expressed as mean ± standard error mean. Statistical difference was considered when $p < 0.05$. **Results:** All the compounds practically abolished the Ang II-induced contraction when compared to the control (Emax: control = 1.45 ± 0.20 g; CTZPA-BipH = 0.03 ± 0.01 g; CTZPApBr = 0.09 ± 0.02 g; CTZAmTo = 0.08 ± 0.03 g). **Conclusion:** Under the evaluated conditions, we can infer that the molecules CTZPA-BipH, CTZPApBr, and CTZPAmTol may antagonize AT1 receptors, since they abolished the cumulative contraction curve for Ang II. However, further studies are needed to test this hypothesis.

06.040 **Glycated Collagen Drives Vascular Remodeling and Smooth-Muscle Dysfunction in Hyperglycemia**. Duarte-Maia S, Silva-Oliveira N, Simões Gaspar R. FCM-Unicamp, Depto Farmacologia, Lab Matriz Extracelular, PPG em Farmacologia.

Diabetes is an important and growing cause of death worldwide due to increased risk of vascular damage even after normalized glucose. We hypothesized that the glycation of collagen in the vascular matrix leads to impaired mechanosensing of aortic smooth-muscle cells leading to dysfunction through the accumulation of Advanced Glycation Endproducts (AGE) and activation of receptors for AGEs (RAGE). Therefore, we tested whether RAGE antagonist Azeliragon would revert vascular dysfunction. Type I collagen was glycated using methylglyoxal (MGO) at different molar proportions (1:0 (CTR) or 1:90 (MGO); 4°C for 7 days) We assessed fibrillogenesis (absorbance), thermostability (circular dichroism), and ultrastructure (atomic force microscopy). Vascular smooth muscle cells (VSMCs) were seeded onto control or MGO collagen for adhesion, migration and immunofluorescence evaluation. Mice (n=44, 6378-1/2024) received streptozotocin (STZ) (ip. 50mg/kg, 5 days) or PBS. After confirmation of hyperglycemia, treatment began with either Azeliragon (AZE, 4mg/kg, i.p., 4 weeks) or PBS. Aorta rings were either put in myographic chamber for vascular reactivity and stretch-force curves, aortas were stained for histological analysis. Data are mean±SEM; ANOVA followed by post-hoc tests. Collagen fibrillogenesis was reduced after glycation (MGO 189.3±16.77 vs. CTR 467.2±15.56; area under curve; n=9; P<0.0001). Glycated collagen was more thermostable (MGO 39.97±0.2127 vs. CTR 39.58±0.2127°C; n=4; p= 0.0453). Glycated collagen fibrils showed increased roughness and a higher prevalence of disorganized fibers (2.311 ± 0.1036 vs. CTR 1.128 ± 0.04283 n=6; FFT Anisotropy Index; p<0.0001). VSMCs seeded onto glycated collagen exhibited greater adhesion(316±18.82 vs. 222.6±6.156; n=4; cell per area; p=0.0033) and migration (68.74±3.219 vs. 58.10±1.807%; n=4; wound closure; p=0,0155). VSMCs cultured onto glycated collagen expressed more COL1(18950±1515 vs. 11006±1112 a.u; n=4 fluorescence/cell; p=0.0055). In mice, STZ aortas showed increased eMax to phenilephrine (STZ 67.14±7.124 n=8 vs. CTR 34.19±10.03 n=13; %KCl, p=0,0334) AZE group showed no effect; STZ aortas generated more force upon stretching (87145±27315 vs. 26963±2475; n=9; AUC; p=0.0346), normalized by AZE(39079±5711; p=0.8511). Medial hypertrophy in the STZ group (STZ 41.94±1.051 vs. 37.44±1.007 N=8; µm; p=0.0294), was reversed by AZE(36.44±1.713; p=0.8079); number of breaks per elastic fiber (STZ 1.648±0.2230 n=9 vs. CTR 0.8056±0.09044 n=6; breaks per fiber; p=0.0434), were reduced after AZE (1.111±0.3247; n=6; p=0.6123). Collagen maturity increased in STZ (7.640±1.844 vs. 2.795±0.3275; n=8; red/green ratio; p=0.0377), and was reduced in AZE (4.883±1.161; n=5; p=0.0377). Taken together, ECM collagen glycation is associated with VSMC dysfunction and vascular tissue remodeling through mechanisms that are partially RAGE- dependent.

06.041 **SGLT2 Inhibition Mitigates Hyperpalatable Diet-Induced Kidney Dysfunction in Ovariectomized Female Mice**. Moraes MC[1,2], Oliveira LBF[2], Parreira LS[1], Avelar CDFL[1], Peruchetti DB[2], Vieira LB[1] [1]ICB-UFMG, Dept Pharmacology, Neuropharmacology Lab, PPG Physiology and Pharmacology, Brazil. [2]ICB-UFMG, Dept Physiology and Biophysics, Renal Physiology, Lab, PPG Physiology and Pharmacology, Brazil.

Introduction: Obesity-associated kidney disease is characterized by metabolic alterations, renal inflammation, renal lipid accumulation, and kidney dysfunction in males. A previous study of our group has shown that sodium-glucose cotransporter 2 (SGLT2) mediates these processes. Interestingly, evidence suggests that estrogen exerts protective effects against obesity- induced metabolic complications. Therefore, we investigated the impact of estrogen deficiency and SGLT2 inhibition on metabolic and renal alterations induced by a hyperpalatable diet in ovariectomized (OVX) female mice. Methods: Female C57BL/6 mice were subjected to OVX or sham surgery and allocated into six experimental groups (n = 8-12 per group). Animals were fed either a standard AIN diet or a high sugar and butter (HSB) diet for 12 weeks. From week 8 onward, animals received dapagliflozin (DAPA, 1 mg/kg/day, gavage) for 4 consecutive weeks. Metabolic, renal, and histological parameters, as well as markers of lipotoxicity, were evaluated (CEUA-UFMG Protocol 71/2023). Statistical analyses were performed using GraphPad Prism 10.4 software, employing two-way ANOVA followed by Tukey's post hoc test ($P<0.05$). **Results:** OVX females fed the HSB diet exhibited greater body weight gain and increased adiposity compared to sham females receiving the same diet, suggesting that estrogen deficiency enhances susceptibility to diet-induced metabolic alterations. In addition, the HSB diet induced in OVX females: (1) glucose intolerance; (2) lipid accumulation in renal tissue; (3) tubular proteinuria; (4) histopathological evidence of tubular injury; and (5) increased expression of renal injury markers. Treatment with DAPAattenuated renal alterations in OVX mice fed with the HSB diet. **Conclusion:** These findings suggest that hyperpalatable diet-induced kidney disease in OVX females involves renal lipid accumulation and tubular injury, contributing to renal dysfunction under estrogen-deficient conditions. In addition, the increased susceptibility observed in OVX animals supports a protective role of estrogen against obesity-associated renal alterations, reinforcing the importance of sex hormones in disease susceptibility. Furthermore, the renoprotective effects observed with DAPA treatment support the potential use of SGLT2 inhibitors as preventive or therapeutic strategies in obesity-associated kidney disease. Collectively, these data expand the understanding of the mechanisms linking obesity, lipid metabolism, and renal dysfunction in females under estrogen- deficient conditions.

06.042 **Oxytocin Promotes Natriuretic Effects by Inhibiting NHE3-Mediated Sodium Reabsorption in the Renal Proximal Tubules of Rats**. Paulino FWV, Oliveira NO, Moura FLC, Pires GS, Lima TDS, Lessa LMA, Pinto EV, Fonteles MC, Girardi ACC, Nascimento NRF, Santos CF [1]ISCB-UECE, Lab Fisiologia Renal, PPG em Ciências Fisiológicas, Brasil, [2]InCor-HCFM-USP, Lab Genetics and Molecular Cardiology, Brasil.

Oxytocin (OT) is a neuropeptide involved in the regulation of fluid and electrolyte balance. The sodium/hydrogen exchanger isoform 3 (NHE3), the major transporter. responsible for sodium reabsorption in the proximal tubule (PT), exhibits sexual dimorphism in rats, with higher expression and activity in males. This study investigated the effects of OT on NHE3 activity in male and female Wistar rats and the mechanisms underlying its natriuretic action. Net bicarbonate reabsorption ($JHCO_3^-$) was measured using the *in vivo* stationary renal microperfusion technique. Three to five animals were used per group, and n represents the number of perfused tubules. Data (mean ± SEM) were analyzed using Excel 2013 and GraphPad Prism 8 by Student's t-test or one-way ANOVA followed by Bonferroni's post hoc test (p < 0.05). OT significantly reduced $JHCO_3^-$ at all concentrations tested [control: 2.18 ± 0.06 (6); OT 10^{-9} M: 1.09 ± 0.05 (8) $nmol \cdot min^{-1} \cdot mm^{-1}$]. Co-perfusion with the selective NHE3 inhibitor S3226 produced no additional effect [0.72 ± 0.04 (10) vs. 0.76 ± 0.04 (7)], indicating that OT acts predominantly through NHE3. A sexually dimorphic response was observed, with greater inhibition in males [2.18 ± 0.06 vs. 1.09 ± 0.05] than in females [1.70 ± 0.09 vs. 1.06 ± 0.03]. Arginine vasopressin (AVP) abolished the inhibitory effect of OT [2.05 ± 0.05 vs. 2.08 ± 0.05], whereas the oxytocin receptor antagonist atosiban did not alter this response [1.37 ± 0.07 vs. 1.40 ± 0.06]. In contrast, the vasopressin V2 receptor antagonist tolvaptan completely prevented the effect of OT [1.86 ± 0.04 vs. 2.02 ± 0.04], suggesting the involvement of vasopressin-sensitive receptors. Inhibition of soluble guanylate cyclase with ODQ partially attenuated the effects of OT, whereas PKG inhibition with KT5823 had no effect, indicating partial involvement of the NO/sGC/cGMP signaling pathway through PKG- independent mechanisms. These findings demonstrate that OT directly inhibits sodium and bicarbonate reabsorption in the PT by modulating NHE3, exhibiting sexual dimorphism, functional interaction with AVP, and partial involvement of the NO/sGC/cGMP signaling pathway.

06.043 **Cardiovascular Effect of Neryl Acetate in an Experimental ModeL of Hypertension and Hemostasis**. Portela, EP[1,2,3], Rêgo, A. F,[2,3], Silva, ND[1,2,3], Albuquerque, BA[1,2,3], Rocha, VA [1,2,3], Almeida, FRC[1], Oliveira, AP[1,2,3,4] [1]UFPI, PPG in Pharmacology, [2]UFPI-NPPM, Lab Cardiovascular Pharmacology-, [3]UFPI, Medicinal Plant Research Center, 4DUFPI, Dept Biophysics and Physiology-UFPI.

Introduction: Nerol is a monoterpene alcohol with anti-inflammatory, antioxidant, and cardioprotective effects described in the literature. Its esterification yields neryl acetate (NAc), the cardiovascular effects of which remain poorly understood.**Objective:** To evaluate the cardiovascular and hemostatic effects of neryl acetate (NAc) in spontaneously hypertensive rats (SHR).**Methods:** Male SHR were used in all protocols (n=5). To assess antiplatelet activity against 20 μM ADP (adenosine diphosphate), NAc concentrations ranging from 10^{-4} to 10^{-9} M were incubated with platelet-rich plasma from SHR. For the evaluation of cardiovascular parameters, SHR were divided into a vehicle group (1% Tween) and NAc groups (treated orally with 25, 50, and 100 mg/kg); systolic blood pressure and heart rate were measured on days 0, 1, 7, and 15 using the tail-cuff plethysmography method. At the end of the treatment, the animals were euthanized, and blood samples were collected for biochemical analyses, prothrombin time (PT), activated partial thromboplastin time (aPTT), and International Normalized Ratio (INR). All protocols were approved by the CEUA/UFPI (Ethics Committee on the Use of Animals at the Federal University of Piauí), under protocol CEUA No. 822/2024. **Results:** Regarding platelet aggregation, the aggregation index induced by ADP (53%) was reduced in the presence of concentrations ranging from 10^{-4} to 10^{-6} M (2.6%, 2.8%, and 2.2%), followed by an almost complete inhibition at lower concentrations, ranging from 10^{-7}; to 10^{-9} M (0.2%, 0.0%, and 0.4%); this can be explained by a dual, dose-dependent effect—in which higher concentrations stimulate aggregation while lower concentrations inhibit it—a phenomenon frequently associated with terpenes. Plethysmography demonstrated an antihypertensive effect of NAc at doses of 50 and 100 mg/kg compared with the vehicle (148.67 ± 0.9 mmHg*; 129.06 ± 0.8 mmHg*; and 213.14 ± 1.0 mmHg, respectively), with no changes in heart rate. Regarding prothrombin time, there was an increase at the 50 mg/kg dose compared with the control (24.2 s vs. 33.7 s), along with a reduction in activated partial thromboplastin time at 25 and 50 mg/kg (33.66 s and 58.5 s) compared with the control group (298.3 s). Calculation of the International Normalized Ratio (INR) revealed an increase in this value at doses of 50 and 100 mg/kg. Regarding biochemical parameters, doses of 25 and 50 mg/kg showed a reduction in cholesterol, glucose, and the hepatic markers ALT and AST. However, at the 100 mg/kg dose, an increase in glucose (196.5 ± 15.5*) and urea (69 ± 0.9*) levels was observed in the treated animals compared with the control group (159.5 ± 8.5 and 34.3 ± 0.9, respectively).**Conclusion:** Treatment with NAc demonstrated an antiplatelet effect, a reduction in systolic blood pressure, and a prolongation of PT and aPTT, with an improvement in biochemical parameters at lower doses.

06.044 **Effects of Isolated (-)-Borneol and Phonophoresis on Resistance Artery Responses to Ischemia-Reperfusion in an Experimental Model**. Anjos MS[1], Sousa CFAJ[1], Martins HRS[2], Acha BT[3], Silva RLT[1], Souza RP[1], Ferreira PMP4, Oliveira AP[1]. [1]UFPI, Health Sciences Center, Medicinal Plants Research Center, Graduate Program in Pharmacology; [2]PIBIC-UFPI, Scientific Initiation Program, Medicinal Plants Research Center, [3]Northeast Biotechnology Network (Renorbio); [4]UFC

Introduction: Mesenteric ischemia followed by reperfusion promotes tissue injury exacerbated by oxidative stress and inflammation, particularly in hypertension. (-)-Borneol, a monoterpene with antioxidant and anti-inflammatory properties, has shown therapeutic potential in reducing such damage. **Objective:** To evaluate the effects of isolated (-)-borneol and (-)-borneol associated with phonophoresis on oxidative stress and inflammatory markers in spontaneously hypertensive rats subjected to mesenteric ischemia-reperfusion (I/R). **Methods**: Forty-seven spontaneously hypertensive rats (SHR) were allocated into six groups (n = 7): hypertensive control (HT), untreated I/R, acute oral (-)-borneol treatment (I/R+B1D), 7-day oral (-)-borneol pretreatment (I/R+B7D), ultrasound treatment after seven days of I/R (US), and topical (-)-borneol gel associated with phonophoresis after seven days (US+B7D). Mesenteric ischemia was induced by occlusion of the superior mesenteric artery for 30 min, followed by 1 h of reperfusion. Oxidative stress and inflammatory markers were evaluated in cardiac, intestinal, and mesenteric tissues, as well as blood leukocyte counts and serum cytokines (TNF-α and IL-6). Data were analyzed using one-way ANOVA followed by Tukey's post hoc test ($p < 0.05$). **Results**: Mesenteric I/R induced oxidative stress and inflammation in SHR rats, evidenced by reduced nitrite and GSH levels and increased MDA, MPO, leukocyte counts, TNF-α, and IL-6 levels. Treatment with (-)-borneol, particularly after 7 days of administration or when associated with phonophoresis, attenuated these alterations by restoring antioxidant parameters and reducing systemic and tissue inflammatory markers. **Conclusion**: (-)-Borneol exerted a protective effect against mesenteric ischemia-reperfusion-induced damage in SHR rats. The most effective strategies were the 7-day pretreatment and its association with phonophoresis, which reduced oxidative stress and inflammatory responses while restoring antioxidant defenses.

06.045 **Carvacrol Attenuates Cardiorenal Damage in Spontaneously Hypertensive Rats by Reducing Oxidative Stress and Fribrosis**. Lima VS[1,2,4], Gonçalves TAF[1,5], Almeida AJPO[1,3], Veras ACMF[2,4], Gomes MLC[1,2,4], Alves AF[2,5], Medeiros IA[1,2,4]. [1]UFPB, Cardiovascular Pharmacology Lab, Institute for Drug and Medicine Research, Brazil. [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil. [3]UFPB, PPG in Development and Technological Innovation in Medicines, Health Sciences Center, Brazil. [4]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil. [5]UFPB, Dept Physiology and Pathology, Health Sciences Center, Brazil.

Introduction: Hypertension causes progressive cardiac and renal damage, partly through oxidative stress. Therefore, investigating compounds with antioxidant properties and beneficial cardiovascular effects may contribute to identifying strategies to attenuate hypertension-induced target-organ injury. Carvacrol, a phenolic monoterpene found in aromatic plants, has demonstrated vasorelaxant and antioxidant activities. **Objective:** To investigate whether carvacrol attenuates blood pressure elevation, cardiac hypertrophy, collagen deposition, and oxidative alterations in the cardiac and renal tissues of spontaneously hypertensive rats (SHR). **Methods:** Male SHR and normotensive Wistar-Kyoto rats were allocated into five experimental groups (n = 6/group): normotensive control (W-CTL), hypertensive control (H-CTL), SHR treated with carvacrol at 50 mg/kg (C50), SHR treated with carvacrol at 100 mg/kg (C100), and SHR treated with resveratrol at 10 mg/kg (RE10). Animals received vehicle, carvacrol, or resveratrol orally once daily for four weeks. Systolic blood pressure (SBP) was measured before and after treatment by non-invasive tail- cuff plethysmography, using the mean of three consecutive measurements. At the end of treatment, heart and kidney mass indices were determined. Collagen deposition in the left ventricular myocardium, renal cortex, and renal medulla was assessed in Masson's trichrome-stained sections and expressed as the collagen volume fraction, corresponding to the percentage of blue-stained area. Superoxide-associated fluorescence was assessed in the same regions using dihydroethidium (DHE). Images were acquired with NIS-Elements 4.02, and fluorescence intensity was quantified using ImageJ. All procedures were approved by CEUA-UFPB (protocol no. 6638150621). Statistical analyses were performed using one-way or two-way ANOVA, followed by Tukey's post hoc test, with $p < 0.05$ considered significant. **Results:** The H-CTL group showed significantly higher SBP than the W-CTL group. At the end of treatment, the C50, C100, and RE10 groups showed reduced SBP compared with the H-CTL group and their respective baseline values. The C50 group also showed a lower heart mass index than the H-CTL group. Although the renal mass index was higher in the H-CTL group than in the W-CTL group, carvacrol did not significantly alter this parameter. The H-CTL group exhibited greater cardiac and renal collagen deposition, which was attenuated by carvacrol and resveratrol. Carvacrol also reduced DHE fluorescence in cardiac and renal tissues compared with the H-CTL group. **Conclusion:** Carvacrol treatment was associated with reduced SBP, collagen deposition, and DHE fluorescence in the cardiac and renal tissues of SHR. A reduction in heart mass index was observed only in the C50 group, whereas renal mass index remained unchanged. These findings suggest that carvacrol may attenuate structural and oxidative alterations associated with hypertension. However, additional morphological and functional assessments are required to determine the extent and relevance of its cardiorenal effects.

06.046 **Burst-Release NO-Donor-Eluting Coatings for Balloon Angioplasty: Endothelial Protection and Restenosis Prevention in Peripheral Arterial Disease**. Silva FAO[1], Chevallier P[2], Lombardo ME[2], Viana LC[2], Mantovani D[2], Gouveia Júnior FS[3], Lopes LGF[3], Jorge RJB[1], Monteiro HSA[1 1]UFC-Porangabuçu, Dept Physiology and Pharmacology, Graduate Program in Pharmacology - Brazil [2]Laval University, CHU de Québec Research Center, Lab Biomaterials and Bioengineering (LBB), Quebec City, QC, Canada [3] UFC-Pici, Dept Organic and Inorganic Chemistry, Lab Bioinorganic Chemistry - Brazil

Introduction: Peripheral arterial disease (PAD) affects millions of people worldwide and is associated with cardiovascular risk factors that promote inflammation, oxidative stress, and endothelial dysfunction, characterized by reduced nitric oxide bioavailability and a shift toward vasoconstriction, thrombosis, and atherogenesis. Although balloon angioplasty can serve as a local drug delivery strategy, its short inflation time limits drug release efficiency, highlighting the need for more effective delivery systems. In this context, ruthenium nitric oxide donor complexes (RuNO) are of particular interest due to their ability to enable controlled nitric oxide (NO) release, exerting vasodilatory, anti-inflammatory, and antiproliferative effects, thereby modulating neointimal hyperplasia and contributing to reduced risk of late restenosis. **Objectives:** The present study aimed to develop a RuNO-functionalized coating for balloon angioplasty applications for the treatment of PAD. **Methods:** For this purpose, balloon angiospasty poly(ethylene terephthalate) (PET) surfaces were activated first by air atmospheric plasma treatment, then functionalized with polydopamine as interlayer, and finally coated with a chitosan-based layer containing RuNO. Three different formulations were developed to evaluate burst release profiles, containing doses of 1 mg/mL, 0.75 mg/mL, and 0.46 mg/mL. Release assays were performed in HEPES solution (pH 7.4) and quantified by UV-Vis spectroscopy at 1, 2, and 5 minutes, simulating the clinical balloon inflation time. Statistical analyses were performed using GraphPad Prism® version 8.0. Results were expressed as mean ± standard deviation (SD). Differences among groups were evaluated using two-way ANOVA followed by Tukey's multiple comparisons test. **Results:** The results, obtained in triplicate, demonstrated rapid and controlled release, with burst release ranging from 50,03 ± 1,80% to 84,85 ± 4,62% at clinically relevant time points. Even at different doses, the formulations maintained a consistent burst release profile, indicating the reproducibility and stability of the release behavior. This finding suggests a predictable dose-response, ensuring the local release of the RuNO complex during the angioplasty procedure, which may contribute to early endothelial protection and the early modulation of mechanisms associated with restenosis. **Conclusion:** Thus, the coatings developed for angioplasty balloons were able to release the RuNO complex within a time frame compatible with the procedure, supporting their potential for clinical translation as endovascular devices for the treatment of peripheral artery disease (PAD). Furthermore, ongoing studies are investigating nitric oxide (NO) release from the RuNO complex and the biological responses induced by the coatings, including processes associated with endothelial dysfunction and vascular restenosis, to assess their therapeutic potential. **Financial support** from CAPES (Brazil).

06.047 **Gut Microbiota in Hypertension: Functional Signatures Linked to Inflammatory Pathways**. Brito DS[1,2], Rodrigues GA[1], Silva LS[1], Cavalcante MAR[1], Peres VCA[1], Soares JA[1], Kistner MC[1], Sena CFS[1], Santana BS, Lopes IS[1], Queiroz ATL[1], [3] Medeiros JMB, [3]Conceição E, [4]Nascimento RJM, Silva DF[1,2] [1]UFBA, Bahia, Brazil, [2]IGM-Fiocruz, PGBSMI, Brazil; [3]UFBA, Dept Nutrition Science, Brazil; [4]UFBA, Dept Bio-Interaction, Brazil.

Introduction: Arterial hypertension (AH) is a clinical issue with a high cardiovascular risk. Recent evidence suggests that the gut microbiota (GM) may modulate inflammatory and metabolic mechanisms involved in its pathophysiology. **Objective:** To investigate associations between GM composition and AH and to identify possible differences in metabolic pathways and lipid markers. **Methods:** Observational, descriptive, cross-sectional study with a quantitative approach, involving individuals stratified into normotensive (NT, n=20) and hypertensive (HAS, n= 20), according to the guidelines of the Brazilian Society of Cardiology. Fecal samples were collected for DNA extraction and sequencing of the V3–V4 region of the 16S rRNA gene. Bioinformatics processing was performed using QIIME2 software, with the application of the DADA2 algorithm for denoising and obtaining amplicon sequence variants. Taxonomic classification used the SILVA database, CAAE 60715922.1.0000.5662. **Results:** No significant differences in bacterial richness were observed between the groups. However, a relevant functional reprogramming was evident: NT showed a reduction of approximately 50% in the abundance of the genus Faecalibacterium, associated with intestinal barrier integrity and butyrate production. While the HAS group showed a three-fold increase in the genus Clostridium, related to the production of trimethylamine, a TMAO precursor, implicated in the reduction of endothelial nitric oxide bioavailability. Differential abundance analysis identified four significantly distinct genera between the groups (CAG-873, Christensenellaceae, Hungatella, and Succinivibrio). There were no significant differences in bacterial diversity metrics, although potentially deleterious microbial interactions were more prevalent in HAS. When evaluating the lipid profile, it was observed that HAS presented VLDL and triglyceride levels positively correlated with the prevalence of Eubacterium coprostanoligenes. Furthermore, there was significant enrichment of pathways related to lipopolysaccharide biosynthesis, bacterial biofilm formation, resistance to antimicrobial peptides, and two-component systems in hypertensive individuals. In contrast, there was a reduction in pathways associated with lipid metabolism, PPAR signaling, and oxidative phosphorylation, suggesting a more pro-inflammatory functional bacterial profile in the HAS group. **Conclusions:** Hypertension is predominantly associated with qualitative alterations in the immune system and not with a global loss of diversity. The reduction of protective taxa, concomitant with the expansion of potentially pro- inflammatory and vasoconstrictive microorganisms, with enrichment of pro- inflammatory pathways and reduction of beneficial metabolic functions, suggests the participation of the microbiota in maintaining the pathophysiological mechanisms of the disease. **Financial support:** FAPESB.

06.048 **Cardioprotective Effect of Trans-4-Methoxy-β-Nitrostyrene in Isolated Rat Hearts Subjected to Ischemia-Reperfusion**. Freitas-Nascimento SR[1], Franco ES[1], Borges RS[2], Silva OA[3], Lahlou S[4], Duarte GP[1] [1]UFPE, Dept Physiology and Pharmacology, Brazil, [2]UFPA, Faculty of Pharmacy, Brazil, [3]UFAL, Physiology Section, Brazil, [4]UFC, Dept Physiology and Pharmacology, Brazil

Introduction: Coronary reperfusion is the essence of the clinical treatment of acute myocardial infarction, but reestablishing blood flow causes irreversible damage to the myocardium, a condition known as myocardial ischemia-reperfusion (I/R) injury. The soluble guanylate cyclase (sGC)/GMPc pathway plays an important role in cardiac protection. We previously showed that the nitroderivative trans-4-methoxy-β-nitrostyrene (T4MN) induces vasodilatory effects in rat aortic rings through sGC stimulation. **Objective:** We investigated whether acute administration of T4MN exerts cardioprotective effects in isolated heart preparations from rats with cardiac I/R injury **Methods:** Male Wistar rats were randomly divided into three experimental infarcted (INF) groups. One group (INF) which received no treatment and two groups which have been pretreated orally during 7 days before I/R injury with vehicle (1 ml/kg/day, INF-V group) or T4MN (70 mg/kg/day, INF-T4MN). A non-infarcted group served as control (CNT). On the day 8 hearts isolated from INF, INF-V, INF-T4MN (n = 6 / group) were perfused with a modified Langendorff preparation. Hearts were subjected to 30 min of regional ischemia, produced by ligation of the left anterior descending coronary artery, followed by 60 min of reperfusion. Staining with triphenyltetrazolium chloride (TTC) was performed to analyze the myocardial infarct size and of the I/R-induced rat heart whereas myocardial histopathological alterations and tissue pathology was examined using hematoxylin and eosin (H&E;) and Masson's trichrome staining. **Results:** Compared to CNT group, infarct area was significantly increased in all INF groups, an effect that was significantly reduced by about 50% in INF-T4MN group when compared to the INF and INF-V groups. In the latter groups and compared to CNT group, a significant reduction in the number of viable nuclei was observed; an effect that was abolished in INF-T4MN. Histopathological analyses revealed that cell viability was preserved in the INF-T4MN group whereas ischemic damage was observed in the INF and INF-V groups. The histopathological score confirmed severe tissue disorganization in the INF (3.60 ± 0.25) and INF-V (3.50 ± 0.50) groups, compared to the CNT group, an effect that was prevented in the T4MN group (1.50 ± 0.50). **Conclusion:** The present study demonstrates that T4MN plays a protective role against myocardial injury by reducing infarct area but further mechanistic studies of these cardioprotective effects of T4MN are warranted. **Financial support**: CAPES, FACEPE, and CNPq.

06.049 **Pharmacological and Immunohistochemical Characterization of Dopamine D_2-Like Receptors in *Chelonoidis carbonarius* Aorta**. Santos EX[1], Britto-Júnior J[1], Mathias Netto FC[1], Cisota FNX [1], Said G[1], Campos R[2], Gonzalez PG[1], Souza VB[1], Antunes E[1], Wang T[3], Leite CAC[4],[1]FCM-Unicamp, Dept Pharmacology, Campinas, SP, Brazil; [2]UFC, Clinical Pharmacology Unit, Drug Research and Development Center, Fortaleza, CE, Brazil; [3]Aarhus University, Section for Zoophysiology, Dept Biosciences, Aarhus, Denmark; [4]UFSCar, Dept Physiological Sciences, São Paulo, Brazil; [5]ICB-USP, Dept Pharmacology, São Paulo, SP, Brazil.

Introduction: Dopamine and 6-nitrodopamine (6-ND) are endothelium-derived

catecholamines released from *Chelonoidis carbonarius* aorta (1,2). Previous studies showed that dopamine-induced contractions in this vessel are modulated by nitric oxide and inhibited by D_2-like receptor antagonists, including 6-ND (3). However, the dopamine D_2-like receptor subtypes involved in reptilian vascular reactivity remain incompletely characterized. We therefore investigated the pharmacological and immunohistochemical profile of D_2, D $_3$ and D₄ receptors in isolated aortic rings from *C. carbonarius* . **Methods:** Aortic rings from *C. carbonarius* were mounted in Krebs–Henseleit solution at 27 °C for isometric tension recording. Dopamine-induced contractions were compared in solution aerated with 97% air/3% CO_2 or carbogen. Concentration–response curves to dopamine, noradrenaline, adrenaline, sumanirole, PD-128907 and A-412997 were obtained in the absence or presence of L-NAME. The effects of 6-ND, the D_2 antagonist L-741,626, the D $_3$ antagonist PG-01037 and the D₄ antagonist sonepiprazole were evaluated. Dopamine receptor expression was assessed by immunohistochemistry. Results – Dopamine induced concentration-dependent contractions that were similar under 97% air/3% CO_2 and carbogen aeration, both in control rings and after nitric oxide synthase inhibition. L-NAME potentiated dopamine-induced contractions and enhanced responses to the D_2 agonist sumanirole. In contrast, the D_3 agonist PD-128907 and the D₄ agonist A-412997 produced contractile responses only in L-NAME-treated preparations. In L-NAME-treated rings, 6-ND reduced contractions induced by sumanirole, PD-128907 and A-412997. Sumanirole responses were inhibited by 6-ND, with Emax reduced from 21.0±1.6 mN to 15.2±1.3 mN at 100 nM and 12.9±2.2 mN at 1 μM 6-ND. 6-ND also reduced PD-128907- and A-412997-induced responses at higher concentrations. L-741,626, PG-01037 and sonepiprazole inhibited dopamine-induced contractions; however, these antagonists also modified noradrenaline- and adrenaline-induced contractions, indicating limited selectivity in this preparation. Immunohistochemistry showed D_2, D $_3$ and D₄ receptor immunoreactivity in the aortic endothelium, while D₄ receptor staining was also detected in smooth muscle cells. **Conclusion**: Dopamine D_2-like receptors are expressed in Chelonoidis carbonarius aorta and participate in the modulation of vascular contraction. Nitric oxide functionally counteracts D_2-like receptor-mediated contractile responses, as shown by the potentiation caused by L-NAME. Among the D_2-like subtypes, D_2 receptors appear to play a prominent role in dopaminergic regulation of reptilian vascular tone, while 6-ND behaves as a selective antagonist of D_2-like receptor-mediated contractions. References 1. Britto-Júnior J, et al. Biomedical Chromatography . 2021;35:e4978. 2. Campos R, et al. Journal of Chromatography B . 2021;1173:122668. 3. Britto-Júnior J, et al. Comparative Biochemistry and Physiology C . 2022;260:109403.

06.050 **Mineralocorticoid Receptors Promote Th17 Polarization in Lymph Nodes while IL-17RA Drives Pro-Inflammatory Phenotypic Changes in Perivascular Adipose Tissue During Obesity**. Dourado TMH[1], Pimenta GF[1], Elias-Oliveira J[2], Rodrigues VF[2], Fazan-Junior R[3], Sartori DC[2], Tirapelli CR[4] [1]FMRP-USP, Depto Farmacologia; [2]FMRP-USP, Depto Bioquímica e Imunologia, [3]FMRP-USP, Depto Fisiologia; [4]FCFRP-USP, Depto Ciências BioMoleculares

Introduction: **and Objective:** Obesity induces phenotypic alterations in perivascular adipose tissue (PVAT), increasing pro-inflammatory and pro-oxidative mediators. Interleukin-17 (IL-17), mainly released by Th17 cells, contributes to cardiovascular dysfunction during obesity and may be stimulated by the renin–angiotensin–aldosterone system (RAAS). This study evaluated the role of IL-17RA signaling in PVAT dysfunction and hypertension during obesity. We hypothesized that obesity activates RAAS, increasing aldosterone production, which stimulates mineralocorticoid receptors (MR) in mesenteric lymph nodes, promoting Th17 differentiation. These cells infiltrate PVAT and release IL-17, activating IL-17RA signaling, increasing reactive oxygen species (ROS) generation and reducing nitric oxide (NO) bioavailability, leading to PVAT dysfunction and elevated blood pressure. **Methods:** Wild-type C57BL/6 (WT) and IL-17RA knockout (IL-17RA-/-; B6.Cg-Il17ratm2.2Koll/J) mice were randomly assigned to: 1) Control: standard chow for 12 weeks; 2) Obese: high-sugar diet (HSD) for 12 weeks; 3) Obese+MRA: HSD for 12 weeks plus potassium canrenoate (30 mg/kg/day, gavage) during weeks 8–12; and 4) Obese+IL-17RA-/-: IL-17RA-/- mice fed HSD for 12 weeks. The role of MR signaling in dendritic cell activation was evaluated in cultured GM-BMDCs incubated with aldosterone (100 nmol/L) and/or eplerenone (5 µmol/L). Body weight was monitored weekly, and blood pressure was assessed by direct recordings through vena cava catheterization at the end of treatment. Th17 populations in lymph nodes and PVAT were analyzed by flow cytometry. Aldosterone, IL-17, IL-10, and IL-6 levels were measured by ELISA. Superoxide production was assessed by lucigenin chemiluminescence, and nitrite concentration was determined by colorimetric assay (Two-way ANOVA followed by Tukey's). **Results:** HSD increased body weight, adiposity index, and circulating aldosterone levels. Obesity increased mean arterial pressure and systolic blood pressure, effects not observed in IL-17RA-/- mice. Obesity increased Th17 populations in iliac/jejunal lymph nodes, effect prevented by MR antagonism. In GM-BMDCs, aldosterone reduced PD-L1 expression and IL-10 production while increasing IL-6 release, effects reversed by eplerenone, indicating MR-dependent dendritic cell activation. In PVAT, obesity increased Th17 infiltration and IL-17A levels, both attenuated by MR blockade. Furthermore, obesity enhanced superoxide generation and reduced nitrite levels in PVAT, whereas IL-17RA deficiency prevented these alterations, demonstrating a critical role for IL-17 signaling in obesity-induced PVAT oxidative stress. **Conclusions:** Obesity promotes MR-dependent Th17 polarization in lymph nodes and IL-17/IL-17RA signaling, contributing to oxidative imbalance in PVAT. These findings identify a novel aldosterone–MR–Th17–IL-17RA axis linking obesity to PVAT dysfunction, highlighting potential therapeutic targets for obesity-associated cardiovascular disease.

06.051 **Effects of γ-Terpinene on Hemodynamic and Oxidative Parameters in Spontaneously Hypertensive Rats**.
Rocha VA[1,2,3], Rego AF[1,2,3], Sena EP[1,2,3], Acha BT[4,5], Silva FAHV[2], Soares HS[2], Costa MRS[2], Nascimento BN[2], Silva ND[1,2,3], Albuquerque BA[1,2,3], Oliveira AP[1,2,3,6] [1]UFPI, Graduate Program in Pharmacology, Brazil. [2]UFPI, Health Sciences Center, Cardiovascular Pharmacology Lab, Brazil. [3]UFPI, Research Center on Medicinal Plants, Brazil. [4]UFPI, Northeast Biotechnology Network (Renorbio), Brazil. [5]UFPI, Lab Functional and Molecular Studies in Physiopharmacology, Brazil. [6]UFPI, Health Sciences Center, Dept Biophysics and Physiology, Brazil.

Introduction: Systemic arterial hypertension (SAH) is a major public health concern associated with an increased risk of cardiovascular complications. γ-Terpinene is a monoterpene found in essential oils with potential cardiovascular activity. This study aimed to investigate the effects of γ-terpinene on hemodynamic and oxidative parameters in spontaneously hypertensive rats (SHR). **Methods:** Male SHR (200–320 g; UFPI Animal Facility; CEUA/UFPI protocol no. 854/2025) were orally treated for 15 days with vehicle, γ-terpinene (50 or 100 mg/kg), or captopril (20 mg/kg). Systolic blood pressure (SBP) and heart rate (HR) were assessed by tail-cuff plethysmography. Oxidative markers were determined by measuring nitrite and reduced glutathione (GSH) levels in heart and liver tissues. **Results:** γ-Terpinene at 50 mg/kg significantly reduced SBP (ΔSBP = -13.4 ± 2.3 mmHg) and HR (ΔHR = -34.6 ± 1.6 bpm), while the 100 mg/kg dose significantly decreased SBP (ΔSBP = -21.9 ± 3.6 mmHg) and HR (ΔHR = -41.1 ± 2.6 bpm). Captopril significantly reduced SBP (ΔSBP = -25.1 ± 3.5 mmHg). In cardiac tissue, the 100 mg/kg dose reduced nitrite levels compared with the vehicle group (5.4 ± 0.8 vs. 8.9 ± 1.0 µM) and increased GSH levels (137.5 ± 5.0 vs. 55.2 ± 4.5 µg/mL). In liver tissue, the 50 mg/kg dose reduced nitrite levels (9.1 ± 0.3 vs. 16.1 ± 1.0 µM in the vehicle group), with no significant changes in hepatic GSH levels. **Conclusion:** These findings suggest that γ-terpinene exerts antihypertensive and antioxidant effects in spontaneously hypertensive rats.

06.052 **The Role of Fluoxetine on Vascular Functions in Endotoxemia**. Santos TM[1], Pedersoli CA[2], Tostes RC[2], Linder AE[1] [1]UFSC, PPG Pharmacology, Brazil; [2]FMRP-USP, Dept. of Pharmacology, Brazil

Introduction: Endotoxemia induced by lipopolysaccharide (LPS) triggers excessive systemic inflammation and vascular damage, leading to hemodynamic instability reminiscent of sepsis. Selective serotonin reuptake inhibitors, such as fluoxetine (FLX), may exert peripheral effects, including regulation of immunological, antimicrobial, metabolic, and vascular function. However, the protective role of FLX pretreatment in this context remains poorly understood. **Objective:** To test the hypothesis of the potential vascular protection of FLX in an experimental model of endotoxemia. **Methods:** Male C57BL/6 mice (10-week-old) received FLX (10 mg/kg) or vehicle (syrup, 4 mL/kg) by gavage daily for 14 days. On day 15, whereas the syrup-treated mice were divided to receive either LPS (10 mg/kg, i.p.) or vehicle (PBS, 4 mL/kg, i.p.), the FLX-treated group received only LPS (10 mg/Kg, i.p.), totaling 3 experimental groups. Hemodynamics (systolic, diastolic, mean blood pressure, and heart rate) were assessed pre-challenge with LPS or PBS and 24 h and 7 days post-challenge (plethysmography). Vascular permeability (Evans blue in peritoneal lavage) and ex vivo reactivity of isolated aortic rings (to phenylephrine, acetylcholine, and sodium nitroprusside) were measured 24 h after LPS or PBS. Data were analyzed by two-way ANOVA with Tukey post hoc test ($p \leq 0.05$). Protocol: CEUA-FMRP/USP 1485/2025R1. **Results:** No significant differences in vascular reactivity were observed between groups ($p > 0.05$). Hemodynamic parameters, notably systolic blood pressure (SBP), decreased at 24 h in both VEI-LPS (75.50 mmHg) and FLX-LPS (78.89 mmHg) compared to control (VEI-PBS, 96.34 mmHg). Vascular permeability increased at 24 h (VEI-LPS 4.71 and FLX-LPS 6.83 vs VEI-PBS 2.83 µg/mL). On the 7th day, SBP fully recovered in all groups (VEI-LPS 90.84 and FLX-LPS 114.10 vs VEI-PBS 106 mmHg). **Conclusion:** In our pilot study, FLX pretreatment did not prevent hypotension or vascular hyporeactivity within 24 h of endotoxemia, despite SBP recovery within 7 days. Future studies will investigate FLX effects at earlier stages (6 h) and against secondary insults in surviving mice 7 days after LPS administration. **Financial support:** FAPESP, CAPES-PPGFMC-UFSC and CNPq.

06.053 **Basal Release of 6-Cyanodopamine from Rabbit Isolated Aorta and its Modulation of Vascular Reactivity**.
Ali K[1], Santos EX[1], Britto-Júnior J[1], Peterson L[2], Morris JJL[2], Miller A[1,3,4], Jacintho FF[1], Moraes ME[3], Santagada V[4], Caliendo G[4], Severino B[4], Antunes E[1], De Nucci G[1,3,5] [1]FCM-Unicamp, Dept Pharmacology, Campinas, SP, Brazil; [2]Rhodes College, Dept Chemistry, Memphis, TN, USA; [3]UFC, Clinical Pharmacology Unit, Drug Research and Development Center, Fortaleza, CE, Brazil; [4]University of Naples Federico II, Dept Pharmacy, School of Medicine, Naples, Italy; [5]ICB-USP, Dept Pharmacology, , São Paulo, SP, Brazil; [6]Dept Pharmacology, São Leopoldo Mandic School of Medicine, Campinas, SP, Brazil.

Introduction: 6-Cyanodopamine (6-CYD) is a recently identified endogenous catecholamine with positive chronotropic and inotropic actions (1). Although 6-CYD has been detected in cardiac and genitourinary tissues, its occurrence in vascular tissue and its role in vascular reactivity remain unclear. Since 6-nitrodopamine is an endothelium-derived vascular modulator (2), we investigated whether rabbit isolated aorta releases 6-CYD and whether this catecholamine modulates vascular smooth muscle contraction and relaxation. **Methods:** Thoracic aortas from male New Zealand rabbits were isolated and mounted in Krebs-Henseleit solution. Basal 6-CYD release was quantified by LC-MS/MS in endothelium-intact and endothelium-denuded preparations and after incubation with GKT137831, L-NAME or tetrodotoxin. Isometric tension recordings were used to construct concentration-response curves to noradrenaline, adrenaline and dopamine in the absence or presence of 6-CYD, and to evaluate 6-CYD-induced relaxation in endothelin-1-precontracted rings. Data are expressed as mean +/- SEM. Concentration-response curves were fitted by nonlinear regression to calculate pEC50 and Emax; independent groups were compared using unpaired Student's t-tests, with $p<0.05$ considered significant. **Results**: Endothelium removal reduced basal 6-CYD release ($p<0.0001$), and GKT137831 reduced release to below the limit of quantification ($p=0.0214$), whereas L-NAME and tetrodotoxin had no significant effect ($p=0.4036$ and $p=0.9981$, respectively). 6-CYD had no direct contractile effect, but significantly increased noradrenaline Emax from 28.88+/-6.30 to 54.81+/-4.40 mN at 1 pM and from 31.88+/-6.09 to 56.44+/-5.10 mN at 10 pM (both $p<0.05$), without changing pEC50. Adrenaline Emax increased from 38.86+/-4.95 to 56.88+/-5.68 mN at 10 pM and from 36.52+/-5.03 to 55.35+/-2.86 mN at 100 pM (both $p<0.05$), also without a significant pEC50 shift. This potentiation was reduced after endothelium removal and was absent for dopamine. In endothelin-1-precontracted rings, 6-CYD produced concentration-dependent relaxation (pEC50 6.8+/-0.1; Emax 62+/-4%), which was significantly reduced by endothelium removal, L-NAME, ODQ and methylene blue ($p<0.05$). **Conclusion**: Rabbit aortic endothelium is a source of 6-CYD. This novel endogenous catecholamine modulates vascular tone through a dual mechanism: potentiation of noradrenaline- and adrenaline-induced contraction at very low concentrations, and NO/sGC-dependent vasorelaxation at higher concentrations. These findings identify 6-CYD as a new endothelium-derived regulator of vascular reactivity. **References**: 1\. Britto-Júnior J, et al. Life Sciences . 2025;366–367:123504. 2\. Santos E, et al. Naunyn-Schmiedeberg's Archives of Pharmacology . 2024. 3\. Alan-Albayrak E, Simonsen U. Basic Clin Pharmacol Toxicol . 2025;137:e70124. **Financial support**: FAPESP 2021/14414-8, 2024/08067-1, 2025/11569-1 and 2019/16805-4; CNPq 155101/2025-0 and 303839/2019-8. Human or Animal Research Ethical Committee Number: CEUA/UNICAMP, protocol 6287-1/2023. **Acknowledgments:** The authors acknowledge FAPESP and CNPq for **Financial support**.

06.054 **Vascular and Endothelial Actions of Rosmarinic Acid: Mechanistic Insights into Nitric Oxide Signaling and Calcium Channel Modulation**. Moser JC[1], Silva RCVAF[1], Valerie SK[2], de Souza P[1]. [1]Univali, PPG Pharmaceutical Sciences, Brazil; [2]UNISTRA, Strasbourg of University, France.

Introduction: Although rosmarinic acid (RA), a polyphenolic compound found in medicinal plants, exhibits diverse biological activities, its vascular effects and the underlying endothelial and smooth muscle mechanisms in hypertension remain incompletely understood. **Objectives:** To investigate the vasorelaxant effects of RA and the underlying mechanisms using isolated aortic rings and mesenteric vascular beds from spontaneously hypertensive rats (SHR), as well as porcine coronary arteries and endothelial cells. **Methods:** Concentration–response curves to RA were assessed in endothelium-intact and denuded SHR aortic rings. Vasorelaxant responses were further evaluated in porcine coronary arteries, while RA-induced changes in perfusion pressure were assessed in mesenteric arterial beds from normotensive and SHR rats. In porcine coronary endothelial cells, NO production and ROS generation were measured by fluorescence assays. **Results:** RA (0.1 – 1000 µg/mL) induced concentration-dependent vasorelaxation in SHR aortic rings, significantly greater in E+ (Emax= 69 ± 8.58%) compared to E- preparations (Emax= 19.57 ± 3.11%). This effect was significantly attenuated by L-NAME (a non-selective inhibitor of NOS (Emax = 35.52 ± 8.87%) and ODQ (an inhibitor of the soluble guanylate cyclase (Emax = 36.75 ± 10.05%). Indomethacin (a non-selective inhibitor of the cyclooxygenase enzyme) propranolol (a non-selective blocker of the β-adrenergic receptor) and atropine (a non-selective blocker of the muscarinic receptor) did not significantly alter the response, compared with their respective controls. Among potassium channel blockers, 4-AP, $BaCl_2$, TEA and glibenclamide had no significant effect, indicating no involvement of K+ channels. RA inhibited $CaCl_2$-induced contractions (EC50 = 6.913) in a similar way to nifedipine, suggesting L-type Ca^2+ channel blockade, with no involvement of intracellular Ca^2+ stores. In the isolated porcine coronary artery, RA (0.1 – 300 µg/mL) promoted concentration-dependent relaxation independent of endothelium (Emax = 96.9 ± 1.46%), unaffected by L-NAME, indomethacin, or TRAN-34 + UCL1648, either alone or in combination, only with a discreet but significantly interference of ODQ without affecting the maximal relaxation (Emax = 96.8 ± 2.3%). In the isolated mesenteric arterial bed, in NTR, RA significantly reduced perfusion pressure at the highest concentration (30 mg/mL; 40.6 mm Hg), whereas in SHR, significant reductions were observed at 10 and 30 mg/mL (23.71 and 44.32 mm Hg respectively). In porcine endothelial cells, RA increased NO production (DAF-FM fluorescence) at concentrations of 10 and 30 µg/mL and significantly reduced TNF-α-induced ROS production. **Conclusion:** RA induces vascular relaxation through mechanisms involving endothelial NO signaling, calcium modulation, and direct smooth muscle effects. Its reduction of vascular resistance and improvement of endothelial function support its potential as a cardiovascular protective agent.

06.055 **Impact of Cilostazol on Cardiac Function and Redox Signaling in Experimental Metabolic Syndrome**. Autran LJ[1,2], Brazão SC[1,2], Lima GF[1,2], Mendes ABA[1], Assis NC[1], Motta NAV[1], Brito FCF[1]. [1] UFF, Lab. of Experimental Pharmacology, Brazil. [2]UFF, PPG Biomedical Sciences (Physiology and Pharmacology), Brazil

Introduction: Metabolic syndrome (MS) is a public health challenge, characterized by a cluster of metabolic alterations, including obesity, hypertension, dyslipidemia, hyperglycemia and hypertension. This condition increases the risk of cardiovascular disease. Cilostazol (CZ), a phosphodiesterase-3 inhibitor used in the treatment of intermittent claudication, exhibits vasodilatory, antiplatelet effects, as well as pleiotropic properties, such as anti-inflammatory and antioxidant properties. We hypothesized that CZ may exert beneficial effects in the treatment of MS. **Objective:** This study aims to evaluate the cardioprotective properties of cilostazol using a model of metabolic syndrome induced in spontaneously hypertensive rats (SHR). **Methods:** Male Wistar Kyoto (WKY) and SHR rats (200-250g) were housed under controlled conditions and a 12 h light/dark cycle. Animals were randomly assigned to four groups (n=8): WKY (normotensive rats) and SHR, both fed a standard diet for 12 weeks; MS (SHR fed a hypercholesterolemic) and MS+ CZ (SHR fed a hypercholesterolemic treated with CZ). The experimental protocol lasted 12 weeks, and during the last 15 days, WKY, SHR, and MS groups received vehicle (tween: ethanol/ water), while the MS + CZ group received CZ (30 mg/kg/day), administered by gavage. Blood pressure was measured at the end of the study using non-invasive tail-cuff plethysmography. Rats were anesthetized for echocardiographic and electrocardiographic assessments. Following euthanasia, tissues were collected for biochemical and molecular analyses (CEUA protocol no. 1479140219). Data were analyzed using one-way ANOVA followed by Bonferroni's multiple-comparisons test. Statistical significance was set at $p < 0.05$. **Results:** The MS group showed prolongaed QT (76.8±0.4 vs. 93.7±4.9 ms),QTc (87.4±0,9 vs. 109.5±5.5 ms), increased SαT (11.6±0.4 vs. 24.7±0.9 ms) and RαT (50.4±0.4 vs. 59.2±0.8 ms) intervals, reduced R-wave (0.4±0.02 vs. 0.19±0.013 mV) and T-wave amplitudes (0.06±0.008 vs 0.03±0.005 mV), decreased SDNN (8.3±1.7 vs. 3.7±0.35ms) and RMSSD (8.2±2.1 vs. 3.0±0.38 ms), and decrease ejection fraction (81.2%±2.2% vs. 68.3%±2.2%) and fractional shortening (44%±2.2% vs 37.3%±1.5%) compared with WKY group ($p<0.05$). The MS+CZ group showed reduced SαT (24.7 ± 0.4 vs.16±1.3 ms), and RαT intervals (59.2±0.8 vs. 50.8±1.6 ms), while increasing R-wave (0.19±0.01 vs. 0.30± 0.01 mV) and T-wave amplitudes (0.03±0.01 vs. 0.06±1.01 mV) and RMSSD (3.04±0.3 vs. 7.40±1.2 ms). Additionally, the MS+CZ group showed reduced SBP (201.0±1.88 vs. 178.9±4.6 mmHg) and LDL cholesterol (75.4±6.2 vs. 58.8±4.10 mg/dL) compared with the MS group ($p < 0.05$). The MS group showed increased NOX2, NOX4, p-AKT, NF-κB, and BAX expression, which was reduced by CZ treatment ($p < 0.05$). **Conclusion:** CZ may exert cardioprotective effects in MS e, likely by improving electrophysiological parameters and modulation of oxidative stress, inflammation, and cell survival pathways.

06.056 **Carvacrol Attenuates TRPV4 Agonist-Induced Calcium Influx and Membrane Depolarization in Rat Pulmonary Artery Smooth Muscle Cells: Experimental and Computational Evidence**. Souza Júnior JF[1,2], Sousa NF[2,3,4], Scotti L[2,3,4], Scotti MT[2,4], Guibert C[5], Quignard J-F[5], Medeiros IA[1,2,3] [1]UFPB, Cardiovascular Pharmacology Lab, Brazil. [2]UFPB, Graduate Program in Bioactive Natural and Synthetic Products, Brazil. [3]UFPB, Dept Pharmaceutical Sciences, Brazil. [4]UFPB, Cheminformatics Lab, Brazil. [5]Université de Bordeaux, Centre de Recherche Cardio-Thoracique de Bordeaux, INSERM, France

Introduction: Pulmonary hypertension involves vascular remodeling, vasoconstriction, and altered calcium homeostasis in pulmonary artery smooth muscle cells (PASMCs). TRPV4 channels contribute to calcium influx and membrane depolarization and are potential therapeutic targets. Carvacrol is a monoterpenoid phenol with vasorelaxant properties; however, its interaction with TRPV4 remains unclear. **Objective:** To investigate the effects of carvacrol on TRPV4-mediated calcium signaling and membrane potential in PASMCs under normoxia and hypoxia and evaluate its interaction with TRPV4 using molecular docking and molecular dynamics. **Methods:** Rat PASMCs were maintained under normoxia (19% O_2, 48 h) or hypoxia (1% O_2, 48 h). Calcium influx and membrane potential were assessed using fluorescent probes after stimulation with the TRPV4 agonist GSK1016790A (0.5 μM) with or without carvacrol (50–300 μM, 3 min). Molecular docking was performed using the human TRPV4 structure (PDB ID: 8FC8), with ATP and GSK1016790A as reference ligands. Molecular dynamics simulations were conducted for 100 ns using GROMACS. **Results:** Hypoxia enhanced TRPV4-mediated calcium influx and membrane depolarization in PASMCs. Carvacrol significantly attenuated GSK1016790A-induced calcium responses, particularly at 100 and 300 μM under hypoxic conditions. Likewise, carvacrol reduced TRPV4-dependent membrane depolarization. Docking analyses revealed interactions involving Asn528, Phe524, and Tyr553. Molecular dynamics simulations demonstrated persistent contacts with Tyr553, Asp531, Gln550, and Lys535 during the 100-ns simulation, supporting stable occupancy of the binding pocket. Carvacrol exhibited greater electrostatic stabilization than GSK1016790A, suggesting favorable receptor interaction. **Conclusion:** Carvacrol attenuates GSK1016790A-induced calcium influx and membrane depolarization in rat PASMCs, with more pronounced effects under hypoxic conditions. Molecular docking and dynamics simulations predict stable interaction of carvacrol within the TRPV4 binding region, supporting the observed cellular effects. These findings suggest that TRPV4 contributes to the effects of carvacrol on calcium signaling and membrane potential. Further studies are needed to define the specificity and mechanism of TRPV4 modulation and determine whether these effects translate into vascular protection in pulmonary hypertension. **Financial support:** CAPES, CNPq, FAPESQ-PB, and Bioprofar-BA – FAPESB PIE0001/2024. Animal Research Ethical Committee Number: APAFIS #53998-2025022815013010 v4, France.

06.057 **Angiotensin II/AT1R Signaling Promotes Vascular NETosis in Ethanol-Treated Mice**. Silva AO[1], Melo BMS[2], Costa VF[2], Marchetti BM[2], Pimenta GF[2], Alves-Filho JC[2], Cunha FQ [2], Tirapelli CR[1] [1]FCFRP-USP, PPG in Pharmaceutical Sciences,Brazil. [2]USP, PPG in Pharmacology, Brazil.

Introduction: Ethanol consumption is associated with activation of the renin–angiotensin–aldosterone system (RAAS). The vascular dysfunction induced by ethanol occurs through multiple mechanisms, including neutrophil infiltration into the vasculature, concomitant with increased levels of pro-inflammatory cytokines. Previous studies have observed that stimulation of isolated neutrophils with angiotensin II induced NETosis; furthermore, angiotensin II infusion in an experimental model promoted neutrophil expansion and the induction of vascular NETosis. Thus, angiotensin II, via Angiotensin II Type 1 Receptor (AT1R), induces neutrophil activation, culminating in the vascular release of neutrophil extracellular traps (NETs) via the NETosis process. **Objectives:** To investigate the contribution of angiotensin II-induced NETosis to vascular dysfunction associated with ethanol consumption. **Methods:** Male C57BL/6 mice were treated with ethanol (solution 20%) for 12 weeks. The involvement of AT1R receptors in neutrophil vascular infiltration and NETosis induction was assessed using losartan (10 mg/kg/day; a selective AT1R antagonist). Flow cytometry was performed to evaluate the total number of leukocytes, neutrophils and neutrophils activation in the aorta. NETs quantification in the aorta and plasma was performed using the Quant-iT PicoGreen kit (Invitrogen). Statistical analyses were performed using Student's t-test or one-way ANOVA, followed by Tukey's post hoc test. The animals were divided into control (C), ethanol (E) and ethanol-losartan (EL). **Results:** An increase in the total number ($p<0.05$; C: 694624 ± 104222; E: 3503008 ± 1050598, n=5/group) and percentage ($p<0.05$; C: 1.824 ± 0.2649; E: 4.548 ± 1.008; n=5/group) of leukocytes, as well as a higher total number of neutrophils ($p<0.05$; C: 14673± 3723; E: 30769 ± 4133, n=5/group) were detected in the aorta of animals treated with ethanol. Concurrently, no increased neutrophil activation is observed ($p>0.05$; C; 137.3 ± 9.393; E: 105.7 ± 17.72). Furthermore, an increase in the concentration of NETs (ng/mg protein) in the aorta ($p<0.05$; C: 7.370 ± 1.306; E: 13.29 ± 1.193; EL: 7.568 ± 1.047, n= 6-7/group) and plasma (ng/mL) ($p< 0.05$; C: 0.4630 ± 0.1345; E: 0.9411 ± 0.1078; EL: 0.9438 ± 0.1258, n= 6-7/group) of animals that consumed ethanol was observed. Losartan reversed the increase in NETs in the aorta ($p<0.05$). **Conclusion:** Ethanol treatment increased neutrophil infiltration into the vasculature, concomitant with elevated NET levels. AT1R antagonism reversed the ethanol-induced increase in vascular NETs concentration, highlighting the role of angiotensin II inducing NETosis. Ethics Committee: Registration No. 24.1.234.60.0. **Financial support:** This study was financed by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), Brazil. Process Number 2024/13353-3.

06.058 **Cilostazol Improves Endothelial Function Via PKA/eNOS/PKG and Nrf2 Signaling and Attenuates Platelet Hyperreactivity in Experimental Model of Metabolic Syndrome**. Brazão SC[1,2], Lima GF[1,2], Pereira NCA[1,2], Mendes ABA[1,2], Autran LJ[1,2], Bragança LAR[1,2], Stein AT[1,2], Alves DS[1,2], Rosa GA[1,2], Alexandre-Santos B[3,4], Motta NAV[1,4], Brito FCF[1,2,4] [1]UFF, Lab. of Experimental Pharmacology, Brazil, [2]UFF, PPG Biomedical Sciences (Physiology and Pharmacology), Brazil, [3]UFF, Research Center on Morphology and Metabolism, Brazil, 4UFF, PPG Cardiovascular Sciences, Brazil.

Introduction: Metabolic syndrome (MS) promotes is characterized by obesity, hypertension, hyperinsulinemia, and dyslipidemia, conditions associated with endothelial dysfunction and platelet hyperactivity. Cilostazol (CZ) is a selective phosphodiesterase-3 (PDE3) inhibitor with antiplatelet and vasodilatory actions, the mechanistic interplay between vascular redox balance, endothelial and platelet function in MS remains poorly defined. **Objectives:** To investigate whether cilostazol restores vascular and platelet homeostasis in experimental MS through modulation of nitric oxide–dependent and antioxidant signaling pathways. **Methods:** Spontaneous hypertensive rats (SHR, 200-250g) were randomized into four groups (n=8/group): a control group (SHR) and control group treated with CZ (100mg/kg) (SHR+CZ) and fed a standard chow diet; MS group, fed a hypercholesterolemic diet; and MS+CZ group, fed a hypercholesterolemic diet and received CZ. The experimental protocol lasted 12 weeks, with CZ or vehicle (tween:ethanol/water) administered by gavage once daily for 30 days. Systolic blood pressure was assessed before the end of the protocol. Following euthanasia by cervical dislocation under ketamine and xylazine anesthesia, blood samples were collected for platelet aggregation and biochemical analysis, and thoracic aortas were excised. Data was analyzed using one-way ANOVA followed by post-hoc Bonferroni multiple comparison test, $p<0.05$. **Results:** MS group showed a cardiometabolic phenotype characterized by increased Δ body mass (SHR: 94.20±4.20 vs. MS: 109.30±3.54 g) and elevated serum total cholesterol (SHR: 90.58±4.38 vs. MS: 124.70±4.56 mg/dL), LDL (SHR: 43.32±1.61 vs. MS: 75.41±6.22 mg/dL), glucose (SHR: 205.30± 20.15 vs. MS: 271.10±13.39 mg/dL) and hepatic triglycerides (SHR: 164.70±6.89 vs. MS: 249.7±18.21 mg/dL) ($p<0.05$). CZ only reduced systolic pressure (MS: 201.80±1.88 vs. MS+CZ: 190.00±3.60mmHg) ($p<0.05$). Endothelium-dependent relaxation was reduced in MS (SHR: 58.04±3.04% vs. MS: 43.11±1.83%) ($p<0.05$), whereas SHR+CZ and MS+CZ showed increased maximal relaxation (SHR+CZ: 70.05±2.24%; MS+CZ: 85.76±5.67%). The wall-to-lumen ratio was increased in MS and reduced in MS+CZ group (MS: 2.99±0.31 vs. MS+CZ: 2.32±0.34). MS disrupted NO-dependent and antioxidant signaling via PKA/eNOS/PKG and Nrf2 downregulation.CZ restored these pathways and endothelial-redox coupling ($p<0.05$). Platelet aggregation induced by ADP (0.5 μM) and collagen (0.5 μg/mL) was increased in MS (ADP: SHR: 43.67±1.90% vs. MS: 50.63±4.31%; collagen: SHR: 51.27±1.78% vs. MS: 77.13±3.76%) and reduced in MS+CZ group (ADP: MS+CZ: 29.00±5.43%; collagen: MS+CZ: 57.11±4.19%). **Conclusion:** Subchronic CZ treatment exerted hypotensive, vasodilatory, and antiplatelet effects, suggesting potential therapeutic benefit in MS, likely through modulation of the PKA/eNOS/PKG and Nrf2 signaling pathways. These findings support CZ as a promising strategy to counteract cardiometabolic vascular disease.

06.059 **Targeted Gi signaling activation exclusively in cardiomyocytes reverses cardiac damage induced by adrenergic overload**. Eliezeck M[1], Scalzo Júnior SRA[1], Costa MC[1], Moura V[1], Silva TM[2], Silva CAA[2], Martins FL[4], Resende CR[1], Fazan Jr R[2], Salgado HC[2], Prado VF[3], Girardi AC[4], Prado MAM[3], and Guatimosim S[1] [1]ICB-UFMG, Dept Physiology and Biophysics, Belo Horizonte, Minas Gerais, Brazil. [2]FMRP-USP, Dept Physiology, Ribeirão Preto, São Paulo, Brazil. [3]The University of Western Ontario, Dept Physiology and Pharmacology, Dept Anatomy & Cell Biology, Robarts Research Institute, London, Ontario, Canada. [4]FMUSP, Lab Fisiologia Renal e Cardiometabolismo, Depto Cardiopneumologia, Brazil.

Introduction: GPCRs are critical regulators of cardiac function. While sustained Gs/Gq signaling contributes to pathological remodeling and heart failure, Gi signaling has been associated with cardioprotective effects. However, the direct contribution of cardiomyocytes-specific Gi activation to myocardial protection and repair during adrenergic stress remains unclear. **Methods:** We used DREADD technology to generate Myh6-Cre/hM4Di mice, enabling selective Gi activation in CMs by clozapine-N-oxide. CEUA:102/2022 and 63/2025. **Results:** First, we characterized the model. To confirm functional Gi activation by hM4Di, isolated CMs were treated with ACh or CNO (100 nM). Myh6-Cre/hM4Di CMs showed reduced shortening after CNO, closely mirroring ACh responses (μm^2: CTR 565±34 vs CNO 342±33 vs ACh 320±30; n=40). *In vivo*, CNO induced rapid and sustained bradycardia (up to 83%), consistent with canonical M2-AChR-Gi signaling. To investigate downstream signaling, ventricular myocytes were acutely treated (5 min) with ISO, with or without CNO. ISO increased phosphorylation of PKA substrates, whereas CNO prevented this response, demonstrating direct Gi-mediated antagonism of β-adrenergic/PKA signaling (a.u: CTR 100±6.9 vs ISO 168.4±8.3 vs CNO+ISO 124.1±6.3; n=5). Littermate controls showed no response, confirming specificity. Likewise, CNO prevented the ISO-induced increase in CM contractility *in vitro* (μm^2: CTR 559.3±25 vs ISO 888.2±63 vs CNO+ISO 672.3±71; n=25). To evaluate cardioprotection *in vivo*, mice received ISO (25 mg/kg) with or without CNO (CNO, 0.5 mg/kg). for 7 days. Gi activation prevented ISO-induced remodeling, including hypertrophy (HW/TL mg/cm: CTR 78±3 vs ISO 95±1 vs CNO+ISO 77±3; n=9). Analyses of isolated CMs confirmed these findings. Importantly, CNO markedly reduced CM death both *in vivo* and *in vitro*, as demonstrated by reduced Evans Blue uptake (marked area %: CTR 0.25±0.07 vs ISO 6.29±1.3 vs CNO+ISO 0.54±0.23; n=7) and restored CM viability (Viability/CTR: ISO 0.73±0.04 vs CNO+ISO 1.00±0.01; n=8). Gi activation also attenuated inflammation, fibroblast activation, and collagen upregulation. To determine the therapeutic potential of CM-Gi activation after injury establishment, mice received three ISO doses followed by late CNO treatment from days 4–7. Remarkably, delayed Gi activation reversed established cardiac damage, including hypertrophy (HW/TL mg/cm: CTR 79±2 vs ISO 97±2 vs CNO+ISO 82±2; n=17), inflammation, collagen upregulation, and cardiac dysfunction (EF%: CTR 54±2 vs ISO 44±1 vs CNO+ISO 51±2; n=9). Flow cytometry revealed reduced inflammatory infiltration, particularly CCR2+ cells (cells/heart: CTR 1348±540 vs ISO 5945±1747 vs CNO+ISO 1544±519; n=8), associated with lower TNF-α, CCL2, and CCL7 expression, consistent with suppression of inflammatory remodeling and promotion of cardiac repair. **Conclusion:** This study identifies CM-specific Gi signaling as a central mediator of cholinergic cardioprotection and myocardial repair during adrenergic stress. By directly antagonizing β-adrenergic/PKA signaling and preserving ventricular myocyte integrity, Gi activation suppresses inflammatory and fibrotic remodeling while restoring cardiac function even after injury establishment. These findings provide compelling mechanistic evidence that CM-targeted modulation of cholinergic/Gi pathways represents a promising precision therapeutic strategy for pathological cardiac remodeling and heart failure.

06.060 **Dual α1-Adrenergic Receptor Antagonism and Voltage-Gated Calcium Channel Blockade Underlie the Vascular Effects of the Pyrimidinone Derivative STI4T-Et in Rat Aorta**. Silva MCC[1], Silva SB[1], Silva MEF[1], Barbosa FM[1], Souza MEVV[1], Feitosa SGD[2], Dos Anjos JV[2], Araújo AV[1] [1]UFPE, Centro Acadêmico da Vitória, Brazil; [2]CCEN-UFPE, Lab Síntese Orgânica, Brazil

Introduction: Cardiovascular diseases are the leading cause of death worldwide, with systemic arterial hypertension being the main risk factor. Among the anti-hypertensive agents are α1-adrenergic receptor (α1AR) antagonists and voltage-dependent calcium channel (CaV) blockers. Pyrimidinone compounds, such as STI4T-Et, are structurally similar to the α1AR antagonists class, and some studies report that these antagonists, like doxazosin, also block CaV. **Objective:** To evaluate the involvement of α1AR and CaV in the vascular effects of STI4T-Et on isolated aorta from Wistar rats. **Methods:** The experiments were performed using endothelium-denuded aortic rings and spleen from Wistar rats. The organs were suspended in organ baths on appropriate conditions. Cumulative concentration-response curves to norepinephrine (NE) or CaCl2 were constructed in the absence and in the presence of STI4T-Et. In addition, the vasorelaxant effect of STI4T-Et was assessed on KCl- or S-(-)-Bay K8644-induced precontraction. Emax and pEC50 values were expressed as the mean and S.E.M. and analyzed by one-way ANOVA followed by Tukey's test ($p < 0.05$, n = 5). **Results:** STI4T-Et inhibited NE-induced cumulative concentration-response curves on rat aorta, reducing both the efficacy and contractile potency of NE (Emax = 3.12 ± 0.17 g; pEC50 = 7.88 ± 0.12) at concentrations of 30 and 100 µmol/L (Emax = 2.14 ± 0.29 and 0.52 ± 0.11 g; pEC50 = 6.80 ± 0.04 and 6.56 ± 0.20, respectively), suggesting an insurmountable α1AR antagonism. STI4T-Et also inhibited KCl-induced contraction at concentrations of 30 (Emax = 52.1 ± 10.4%) and 100 µmol/L (Emax = 63.8 ± 5.4%). STI4T-Et induced equipotent relaxation of aorta precontracted with KCl 30 or 80 mmol/L (Emax = 90.9 ± 7.5 and 99.3 ± 2.9%; pEC50 = 4.25 ± 0.01 and 4.26 ± 0.01, respectively), suggesting a negative modulation of Ca2+ channels. This hypothesis was further supported by the reduction in both the efficacy and contractile potency of CaCl2, in a concentration-dependent manner. Furthermore, it was observed a greater relaxant efficacy and potency of STI4T-Et (Emax = 109.7 ± 2.7%; pEC50 = 4.69 ± 0.04) on contractions induced by Bay K8644 than on KCl 80 mmol/L. In addition, STI4T-Et reduced NE-induced contraction in rat spleen at concentrations of 30, 100 and 300 µmol/L (Emax = 0.25 ± 0.02, 0.19 ± 0.02 and 0.02 ± 0.02 g; pEC50 = 5.48 ± 0.10, 5.08 ± 0.26 and not determined, respectively) compared to control (Emax = 0.35 ± 0.03 g and pEC50 = 5.73 ± 0.07). **Conclusions:** Taken together, these findings indicate that STI4T-Et exerts its vascular effects through a dual mechanism of action, involving both α1AR antagonism and blockade of CaV, in isolated endothelium-denuded aortic rings from Wistar rats. **Acknowledgments:** UFPE, CAV.

06.061 **Structural Features of a Marine Sulfated Galactan Drive its Potent Prothrombotic Activity in Venous and Arterial Thrombosis Models.** Fonseca RJC[1], Imilhão BM[1], Cinelli LP[2], Mourão PAS[3] [1]CCS-ICB-UFRJ. Lab Coagulação e Trombose, Hospital Universitário Clementino Fraga Filho, Rio de Janeiro, RJ, Brasil. [2]IBqM-UFRJS, Lab Prospecção em Produtos Bioativos, Grupo de Glicofármacos, Rio de Janeiro, Brasil. [3]Lab Tecido Conjuntivo, Rio de Janeiro, Brasil.

Sulfated polysaccharides (SPs) from marine organisms display a wide range of pharmacological properties, including potent and sometimes contrasting effects on hemostasis. In this study, two sulfated galactan fractions (F23 and F44) were isolated from the green alga Penicillus capitatus and characterized by chromatographic and NMR analyses. Both fractions contained 3-linked 4,6-disulfated galactose and 6-linked 4-sulfated galactose units, but differed in molecular mass, sulfation degree, and heterogeneity. F44 exhibited higher sulfation and stronger anticoagulant activity *in vitro*, potentiating antithrombin-mediated inhibition of factors Xa and IIa, whereas F23 showed lower anticoagulant potency and a concentration-dependent procoagulant effect in the recalcification assay. *In vivo*, F23 markedly increased thrombus weight by ~60% at 2.5 mg kg^{-1} in a venous thrombosis model and reduced carotid artery occlusion time by 50% in the ferric chloride–induced arterial thrombosis model. Moreover, F23 significantly shortened bleeding time, confirming a prothrombotic and hemostatic-enhancing profile. Both F23 and F44 activated factor XII, with F23 showing potency comparable to fucosylated chondroitin sulfate. These results demonstrate that subtle structural variations among sulfated galactans from P. capitatus can shift their biological activity from anticoagulant to procoagulant, revealing key structure–activity relationships relevant to hemostasis modulation. Key words: sulfated polysaccharides; sulfated galactan; procoagulant effect

06.062 **Cytomegalovirus m33-Dependent Chemokine Signaling Drives Endothelial Inflammation and Oxidative Dysfunction: Evidence from Cell Culture and Human Hypertension**. Santos CV[1,2], Gonçalves ES[3], Velasco DS[2], Carneiro FS[1], Sinhorin VDG[3], Tostes RC[1], Priviero F[2], Webb RC[2], Bomfim GF[2,3] [1]USP-RP; [2]University of South Carolina, CTRC - Cardiovascular Translational Research Center, USA; [3]UFMT-Sinop, MT.

Introduction: Cytomegalovirus (CMV) is a ubiquitous betaherpesvirus linked to vascular pathologies and hypertension. CMV infects endothelial cells and activates inflammatory mechanisms, including upregulation of chemokines and adhesion molecules. Murine CMV (mCMV) encodes M33, a viral G protein-coupled receptor (vGPCR) homologous to cellular chemokine receptors, necessary for *in vivo* pathogenesis and implicated in cardiovascular dysfunction. The role of M33 in endothelial inflammation and oxidative stress, however, remains poorly defined. **Objective:** To characterize M33-dependent inflammatory and oxidative responses in mCMV-infected endothelial cells and to assess the association between CMV seropositivity and oxidative stress markers in hypertensive and normotensive subjects. **Methods:** Primary C57BL/6 mouse mesenteric endothelial cells were infected with mCMV (wild-type) or ΔM33 mCMV (M33-deficient mutant) (MOI 0.5) and analyzed at 3, 10, and 14 days post-infection (dpi). Viability and endothelial phenotype were evaluated by flow cytometry, inflammatory mediators by multiplex assay, and antioxidant enzymes by western blot. In parallel, blood samples from normotensive and hypertensive individuals were analyzed for CMV IgG and oxidative stress markers. **Results:** mCMV infection reduced endothelial cell viability at 10 and 14 dpi and promoted phenotypic alterations characterized by increased α-actin expression, reduced CD31, and increased α-actin/CD31 double-positive cells, indicating endothelial-to-mesenchymal transition. Infection induced an inflammatory response, with increased IL-6 at all time points and transient elevations of CXCL1, CCL2, and RANTES. Late-stage infection revealed reduced CX3CL1 and CXCL1 in ΔM33-infected cultures, whereas only mCMV-infected cells maintained elevated RANTES. Antioxidant defenses were impaired, with reduced SOD and catalase expression at 10 dpi. In humans, hypertensive individuals exhibited increased protein carbonylation and reduced catalase activity. CMV IgG levels correlated negatively with catalase ($r=-0.366$, $p=0.004$) and SOD activity ($r=-0.374$, $p=0.003$) only in hypertensive subjects. **Conclusion:** mCMV exploits M33-mediated chemokine signaling - via CCL2, RANTES, and CX3CL1 - to drive endothelial activation, phenotypic transition, and antioxidant depletion. The divergent profiles between wild-type and ΔM33 mCMV establish M33 as a key mediator of CMV-induced endothelial dysfunction. Translationally, human data reinforce this model by linking CMV exposure to compromised antioxidant defenses in hypertensive individuals. Together, these findings suggest that mCMV, through M33-dependent mechanisms, contributes to endothelial inflammation and dysfunction, potentially favoring cardiovascular disease development.

06.063 **Subchronic Exposure to a Glyphosate-Based Herbicide causes Changes in Perivascular Innervation Function in the Superior Mesenteric Artery of Rats**. Alves KSS[1], Polo-Norte ME[1], Alves OS[2], Duarte-Filho LD[3], Menezes PMN[4], Ribeiro LAA[5], Silva FS[5], de Queiroz DB[1] [1]UP, [2]UFAL, [3]UFPE, [4]FACAPE, [5]UFVSF

Background: Glyphosate-based herbicides (GBHs) are widely used, yet their cardiovascular effects, particularly on perivascular innervation, remain underexplored despite evidence of neurotoxicity and vascular dysfunction at low doses. **Methods:** Adult male Wistar rats received oral glyphosate (200 mg/kg/day, equivalent to 0.4% commercial formulation, below NOAEL) or water subchronically. Superior mesenteric artery segments underwent isometric tension recording. Electrical field stimulation (EFS, 1-16 Hz) elicited frequency-dependent contractions in endothelium-intact/denuded segments; blockers assessed neural components (TTX, phentolamine, suramin, CGRP8-37, L-NAME). **Results:** Glyphosate enhanced EFS-induced vasoconstriction (endothelium- independent), abolished by TTX. Adrenergic (noradrenaline) and purinergic (ATP) contributions increased (greater phentolamine/suramin effects); nitrergic (NO) activity rose (enhanced L-NAME response); sensory (CGRP) unchanged. No alterations in body weight, KCl/NA responses, ACh relaxation, or DEA-NO vasodilation. **Conclusion:** Low-dose glyphosate exposure augments sympathetic and nitrergic perivascular innervation in mesenteric arteries, disrupting neural vascular control. This may contribute to cardiovascular risks and the need for revised exposure guidelines of safe exposure limits.

06.064 **Carvacrol Enhances Endothelial Repair by Modulating Oxidative Stress and eNOS/Nrf2 Pathways in Endothelial Progenitor Cells**. Gonçalves TAF[1], Lima VS[1], Almeida AJPO[1,2], Soares EMC[1], Santos AC[1], Pontes LVS[1,3], Almeida Feitosa MS[1], Veras RC[1], Almeida IA[1]. [1]UFPB, Dept Pharmaceutical Sciences, Brazil, [2]University of Utah, Nora Eccles Harrison Cardiovascular Research and Training Institute, USA, [3]University of Utah, Dept Nutrition and Integrative Physiology, USA

Introduction: Carvacrol is a phenolic monoterpene with a broad range of biological activities, particularly antioxidant and antihypertensive effects. However, limited evidence is available regarding its role in vascular regeneration, especially in neovascularization mediated by endothelial progenitor cells (EPCs). **Objectives:** Therefore, this study evaluated whether carvacrol modulates EPC-mediated endothelial repair. **Methods:** Experimental protocols were approved by the CEUA-UFPB (No. 2171120320). EPCs were isolated from the bone marrow of Wistar rats and cultured for seven days in endothelial growth medium (EGM-2). Initially, an oxidative stress model was standardized using different concentrations of angiotensin II (ANG; 0.1, 1.0, and 10 μM), which were evaluated for cytotoxicity and reactive oxygen species (ROS) production. Cell viability was assessed using the MTT assay, while ROS production was analyzed by flow cytometry. Subsequently, EPCs were divided into four experimental groups: Control (CTL), Angiotensin II (ANG; 1.0 μM), Carvacrol (CTL-CAR; 0.1 μM), and Angiotensin II + Carvacrol (ANG-CAR; 1.0 μM ANG + 0.1 μM carvacrol). All treatments were performed for 24 h. Cell viability, ROS production, nitric oxide (NO) levels, and the expression of endothelial nitric oxide synthase (eNOS), catalase (CAT), superoxide dismutase (SOD), and Nrf2 were evaluated by flow cytometry. Cell adhesion and migration assays were performed using light microscopy. Statistical analyses were conducted using one-way ANOVA followed by Tukey's post hoc test, with significance set at $p < 0.05$. **Results:** ANG significantly reduced EPC viability at 1.0 μM (87.8 ± 1.3%) and 10 μM (87.9 ± 2.4%) compared with the CTL group (100.0 ± 1.6%), with no difference between the two concentrations. In contrast, ROS production increased at all ANG concentrations relative to CTL. Treatment with carvacrol in the ANG-CAR group restored cell viability (104.9 ± 5.7%) and reduced oxidative stress (74.6 ± 8.3%) compared with the ANG group (148.4 ± 10.5%). Carvacrol also significantly improved EPC adhesion (181.6 ± 6.1) and migration (T0 = 5.5 ± 0.2 mm; T24 = 4.0 ± 0.5 mm) compared with ANG-treated cells. The improvement in EPC function in the carvacrol-treated group was associated with higher eNOS expression (47.4 ± 1.5%) and NO production (158.2 ± 12.3%), compared with the ANG group (eNOS: 9.9 ± 1.1%; NO: 66.7 ± 14.6%). Moreover, EPCs treated with carvacrol showed increased expression of SOD, CAT, and Nrf2 compared with cells treated with ANG alone. **Conclusion:** ANG impaired EPC viability and increased oxidative stress, whereas carvacrol treatment restored viability and attenuated ANG-induced oxidative damage. These protective effects were associated with improved EPC function and enhanced expression of antioxidant and endothelial regulatory factors.

06.065 **The Role of Potassium Channels in the Vasodilation Induced by a Novel Nitrosyl–Ruthenium Nitric Oxide Donor Complex**. Monteiro HSM[1], Silva FAO[1], Sousa AS[2], Lima NCB[1], Simonato SG[1], Franco VMF[1], Souza ARL[1], Viana LC[1], Souza RM[1], Jamacaru FVF[1], Lopes LGF[2], Jorge RJB[1] [1]UFC-Porangabuçu, Dept Physiology and Pharmacology, Graduate Program in Pharmacology – Brazil; [2]UFC-Pici, Dept Organic and Inorganic Chemistry, Lab Bioinorganic Chemistry - Brazil

Introduction: Nitrosyl–ruthenium complexes (RuNO) are promising candidates for the controlled release of nitric oxide (NO), a key mediator of vascular homeostasis. Beyond activating the NO/soluble guanylate cyclase/cGMP pathway, evidence suggests that NO-donor compounds may also modulate potassium channels in vascular smooth muscle. Although related ruthenium complexes have shown significant vasorelaxant activity, the involvement of these channels in the response to $Ru(bpy)_2(Bzim)NO_3$ (FOR0803) remains unclear. **Objective:** To evaluate the vasodilatory effect of the ruthenium complex FOR0803 in aortic rings from Wistar rats and determine the contribution of potassium channels to this response. **Methods:** Male Wistar rats (Rattus norvegicus), weighing 250–300 g, were used. Thoracic aorta segments were mounted in an ex vivo isolated organ bath system. Rings were precontracted with phenylephrine (1 µmol/L) and incubated in the absence (control) (n=6) or presence of tetraethylammonium (TEA, 10 mmol/L) (n=6), a non-selective potassium channel blocker. A cumulative concentration–response curve for FOR0803 (3×10^{-10} to 10^{-5} mol/L) was then generated. Statistical analyses were performed using GraphPad Prism® version 8.0. Data are presented as mean ± standard error of the mean (SEM). Differences between two independent groups were evaluated using Student's t-test, and results were considered statistically significant when $p < 0.05$. **Results:** TEA pre-incubation significantly attenuated the vasorelaxation induced by FOR0803, reducing maximal efficacy (EMAX = 83.21 ± 4.14%) compared with control (107.59 ± 6.71%). The blocker also increased the EC_{50} from 0.215 µmol/L to 1.584 µmol/L, indicating decreased potency. These findings support a relevant contribution of potassium channel activation to the vascular relaxation elicited by FOR0803. **Conclusion:** The ruthenium complex FOR0803 exhibited vasorelaxant effects in rat aortic rings, with a significant involvement of potassium channels in this mechanism. Further studies are needed to identify the specific potassium channel subtypes involved and to deepen the understanding of the mechanisms underlying the observed vascular response. **Financial support:** CNPq.

06. Biology and Metabolic and Reproductive Diseases

06.001FR **Evaluation of Reproductive Parameters in Wistar Male and Female Rats Subjected to Acute Physical Exercise**. Santos-Júnior JCS[1], Morgado VCC[1], Salustiano IM[1], Lopes RA[1], Melo MTBV[1], Noronha GL[1], Brandão CFCCM[2], Lacerda LT[3], Andrade MJO[4], Campos HO[6], Leite LHR[7], Coimbra CC[8], Drummond LR[1,2] [1]UEMG, Experimental Exercise Physiology Lab, [2]UEMG, Research Lab in Metabolism, Physiology and Physical Exercise, [3]UEMG, Strength Training in Health and Physical Conditioning Lab, [4]UEMG, Neuroscience, Chronobiology and Sleep Psychology Lab, [5]UFOP Animal Science Center, [6]UEMG Ubá Unit, [7]UFJF, [8]UFMG Endocrinology and Metabolism Lab, [9]UEMG, Brazil.

Introduction: The reproductive cycle of female rats is subdivided into diestrus I and II(D), proestrus(P), and estrus(E), and is known as the estrous cycle. Due to the hormonal variations inherent to the estrous cycle, studies involving different physical exercise protocols in females are scarce in the literature. Consequently, the effects of acute physical exercise on female reproductive function remain unclear. **Objective:** To evaluate the effects of acute physical exercise on the weight of reproductive organs across the different phases of the estrous cycle in Wistar rats. **Methods:** Male(n=18) and female(n=56) Wistar rats were used, housed at the Experimental Exercise Physiology Laboratory of the State University of Minas Gerais(UEMG), Divinópolis Unit. Procedures were approved by the Animal Ethics Committee(protocol002/2025). Vaginal cytology was monitored; only animals exhibiting three regular estrous cycles were included, and females assigned to the acute exercise group were acclimated to treadmill running for 5 days. Animals were divided into progressive exercise-to-fatigue groups D-Ex(n=11), P-Ex(n=7), E-Ex(n=12), and M-Ex(n=11) and resting groups D-R(n=9), P-R(n=8), E-R(n=11), and M-R(n=7). Following the exercise protocol, the animals were euthanized for the removal and weighing of reproductive organs. Data were expressed as mean ± standard deviation of the mean(SDM), with a significance level of 5%. **Results:** The frequency of estrous cycle phases was lower in P(23.97±6.75) compared to D(35.17±11.16) and E(39.93±8.01); $p< 0.0001$. Considering rats subjected to exercise or not, the frequency of P-R(26.92±12.58) was lower than that of D-R(35.64±17.68) and E-R(37.18±11.50); $p<0.005$, whereas E-Ex(43.10±10.81) was higher than D-Ex(27.14±9.36) and P-Ex(29.76±9.16); $p<0.0001$. When comparing resting and exercising groups within each estrous cycle phase, only phase D showed a difference in frequency, with D-R(35.64±17.68) being higher than D-Ex(27.14±9.36); $p<0.001$. Regarding the analysis of female reproductive organs, uterine weight showed the expected physiological variations across estrous cycle phases, being higher in P-R(0.44±0.25g) compared to D-R(0.23±0.09g) and E-R(0.31±0.04g); $p<0.005$. However, when comparing resting and exercising groups within each phase, a difference was observed only in phase P, with lower uterine weight in P-Ex(0.26±0.14g) compared to P-R(0.44±0.25g); $p<0.01$. Acute exercise did not alter ovarian weight. In males, no changes were observed in the weights of the prostate, testes, or seminal vesicles between groups subjected to progressive exercise to fatigue and those that were not. **Conclusion:** Progressive exercise reduced uterine weight during proestrus, which may be related to changes in circulating estradiol levels and a possible reduction in uterine responsiveness to this hormone. In males, acute exercise did not alter reproductive organ weights. These findings demonstrate sexual dimorphism regarding the reproductive organs' response to acute exercise, with females appearing to be more sensitive than males. **Financial support:** UEMG, FAPEMIG, CNPq, and CAPES.

06.002FR **Analysis of Thermoregulation During the Estrous Cycle of Female and Male Rats**. Salustiano IM[1], Melo MTBV[1], Morgado VCC[1], Noronha GL[1], Martins JA[1], Santos JCS[1], Brandão CFC[1,2], Lacerda LT[1,2], Andrade MJO[1,2], Campos HO[3], Leite LHR[4], Coimbra CC[5], Lopes RA[1,2], Drummond LR[1,2]. [1]UEMG-Divinópolis, [2]UEMG, PPG em Biociências e Saúde Humana, [3]UEMG-Ubá, [4]UFJF, [5]UFMG.

Introduction: The reproductive cycle of female rats is characterized by variations in ovarian steroids and lasts 4 to 5 days, divided into four phases: proestrus (P), estrus (E), metestrus (M), and diestrus (D). Gonadal steroids influence thermoregulatory control, but how this occurs during the estrous cycle of rats remains not elucidated. **Objectives:** This study aimed to evaluate whether oscillations in internal temperature (Ti) and tail temperature (Tc) occur during the estrous cycle and to investigate possible sexual dimorphism in thermoregulation in rats. **Methods:** Were used 27 female and 17 male Wistar rats from the Animal Science Center (CCA) of the Federal University of Ouro Preto. The female rats were transferred to the animal facility of the Experimental Exercise Physiology Laboratory (LAFEEX) at the State University of Minas Gerais (UEMG), Divinópolis. The procedures were approved by the Ethics Committee on Animal Use (protocol - 002/2025). At 2 months of age, vaginal smears were taken daily and only rats showing at least three consecutive regular estrous cycles were included in the study. The animals underwent surgery for implantation of the abdominal and tail temperature sensor. After the recovery period, the female rats that showed regular cycle were kept in metabolic cages during the phases of D (n = 14), P (n = 15), and E (n = 14). Ti was recorded by telemetry for 24 h, and Tc was recorded by the Tag reader every 30 minutes from 7 a.m. to 6 p.m. The male rats (M; n = 17), were subjected to the same experimental protocol as the females. Data were presented as mean ± S.E.M. For comparison of Ti and Tc data, two-way ANOVA followed by Tukey's post hoc test was used. Data were analyzed using GraphPad Prism software. **Results:** No interaction between estrous cycle phase and time was observed for Ti. In all groups, Ti was lower during the light phase, corresponding to the resting period, and higher during the dark phase, corresponding to the active period ($p < 0.0001$). In contrast, Tc showed a significant interaction between cycle and time ($p < 0.001$). At 15:00 h, Tc was lower in males (31.59 ± 1.17 °C) compared with females during diestrus (33.32 ± 1.64 °C), proestrus (32.38 ± 1.32 °C), and estrus (33.15 ± 1.76 °C) ($p < 0.005$). At 17:00 h, Tc in females during diestrus (33.72 ± 1.76 °C) was higher than that observed in males (32.21 ± 1.20 °C) ($p < 0.005$). **Conclusion:** Although no variations in Ti were found between males and females, nor among the different phases of the estrous cycle, our results demonstrating a circadian variation of Ti in all groups. The differences of Tc between male and female in the end of the light phase, can be associated to hormonal oscillations in females, indicating a possible sexual dimorphism in thermoregulatory control.

06.003FR **Maternal Resistance Training Differentially Affects Growth and Developmental Milestones in Male and Female Offspring of Obese Dams**. Silva MLB[1], Silva RAA[2], Nelo SRB[2], Barros MRM[3], Oliveira MCMC[4], Martins MVA[4], Lima RS[1], Pereira TKM[4], Oliveira TRP[5], Antonio-Santos J[5], Da Silva Aragão R[5]. [1]UFPE, Physical Education Undergraduation, Brazil, [2]UFPE, PPG Nutrition, Brazil, [3]UFPE, PPG Nutrition, Physical Activity and Phenotypic Plasticity, Brazil, [4]UFPE, Nutrition Undergraduation, Brazil [5]UFPE, Dept Physical Education, Brazil.

Introduction: Maternal nutritional status and lifestyle during pregnancy play a critical role in offspring development and may influence growth and maturation trajectories throughout life. Maternal obesity and physical exercise are important factors that can modulate developmental outcomes in offspring. **Objective:** To evaluate the effects of an obesogenic diet and maternal resistance training during pregnancy on growth parameters and physical development in rat offspring. **Methods:** Female Wistar rats were assigned to either a control diet (CD; 3.6 kcal/g, 14% fat; n = 9) or an obesogenic diet (OD; 4.6 kcal/g, 49% fat; n = 13), supplemented with condensed milk, for eight weeks before mating and throughout lactation. During pregnancy, half of the dams from each dietary group performed resistance training on a ladder (5 days/week; 50% of maximal load during the first gestational week and 80% during the second and third gestational weeks), forming the trained groups (CD-T; n = 4 and OD-T; n = 7), while the remaining dams constituted the untrained groups (CD-U; n = 4 and OD-U; n = 6). Offspring were evaluated for growth and physical development parameters throughout postnatal development. The Shapiro-Wilk test was used to assess normality, and the groups were compared using a two-way ANOVA followed by Tukey's post-hoc test. **Results:** Offspring from the OD-T group exhibited lower birth weight than those from the CD-T group in both males (6.32 ± 0.20 vs. 7.93 ± 0.25 g, p = 0.01) and females (6.25 ± 0.20 vs. 7.17 ± 0.39 g, p = 0.01). In male offspring, differences were observed in the laterolateral head axis at birth (CD-U: 10.83 ± 0.63 mm vs. CD-T: 12.15 ± 0.55 mm, p = 0.04; CD-T: 12.15 ± 0.55 mm vs. OD-T: 10.53 ± 0.31 mm, p = 0.01). On postnatal day 7, female offspring from the OD-T group exhibited greater body length (68.03 ± 0.94 vs. 63.78 ± 0.84 mm, p = 0.0001) and laterolateral head axis (15.55 ± 0.30 vs. 14.70 ± 0.44 mm, p = 0.01) than those from the OD-U group. On postnatal day 28, female offspring from the OD-U group exhibited lower body weight than those from the OD-T group (81.92 ± 1.80 vs. 89.09 ± 0.78 g, p = 0.03). Additionally, female offspring from obese dams showed delayed ear unfolding (OD-T: 2.85 ± 0.26 vs. CD-T: 2.00 days, p = 0.04) and delayed sexual maturation (OD-U: 36.33 ± 1.71 vs. CD-U: 32.20 days, p = 0.02). **Conclusion:** Maternal consumption of an obesogenic diet affected offspring growth and developmental milestones. Although offspring from trained obese dams exhibited lower birth weight, they showed improved growth-related parameters during postnatal development, particularly among females.

06.004FR **Evaluation of Metabolic Parameters During the Estrous Cycle in Rats**. Melo MTB[1], Salustiano IM[1], Morgado VCC[1], Noronha GL[1], Martins JA[1], Santos JCS[1], Brandão CFC[1,2], Lacerda LT[1,2], Andrade MJO[1,2], Campos HO[3], Leite LHR[4], Coimbra CC[5], Lopes RA[1,2], Drummond LR[1,2] [1]UEMG-Divinópolis, [2]UEMG, PPG em Biociências e Saúde Humana, [3]UEMG-Ubá, [4]UFJF, [5]UFMG.

Introduction: The estrous cycle in rats is characterized by cyclical variations in ovarian steroid levels over 4 to 5 days and is divided into proestrus (P), estrus (E), and diestrus I and II (D). However, the metabolic responses and mechanisms involved in this regulation in the different phases are not yet fully understood. **Objective:** Investigate the effects of the estrous cycle on metabolic responses in rats by quantifying oxygen consumption (VO_2) and the respiratory quotient (RQ). **Methods:** Eight-week-old Wistar rats (male and female) from the Animal Science Center of the Federal University of Ouro Preto were housed in the Experimental Exercise Physiology Laboratory of the State University of Minas Gerais, Divinópolis Unit. Vaginal cytology of the rats was monitored daily. Basal metabolism was recorded over 24 hours during D (n=14), P (n=14), E (n=13) and in males (M; n=17). The experimental procedures were approved by CEUA/UEMG (protocol 002/2025). Data were expressed as mean ± standard deviation (SD), with a significance level of 5%. Data were initially organized in Microsoft Excel and subsequently analyzed using GraphPad Prism with two-way ANOVA followed by Tukey's post hoc test. **Results:** During the light phase (7:00–19:00 h), a reduction in metabolism was observed. There was an interaction between the time of day and VO2 consumption ($p<0.005$). VO_2 was lower in group D compared to the other groups between 9:00 and 15:00 hours (9:00h, D: 14.22±1.18; P: 18.82±4.38; E: 18.80±3.44; and M: 17.21±2.82, $p<0.001$). During the dark phase (after 19h), basal metabolism was higher compared to the light phase. Significant differences in VO_2 were observed at 21h: P (18.62±1.57) vs M (16.73±1.53); $p<0.005$; at 1am: P (16.67±1.85) vs E (18.57±1.51); $p<0.005$; At 4am: P (19.07±2.29) and E (18.94±1.75) vs M (15.91±1.82); $p<0.0001$; at 5am: P (18.90±2.70) and E (18.93±1.68) vs M (16.00±2.40); $p<0.001$; and at 7am: E (15.53±1.93) vs M (13.23±1.85); $p<0.005$. For RQ, a significant difference was observed only at 12h: D (0.93±0.06) vs P (0.85±0.08) and E (0.84±0.06); $p<0.005$. **Conclusion:** The results suggest that the metabolic variations observed among the groups may be associated not only with sex differences between males and females but also with the animal's circadian rhythm, characterized by lower metabolic activity during the light period, as well as with hormonal fluctuations throughout the estrous cycle. These findings indicate that ovarian steroids play an important role in the modulation of energy metabolism. From an experimental perspective, the results reinforce the importance of considering both the phase of the estrous cycle and the timing of metabolic assessments in studies involving female animals, thereby improving methodological accuracy and scientific reproducibility. Finally, this study expands current knowledge of female metabolic physiology by providing the first continuous 24-hour characterization of these metabolic variables throughout the estrous cycle.

06.005FR **Influence of Volume Reduction on Heart Rate Behavior after Strength Training**. Luiz CM, Pires KC, Vieira YLM, Rodrigues IJS, Flora JMG, Lacerda LT, Brandão CFCCM, Andrade MJO, Drummond LR UEMG-Universidade Divinópolis, Depto Educação Física, Brasil; UEMG-Universidade Divinópolis, Depto Psicologia, Brasil

Introduction: Strength training performed to muscle failure (STM) has been widely used to maximize strength and muscle hypertrophy because the high levels of fatigue generated may increase muscle activation. However, exercising to muscle failure also imposes greater cardiovascular stress. Although heart rate (HR) is a practical, low-cost, and noninvasive measure of cardiovascular response, few studies have compared HR recovery following strength training performed to muscle failure with protocols performed at different proximities to muscle failure. Therefore, investigating these responses may help optimize training prescription while reducing cardiovascular overload. **Objective:** To compare heart rate responses following strength training performed to muscle failure and protocols with different reductions in training volume over an 8-week intervention. **Methodology:** This study was approved by the Research Ethics Committee of the Federal University of Minas Gerais (UFMG) (CAAE: 79108117.5.0000.5149). Eleven healthy male volunteers (18–35 years) who had not participated in strength training during the previous six months were recruited. Participants had no history of musculoskeletal injuries, cardiovascular or metabolic diseases, were non-smokers, reported no excessive alcohol consumption, and did not use pharmacological ergogenic aids. Each participant performed bilateral knee extension exercise to muscle failure (STM) and five additional protocols with training volumes reduced by 10%, 20%, 30%, 40%, or 50% relative to STM. Sessions were separated by a seven-day interval over an 8-week period. HR was recorded at rest and at 5 and 15 minutes after exercise using a Polar M30 heart rate monitor (Polar Electro Oy, Oulu, Finland), a device based on validated heart rate monitoring technology. Data were analyzed using SigmaPlot 11.0 and are presented as mean ± standard deviation. One-way ANOVA followed by Tukey's post hoc test was used, with statistical significance set at $P \leq 0.05$. **Results:** Resting HR did not differ significantly among the exercise protocols ($P = 0.553$). At 5 minutes post-exercise, the protocols with 30% ($P = 0.02$), 40% ($P = 0.03$), and 50% ($P < 0.01$) reductions in training volume showed significantly lower HR compared with the STM protocol. No significant differences were observed among protocols after 15 minutes of recovery. **Conclusion:** Strength training performed to muscle failure elicited a greater acute cardiovascular response during early post-exercise recovery than protocols performed with reduced training volumes. These findings suggest that training at a greater distance from muscle failure may reduce acute cardiovascular overload while potentially preserving the benefits of strength training.

06.006FR **Maternal Diet-Induced Obesity Increases Adiposity and Modifies Triglyceride Levels During Pregnancy**. Pereira TKM[1], Silva RAA[2], Lima RS[3], Silva MLB[3], Oliveira PGS[1], Oliveira DKS[4], Oliveira DPL[5], Nelo SRB[2], Barros MRM[4], Oliveira RRP[6], Antonio-Santos J[1,5], Da Silva Aragão R[5]. [1]UFPE, Nutrition; [2]UFPE, PPG Nutrition; [3]UFPE, Physical Education; [4]UFPE, PPG Nutrition, Physical Activity and Phenotypic Plasticity; [5]FPS, Physical Education.

Introduction: Maternal obesity is associated with alterations in nutrient metabolism and body composition that may affect maternal health during pregnancy. Experimental models of diet-induced obesity can provide insights into the metabolic consequences of excessive adiposity during gestation. **Objective:** To evaluate the effects of diet-induced obesity on maternal adiposity, macronutrient intake, and biochemical parameters during pregnancy. **Methods:** Female Wistar rats were allocated to one of two experimental groups and fed their respective diets for six weeks before mating and throughout gestation: a control diet (CD; 3.6 kcal/g, 14% fat; n = 8) or an obesogenic diet (OD; 4.6 kcal/g, 49% fat; n = 9), supplemented with condensed milk. Total food intake during pregnancy was quantified, and dams were euthanized at the end of gestation for collection of retroperitoneal adipose tissue and blood samples for biochemical analyses. Comparisons between groups were performed using an unpaired Student's t-test. **Results:** Dams fed the obesogenic diet exhibited higher lipid intake and lower protein and carbohydrate intake throughout pregnancy ($p < 0.0001$).At gestational day 20, the OD group also showed greater retroperitoneal adipose tissue accumulation than control dams ($p = 0.002$).In addition, serum triglyceride concentrations were lower in the OD group than in controls ($p = 0.018$). No significant differences were observed in albumin ($p = 0.38$), total cholesterol ($p = 0.92$), HDL cholesterol ($p = 0.55$), total protein ($p = 0.79$), aspartate aminotransferase (AST; $p = 0.67$), or alanine aminotransferase (ALT; $p = 0.58$). **Conclusion:** Diet-induced obesity increased maternal adiposity and altered macronutrient intake patterns during pregnancy. These changes were accompanied by modifications in circulating triglyceride concentrations, whereas other biochemical markers of nutritional status and liver function remained unchanged.

06.007FR **Effects of Physical Training on Physical Performance and Dopaminergic Activity in the Preoptic Area in Hypertensive Rats**. Noronha GL[1], Martins JA[1], Lopes RA[1], Campos HO[2], Rodrigues QT[3], Silva KSC[3], Prímola-Gomes TN[4], Lacerda LT[1]; Brandão CFCCM[1]; Andrade MJO[5], Natali AJ[4], Szawka RE[3], Coimbra CC[3], Drummond LR[1] [1]UEMG, Dept Physical Education, Brazil; [2]UEMG, Dept Biological Sciences, Brazil; [3]UFMG, Dept Physiology and Biophysics, Brazil; [4]UFV, Dept Physical Education, Brazil; [5]UEMG, Dept Psychology, Brazil.

Introduction: Spontaneously hypertensive rats (SHR) exhibit an imbalance in body temperature regulation during physical exercise, which may be related to the level of activation of dopaminergic neural pathways. **Objective:** This study aimed to evaluate dopaminergic activity in the preoptic area of hypertensive rats subjected to physical training. **Methods:** Were used 32 rats divided into four groups: untrained normotensive Wistar rats (NWR NTs; n = 8); trained normotensive Wistar rats (NWR Ts; n = 8); untrained spontaneously hypertensive Wistar rat (SHR NTs; n = 8); and trained spontaneously hypertensive Wistar rat (SHR Ts; n = 8), all SHR animals had systolic blood pressure below 150mmHg. Physical training was performed on a treadmill for 8 weeks, 5 days per week, reaching a speed of 18 m.min-1 for 60 minutes. Before and after physical training the animals were subjected to a progressive exercise session until fatigue in order to determine physical performance. At 16 weeks of age, blood pressure was measured by tail plethysmography. Forty-eight hours after blood pressure assessment, the animals were euthanized by decapitation. Subsequently, the brains were removed and stored at -80°C. Dopamine and DOPAC levels were measured by high- performance liquid chromatography (HPLC), and dopaminergic activity was assessed using the DOPAC/DA ratio. All procedures were approved by the Ethics Committee on Animal Use of the State University of Minas Gerais (# 04/2024). Data were presented as mean ± S.E.M. **Results:** Physical training increased exercise time both in NWR groups (NWR T 14.8 ± 4.1 min, vs. NWR NT -9.4 ± 3.5 min, $p < 0.05$) and in SHR groups (SHR T 11.1 ± 3.8 min, vs. SHR NT -9.5 ± 2.9 min, $p < 0.05$). The concentration of DOPAC, in APO, did not show statistically significant differences between the groups (SHR NT 14.29 ± 1.31; SHR T 18.60 ± 13.31; NWR NT 12.13 ± 3.08; NWR T 14.13 ± 5.66; $p < 0.05$). SHR T showed a higher concentration of dopamine compared to NWR T (SHR T 33.11 ± 13.56 vs. NWR T 8.2 ± 3.81 $p < 0.05$). However, NWR T presented greater dopaminergic activity when compared to all other groups. (NWR T 1.93 ± 0.62, vs. NWR NT 0.80 ± 0.10, SHR T 0.52 ± 0.15, SHR NT 0.66 ± 0.26, $p < 0.05$). **Conclusion:** The study results indicate that physical training increased physical performance, but did not modify dopaminergic activity in the preoptic area of SHR, only in NWR rats.

06.008FR **Effect of Physical Training on Serotonergic Activity in the Preoptic Area of Hypertensive Rats**. Martins JA[1], Lopes RA[1], Noronha GL[1], Campos HO[2], Rodrigues QT[3], Silva KSC[3], Prímola-Gomes TN[4], Lacerda LT[1]; Brandão CFCCM[1]; Andrade MJO[5], Natali AJ[4], Szawka RE[3], Coimbra CC[3], Drummond LR[1] [1]UEMG, Dept Physical Education, Brazil; [2]UEMG, Dept Biological Sciences, Brazil; [3]UFMG, Dept Physiology and Biophysics, Brazil; [4]UFV, Dept Physical Education, Brazil; [5]UEMG, Dept Psychology, Brazil.

Introduction: Thermoregulation results from a balance between the mechanisms of heat production and heat dissipation in the body, and its central control is located in the preoptic area of the hypothalamus. Spontaneously hypertensive rats(SHR) exhibit impaired body temperature regulation during physical exercise, which may be related to the activation of serotonergic neural pathways. **Objective:** To evaluate serotonergic activity in the preoptic area of hypertensive rats subjected to physical training. **Methods:** All procedures were approved by the Ethics Committee on Animal Use of the State University of Minas Gerais(CEUA/UEMG; protocol no.04/2024). Thirty- two rats were divided into four groups: non-trained normotensive Wistar rats(NWR NT;n=8), trained normotensive Wistar rats(NWR T;n=8), non-trained spontaneously hypertensive rats(SHR NT;n=8), and trained spontaneously hypertensive rats(SHR T;n=8). Physical training was performed on a treadmill for 8 weeks, 5 days per week, at a speed of 18 $m \cdot min^{-1}$ for 60 minutes per session. After completion of the training period, the animals were subjected to a progressive exercise session until fatigue in order to determine maximum running speed. At 16 weeks of age, blood pressure(SBP) was measured by tail plethysmography. 48 hours after SBP assessment, the animals were euthanized by decapitation. Subsequently, the brains were removed and stored at -80 °C. Serotonin(5-HT) and 5-hydroxyindoleacetic acid(5-HIAA) levels were measured by high-performance liquid chromatography (HPLC), and serotonergic activity was assessed using the 5-HIAA/5-HT ratio. The data were analyzed and expressed as mean ± standard error. **Results:** Physical training reduced SBP only in the SHR T (160.1±5.4mmHg) vs. SHR NT (183.5±5.3mmHg, $p<0.05$). SHR animals presented higher SBP when compared to NWR animals, SHR NT (183.5±5.3mmHg) vs. NWR NT (118.8±5.4mmHg, $p<0.05$) and SHR T (160.1±5.4mmHg) vs. NWR T (121.2±6.4mmHg, $p<0.05$). Physical training increased peak VO2 in both NWRs (6.50±2.23ml.kg-0.75.min-1 vs. -2.03±1.88 ml.kg-0.75.min-1, $p<0.05$) and SHRs (5.71±1.76ml.kg-0.75.min-1 vs. 0.26±1.57 ml.kg-0.75.min-1, $p<0.05$). Animals from the SHR group presented lower body mass when compared to animals from the NWR groups, both in the untrained groups (289.3±8.9g vs. 397.3±8.9g, $p<0.05$) and in the trained groups (304.7±9.5g vs. 394.8±9.5g, $p<0.05$) respectively. Physical training promoted an increase in serotonin(5-HT) levels only in SHR animals SHR T(25.65±10.63) vs NWR T(13.10±5.37, $p<0,01$). Physical exercise did not change the 5-hydroxyindoleacetic acid(5-HIAA) levels. SHR T animals showed lower serotonergic activity when compared to NWR T animals (1.22±0.38 vs. 3.79±1.30, $p<0,05$). **Conclusion:** Physical training reduced blood pressure in SHR animals, increased the VO2peak in both SHR's and NWR's groups, but did not modify the serotonergic activity in the preoptic area in both SHR's and NWR's groups.

06.009FR **Influence of the Polar Fraction of *P. aculeata* on Glycemia and Food Intake in Female Wistar Rats**. Silva EKL[1], Silva JCF[1], Franco ES2, Maia MBS2, Souto VS[1], Feitoza LHS[1], Barros CFN[1], Francelino JO[1], Araújo FWC[1], Nascimento E[1]. [1]UFPE, Dept Nutrition, Brazil. [2]UFPE, Dept Physiology and Pharmacology, Brazil.

Parkinsonia aculeata is a plant with phytotherapeutic potential, given its effects in attenuating of glycemic and lipidemic levels in the context of excess weight and its associated deleterious outcomes. The aim of this study was to investigate the repercussions of the polar fraction of P. aculeata on physio-metabolic parameters and food intake in young eutrophic female Wistar rats (n = 17). The animals were fed a standard diet throughout the entire experiment, from post-weaning (21 days of age) until 13 weeks thereafter. In the 9th week, the female rats were divided into two groups: control (C, n = 7) and treated with P. aculeata (P, n = 10). The polar fraction of the hydroalcoholic extract of P. aculeata was administered by gavage for 30 days at 12:00p.m., at a dose of 140mg/kg for the P group, whereas the C group received filtered water at 1.5mL/kg to match the stress associated with the gavage procedure. The female rats were euthanized in the 13th week. Statistical significance was considered at $p < 0.05$. The body weight gain was significantly higher in group P in the 1st week (C = 65.04 ± 8.01g; P = 82.10 ± 5.82g; p = 0.0002) and in the 13th week (C = 201.00 ± 18.67g; P = 226.20 ± 19.85g; p = 0.0186). Regarding visceral adiposity fat was significantly increased in the P group (C = 2.03 ± 1.73g/100g; P = 3.42 ± 0.92g/100g; p = 0.0485). Cumulative food intake did not differ significantly between groups (C = 1433.00 ± 79.52g; P = 1504.00 ± 150.70g; p = 0.2747). Regarding glycemic patterns, no significant differences were found during the light phase (C = 119.20 ± 5.68mg/dL; P = 116.40 ± 9.10mg/dL; p = 0.2268); however, the P group exhibited significantly lower glycemic levels during the dark phase (C = 122.80 ± 7.83mg/dL; P = 117.30 ± 6.37mg/dL; p = 0.0085). In relation to feeding patterns, the P group showed a significant increase in food intake during the light phase (C = 0.80 ± 0.70g; P = 1.77 ± 1.13g; p = 0.0011) whereas no changes were observed during the dark phase. In conclusion, P. aculeata differentially modulated glycemic and feeding patterns across light and dark phases. The glycemia was attenuated during the dark phase despite equivalent food intake, and the increased feeding intake during the light phase did not result in higher glycemic levels. This study was supported by the Fundação de Amparo à Ciência e Tecnologia do Estado de Pernambuco (FACEPE) (No. IBPG-0676-4.05/25). Local Ethics Committee approval (No. 0017/2022).

06.010FR **Effects of the Polar Fraction of *P. aculeata* on Acute Stress Responses in Young Female Wistar Rats Subjected to Rest-Phase Time-Restricted Feeding**. Feitoza LHS[1], Silva JCF[1], Franco ES[2], Maia MBS[2], Souto VF[1], Araújo FWC[1], Barros CFN[1], Silva EKL[1], Francelino JO[1], Nascimento E[1]. [1]UFPE, Dept Nutrition, Brazil. [2]UFPE, Dept Physiology and Pharmacology, Brazil.

Feeding at times incompatible with the light phase of the circadian system promotes misalignment and deleterious outcomes in body weight and hedonic eating behavior, contributing to overweight and greater stress responsiveness. In this context, plants with phytotherapeutic potential, such as Parkinsonia aculeata, act as modulators of the metabolic profile, although their effects on acute stress in a chronodisruption model using young female rats remain poorly elucidated. The present study aimed to investigate the effects of treatment with P. aculeata on tail-pinch responses in young female rats subjected to time-restricted feeding (TRF) during the rest phase. Female Wistar rats (n = 26) were weaned at 21 days of age and, during the first 8 weeks, maintained on a standard chow diet ad libitum. From the 9th to the 12th week, the animals were divided into Control (n = 7), Restricted (R, n = 10), and Restricted with P. aculeata (RP, n = 9). The R group was exposed exclusively to the TRF protocol during the light phase, whereas the RP group received both the TRF protocol and the polar fraction of the hydroalcoholic extract of P. aculeata (140mg/kg) by gavage at 12:00 p.m. In the 13th week, the acute nociceptive stress test tail-pinch was performed using palatable food (Kellogg's®) or standard chow diet, with food intake evaluated at 30 and 60 minutes. Statistical significance was considered at $p < 0.05$. R and RP presented higher initial body weight compared to the C in the first week (C = 65.04 ± 8.01 g; R = 82.46 ± 2.87 g; RP = 75.42 ± 9.66 g; p = 0.0009). In the last week, RP showed higher body weight compared to C (C = 201.00 ± 18.67 g; R = 208.20 ± 16.46; RP = 222.40 ± 9.91 g; p = 0.0274). The cumulative food intake was lower in R compared to C (C = 1433.00 ± 79.52 g; R = 1346.00 ± 70.16 g; RP = 1399.00 ± 50.16; p = 0.0401). During the manual restraint, at 30 minutes, the R and RP groups showed higher palatable food intake than standard chow diet intake (Rpalatable = 3.09 ± 0.73 g; Rstandardchow = 1.36 ± 0.50 g; p = 0.0225; RPpalatable = 4.02 ± 1.31 g; RPstandardchow = 0.80 ± 0.64 g; p = 0.0009). At 60 minutes, the RP showed higher palatable food intake compared to standard chow diet intake (RPpalatable = 4.36 ± 1.58 g; RPstandardchow = 1.52 ± 1.11 g; p = 0.0166). In the tail-pinch test, R and RP showed higher palatable food intake than standard chow diet intake at 30 minutes (Rpalatable = 4.85 ± 2.75 g; Rstandardchow = 1.36 ± 0.82 g; p = 0.0053; RPpalatable = 5.17 ± 2.39 g; RPstandardchow = 1.67 ± 0.89 g; p = 0.0110), and at 60 minutes (Rpalatable = 6.61 ± 2.48 g; Rstandardchow = 2.11 ± 0.60 g; p = 0.0007; RPpalatable = 6.58 ± 2.76 g; RPstandardchow = 2.59 ± 1.54 g; p = 0.0054). Thus, the treatment with the polar fraction of P. aculeata failed to attenuate the preference for palatable food in female Wistar rats subjected to rest- phase TRF. This study was supported by the Fundação de Amparo à Ciência e Tecnologia do Estado de Pernambuco (FACEPE) (No. IBPG-0676-4.05/25). Local Ethics Committee approval (No. 0017/2022). Local Ethics Committee approval (No. 0017/2022). This study was supported by the Fundação de Amparo à Ciência e Tecnologia do Estado de Pernambuco (FACEPE) (No. IBPG-0676-4.05/25).

06.011FR **Outcomes of Rest Phase Time-Restricted Feeding on Phenotypic and Metabolic Parameters of Young Female Wistar Rats**. Barros CFN[1], Silva JCF[1], Franco ES[2], Souto VF[1], Feitoza LHS[1], Silva EKL[1], Francelino JO[1], Araújo FWC[1], Nascimento E[1]. [1]UFPE, Dept Nutrition, Brazil. [2]UFPE, Dept Physiology and Pharmacology, Brazil.

Circadian rhythms regulate metabolism and energy homeostasis, particularly in youth. Inverted feeding schedules can induce physiometabolic imbalances,promoting obesity, glycemic and lipid alterations, and hormonal dysregulation. In this context, the aim of this study is to investigate the effects of time-restricted feeding during the light phase on body weight, food intake, glycemia and lipemia of young female Wistar rats. Female Wistar rats (n = 17), aged 21 days, received a standard diet ad libitum for 8 weeks. From the 9th week onward, animals were divided into control (C, n = 7) and restricted (R, n = 10) groups. The R group was subjected to 12-hour time- restricted feeding during the rest (light phase) from the 9th to the 12th week. Euthanasia was performed in the 13th week. Statistical significance was considered at $p < 0.05$. Although significant differences in body weight were observed at week 1 (C = 65.04 ± 8.01 g; R = 82.46 ± 2.87 g; p = 0.0105) and week 8 (C = 178.41 ± 6.08 g; R = 199.75 ± 13.19 g; p = 0.0086), no significant differences were found between groups in the final week of the experiment (C = 201 ± 18.67 g; R = 208.20 ± 16.46 g; p = 0.9993). Weekly food intake showed a significant reduction of 42% in the R group compared with the C group in week 9 (C = 149.79 ± 9.54 g; R = 86.26 ± 14.03 g; $p < 0.0001$), and was 33% lower in the R group in week 13 (C = 113.74 ± 5.35 g; R = 76.02 ± 19.50 g; p = 0.0016). The total cholesterol was 48% higher in the R group compared with the C group (C = 58.82 ± 6.23 mg/dL; R = 87.60 ± 10.76 mg/dL; $p < 0.0001$). HDL levels increased by 48% (C = 42.68 ± 4.80 mg/dL; R = 63.50 ± 12.39 mg/dL; p = 0.0016). LDL levels also showed an increase of 149% in the R group compared to the C group (C = 6.89 ± 1.99 mg/dL; R = 17.18 ± 6.79 mg/dL; p = 0.0031). However, no significant differences were observed in the LDL/HDL ratio (Castelli Index II) between groups (C = 0.17 ± 0.06; R = 0.29 ± 0.16; p = 0.0963). In contrast, triglyceride levels were reduced by 52% in the R group compared with the C group (C = 47.56 ± 10.00 mg/dL; R = 22.60 ± 10.10 mg/dL; p = 0.0001). Likewise, plasm glucose levels did not differ between groups (C = 104.70 ± 15.62 mg/dL; R = 111.60 ± 16.00 mg/dL; p = 0.4092). Therefore, rest- phase time-restricted feeding in young female Wistar rats reduced food intake without decreasing body weight and increased of LDLc levels without altering cardiovascular risk. This study was supported by the Fundação de Amparo à Ciência e Tecnologia do Estado de Pernambuco (FACEPE) (No. IBPG-0676-4.05/25). Local Ethics Committee approval (No. 0017/2022). Local Ethics Committee approval (No. 0017/2022). This study was supported by the Fundação de Amparo à Ciência e Tecnologia do Estado de Pernambuco (FACEPE) (No. IBPG-0676-4.05/25).

06.012FR **Effects of Combined Physical Exercise and Symbiotic Supplementation on Gut Microbiome and Inflammasome-Related Genes in the Gut-Kidney Axis of Obese Rats**. Coutinho DO[1], Costa PCT[1], Freire MOL[1], Cruz Neto JPR[1], Magnani M[2], Vidal H[3], Alves JLB[1] [1]UFPB, Dept Nutrition, Health Sciences Center, PPG Nutrition Sciences, Brazil; [2]UFPB, Dept Food Engineering, Lab Microbial Processes in Foods, Brazil; [3]Claude Bernard Lyon 1 Université, CarMeN Lab, France

Introduction: Obesity is characterized by chronic low-grade inflammation and gut dysbiosis. The gut-kidney axis represents a relevant mechanism through which gut microbiome (GM) alterations may drive renal dysfunction in adverse metabolic contexts. However, the combined effects of aerobic exercise and synbiotic supplementation on GM composition and inflammasome-related gene expression along this axis remain poorly investigated in high-fat, high-sugar (HFHS) diet-induced obesity models. **Objective:** To evaluate the effects of combined aerobic physical exercise and synbiotic supplementation on GM composition and the expression of inflammasome-related genes in colon and kidney tissues of obese Wistar rats submitted to a HFHS diet. **Methods:** Male Wistar rats (n = 5 per group) were allocated into three groups: standard diet (SD), HFHS diet, and HFHS diet combined with aerobic exercise and synbiotic supplementation (HFHS+PE+Synb). Animals were maintained on their respective diets from postnatal day 21 to day 80. From day 80 to 120, rats in the HFHS+PE+Synb group received daily a synbiotic containing Limosilactobacillus fermentum strains 139, 263, and 296 (1.2×10^{10} CFU), quercetin (64 mg), and resveratrol (60 mg), and performed aerobic training on a treadmill. Inflammasome-related gene expression was assessed in colon and kidney tissues by RT-qPCR. GM composition was evaluated by 16S rRNA gene sequencing. Data are presented as mean ± standard deviation (SD). Parametric data were analyzed by one-way ANOVA followed by Tukey's post hoc test, using GraphPad Prism 10 ($p < 0.05$). **Results:** In colon tissue, the intervention significantly downregulated IL-1β gene expression ($p = 0.004$; $F = 9.42$), with no significant effects on NLRP3 ($p = 0.22$), Caspase-1 ($p = 0.25$), or TNF-α ($p = 0.15$). In kidney tissue, IL-1β expression was also significantly reduced ($p = 0.002$; $F = 10.45$), while Caspase-1 ($p = 0.95$) and TNF-α ($p = 0.49$) remained unchanged. Alpha diversity indices (Chao1 and Shannon) did not differ among groups ($p > 0.05$). Bray- Curtis analysis revealed significant differences in beta diversity ($p = 0.001$; $R^2 = 0.462$). The HFHS+PE+Synb group showed enrichment of Paraprevotella, Alistipes, and Parabacteroides, alongside reduced abundance of Coriobacteriaceae UCG-002 and Dubosiella ($p < 0.05$; $q < 0.05$). **Conclusion:** The combined intervention modulated GM composition and attenuated IL-1β expression in both colon and kidney tissues. These findings are consistent with a modulatory effect extending across the gut-kidney axis, in parallel with inflammatory gene suppression in both tissues. Overall, the results support non-pharmacological strategies as promising tools for managing obesity related metabolic dysfunction. **Acknowledgments:** The authors thank the Coordination for the Improvement of Higher Education Personnel (CAPES). This work was carried out with the support of the CAPES-COFECUB program.

06.013FR **Maternal Obesity Induced by an Obesogenic Diet Reduces Exercise Capacity and Increases Adiposity in Rats**. Silva RAA[1], Silva RL[2], Silva MLB[2], Oliveira PGS[3], Oliveira DKS[4], Lima DPO[6], Oliveira TRP[6], Antonio-Santos J[6], Da Silva Aragão R[6] [1]UFPE, PPG Nutrition, Brazil; [2]UFPE, Physical Education Undergraduation, Brazil; [3]UFPE, Nutrition Undergraduation, Brazil; [4]UFPE, PPG Nutrition, Physical Activity and Phenotypic Plasticity, Brazil; [5]FPS, Dept Physical Education, Brazil. [6]UFPE, Dept Physical Education, Brazil.

Introduction: Maternal obesity is associated with metabolic alterations. Models of diet-induced obesity provide an opportunity to investigate the effects of excessive adiposity on maternal metabolic status and physical performance. **Objective:** To evaluate the effects of maternal obesity and resistance training on metabolic, nutritional, and body composition parameters before mating, during pregnancy, and after lactation. **Methods:** Wistar rats were assigned to either a control diet (CD; 3.6 kcal/g, 14% fat; n = 9) or an obesogenic diet (OD; 4.6 kcal/g, 49% fat; n = 13), supplemented with condensed milk, for eight weeks before mating and throughout gestation and lactation. During pregnancy, half of the dams (CD-T and OD-T) performed resistance training on a ladder (5 days/week; 50% of maximal load during the first gestational week and 80% during the second and third gestational weeks), whereas the remaining dams constituted the untrained groups (CD-U and OD-U). **Results:** Before mating, dams fed the obesogenic diet exhibited higher body weight (302.8 ± 7.57 vs. 271.42 ± 9.15 g, p = 0.005), greater percentage weight gain (120.8 ± 7.32 vs. 95.45 ± 5.83%, p = 0.016), and impaired glucose tolerance, evidenced by higher blood glucose concentrations at 120 min during the glucose tolerance test (141.5 ± 21.3 vs. 106.3 ± 32.6 mg/dL, p = 0.04), despite lower food and energy intake (749.2 ± 26.9 vs. 1249 ± 32.6 g, p < 0.0001; 3887 ± 108.6 vs. 4496 ± 117.4 kcal, p = 0.002). During the first maximal load test performed in pregnancy, the OD-T group exhibited lower relative overload capacity than the CD-T group (155.05 ± 8.33 vs. 189.32 ± 0.57 g, p = 0.02). Lower food and energy intake persisted throughout gestation and lactation in obese dams gestation: OD-U 275.8 ± 25.5 vs. CD-U 530.9 ± 18.8 g, p = 0.0003; OD-T 303.6 ± 21.4 vs. CD-T 503.3 ± 26.9 g, p = 0.0001; Lactation: OD-U 587.7 ± 44.8 vs. CD-U 1232.1 ± 54.09 g, p < 0.0001; and OD-U 2910.8 ± 196.9 vs. CD-U 4435.6 ± 194.7 kcal, p = 0.0004; OD-T 634.8 ± 35.4 vs. CD-T 1190.4 ± 98.8 g, p < 0.0001; and OD-T 3103.5 ± 172 vs. CD-T 4285.5 ± 355.8 kcal, p = 0.01), although no differences in body weight or body weight gain were observed during these periods. After weaning, both OD-U and OD-T dams exhibited greater retroperitoneal adipose tissue accumulation than their respective control groups (absolute: OD-U 9.98 ± 0.91 vs. CD-U 2.64 ± 0.27 g, p = 0.0005; relative: OD-U 2.56 ± 0.91 vs. CD-U 0.94 ± 0.31%, p = 0.002; absolute: OD-T 6.50 ± 2.27 vs. CD-T 2.82 ± 1.00 g, p = 0.02). **Conclusion:** The obesogenic diet induced maternal obesity, characterized by increased body weight, adiposity and impaired glucose tolerance, associated with reduced relative exercise capacity at the beginning of the training protocol. Despite persistent reductions in food and energy intake, obese dams maintained increased adipose tissue accumulation throughout the reproductive period. Resistance training did not significantly modify the outcomes.

06.014FR **Metabolic Benefits of Tauroursodeoxycholic Acid, Alone or Combined with Resistance Exercise, in Aging Mice**. Carvalho MS, Zangerolamo L, Barrios NMF, Oliveira KM, Carneiro EM, Barbosa HCL. Unicamp, Obesity and Comorbidities Research Center, PPG Molecular and Morphofunctional Biology, Brazil. Université de Montréal, Dept Pharmacology and Physiology, Faculty of Medicine, Canada. Unicamp, Lab Nutrition and Cancer, PPG Molecular and Morphofunctional Biology, Brazil.

Introduction: Aging is associated with adverse metabolic changes, including increased adiposity, impaired glucose homeostasis, and reduced insulin sensitivity, which increases the risk of metabolic disorders. Physical exercise is among the most effective non-pharmacological strategies to counteract aging-related metabolic decline by improving insulin sensitivity, boosting energy expenditure, reducing chronic low-grade inflammation, and preserving lean mass. However, there is growing interest in combining exercise with complementary interventions, as exercise alone may not fully prevent metabolic dysfunction with age. Tauroursodeoxycholic acid (TUDCA) has emerged as a promising candidate due to its reported metabolic benefits in aging models. **Objectives:** Therefore, combining lifestyle and pharmacological interventions may be a more effective approach to address age-related metabolic decline. Here, we examined TUDCA alone or with resistance exercise (RE) on glucose homeostasis and metabolism in aged mice. **Methods:** C57BL/6J early-aging mice (18 months old) were divided into 4 groups: Old (i.p. PBS), TUDCA (i.p. TUDCA 300 mg/kg), RE (exercise + PBS), and T+RE (exercise + TUDCA). RE was performed once daily, 5 days/week, for 4 weeks. Each session consisted of 8 climbs at 4 loads (50, 75, 90, and 100% of each mouse's maximum load), administered alongside i.p. injections. **Results:** Mice in the TUDCA, RE, and T+RE groups showed reduced body weight gain from the fourth day of intervention. These groups also had less accumulation of white adipose tissue (iWAT and eWAT) and increased skeletal muscle mass (gastrocnemius, tibialis anterior, and quadriceps), along with improved whole-body strength (MVCC/grip strength). Additionally, serum triglyceride levels were reduced, and circulating IGF-1 levels were increased in treated and/or exercised mice. TUDCA and RE mice also presented elevated energy expenditure and increased BAT temperature, indicating enhanced energy metabolism compared to Old mice. Notably, only TUDCA mice, alone or combined with exercise, demonstrated improved glucose tolerance and insulin sensitivity, as well as enhanced muscle-specific insulin sensitivity (all $p<0.05$), compared to both Old and RE groups. **Conclusion:** Taken together, our findings indicate that both TUDCA and resistance exercise exert beneficial effects on body weight regulation, adiposity, and energy expenditure in aging mice. Importantly, TUDCA appears to be more effective in improving glucose homeostasis and insulin sensitivity, supporting its potential as an adjunct therapy for age-related metabolic dysfunction. Animal Research Ethical Committee Number: 6405-1/2024. **Financial support**: FAPESP nº: 2024/02598-5.

06.015FR **Sexual Dimorphism in Thermoregulatory and Metabolic Responses in Cycling Rats and male**. Lopes RA[1],2; Melo MTB[1], Salustiano IM[1], Morgado VCC[1], Noronha GL[1], Martins JA[1], Santos JCS[1], Brandão CF[1,2], Lacerda LT[1,2], Andrade MJO[1,2], Campos HO3, Leite LHR4, Coimbra CC5, Lopes RA[1],2, Drummond LR[1],2[1]UEMG-Divinópolis, Brazil, [2]PPG em Biociências e Saúde Humana; Brazil; 3UEMG-Ubá, Brazil; 4UFJF, Brazil; 5UFMG, Brazil

Introduction: Rats, like women, exhibit cyclical variations in ovarian steroid levels throughout estrous cycle, which is divided into proestrus (P), estrus (E), diestrus I and II (D). The thermoregulatory and metabolic axes appear to be interconnected via gonadal steroids, but this is not fully understood. **Objectives:** To evaluate if hormonal variations during the estrous cycle of rats influence thermoregulation and metabolism, as well as to investigate possible sexual dimorphism in these parameters. **Methods:** Male and female Wistar rats from the Animal Science Center (CCA) of the Federal University of Ouro Preto were transferred to the animal facility of the Experimental Exercise Physiology Laboratory (LAFEEX) at the State University of Minas Gerais (UEMG), Divinópolis. The procedures were approved by the Ethics Committee on Animal Use (protocol - 002/2025). Vaginal smears were taken daily during 4 weeks. The rats underwent surgery for implantation of the abdominal and tail temperature sensor. The animals were kept in metabolic cages during D (n=14), P (n= 5), and E (n=14). Ti was recorded by telemetry for 24 h, and Tc was recorded by the Tag reader every 30 min from 7am to 6 pm. The male rats (M; n=17), were subjected to the same experimental protocol as the females. Data were presented as mean ± S.D.M. **Results:** The frequency of P (21.87±6.26) was lower than D (32.9±11.75) and E (37.96±11.13); p<0,0001. The variation of Ti followed a circadian pattern in all groups (p<0.0001). Tc showed a significant interaction between cycle and time (p<0.001). At 3pm, Tc was lower in M (31.59±1.17 °C) vs D (33.32±1.64 °C), P (32.38 ± 1.32 °C), and E (33.15 ± 1.76 °C); $p < 0.005$. At 5pm, Tc in D (33.72 ± 1.76 °C) was higher than M (32.21 ± 1.20 °C); $p < 0.005$. There was an interaction between time of the day and VO2 consumption (p<0.005). The VO_2 was lower at 9am of D (14.22±1.18) vs P (18.82±4.38), E (18.80±3.44), and M (17.21±2.82); p<0.001; at 10am of D (13.18±0.77) vs P (16.19±3.56) and M (15.39±2.69); p<0.005; at 11am of D (12.34±1.0) vs P (13.82±1.64), E (15.17±3.13), and M (14.31±2.57); p<0.005; in D midday (11.69±1.30) vs E (13.81±1.87) and M (13.41±1.73); p<0.005; at 1pm: D (11.22±1.59) vs P (12.88±1.38) and E (13.37±1.85); p<0.005; at 2pm: D (11.24±1.61) vs P (13.00±1.58) and E (13.38±1.73); p<0.05; and at 3pm: D (11.76±1.73) vs E (13.49±1.48); p<0.005. VO_2 was higher at 9pm: P (18.62±1.57) vs M (16.73±1.53); p<0.005; at 1am h: E (18.57±1.51); p<0.005; at 4am: P (19.07±2.29) and E (18.94±1.75) vs M (15.91±1.82); p<0.0001; at 5am P (18.90±2.70) and E (18.93±1.68) vs M (16.00±2.40); p<0.001; and at 7am: E (15.53±1.93) vs M (13.23±1.85); p<0.005. For RQ, a significant difference was observed only in D midday (0.93±0.06) vs P (0.85±0.08) and E (0.84±0.06); p<0.005. **Conclusion:** Hormonal fluctuations during the estrous cycle of rats promote sexual dimorphism in the Tc and VO2 parameters.

07. Endocrine, Reproductive and Urinary Pharmacology

07.001 **Effect of Systemic Matrix Metalloproteinases Blocking in A Pre-Clinical Model of Menopause**. Baltazar RS[1], Pozes AB[1], Mendes, L. [1], Gonçalves, F. [1], Santos CED[1], Filho FLS[1], Maranhão, M[1], Santos, MLF[1], Belfort MFA[1], Palhano NBM[1], Moreno AVP[1], Borges, MOR[12], Borges, ACR[12],Oliveira RMGC[1], Brito HO[1] [1]UFMA, Research Center For Experimental and Clinical Physiopathology and Pharmacology (NEC), Bioanalyses Lab (LabIO), Brazil; [2]UFMA, Pharmacology Lab, Federal University of Maranhão, Brazil

Introduction: Menopause is associated with physical and psychological symptoms resulting from hormonal decline. During this stage, extracellular matrix disruption may contribute to tissue damage and functional alterations, favoring the development of pathological conditions. Therefore, new pharmacological targets should be investigated to improve therapeutic approaches for menopausal patients. **Objectives:** To evaluate the effects of metalloproteinases inhibition on menopausal symptoms in ovariectomized animals. **Methodology:** Wistar rats and Swiss mice underwent sham-operated (SHAM) or ovariectomy (OVX) surgeries and were distributed into six groups: SHAM treated with saline; SHAM treated with doxycycline; OVX treated with saline; OVX treated with doxycycline; OVX treated with estrogen-progestogen therapy; and OVX treated with doxycycline associated with estrogen-progestogen therapy. Treatments were administered for 30 days. Body weight, feed intake, adipose and uterine tissue weight, serum biochemical parameters, hot flushes induced by physical exercise, and estrous cycle were evaluated. Statistical analyses were performed using ANOVA followed by Bonferroni's test using GraphPad Prism 6.0, considering $p<0.05$ as statistically significant. **Results:** Animals treated with doxycycline associated with estrogen-progestogen therapy showed increased alkaline phosphatase, magnesium, total cholesterol, creatinine, adipose tissue weight, and uterine weight. In the same group, reduced cutaneous body temperature variation and increased frequency of the diestrus phase were also observed. No statistically significant differences were found regarding total serum proteins, urea, triglycerides, TGO, TGP, body weight, or feed intake. Metalloproteinases appear to play a relevant role in some menopausal symptoms, especially when doxycycline is associated with estrogen-progestogen therapy. **Conclusion:**These enzymes may participate in the modulation of renal, hepatic, bone, obesity-related, uterine, and vaginal alterations, as well as hot flushes associated with menopause.

07.002 Evaluation of the Effects of *Morus nigra* L. (Black Mulberry) in Animal Models of Menopausal-Hot Flashes.
Cavalcante DCS, Rodrigues TAR, Santos CED, Bezerra HRR, Lima LAS, Bastos HAC, Belfort MFA, Palhano NBM, Baltazar RS, Moreno AVP, Borges, MOR, Borges, ACR, Oliveira RMGC, Brito HO UFMA, Research Center for Experimental and Clinical Physiology and Pharmacology, Bioanalyses Lab, Pharmacology Lab, Brazil

The transition between reproductive and non-reproductive stages in a woman's life is called climacteric, this involves a myriad of physical, endocrine and psychological changes that are influenced by ethnic, psychological and sociocultural factors. For the treatment of these outcomes, hormone replacement therapy (HRT) is used, however, there are several side effects, with contraindications, such as previous treatment of hormone-dependent tumors and history of previous thromboembolic events. Alternatives to HRT include herbal medicines such as Morus nigra L., a plant species used to combat menopausal symptoms, whose leaves contain phytoestrogenic substances. This study was of the randomized experimental type, with the experimental protocols approved by the CEUA of the Federal University of Maranhão. The objective of this work was to evaluate the effect of the chronic treatment of the aqueous (FAQ) and ethyl acetate (FACET) fractions of Morus nigra L. leaf extract in animals with hypoestrogenism. For the experiments, rats of the species Rattus norvegicus, Wistar strain and female *Mus musculus* Swiss strain mice, from the Central Animal Facility of the Federal University of Maranhão (UFMA), were used. The animals were divided into 05 groups: False operated (SHAM); Saline- treated ovariectomized patient (OVX-SAL); Ovariectomized treated with an aqueous fraction of 100 mg/kg (OVX-FAQ); Ovariectomized treated with 400 mg/kg acetate fraction (OVX-FACET); Ovariectomized treated with estrogen associated with medroxyprogesterone 1 mg/Kg (OVX-E2+P). During treatment (30 days) the estrous cycle, body weight and body temperature were measured. At the end, the serum and hormonal biochemical parameters of the samples were evaluated. The OVX-SAL group exhibited a significant negative change in body weight, total fat, lipid profile and in different hormone markers, eg estradiol and FSH. A significant increase in skin temperature and reduction in serum calcium levels was also found compared to the SHAM group. Changes in the estrous cycle and uterine atrophy were also observed. The OVX-E2+P group significantly improved these deleterious effects of hypoestrogenism compared to the OVX-SAL group. On the effect of treatment with fractions of M. nigra in relation to body weight and total fat, it was observed that this significant reducing effect with the two fractions of M. nigra. In addition, the positive effect on the lipid profile of the animals that received the two fractions of M. nigra was remarkable. However, the OVX-FACET group was more efficient in controlling hot flashes, fat accumulation, lipid and hormonal profile. Thus, it is concluded that the two fractions of M. nigra have beneficial anti-osteoporotic, anti- dyslipidemic and anti-atherosclerotic effects. However, more studies should be carried out regarding the effect of estrogenic activity on the main symptoms of menopause.

07.003 **Low-Dose Cannabidiol plus β-Estradiol Improve Symptoms Compared with Estrogen Replacement Therapy in a Rat Model of Menopause**. Santos CED[1], Moreno AVP[1], Bezerra HRR[1], Belfort MFA[1], Palhano NBM[1], Baltazar RS[1], Borges, MOR[1,2], Faria, M[1], Teixeira, CVP[1], Crippa, A[3], Hallak, JEC[3], Borges, ACR[1,2], Brito HO[1]. [1]NEC-UFMA, Research Center for Experimental and Clinical Physiopathology and Pharmacology, Brazil; [2]UFMA, Pharmacology Lab, Brazil; [3]FMRP-USP, Brazil

Introduction: The climacteric is characterized by hormonal alterations that frequently reduce quality of life due to symptoms such as hot flushes and metabolic disturbances resulting from estrogen deficiency. Therefore, new therapeutic strategies, including phytocannabinoids, have been investigated as alternatives or adjuncts to conventional hormone replacement therapy. **Objectives:** To evaluate the effects of chronic treatment with cannabidiol (CBD), a derivative of Cannabis ativa, on menopausal symptoms in an ovariectomized animal model. **Methods:** A randomized experimental study was conducted using ovariectomized Wistar rats. Animals were allocated into five groups: SHAM treated with mineral oil; OVX VEHICLE; OVX E2 treated with β-estradiol (1 mg/kg); OVX CBD treated with cannabidiol (10 mg/kg); and OVX CBD E2 treated with low-dose β-estradiol (0.5 mg/kg) plus cannabidiol (5 mg/kg). During the 15-day treatment period, estrous cycle, body weight, and caudal skin temperature were monitored. At the end of the experiment, biochemical, hormonal, and histological analyses were performed. **Results:** The OVX VEHICLE group exhibited significant increases in body weight, total cholesterol, follicle-stimulating hormone (FSH), caudal skin temperature, and uterine atrophy, accompanied by reduced estrogen levels. The OVX E2 group significantly attenuated these alterations. The OVX CBD E2 group showed significant improvements in body weight, total cholesterol, and estrogen levels, in addition to presenting the lowest degree of uterine atrophy among ovariectomized groups. Furthermore, 57.14% of the animals remained in the estrus phase, indicating preservation of reproductive cyclicity. **Conclusion:** Cannabidiol demonstrated relevant effects on menopausal symptoms, especially when combined with low-dose β-estradiol. These findings suggest a potential therapeutic role for cannabidiol in menopause and reinforce the need for further studies to clarify the mechanisms involved.

07.004 **COX-Derived Prostanoid Signaling Mediates the Anticontractile Effect of MRPs Inhibition in Human Prostatic Tissue**. Cardoso JS[1], Passos GR[1], Moretti, MB[1], D'Ancona CA2, Fregonesi A2, Antunes E[1], Monica FZ[1] [1]FCM-Unicamp, Dept Pharmacology, Brazil; [2]Dept Surgery (Urology), Brazil

Introduction: Benign prostatic hyperplasia (BPH) is a highly prevalent condition in older men, characterized by proliferation of epithelial and stromal cells and associated with lower urinary tract symptoms (Berry et al., 1984; Roehrborn, 2008). Prostatic smooth muscle tone is regulated, among other mechanisms, by cyclic nucleotide signaling pathways involving cAMP and cGMP (Christ & Andersson, 2007). While phosphodiesterases hydrolysis these cyclic nucleotides, multidrug resistance proteins 4 and 5 (MRP4 and MRP5) actively transport them out of the cytosol. The MRP inhibitor MK571, studied *in vitro* (Bertollotto et al., 2018; de Oliveira et al., 2023; Gomes et al., 2024; Passos et al., 2025) and *in vivo* (de Oliveira et al., 2023), reduces smooth muscle reactivity in bladder, prostate, and corpus cavernosum by increasing intracellular cAMP/cGMP. In addition to cyclic nucleotides, MRP4 actively exports prostaglandin E_2 (PGE_2), a cyclooxygenase-derived prostanoid involved in the regulation of cAMP signaling (Reid et al., 2003). Therefore, we investigated whether prostanoid signaling contributes to the effects of MRP inhibition on prostatic smooth muscle contractility. **Methods:** Prostatic tissue was obtained from patients with BPH undergoing **Transurethral Resection of the Prostate (TURP)**. Tissue strips were mounted in a myograph, and concentration–response curves to phenylephrine (Phe) were generated in the absence or presence of the MRP inhibitor MK571 (20 μM), alone or combined with inhibitors of cyclooxygenase (indomethacin, 1 μM), cyclooxygenase-2 (celecoxib, 1 μM), leukotriene synthesis (zileuton, 6 μM), or antagonists of EP2 (TG6-10, 1 μM), EP4 (ONO-AE3-208, 100 nM), and IP (CAY10441, 1 μM) receptors. MRP4 and MRP5 expression was evaluated by immunohistochemistry in healthy and hyperplastic prostate tissues. **Results:** The anticontractile effect of MK571 was attenuated by indomethacin (Emax: 110.0 ± 24.5; n = 6), celecoxib (Emax: 109.7 ± 46.0; n = 6), CAY10441 (Emax: 95.1 ± 26.9; n = 6), and ONO-AE3-208 (Emax: 107.7 ± 40.0; n = 5). In contrast, TG6-10 (Emax: 72.1 ± 29.6; n = 5) and zileuton (Emax: 78.7 ± 50.7; n = 5) did not significantly affect the response. MRP4 expression was significantly higher in hyperplastic than in histologically normal stromal smooth muscle from TURP specimens (32.51 ± 5.09 vs. 16.35 ± 5.39; $p = 0.004$; n = 4), whereas MRP5 expression did not differ between hyperplastic and histologically normal tissues (38.66 ± 3.58 vs. 34.18 ± 2.67; n = 4). **Conclusion:** Our findings suggest that the anticontractile effect of MRP4 inhibition involves COX-derived prostanoid signaling, likely through Gs-coupled receptors associated with increased intracellular cAMP. **Financial support:** FAPESP 2026/09119-0; 2022/11621-5

07.005 **Full-Spectrum Cannabis Oil Combined with Insulin Promotes Glycemic and Antioxidant Benefits in an Experimental Model of Type 1 Diabetes Mellitus**. Barboza, ACS[1], Martins, JRN2, Silva ALM[1], Carmo DMQ[1], Lima GGS[1], Oliveira CC[2], Silva JGG[2], Cruz JC[1] [1]UFPB, [2]APEPI – Associação de Apoio à Pesquisa e Pacientes de Cannabis Medicinal, Rio de Janeiro, Brasil

Type 1 diabetes mellitus (T1DM) is an autoimmune disease characterized by pancreatic β-cell destruction, resulting in insulin deficiency, chronic hyperglycemia, and metabolic, inflammatory, and oxidative alterations. Although insulin therapy is essential for glycemic control, it does not fully prevent diabetes-associated complications, highlighting the need for adjunctive therapeutic strategies. In this context, cannabidiol (CBD), a non- psychoactive phytocannabinoid derived from *Cannabis sativa*, exhibits antioxidant and anti-inflammatory properties that may be beneficial in T1DM. Therefore, this study evaluated the effects of a CBD-rich Cannabis oil administered alone or in combination with insulin on metabolic, biochemical, and oxidative parameters in an experimental model of T1DM. T1DM was induced in Wistar rats by streptozotocin administration (65 mg/kg, i.p.). Animals were allocated into five groups (n/group = 8–10): non-diabetic controls, diabetic rats treated with vehicle, diabetic rats treated with CBD-rich Cannabis oil (30 mg/kg, intragastric gavage, twice daily), diabetic rats treated with insulin plus vehicle (5 IU/day, i.p.), and diabetic rats treated with insulin plus CBD-rich Cannabis oil for 14 days. Metabolic parameters, including fasting and postprandial glycemia, water and food intake, and insulin sensitivity (kITT), were evaluated. Serum biochemical parameters, including lipid profile, fructosamine, albumin, uric acid, creatinine, and alanine aminotransferase (ALT), were measured using commercial diagnostic kits. Oxidative stress in liver and heart tissues was indirectly assessed through lipid peroxidation by quantifying malondialdehyde (MDA) levels using the thiobarbituric acid reactive substances (TBARS) assay. Compared with vehicle- treated diabetic rats, CBD treatment alone did not reduce fasting glycemia (AUC: 606.20 ± 43.44 vs. 592.5 ± 36.07), but significantly decreased postprandial glycemia (AUC: 804.2 ± 38.34 vs. 1496 ± 51.38). Combined therapy potentiated the effects of insulin treatment, reducing fasting glycemia (AUC: 218.7 ± 12.48 vs. 592.5 ± 36.07) and postprandial glycemia (AUC: 812.2 ± 51.04 vs. 1496 ± 51.38). Furthermore, it increased insulin sensitivity, as evidenced by kITT values (1.45 ± 0.410 vs. 0.60 ± 0.09 %/min), and reduced polydipsia (136.38 ± 2.98 vs. 245.09 ± 15.30 mL/24 h) and polyphagia (36.76 ± 0.95 vs. 58.49 ± 2.30 g/24 h). No significant changes were observed in the lipid profile, fructosamine, albumin, uric acid, or creatinine levels. However, the combination of insulin and CBD significantly reduced serum ALT levels (7.23 ± 0.62 vs. 21.84 ± 4.58 U/L), as well as MDA levels in the liver (0.95 ± 0.12 vs. 3.05 ± 0.38 nmol/mg protein) and heart (1.98 ± 0.23 vs. 3.72 ± 0.40 nmol/mg protein). Collectively, these findings demonstrate that CBD-rich Cannabis oil enhances the metabolic effects of insulin therapy and attenuates oxidative stress and liver damage associated with T1DM, supporting its potential as an adjunctive therapeutic strategy for the management of the disease. Animal Ethics Committee Approval No. 6271110324.

07.006 *Arthrospira platensis* **Prevents Oxidative Stress and Testicular Alterations in Wistar Rats Subjected to a Hypercaloric Diet**. Melo MB[1], Sousa-Filho JEC[1], Barros BC[1,2], Arruda RRA[1,2], Silva JMA[1,2], Santos TJ[1], Claudino BFO[1,2], Barbosa YV[1,2], Diniz AFA[1,2], Alves AF[2,3], Silva BA[1,2,3] [1]UFPB, Lab Functional Pharmacology Prof. George Thomas, Institute of Research in Drugs and Medicines, Brazil; [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil; [3]UFPB, Dept Biomedical Sciences, Health Sciences Center, Brazil; [4]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil

Obesity is a metabolic disease associated with low-grade chronic inflammation and systemic redox imbalance, conditions that impair testicular homeostasis and may negatively affect male fertility. Excess reactive oxygen and nitrogen species, together with insufficient endogenous antioxidant defenses, promote lipid peroxidation, cellular damage, and structural dysfunction of the seminiferous epithelium. In this context, *Arthrospira platensis* (AP) stands out as a cyanobacterium rich in bioactive compounds with well-recognized antioxidant and anti-inflammatory activity, although its protective effects on testicular tissue under obesity conditions are still not fully understood. Thus, this study investigated the preventive potential of AP on oxidative stress and histomorphometric alterations in the testes of male Wistar rats subjected to a hypercaloric diet. Animals were distributed into four groups (n=5): standard diet (SD), SD supplemented with AP (SD+AP25), hypercaloric diet (HCD), and HCD supplemented with AP (HCD+AP25). Powdered AP was suspended in saline (0.9% NaCl) to provide a dose of 25 mg/kg. The suspension was administered daily by intragastric gavage for 8 weeks. After euthanasia, testes were collected for histomorphometric analysis using hematoxylin and eosin staining and for biochemical assessment of nitrite, NOx (nitrite+nitrate), and antioxidant enzyme activities, including superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) by spectrophotometry. Animals in the HCD showed increased nitrite levels (172.9 ± 3.8 µM/g) and NOx (657.0 ± 26.0 µM/g) compared with the SD (108.1 ± 15.8 µM/g; 447.0 ± 28.9 µM/g, respectively), indicating testicular nitrosative stress. AP supplementation prevented this increase in the HCD+AP25 (120.7 ± 10.9 µM/g and 374.3 ± 36.1 µM/g, respectively). In addition, antioxidant enzyme activities (SOD, CAT, and GPx) were reduced in the HCD (2.2 ± 0.2 U/mL; 70.7 ± 4.1 nmol/min/mL; 1.4 ± 0.2 mol/min/mL, respectively) compared with the SD (2.8 ± 0.05 U/mL; 108.8 ± 3.4 nmol/min/mL; 2.6 ± 0.2 mol/min/mL, respectively), an effect prevented by AP supplementation (2.9 ± 0.05 U/mL; 93.6 ± 1.4 nmol/min/mL; 2.8 ± 0.3 mol/min/mL, respectively). Histomorphometric analysis showed a reduction in seminiferous tubule area in the HCD (5946.0 ± 182.4 μm^2) compared with the SD (7698.0 ± 292.2 μm^2), which was prevented in the HCD+AP25 (6974.0 ± 87.8 μm^2). The number of Leydig and Sertoli cells was also reduced in the HCD (1.9 ± 0.2 and 6.6 ± 0.6, respectively) compared with the SD group (3.8 ± 0.5 and 10.6 ± 0.8), with partial restoration by AP supplementation (3.0 ± 0.2 and 12.0 ± 1.0, respectively). Thus, *Arthrospira platensis* prevents redox imbalance and hypercaloric diet-induced testicular alterations, preserving antioxidant defenses, reducing nitrosative stress, and attenuating histomorphometric damage, suggesting a potential therapeutic role in obesity- associated testicular dysfunction.

07.007 **Effects of Topiramate on Rat Sperm Parameters**. Chaves HJC, Sena MO, Carvalho YV, Costa ML, Gavioli EC, Silva-Junior ED UFRN, Dept. of Biophysics and Pharmacology, Brazil.

Introduction: The effects of topiramate, a widely used anticonvulsant, on male fertility are not fully understood, especially considering the epididymis as a potential target. **Objectives:** Evaluate the effect of *in vivo* treatment with topiramate on testicular and epididymal sperm parameters. **Methods:** Wistar rats were divided into groups and subsequently treated orally via gavage with saline (control) or topiramate (40 or 160 mg/kg) for 21 days. After euthanasia, the testes and epididymides were isolated and processed to determine daily sperm production (DSP), sperm transit time throughout the epididymis, and sperm concentration in different epididymal regions. Data are expressed as mean ± S.E.M. Statistical significance was assessed using one-way ANOVA followed by Dunnett's test ($p < 0.05$). **Results:** The results demonstrated that topiramate 160 mg/kg significantly reduced the number of spermatids and daily sperm production, indicating impaired testicular spermatogenesis. In the caput/corpus segment of the epididymis, a significant reduction in spermatozoa number was observed only in the group topiramate 160 mg/kg. In the cauda epididymis, the number of spermatozoa was similar among the groups. However, sperm transit time was significantly increased at both tested doses. **Conclusion:** The data indicate that topiramate may impair reproductive capacity in rats by reducing testicular sperm production and altering sperm transit time in the epididymis.

07.008 **Evaluation of the Effects of an Incretin Mimetic on Depressive-Like and Compulsive-Like Behaviors in a Murine Model of Early Diet-Induced Obesity**. Lemos IL[12], Silva JGM[12], Weber IH[2], Moraes GR, Silva ABC[1], Miranda KKB[1], Bellozi PMQ[1] [1]UnB, Faculty of Health Sciences, Brazil, [2]UnB, Institute of Biological Sciences, PPG Animal Biology, Brazil

Introduction: Type 2 diabetes mellitus (T2DM) and obesity represent growing challenges to global public health, as they are associated with significant metabolic alterations and central nervous system (CNS) dysfunction. Tirzepatide (TZP), a dual GIP/GLP-1 receptor agonist, has gained attention due to its beneficial effects on glycemic control and adiposity reduction. However, the effects of TZP on obesity-associated behavioral alterations, particularly in young female individuals, remain poorly understood. **Objective:** To evaluate the effects of TZP on metabolic and behavioral alterations associated with exposure to a high-fat diet (HFD) in female C57BL/6 mice. **Methods:** The study was approved by the Animal Ethics Committee of the University of Brasília (CEUA/UnB; SEI No. 23106.067420/2023-98). Five-week-old female C57BL/6 mice were allocated to groups receiving either a control diet (CD; 15% lipids) or a HFD (45% lipids) for 10 weeks. During the last four weeks of the protocol, animals received tirzepatide (TZP; 10 nmol/kg/day, subcutaneously) or vehicle. Thus, the experimental groups were: CD + Vehicle, CD + TZP, HFD \+ Vehicle, and HFD \+ TZP. Metabolic parameters were assessed through body weight monitoring, food intake, and the glucose tolerance test (GTT). Behavioral parameters were evaluated using the Splash Test and the Marble Burying Test. Data were analyzed using two-way ANOVA, with $p < 0.05$ considered statistically significant. **Results:** HFD promoted greater body weight gain compared with the CD from the sixth week after diet Introduction: onward. During treatment, TZP reduced body weight in both groups, with a more pronounced effect in HFD+TZP animals compared with CD+TZP animals. TZP significantly reduced food intake during the first week of treatment. Over the subsequent three weeks, the CD+TZP group maintained lower food intake than its respective control group, although with attenuation of the initial effect, whereas the HFD+TZP group exhibited a sustained reduction in food intake throughout the treatment period. In addition, TZP improved glucose tolerance, as demonstrated by the GTT. In the Splash Test, HFD induced behavioral alterations consistent with impaired self-grooming. However, TZP-treated groups showed a positive influence on this parameter, suggesting modulation of behaviors associated with a depressive- like phenotype. In the Marble Burying Test, TZP significantly reduced marble- burying behavior, indicating attenuation of behaviors associated with compulsivity. **Conclusions:** Tirzepatide promoted significant metabolic improvement and exerted beneficial effects on behaviors associated with depressive-like and compulsive-like phenotypes.

07.009 **Assessing Temporal Effects of Bladder Dysfunction in C57BL/6JUnib Mice Using Multiple-Low Dose of Streptozotocin-Induced Diabetes**. Barbalho TM, Horioka CP, Leutz MC, Medeiros ML, Oliveira AL, Antunes E. Unicamp, PPG Farmacologia, Brasil.

Diabetes mellitus (DM) leads to severe lower urinary tract complications, such as diabetic bladder dysfunction (DBD), which affects over 50% of patients. DBD progresses from an initial phase of hypercontractility to a late phase of bladder emptying failure. The objective of this study was to characterize DBD in male C57BL/6JUnib mice with streptozotocin (STZ)-induced DM, using the void spot assay (VSA; 4 h/day/4 days) as a non-invasive tool to monitor the transition between the bladder hyperactivity and decompensation phases. Animals were divided into Control (CT) and DM groups (Ethical approval no. 6770-1/2025). DM group received STZ (40 mg/kg, i.p., 5 consecutive days) whereas CT received citrate buffer alone. Fasting blood glucose (FBG) was measured 48h after induction. After 4 to 12 weeks, VSA was analyzed as total/mean volume, number of spots, and distribution (corners/center). *In vitro* bladder contractility in response to KCl (80 mM), electrical-field stimulation (EFS), and carbachol (CCh) were also investigated. Data (Mean ± SEM) were analyzed by unpaired Student's t-test. Compared to CT groups, STZ at 4 weeks showed a 12.6% reduction in body weight ($p<0.05$), concomitant with significant increases ($p<0.05$) in relative bladder weight, FBG and ketone levels by 27%, 368% and 108%, respectively. STZ group also exhibited polydipsia and polyuria, with increases in total void volume (80.5%, $p<0.05$) and spot numbers (95%, $p<0.05$), especially in the center region of the filter paper ($p<0.05$), indicating an altered voiding pattern. Similar reductions in body weight and increases in relative bladder weight, along with increases in FBG and ketone levels were observed at 8 and 12 weeks of STZ (n=6-11). At 4 weeks STZ, the *in vitro* bladder contractions to CCh were elevated in STZ compared with CT group (Emax = 2.6±0.37 and 2.0±0.29 mN/mg, respectively). Similarly, EFS-induced contractions were higher in STZ compared with CT groups (32Hz: = 3.2±0.55 and 2.6±0.36 mN/mg, respectively), whereas no differences were found in KCl-induced contractions. At 8 and 12 of STZ (n=6-11), no significant alterations in bladder contractions induced by CCh at the level of Emax (8 weeks: 1.1±0.18 and 1.0±0.17 mN/mg control and STZ, respectively; 12 weeks: 1.3±0.17 and 1.3±0.19 mN/mg control and STZ, respectively). Likewise, the EFS (32Hz) - induced contractions at 8 and 12 weeks of STZ (1.6±0.37 and 1.8±0.27, respectively) did not significantly differ from control and (1.7±0.36 and 2.0±0.32, respectively). In summary, our findings indicate that 4 weeks STZ induces some degree of bladder hyperactivity, likely reflecting the initial compensatory state of DBD in mice. At 8 and 12 weeks STZ, bladder hyperactivity is not observed anymore, suggesting a progression to the decompensated, hypoactive, phase of diabetes. The effect of STZ at 16 weeks on mouse DBD is under current investigation. Financial Support: CAPES.

07.010 **Effect of Taurine on Time in Range in Individuals with Type 2 Diabetes Mellitus: A Secondary Analysis of a Randomized Clinical Trial**. Bispo ACC, Vidal BA, Cavalheiro LS, Selau B, Laurentino AOM, Leal MB, Bock PM, Gomez R. UFRGS, ICBS, PPG em Farmacologia e Terapêutica, Brasil.

Introduction: Taurine has been proposed as an adjuvant for glycemic control in type 2 diabetes mellitus (T2DM) due to its antioxidant and anti-inflammatory properties. In a randomized clinical trial, its effects were assessed using both conventional glycemic parameters and continuous glucose monitoring (CGM), allowing a detailed evaluation of daily glucose patterns. **Objective:** To investigate the effect of taurine supplementation on Time in Range (TIR) over 14 days in individuals with T2DM monitored with a CGM. **Methods:** This secondary analysis used data from a double-blind, randomized, placebo-controlled clinical trial conducted in individuals with T2DM (CEP/HCPA: 4380148). Participants received taurine (6 g/day) or placebo for 90 days. During the final 14 days of the intervention, interstitial glucose levels were continuously monitored using the FreeStyle Libre® system. CGM-derived metrics, including TIR (70–180 mg/dL), Time Above Range (TAR), and Time Below Range (TBR), were obtained through the LibreView® platform and compared between groups. Data normality was assessed using the Shapiro-Wilk test, and between- group comparisons were performed using the Mann-Whitney test in SPSS, with $p < 0.05$ considered statistically significant. **Results:** Of the 94 participants initially randomized, 86 completed the study. Among these, 69 had valid CGM data for this secondary analysis (placebo: n = 31; taurine: n = 38), 52.2% were men, and the mean age was 57.2 years ± 9.5 years. Both groups showed comparable baseline characteristics, with no significant differences in HbA1c (8.5 vs. 8.3%), fasting glucose levels (184.5 ± 55.3 vs. 185.9 ± 46.2 mg/dL), or glycemic variability coefficient (27.1 ± 5.1 vs. 27.4 ± 6.5%). TIR was below the recommended target (53.9 ± 27.9 vs. 51.6 ± 28.3%; p = 0.534), while TAR was elevated (44.9 ± 28.9 vs. 49.2 ± 29.9%) in both groups, indicating prolonged exposure to hyperglycemia status. In contrast, TBR values were low (1.1 ± 3.8 vs. 1.1 ± 3.2%; p = 1.000), indicating infrequent hypoglycemic episodes. **Conclusion:** In this secondary analysis, taurine supplementation did not significantly affect CGM-derived glycemic parameters in individuals with T2DM. Mean TIR values remained below the recommended target in both groups, suggesting persistent inadequate glycemic control.

07.011 **Effects of Lycopene on the Morphometry of Seminiferous Tubules in Diabetic Rats**. Gomes PD, Medeiros BC, Mota LSF, Silva JL, Leite TCR, Lima WG, Paula-Gomes S, Morais DB. UFRN, UFOP.

Introduction: Lycopene, a natural antioxidant found in our diet, has been associated with protective properties for various body tissues, such as testicles. This tissue is severely impacted in cases of diabetes, compromising male fertility, even in patients treated with Metformin. **Objectives:** To evaluate the ability of Lycopene to prevent testicular damage in diabetes, with emphasis on seminiferous tubule morphometry. **Methods:** Twenty adult Wistar rats were distributed into the experimental groups: C-Control (normoglycemic rats treated with natural yogurt), DM-Diabetes Mellitus (diabetic rats treated with natural yogurt), L-Lycopene (45 mg/kg/day in natural yogurt), and M-Metformin (250 mg/kg/day in natural yogurt). After a 40-day experimental period, the animals were euthanized for testicular collection, followed by histological processing for paraffin embedding, HE staining, and histomorphometric analysis (ImageJ®). Variables were subjected to Shapiro-Wilk normality test followed by one-way ANOVA and SNK post-hoc test, or Kruskal-Wallis test followed by Dunn's post-hoc test, (5% significance level). **Results:** Significant weight loss ($p<0.05$) was observed in body weight (BW) and gonadal weight (GW) in animals from the DM (BW and GW, respectively, 229.00±16.93 and 2.86±2.65), L (BW and GW, respectively, 289.60±17.18 and 3.29±3.16) and M (BW and GW, respectively, 298.67±10.10 and 1.70±1.60) groups, compared to C (BW and GW, respectively, 327.40±17.52 and 3.59±3.52); while in the L and M treatments, a higher BW was observed compared to animals with DM ($p<0.05$). The tubulosomatic index (TSI) was significantly higher in DM (1.03±0.21) compared to C (0.77±0.10), indicating an attempt by the seminiferous tubule (ST) to maintain its activity in face of diabetes. Comparing groups M and C, M showed higher percentages of ST (86.02±2.61 versus 70.07±7.26) and seminiferous epithelium (60.63±2.00 versus 49.86±5.96), as well as a higher percentage of tubular lumen in M (19.35±1.60) compared to the other groups ($p<0.05$). The diameter of the ST was also larger in M (217.50±5.45) and L (195.80±6.76) compared to C (193.94±4.98) and DM (211.81±34.04), which may be associated with a possible stimulation of seminiferous epithelium proliferation in M and L. In normoglycemic animals treated with L, a tendency was observed for the evaluated parameters to remain close to the values of group C. **Conclusion:** These preliminary results suggest that Lycopene exerts beneficial effects on the structural preservation of the ST, and that Metformin does not promote apparent testicular toxicity. Further analyses with a larger sample size are necessary to elucidate the isolated and combined effects of these substances on testicular tubular histoarchitecture and, consequently, on the preservation of male fertility in face of DM. Animal Research Ethical Committee from UFOP: protocol number 7807301122. **Financial support:** FAPEMIG (Undergraduate research).

07.012 Impact of Chronic Administration of Methylglyoxal in Diabetic Bladder Dysfunction in Obese Model (ob/ob).
Horioka CP, Barbalho TM, Oliveira AL, Medeiros ML, Antunes E. FCM-LABEA Unicamp, PGP Pharmacology, Brazil

Methylglyoxal (MGO) is a dicarbonyl compound found at high levels in the blood of diabetic patients. Studies from our group have shown that chronic MGO administration induces bladder dysfunction. Here, we investigated whether the consumption of exogenous MGO enhances the bladder dysfunction observed in obese ob/ob mice (type 2 diabetic model), as this animal model already presents elevated levels of endogenous MGO by hyperglycemia. The protocol was approved by CEUA-UNICAMP (N°. 6653-1/2025). C57BL/6JUnib and B6.Cg-Lepob/Junib female mice aged 20 weeks-old were used. Animals were divided into three groups, namely, lean control (WT), obese control and obese treated with MGO 0,5%. Methylglyoxal 0,5% was administered to the obese group in drinking water for 12 weeks. The body weight and glycemic levels were significantly elevated in ob/ob compared with WT group ($p<0.05$), whereas the water consumption did not significantly change between these groups. Ob/ob mice also exhibited marked insulin resistance (KITT test). However, any of these parameters in ob/ob group were significantly changed by 12-week MGO ingestion. The voiding behavior in awake ob/ob mice revealed significant increases in total volume, which was not modified by MGO intake. The *in vitro* bladder contractions to carbachol (1 nM–100 μM) and EFS (1-32 Hz) were reduced in ob/ob compared with WT group, but MGO intake in ob/ob did not affect the contractile responses compared with untreated animals. Bladder contractions to α,β-methylene ATP (1, 3 and 10 μM) and KCl (80 mM) were not modified in ob/ob treated or not with MGO. Our data indicate that exogenous 0.5% MGO intake for 12 weeks does not worsen the bladder dysfunction of 20-week-old ob/ob mice.

07.013 **Effects of Tirzepatide on Neurobehavioral Alterations in Mice Exposed to a High-Fat Diet Early in Life**. Melo Silva JG[1,2], Lemos IL[1,2], Weber IH[1], Moraes GR[1], Silva ABC[1,2], Miranda KKB[1,2], Bellozi PMQ[1,2] [1]UnB, Faculty of Health Sciences, Brazil, [2]UnB, Institute of Biological Sciences, PPG Animal Biology, Brazil

Introduction: Childhood and adolescent obesity, linked to western diets, is a growing public health challenge. Tirzepatide (TZP), a dual GIP/GLP-1 receptor agonist, is a promising therapeutic strategy, however, its effects on neurobehavioral changes associated with early-life exposure to a high-fat diet (HFD) remain unclear. **Objectives:** This study evaluated the effects of TZP on feeding behavior, anxiety-like behavior, and food motivation in young female C57BL/6 mice fed with a HFD. **Methods:** Thirty-three female C57BL/6 mice (5 weeks old) were fed a control diet (CD; 15% fat) or a HFD (45% fat) for 10 weeks. After 6 weeks on diet, animals were allocated into four experimental groups: CD + Vehicle (V), CD + TZP, HFD + V, and HFD + TZP. TZP (10 nmol/kg/day, s.c.) or V were administered daily for 4 weeks. Body weight and food intake were measured twice weekly. Behavioral assessments included the Open Field Test (OFT), Elevated Plus Maze (EPM), and Novelty-Suppressed Feeding (NSF) test to evaluate locomotor activity, anxiety-like behavior, and food motivation and aversion. Data were analyzed by two-way ANOVA, with $p < 0.05$ considered statistically significant. The study was approved by CEUA/UnB under protocol n° 23106.067420/2023-98. **Results:** HFD induced greater weight gain than the CD from week 3 of the experiment onward. While vehicle-treated animals showed progressive weight gain, TZP treatment significantly reduced body weight from the first week of treatment onward, with the HFD + TZP group showing the most pronounced weight loss. From experimental week 7 onward, TZP-induced weight loss gradually declined. Food intake was similar among all groups until week 6 of the experiment. During the first week of treatment, TZP induced a marked reduction in food consumption, followed by a gradual recovery during the subsequent weeks, although intake remained lower than in vehicle-treated groups. In the OFT, no significant differences occurred in locomotor and exploratory parameters. In the EPM, the diet had a positive influence on the number of closed arm entries. Moreover, time spent in the center was greater in the HFD + V group compared to CD + V, as well as in the HFD + TZP group relative to CD + TZP, without any other alterations. In the NSF, TZP significantly increased the latency to feed after an 18-h fast in both CD + TZP and HFD + TZP groups compared with CD + V and HFD + V groups, respectively. Further, TZP markedly reduced subsequent food intake regardless of diet. Locomotor and exploratory measures did not differ among the groups. **Conclusion:** TZP reversed early-induced obesity, reducing body weight and food intake. Behavioral effects were modest, with limited effects on anxiety-like behaviors, but a relevant impact on feeding-aversion conflict after fasting.

07.014 *Arthrospira platensis* **Prevents Macroscopic Inflammatory Alterations in Uterus and Ovaries in a Wistar Rat Model of Primary Dysmenorrhea**. Barbosa YV[1,2], Silva JMA[1,2], Claudino, BFO[1,2], Barros BC[1,2], Diniz AFA[1,2], Arruda RRA[1,2], Santos ABR[2], Melo MB[1], Sousa-Filho JEC[1], Santos TJ[1], Sousa TR[1], Soares MFS[2], Alves, AF[3], Silva BA[1,2,4] [1]UFPB, Lab Functional Pharmacology Prof. George Thomas, Institute of Research in Drugs and Medicines, Brazil. [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil. [3]UFPB, Dept Biomedical Sciences, Health Sciences Center, Brazil. [4]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil.

Primary dysmenorrhea (PD) is a gynecological condition characterized by painful menstruation resulting from inflammation and uterine hypercontractility. Pharmacotherapy includes tocolytics, but therapeutic refractoriness and adverse reactions limit their uses, reinforcing the search for new approaches. In this context, *Arthrospira platensis* (AP) emerges, an aquatic cyanobacterium with anti-inflammatory and antioxidant effects. Premises indicated that AP prevents increase in writhing, contractile reactivity, cytokines and prostanoids in PD model, so the objective of the study was to continue the investigation of the preventive effects of AP against the morphological changes induced by an experimental model of PD. Virgin female Wistar rats were used and randomly allocated in 3 groups (n = 5): control (CG), primary dysmenorrhea (PD), and PD supplemented with AP at dose 100 mg/kg (PD + AP100). Powdered AP was suspended in saline (0.9% NaCl) and the suspension was administered daily by intragastric gavage for 8 weeks, PD was induced in the PD and PD + AP100 by subcutaneous injections of diethylstilbestrol. Finally, the rats were euthanized and the uterine horns and ovaries collected for macroscopic analysis of relative weight and size. Macroscopic analyses evidenced in the PD an increase in uterine volume, with distended and irregular horns when compared to the CG, in addition a increase in the number of apparent vessels on the surface, which, combined with intense edema, suggests acute inflammation. Ovaries in PD were found to be slightly edematous, with surface irregularities similar to the CG. In PD + AP100, an attenuation of these changes was observed, with a prevention of the volumetric increase and hyperemia of the uterine horns, with a more uniform coloration, while the ovaries were found to be redder than those found in the CG and PD. Relative weight of the uterine horns and ovaries was higher in PD (0.21 ± 0.02; 0.04 ± 0.004%, respectively) compared to CG (0.1 ± 0.004; 0.02 ± 0.002%, respectively). Supplementation with AP prevented these changes in PD + AP100 (0.15 ± 0.012; 0.02 ± 0.002%). Regarding the average size of the uterine horns and ovaries, there was an increase in PD (4350 ± 158.11; 660 ± 10 mm, respectively) compared to CG (2950 ± 139.94; 560 ± 10 mm, respectively), while supplementation prevented this increase in PD + AP100 (2812 ± 158.60; 540 ± 33 mm, respectively). Results demonstrate for the first time that AP supplementation exerts anti-inflammatory effect that go beyond functional and molecular changes, impacting the anatomy of these organs. Finally, it is concluded that supplementation with this cyanobacterium prevents anatomical alterations through possible negative modulation of the inflammatory component, building its therapeutic potential for the clinical management of PD. All experiments were approved by the CEUA/UFPB (n° 535100625/UFPB). This study was founded by CNPq, CAPES and FAPESQ.

07.015 **Probenecid Reduces Phenylephrine-Induced Contractions in Human Prostate Tissue**. Moretti MB, Passos GR, Barros JVC, Lima JM, Antunes E, Monica FZ Unicamp, Lab of Lower Urinary Tract and Erectile Disfunction, Dept Pharmacology

Benign prostatic hyperplasia (BPH) is one of the most prevalent urological disorders affecting aging men and is characterized by prostate enlargement due to cell proliferation and increased prostate smooth muscle tone, leading to lower urinary tract symptoms and reduced quality of life. Although several pharmacological therapies are available, treatment efficacy may be limited by adverse effects or insufficient symptom relief, highlighting the need for novel therapeutic approaches. Probenecid is a drug recognized as an inhibitor of organic acid transporters, multidrug resistance transporters and pannexin-1 proteins and activator of TRPV2 transporters and has been using in the clinical setting for the treatment of gout and as coadjuvant to beta-lactam antibiotics. In rat prostate, probenecid (0.1, 0.3 and 1 mM) significantly potentiated the relaxation induced by beta-adrenoceptors. The present study aims to assess the *in vitro* effect of probenecid in isolated prostate patients undergoing transurethral resection of the prostate. Prostate strips were mounted in organ baths containing 5 mL Krebs–Henseleit solution maintained at 37 °C. Tissues were incubated with probenecid (1, 10, or 100 μM) for 30 minutes before concentration-response curves to phenylephrine were generated. Maximum response (Emax) and potency (pEC50) were determined. Statistical analyses were performed using unpaired Student's *t*-test, and differences were considered statistically significant when $p < 0.05$. At 1 μM and 10 μM probenecid significantly reduced pEC50 from 5.42 ± 0.07 to 5.16 ± 0.04 (N=5, P=0.0002) and 5.30 ± 0.06 vs 4.91 ± 0.05 (N=5, P<0.0001), respectively without altering significantly the Emax values (130.2 ± 12.9% vs 123.8 ± 9.3%, P=0.3984 and 139.1 ± 15.9% vs 122.3 ± 11.4%; N=5, P=0.0920, respectively). At 100 μM, probenecid significantly reduced both pEC50 (4.98 ± 0.11 vs 4.76 ± 0.15; N=5; P=0.031) and Emax (117.4 ± 26.7% vs 66.1 ± 15.8%; N=5; P=0.0061). These findings demonstrate that probenecid attenuates α1-adrenergic agonist-induced contraction, suggesting that it may represent a potential therapeutic target for alleviating the hypercontractile effects observed in patients with BPH. However, the mechanisms underlying this effect remain to be elucidated and are currently under investigation.

07.016 *Arthrospira platensis* **Prevents Alterations in Histology and Increase of Eosinophilic Infiltrate Homogeneously along the Uterine Topography of Female Wistar Rats with Primary Dysmenorrhea**. Silva JMA[1,2], Barborsa YV[1,2], Claudino, BFO[1,2], Diniz AFA[1,2], Arruda RRA[1,2], Barros BC[1,2], Santos ABR[2], Santos TR[1], Santos TJ[1], Melo MB[1], Sousa-Filho JEC[1], Soares MFS[2], Alves AF[2,3], Silva BA[1,2,4] [1]UFPB, Lab Functional Pharmacology Prof. George Thomas, Institute of Research in Drugs and Medicines, Brazil; [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil; [3]UFPB, Dept Biomedical Sciences, Health Sciences Center, Brazil; [4]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil

Primary dysmenorrhea (PD) is the most prevalent gynecological dysfunction in young women, being characterized by uterine hypercontractility, inflammation and pelvic pain. Pharmacotherapy consists in tocolytics, however, there is therapeutic refractoriness, making new treatment options necessary. In this context, the aquatic cyanobacterium *Arthrospira platensis* (AP) emerges as a promising alternative, as it has compounds with antioxidant and anti-inflammatory effects. Previous studies demonstrated that AP has anti- dysmenorrheic effect by preventing the increase of writhing, contractile reactivity and pro-inflammatory mediators in this experimental model. Thus, the aim of this study was to continue the investigation of effects of AP on histological and eosinophilic infiltration alterations in uterine topography induced by PD. For this, female virgin Wistar rats were randomly allocated into 3 groups (n = 5): control (CG), primary dysmenorrhea (PD) and PD supplemented with AP (PD + AP100; 100 mg/kg, i.g.). Powdered AP was suspended in saline (NaCl 0,9%) and was administered daily for 8 weeks, while experimental induction of PD occurred in the last 10 days of the protocol with administration of diethylstilbestrol (s.c.). For histological assays, uterine sections from 3 regions were collected: cranial (Cr), medial (Md) and caudal (Cd), processed and stained with hematoxylin-eosin for subsequent quantification of endometrium (ENDO) and myometrium (MYO) thickness and eosinophilic infiltration. ENDO thickness was reduced in PD in the Cr, Md and Cd regions (40.07 ± 3.20, 42.37, ± 4.08, 32.45, ± 2.23 µm, respectively), compared to CG (72.64 ± 8.79, 69.45, ± 4.28, 81.23, ± 4.98 µm, respectively), while supplementation with AP completely prevented these alterations in PD + AP100 (69.96 ± 5.07, 70.81, ± 5.98, 65.54, ± 4.52 µm, respectively). By contrast, MYO thickness was greater in PD in the Cr, Md and Cd regions (70.64 ± 2.88; 71.63 ± 3.28; 81.86 ± 3.77 µm, respectively), compared to CG (46.72 ± 2.62; 49.32 ± 2.92; 57.88 ± 2.02 µm, respectively), findings partially prevented by AP in PD + AP100 (60.65 ± 1.72; 62.58 ± 3.70; 71.45 ± 1.60 µm, respectively). Similarly, the number of eosinophils were elevated in PD in the Cr, Md and Cd segments (30 ± 3; 29 ± 1; 38 ± 2 cells/mm^2, respectively), compared to CG (19 ± 3; 20 ± 2; 21 ± 2 cells/mm^2, respectively), findings that were completely prevented in PD + AP100 (13 ± 2; 15 ± 3; 13 ± 3 cells/mm^2, respectively). No difference was observed between the same uterine regions when the same experimental group was evaluated. Together, these results indicate that AP exerts a global uterine protective effect, preventing alteration in ENDO and MYO, as well as the increase in eosinophilic infiltrate associated with uterine inflammation, reinforcing the therapeutic potential in the clinical management of this dysfunction. All experiments were approved by the CEUA/UFPB (nº 2535100625). This study was funded by CAPES and CNPq.

07.017 **Sexually Dimorphic Responses to Oral Sodium Nitrite Treatment on Metabolic Parameters and Glucose Tolerance in an Experimental Model of Type 2 Diabetes Mellitus**. Silva-Cunha MS, Sanches-Lopes JM, Conde-Tella SO, Medeiros CFA, Rebelo MA, Tostes RC, Tanus-Santos JE FMRP-USP, Dept Pharmacology, PPG Pharmacology, Brazil; Unicamp, Faculty of Medical Sciences, Dept Translational Medicine, PPG Pharmacology, Brazil

Introduction: Type 2 diabetes mellitus (T2DM) is characterized by insulin resistance, which is frequently associated with reduced nitric oxide (NO) bioavailability. Oral nitrite supplementation emerges as a promising therapeutic strategy to restore systemic NO pools independently of the classic endothelial nitric oxide synthase (eNOS) pathway. Although the leptin receptor-deficient (db/db) mouse model replicates the clinical features of T2DM, the evolutionary characterization of the metabolic profile and the efficacy of nitrite in both sexes remain poorly explored. **Objectives:** This study evaluated the metabolic effects of chronic oral sodium nitrite ($NaNO_2$) supplementation in male and female diabetic db/db mice and their respective healthy db/+ controls. **Methods:** The experimental protocol was approved by the Ethics Committee on Animal Use of the Ribeirão Preto Medical School - USP (CEUA FMRP-USP, protocol no. 1547/2025). Male and female diabetic mice (db/db) and their respective heterozygous controls (db/+) were treated with $NaNO_2$ (50 mg/L) or vehicle in their drinking water for 6 weeks ($n = 6$-10 for males and $n = 4$-10 for females). Body weight and fasting blood glucose were monitored longitudinally throughout the experimental period. In the 6th week, an Oral Glucose Tolerance Test (OGTT) was performed. Plasma nitrate and nitrite concentrations were measured using ozone-based reductive chemiluminescence. Longitudinal comparisons were analyzed by two-way repeated-measures ANOVA, whereas endpoint data were evaluated by two-way ANOVA, followed by Tukey's post-hoc test. **Results:** The obesity observed in db/db mice of both sexes was not altered by the treatment. However, a sexual dimorphism emerged regarding glycemic control: chronic $NaNO_2$ promoted a significant reduction in fasting blood glucose restricted entirely to male db/db mice at weeks 5 and 6 ($p < 0.05$), whereas female db/db mice were non-responsive. Similarly, oral glucose tolerance improved significantly only in diabetic males ($p < 0.05$). Systemically, $NaNO_2$ selectively increased plasma nitrate concentrations in females (db/+ and db/db, $p < 0.05$), without altering plasma nitrite in either sex. **Conclusion:** Our findings demonstrate a sex-specific efficacy of chronic oral $NaNO_2$, which improves glucose intolerance and fasting hyperglycemia in diabetic male mice, but not in females. These metabolic responses did not interfere with the obesity phenotype and, in males, were not accompanied by an increase in systemic nitrate and nitrite levels. This indicates that the therapeutic effects of nitrite in males are mediated by specific peripheral targets, such as skeletal muscle or hepatic tissue.

07.018 **Inactivated SARS-CoV-2 Exposure Induces Pulmonary Inflammation Associated with Male Reproductive Dysfunction in K18-hACE2 Mice**. França PRC[1], Paiva JPB[1], Valente AG[1], Minho AS[1], Carvalho RS[1], Carvalho RR[2], Berbert LR[3], Frajblat M[3], Figueiredo MM[4], Marques DPA[5], Coelho-dos-Reis JGA[5], Fernandes PD[1]. [1]ICB-UFRJ, Lab Pharmacology of Pain and Inflammation, PPG Pharmacology and Medicinal Chemistry, Brazil, [2]ENSP-Fiocruz, Dept Biological Sciences, Lab Environmental Toxicology, Brazil, [3]UFRJ, Coordination of Activities with Experimental Biological Models, Brazil, [4]UEMG, Dept Natural and Earth Sciences, Brazil, [5]ICB-UFMG, Dept Microbiology, Lab Basic and Applied Virology, Brazil.

Introduction: Angiotensin Converting Enzyme 2 (ACE2) receptors are expressed in several organs and tissues. The Spike protein of SARS-CoV-2 binds to ACE2 receptors, promoting viral entry into host cells. Previous studies have demonstrated ACE2 expression in Leydig and Sertoli cells, as well as in spermatogonia, suggesting that the testes may represent a potential target of SARS-CoV-2-related alterations. In addition, inflammatory responses, oxidative stress, and apoptotic pathways may contribute to the disruption of male reproductive function. **Objectives:** This study aimed to evaluate the impact of inflammation induced by inactivated SARS-CoV-2 (iSARS-CoV-2) exposure on spermatogenesis and reproductive performance in K18-hACE2 transgenic male mice. **Methods:** Male K18-hACE2 transgenic mice (20g, n=8) were intranasally instilled (5 µL/nostril) once daily for 14 consecutive days with iSARS-CoV-2 corresponding to 1x105 PFU equivalents of the original infectious stock prior to inactivation. On the last day, animals were euthanized, and testes and epididymides were collected for organ weighing, total sperm count, sperm morphology, and motility classification analyses. Epididymides and vas deferens were placed in a specific gamete buffer to allow sperm migration into the solution, and aliquots were analyzed in a Neubauer chamber. In addition, lungs were collected for histopathological evaluation and cytokine quantification. The results were expressed as mean ± SD. Statistical analysis was performed by T-test followed by Mann-whitney (*$p<0.05$). This protocol was approved by CEUA/UFRJ and received the number 93/22. **Results:** iSARS-CoV-2 instillation significantly increased inflammatory cytokine levels in lung homogenates, including TNF-α (54% increase; 38.5±8.3 pg/µg protein vs. 25.0±1.9 pg/µg protein), IFN-γ (32.3% increase; 20.5±2.6 pg/µg protein vs. 15.5±0.6 pg/µg protein), and IL-6 (two-fold increase; 10.4±2.0 pg/µg protein vs. 5.2±1.1 pg/µg protein) compared to the vehicle group. Furthermore, iSARS-CoV-2 exposure significantly reduced total sperm count by 18% (7.7±1.3 sperm cells/mL vs. 9.7±1.5 sperm cells /mL) and impaired sperm motility, characterized by a 70.5% reduction in progressive spermatozoa (15.8±8.1% vs. 54.2±6.3%), accompanied by increases of 127% in non-progressive sperm (32.5±5.4% vs. 14.3±5.5%) and 76% in immotile sperm (51.0±5.5% vs. 29.1±5.6%) compared to the vehicle group. **Conclusion:** Our findings demonstrate that exposure to iSARS-CoV-2 promotes pulmonary inflammatory responses associated with impaired male reproductive parameters in K18-hACE2 mice, including reduced sperm count and altered sperm motility. These results suggest that inflammation induced by iSARS-CoV-2 exposure may contribute to male reproductive dysfunction. **Financial support:** CNPq, CAPES, FAPERJ.

07.019 **Association of Probenecid and Tadalafil Enhances Corpus Cavernosum Relaxation in Spontaneously Hypertensive Rats**. Leonardi GR, Moretti MB, De Barros JVC, De Lima JM, Passos GR, Antunes E, Mónica FZ. Unicamp, Lab. of Lower Urinary Tract Disorders & Erectile Dysfunction, PPG Pharmacology, Brazil.

Introduction: Among the most prevalent male sexual disorders, erectile dysfunction is characterized by the persistent inability to achieve and maintain an erection sufficient for a satisfactory sexual experience. Probenecid, classically known as an uricosuric agent, has emerged as a compound of interest in drug repurposing research owing to its multiple pharmacological targets. **Objectives:** The aim of this study was to evaluate the effect of oral treatment with probenecid, tadalafil, or their association, in corpus cavernosum (CC) smooth muscle relaxation in spontaneously hypertensive rats (SHR). **Methods:** Wistar Kyoto Rats (WKY) were used as control group. SHR (24 weeks) were treated with probenecid (200 mg/Kg/day), tadalafil (10 mg/Kg/day), or both, in drinking water for 4 weeks. Subsequently, the CC was isolated and concentration-response curves (CRCs) were performed using an isolated organ bath system to determine potency (pEC50) and maximal response (Emax). cGMP levels were also quantified in these tissues by liquid chromatography. Statistical comparisons were performed using the unpaired Student's t-test. **Results:** SHR showed lower Emax values compared to control group (WKY) in CRC to acetylcholine (43.7%±16.6 vs 22.7%±7.7, n=6, $P<0.05$), salbutamol (60.6%±8.8 vs 43.4%±14.4, n=5, $P<0.05$) and DETA NONOate (41.5%±2.3 vs 28.8%±7.7, n=5, $P<0.05$). Combined treatment (probenecid + tadalafil) was the only intervention capable to restore Emax significantly nearly to WKY levels, but just in CRC to acetylcholine (35.2%±7.1, n=5, $P<0.05$) and DETA NONOate (40.5%±7.7, n=5, $P<0.05$). In the CRC to DETA NONOate, a leftward shift was also observed in the combined treatment group compared to both WKY (pEC50: 6.25±0.31 vs 7.15±0.52; n=5, $P<0.05$) and untreated SHR rats (pEC50: 6.37±0.46 vs 7.15±0.52; n=5, $P<0.05$). In CRC against isoprenaline, Emax was significantly increased following combined treatment compared to untreated SHR (39.9%±6.8 vs 50.8%±6.2, n=5, $P<0.05$). Relaxation induced by electrical field stimulation (EFS) was significantly reduced in the untreated SHR group across all frequencies (2–32 Hz), however, none of the treatment approaches were capable of reversing this impairment. cGMP quantification revealed an increase in samples stimulated with acetylcholine compared to the unstimulated (basal), however, no significant differences were observed between the control WKY and untreated SHR group. **Conclusion:** Combined treatment enhanced responses to some relaxant agents, particularly those dependent on the cGMP pathway, restoring CC relaxation to levels comparable to those observed in the control group. However, cGMP quantification did not reveal significant differences in the pathological model, indicating that further studies are needed to elucidate better the underlying mechanisms.

07.020 **Taurine as a Potential Modulator of Metabolic Aging and AGE–RAGE-Associated Pathways: Integrated *in silico* and Antiglycation Analyses**. Andrade EM, Souza VL, Santos PA. UFRGS, Institute of Basic Health Sciences, Dept Pharmacology, Lab Neuropharmacology and Clinical Toxicology, PPG in Pharmacology and Therapeutics. Brazil

Introduction: Metabolic aging and type 2 diabetes mellitus (T2DM) are strongly associated with oxidative stress, mitochondrial dysfunction, chronic inflammation, and accumulation of advanced glycation end-products (AGEs). Taurine, a sulfur-containing amino sulfonic acid abundant in metabolically active tissues, has emerged as a promising regulator of redox homeostasis, mitochondrial function, calcium signaling, and glyco-oxidative stress. Recent evidence suggests that taurine may contribute to modulation of aging- associated metabolic dysfunction and AGE–RAGE signaling pathways. **Objectives:** To investigate the pharmacokinetic, toxicological, molecular interaction, and antiglycation potential of taurine using integrated *in silico* and experimental approaches focused on metabolic aging and AGE-associated pathways. **Methods:** A structure-based and ligand-centric computational workflow was performed using taurine as the central compound of interest. Physicochemical, pharmacokinetic, and toxicological parameters were predicted using SwissADME, pkCSM, ADMET-AI, and ProTox-II platforms. Ligand-based target prediction and biological activity profiling were performed using SwissTargetPrediction and PASS Online. Molecular targets associated with metabolic aging, oxidative stress, nutrient sensing, and glyco-oxidative signaling, including DPP-4, AMPK, mTOR, SIRT1, KEAP1–NRF2, and RAGE, were selected for interaction analysis. Multi-omics integration using transcriptomic and proteomic datasets associated with aging and T2DM was conducted to identify signaling pathways potentially modulated by taurine. In parallel, an *in vitro* antiglycation assay was performed using a bovine serum albumin (BSA)-glucose system in 96-well plates, including aminoguanidine as a positive control. **Results:** Taurine demonstrated a highly hydrophilic profile characterized by low molecular weight, high aqueous solubility, low lipophilicity, and intermediate blood–brain barrier permeability. Favorable safety-related parameters were observed, including low predicted hERG inhibition and low ClinTox probability. Systems-level analyses identified convergence between taurine-responsive pathways and molecular networks associated with oxidative stress regulation, mitochondrial homeostasis, inflammatory signaling, and AGE–RAGE-associated pathways. Taurine-associated signaling demonstrated overlap with AMPK–mTOR–NRF2 regulatory axes implicated in metabolic aging.Experimental antiglycation analyses showed that taurine significantly reduced AGE formation by approximately 29% compared with the glycated control (199.0 ± 3.5 vs. 280.0 ± 2.8 Relative Fluorescence Units (RFU), $p < 0.001$), supporting its glyco- oxidative modulatory activity. **Conclusion:** The present integrated analysis supports taurine as a promising metabolic and redox-regulatory compound with potential relevance in aging-associated metabolic dysfunction and AGE-related pathways. The combined *in silico* and antiglycation findings reinforce the translational potential of taurine as an adjunct strategy targeting oxidative stress, mitochondrial dysfunction, and glyco-oxidative damage associated with metabolic aging and T2DM.

07.021 **Modulation of Prostatic Carcinogenesis by Raloxifene: Histopathological and Immunohistochemical Evidence in Rats**. Pinho CF[1], Chamelete JLG[1], Silva LB[1], Takehara BAD[1], Fonseca MCBS[1], Cózaro LC[1], Santana ACP[2], Pereira S[1]. [1]Unesp-Bauru, Brazil, [2]IBB-Unesp-Botucatu, Brazil.

Introduction: Prostate Cancer is the second most frequently diagnosed malignancy in Brazil and the fifth leading cause of cancer-related mortality among men worldwide. The ability of prostate cancer to progress to an androgen deprivation therapy–resistant stage highlights the importance of investigating adjuvant therapeutic strategies. Recent studies have suggested estrogen receptors as potential therapeutic targets in neoplastic diseases, which may be modulated by drugs such as raloxifene. **Objectives:** This study aimed to evaluate the effects of raloxifene therapy on the prostate of rats subjected to chemically induced carcinogenesis through exposure to the carcinogen N-methyl-N-nitrosourea (MNU). **Methods:** Thirty adult male Fisher 344 rats were allocated into 3 groups: Control, Induced, and Raloxifene. The Induced and Raloxifene groups received intraprostatic inoculation of MNU (15 mg/kg) associated with testosterone cypionate administration twice weekly for 220 days. Another 10 animals belonging to the Control group received only corn oil for the same period. Following euthanasia, the ventral prostates were subjected to morphological analyses using hematoxylin–eosin and toluidine blue staining, as well as immunohistochemical evaluation. **Results:** The Induced group exhibited marked disruption of prostatic glandular morphology, characterized by the presence of hyperplastic lesions, dysplasia, prostatic intraepithelial neoplasia, and adenocarcinoma compared with the Control group (Kruskal–Wallis and Dunn's tests, $p \leq 0.05$). This group also demonstrated increased immunolabeling of the pro-inflammatory proteins TNF-α, NF-κB, and TLR4, accompanied by enhanced mast cell recruitment and a higher number of inflammatory foci (Kruskal–Wallis and Dunn's tests, $p \leq 0.05$). In contrast, the Raloxifene group showed a significant reduction in these lesions compared with the Induced group (Kruskal–Wallis and Dunn's tests, $p \leq 0.05$), and no animals developed adenocarcinoma. Raloxifene treatment also increased the apoptotic index in the prostate and reduced the immunolabeling of TNF-α, NF- κB, and TLR4 (Kruskal–Wallis and Dunn's tests, $p \leq 0.05$), which are associated with cell survival and proliferation, tumor progression, and metastasis. Furthermore, quantification of androgen receptor (AR) immunolabeling area revealed increased expression in both the Induced and Raloxifene groups compared with the Control group (Kruskal–Wallis and Dunn's tests, $p \leq 0.0001$), indicating maintenance of androgen receptor expression following carcinogenic induction. **Conclusion:** The findings obtained thus far suggest a protective effect of raloxifene on the ventral prostate during experimental prostatic carcinogenesis, attenuating the histopathological alterations triggered by MNU exposure.

07.022 **Effects of Oral Gestrinone Administration on Adiposity and Hepatic Lipids in Obese Female Rats**. Ribeiro RA, Moreira AC, Santos AS, Silva RN, Scomparin DX, Rosa EPCC UEPG, Ponta Grossa, PR, Brazil.

Introduction: Gestrinone is a progestin used for the treatment of endometriosis and myomas; however the internet has been promoted it for body fat reduction, which is worrying since misuse of steroid hormones can cause liver damage. **Objectives:** This study investigated the effects of oral gestrinone administration on adiposity and hepatic lipid metabolism in female obese rats. **Methods:** Adult female Wistar rats were subjected to obesity induction through a high-fat diet (HFD) for 8 weeks. After, obese HFD-fed females remained on the same diet for an additional 8 weeks and received, 3 times per week, a gavage of soybean oil containing 0.2% DMSO (HFD group), either without or with gestrinone at the doses of 0.13 (H0.13 group), 0.26 (H0.26 group), or 0.52 mg/kg body weight (H0.52 group). **Results:** Gestrinone treatment reduced body weight and abdominal adiposity in H0.13 (302.2 ± 8.6 g and 20.30 ± 2.2 g), H0.26 (286.8 ± 5.0 g and 24.3 ± 2.4 g) and H0.52 groups (288.5 ± 10.2 g and 21.2 ± 3.3 g), compared to HFD (332.4 ± 7.5 g and 42.6 ± 4.1 g). Also, carcass fat percentage, which represents subcutaneous adiposity, was lower in H0.13 (14.0 ± 1.5 %), H0.26 (14.6 ± 0.9 %) and H0.52 (11.3 ± 1.3 %), than in HFD females (21.5 ± 2.2 %). Gestrinone regulated gene expression in the inguinal white adipose tissue (WAT) in a dose-dependent manner. H0.13 group showed reduced Fabp-4 (0.2 ± 0.1) and increased Adrβ3 gene expressions (6.5 ± 2.1), compared to HFD (1.0 ± 0.3 and 1.0 ± 0.2). In contrast, inguinal WAT of H0.26 and H0.52 groups exhibited increased Pgc-1α mRNA levels (2.2 ± 0.6 and 4.0 ± 1.2), compared with HFD (1.0 ± 0.1). Gestrinone also reduced fasting plasma cholesterol (CHOL) levels in H0.26 (72.7 ± 7.2 mg/dL) and H0.52 (66.5 ± 5.0 mg/dL), compared to HFD (98.77 ± 5.9 mg/dL), without altering triglyceride (TG) levels (HFD: 59.8 ± 3.1; H0.13: 48.7 ± 3.5, H0.26: 54.0 ± 3.6 and H0.52: 53.5 ± 2.8 mg/dL). In the liver, gestrinone did not affect TG concentrations, but increased hepatic CHOL in H0.13 (4.07 ± 0.39 and 0.72 ± 0.02 ug/mg liver), H0.26 (3.61 ± 0.34 and 0.77 ± 0.06 ug/mg liver), and H0.52 (3.48 ± 0.49 and 0.87 ± 0.09 ug/mg liver), compared with HFD (4.71 ± 0.59 and 0.57 ± 0.07 ug/mg liver, respectively). Also, gestrinone upregulated the hepatic Srebp-2 and Hmgrc genes, in H0.13 (14.8 ± 3.8 and 9.3 ± 2.9), H0.26 (14.0 ± 2.8 and 10.4 ± 2.2) and H0.52 (13.7 ± 3.0 and 9.4 ±2.7), compared to HFD (1.0 ± 0.2 and 1.0 ± 0.3). In addition, the liver of H0.13 (22.6 ± 4.4), H0.26 (20.25 ± 2.4) and H0.52 (22.4 ± 1.1) displayed increased Cpt-1a gene, than HFD group (1.0 ± 0.5). **Conclusion:** At 0.13 mg/kg, gestrinone reduced adiposity, possibly by decreasing fatty acid uptake and increasing adrenergic sensitivity in inguinal WAT. At 0.26 and 0.52 mg/kg, reduced fat accumulation was associated with increased Pgc-1α expression. The increased hepatic CHOL content induced by the steroid in part may be due to CHOL biosynthesis. Increased Cpt-1a expression also suggests enhanced hepatic fatty acid oxidation in the liver of gestrinone-treated obese rats.

07.023 **Tirzepatide Induces Sex-Dependent Metabolic Rescue, Anxiolytic-Like Effects, and Adipose Tissue Bioenergetic Restoration in Obese Mice**. Arancibia, JMDV[1], Domingues, DM[2], Sousa, ABS[1], Moschen, HTS[2], Ribeiro, SGPS[1], Lopes, NMCP[2], Ferreira, LD[2], Barros, WM[2], Gontijo, FSN[3], Costa, MRD[3], Goulart, JT[2], de Bem, AF[2], Amato, AA[1], Bellozi, PMQ[1] [1]UnB, Faculty of Health Sciences, Brazil, [2]UnB, Institute of Biological Sciences, Brazil, [3]UnB, Faculty of Medicine, Brazil

Introduction: Type 2 diabetes mellitus (T2DM) and obesity are major public health concerns associated with metabolic and central nervous system (CNS) complications. Tirzepatide (TZP), a dual GIP/GLP-1 receptor agonist, has shown superior metabolic efficacy, but its sex-dependent neuroprotective and tissue- specific bioenergetic impacts require elucidation. **Objectives:** This study evaluated the potential neuroprotective and metabolic effects of TZP in male and female C57BL/6 mice subjected to a high-fat diet (HFD) model of T2DM and obesity. **Methods:** The present project was approved by CEUA/ UnB under protocol number 23106.067420/2023-98. Male and female mice (8 weeks old) received a control diet (CD, 15% lipids) or HFD (60% lipids) for 12 weeks. During the final 4 weeks, subgroups received TZP (10 nmol/kg/day, s.c.) or vehicle. Metabolic profiles were assessed via body weight trajectories and glucose tolerance tests (GTT). Behavioral parameters were evaluated using the Open Field test and the Splash Test. Tissue bioenergetics was evaluated by high-resolution respirometry (Oxygraph-2k) in the hippocampus and subcutaneous white adipose tissue (scWAT). Data were analyzed using ANOVA and ANCOVA models. **Results:** HFD effectively expanded body mass in both sexes, with a disproportionately higher acceleration in males (+1.016 g/week) than in females (+0.340 g/week, $p<0.001$). TZP treatment induced active weight loss in both sexes, completely abolishing terminal weight sex differences. GTT and fasting glucose were significantly normalized by TZP in both sexes; however, females exhibited a superior dominant response in glucose disposal efficiency beyond fasting correction, while males showed a larger absolute reduction in fasting glucose ($p=0.001$). Behaviorally, HFD induced significant thigmotaxis and hypoactivity in the Open Field; TZP significantly reversed this anxiety- like phenotype specifically in males, increasing distance traveled (+9.6 m, $p=0.001$) and center ratio ($p=0.007$) through a metabolically independent mechanism. In the Splash Test, HFD induced depressive-like behavior (reduced self-grooming) that was not reversed by TZP in either sex. In scWAT, HFD suppressed pyruvate/malate and Complex I-linked respiration across both sexes, and TZP partially rescued Complex I-linked capacity selectively in males ($p=0.007$). In the hippocampus, neither HFD nor TZP induced localized univariate changes in mitochondrial respiration state variables. **Conclusions:** Tirzepatide exerts robust metabolic rescue and tissue-specific bioenergetic restoration in scWAT alongside anxiolytic-like effects in the Open Field. Crucially, these central and peripheral outcomes display a profound sex-modulated dimorphism, emphasizing the importance of sex-balanced preclinical evaluations for incretin-based therapies.

07.024 **Trazodone Compromises Male Reproductive Function by Damaging Testicular Tissue and Sperm Quality in Rats**. Silva Junior ED, Silva MS, Gavioli EC UFRN, Depto Biofísica e Farmacologia

Introduction: Trazodone is a widely prescribed antidepressant. However, its effects on male reproductive function remain poorly understood. **Objective:** This study evaluated the effects of trazodone on testicular histology and sperm parameters in adult Wistar rats. **Methods:** Animals (3-4 months old) received trazodone (10 or 20 mg/kg/day) or vehicle by gavage once daily for 21 consecutive days. Histological and morphometric analyses of the testes, as well as quantitative and qualitative sperm evaluations, were subsequently performed. **Results:** Treatment with trazodone induced marked histological alterations in the testes, characterized by seminiferous epithelium disorganization, vacuolization, epithelial desquamation, and enlargement of the tubular lumen. Quantitative histological analysis demonstrated a reduction in tubular epithelium height from 128.0 ± 5.1 µm in controls to 104.5 ± 9.6 µm and 102.1 ± 3.1 µm in animals treated with trazodone 10 and 20 mg/kg, respectively ($p < 0.05$). In contrast, lumen diameter increased from 78.8 ± 4.0 µm in controls to 108.1 ± 11.1 µm (trazodone 10 mg/kg) and 121.1 ± 7.7 µm (trazodone 20 mg/kg) in treated rats ($p < 0.05$). Sertoli cell density was reduced from 6.1 ± 1.3 cells/mm2 in controls to 3.0 ± 0.2 and 2.2 ± 0.7 cells/mm2 after treatment with trazodone 10 and 20 mg/kg, respectively. Leydig cell density also decreased in treated animals ($p < 0.05$). Daily sperm production decreased from 25.6 ± 0.8 x 106 sperm/g/testis/day in controls to 18.2 ± 1.0 and 19.0 ± 1.0 x 106 sperm/g/testis/day in the trazodone 10 and 20 mg/kg groups, respectively ($p < 0.05$). Cauda epididymal sperm count was reduced from 723.1 ± 32.8 x 106 sperm/g/organ in controls to 547.8 ± 45.3 and 579.9 ± 40.9 x 106 sperm/g/organ after trazodone treatment at 10 and 20 mg/kg, respectively ($p < 0.05$). Progressive sperm motility was reduced by approximately 23% and 62% in the 10 and 20 mg/kg groups, respectively. In addition, sperm morphological abnormalities increased by 24.5% and 43% in animals treated with 10 and 20 mg/kg trazodone, respectively. **Conclusion:** Trazodone induced significant histological damage to the testes and impaired sperm production and quality in rats, suggesting potential adverse effects on male fertility. Human or Animal Research Ethical Committee Number: 031/2023.

07.025 **Effects of Herbal Supplements Based on** *Tribulus terrestris* **and** *Lepidium meyenii* **on the Female Reproductive System of Wistar Rats**. Lorenzon DN[1,2], Dunga CEC[1,2], Moura MJN[1,2], Oliveira LGG[1,2], Ângelo ABS[1,2], Silva AGG[1,2], Neto FES[1,2], Gomes FTS[3], Borges CS[1,2] [1]UFERSA, Lab Tissue Biology and Developmental Toxicology, Brazil, [2]UERN, Multicenter Graduate Program in Biochemistry and Molecular Biology, Brazil and [3]UERN, Lab. of Experimental Neurology, Brazil.

Introduction: Interest in herbal remedies, such as Tribulus terrestris (Tribulus) and Lepidium meyenii (Maca), has been increasing as therapeutic alternatives for female reproductive health. However, evidence regarding their effects, both isolated and combined, is still limited. This study was approved by the Ethics Committee of UFERSA. **Objectives:** Evaluated the effects of these extracts on the reproductive system, metabolism, and behavior of adult female Wistar rats. **Methods:** 46 females were used, distributed into four experimental groups: Control (saline solution), Maca (100 mg/kg/day), Tribulus (100 mg/kg/day), and Combination (Maca + Tribulus), treated by gavage for 15 days, with estrous cycle monitoring. Following treatment, toxicological, morphometric (organ weight), reproductive (pregnancy rate, number of implantations, and live fetuses), and behavioral (sexual activity, exploratory activity, and memory) parameters were analyzed. Data were evaluated using $p < 0.05$, with ANOVA followed by Tukey's test for parametric data and the Kruskal- Wallis test followed by Dunn's test for nonparametric data. **Results:** Our data indicated that Maca acted as a neuroendocrine modulator, prolonging the diestrus phase, while Tribulus exerted a phytoestrogenic effect, intensifying estrus but compromising the regularity of the cycle. Combined administration of the extracts resulted in greater estrous irregularity, suggesting an antagonistic interaction. A significant increase in body mass was observed in the treated groups, with a potential synergistic effect in the combination. From a morphometric point of view, the association of the phytotherapeutics increased uterine weight, indicating an additive estrogenic action. Regarding fertility, Tribulus increased fetal weight, but all treated groups showed a reduction in pregnancy rate (66.7%) compared to the control group (100%). In terms of behavior, Tribulus reduced sexual receptivity and impaired long-term memory, effects partially attenuated by Maca when combined. **Conclusion:** Lepidium meyenii and Tribulus terrestris have significant physiological modulating potential; however, their combined administration may disrupt the reproductive cycle, and caution is advised in their use, especially in contexts related to women's health.

07.026 *Citrus sinensis* (L.) Osbeck var. Moro extract (MOROSIL®): A Potential Adjuvant in the Treatment of Male Infertility. Rosa GA[1], Feres MP[1], Oliveira LV[1], Lima GF, Brazão SC[1], Bragança LAR[1], Ribas JAS[1], Santos CM[2], Martins MA[3], Brito FCF[1], Marostica E[1]. [1]UFF, Dep. Physiology and Pharmacology, Lab Experimental Pharmacology, PPG Biomedical Sciences, Niterói, RJ, Brazil. [2]LEPHEC-UFF, Dep. Morphology, Niterói, RJ, Brazil. [3]UERJ, Dep. Pharmacology and Psycology, RJ, Brazil.

Introduction: Factors that can contribute to infertility include obesity and dyslipidemia which result in a chronic state of inflammation and oxidative stress (Aitken RJ. Reproduction. v. 164(6):79, 2022). More than 20 are commercially available natural anti-obesity products and among them is the *Citrus sinensis* (L.) Osbeck extract (Morosil®), with diverse pharmacological effects including, anti-inflammatory and cardiovascular protective action, attributed to its important antioxidant activity (Grosso, G. Oxid Med Cellular Long . v.1:01, 2013). However, its impact on the male reproductive system is unclear. Objective: to evaluate the effects of Morosil® on the testes, epididymis and spermatozoa of hypercholesterolemic rats. Methods: Adult male Wistar rats were randomly divided into 4 groups: CO (control - standart rodent chow + saline), CM (CO + Morosil®, 150mg/kg, 15 days by gavage), HF (high fat diet - standart rodent chow 87.7%, cholesterol 2%, lard oil 10%, cholic acid 0,3%+ saline) (Da Motta, NA. J Pharmacol Sci . v.123:47, 2013) and HM (HF + Morosil®). The animals were anesthetized with ketamine/xylasin (80/10mg.Kg-1, i.p.), the testes and epididymis were removed, weighed and processed for morphological analysis or homogenate (CEUA 7582240224). Sperm were obtained from the cauda epididymis for sperm evaluation (progressive motility, vigor, membrane functionality, concentration, morphology and acrosome reaction). Oxidative stress in the testis was assessed by using TBARs assay, and SOD and catalase activity, as well as protein carbonylation were determined. The values are mean±SEM (ANOVA, Newman-Keuls), p <0.05. Results: HF diet increased the gonadosomatic index (CO:0.395±0.01; CM:0.407±0,04; HF:0.678±0.06*; HM:0.363±0.02 %), decreased the epithelium/tubule ratio (CO:63.0±0,9; CM:60,3±0.8; HF:57.4±0.7*; HM:68.1±0.7 %) and disrupted the seminiferous epithelium. Furthermore, it increased inflammatory cells and decreased clear cells in the epididymis, effects that were recovered in the HM group. Deleterious effect of HF on the testis was accompanied by an increase in lipid peroxidation (MDA) (CO:9.45±0.78; CM:8.40±0.79; HF:12.63±0.49*; HM:6.56±0.76 nmol/mg protein), showing local oxidative stress, with consequent loss of sperm motility, vigor and membrane functionality, as well as 50% increase in spontaneous acrosome reaction. Treatment with Morosil® for only 15 days was able to reverse these effects of the HF diet on all the above parameters, except on the vigor. SOD activity increased in the CM, HF and HM groups and protein carbonylation was not different among de groups. Conclusion: In addition to its indication for weight loss, our data suggest that Morosil® may combat oxidative stress generated by dyslipidemia in the male reproductive system, due to its various antioxidant phytochemicals, and may be a therapeutic adjuvant to reduce the global rate of male infertility. Financial support: FAPERJ, CNPq, CAPES, PROPPI/UFF.

08. Respiratory and Gastrointestinal Pharmacology

08.001 Characterization of the Herbal Drug Obtained from the Leaves of Spondias purpurea and Antiulcer Activity of Its Infusion Morais FS[1], Barbosa YV[1], Rodrigues CVS[1], Andrade Junior MA[1], Sales AO[1], Santos VL[1] [1]UEPB, Laboratory of Pharmacological Assays, Brazil

Introduction: *Spondias purpurea* L., popularly known as seriguela, is a species belonging to the Anacardiaceae family and is traditionally used in folk medicine as a tea for the treatment of gastritis and diarrhea. Previous studies have demonstrated the antioxidant and gastroprotective activities of ethanolic and hexanic extracts obtained from *S. purpurea* leaves. These activities are likely related to the presence of flavonoids, cinnamic acid derivatives, terpenes, and steroids in the extracts. However, studies addressing the characterization of the herbal drug and its pharmacological activities remain limited. **Objective:** Therefore, this study aimed to characterize the herbal drug obtained from *S. purpurea* leaves and to verify its antiulcerogenic activity based on its traditional use, specifically in the form of an infusion. **Methods:** The leaves were dried in an oven and ground using a knife mill. Characterization was performed through tests for bulk and tapped density, loss on drying, total and acid-insoluble ash content, pH, and swelling index. The antiulcerogenic activity of the infusion at concentrations of 5% and 10% was evaluated using the ethanol-induced gastric ulcer model. Animal experimental protocols were approved by the CEUA/UEPB Ethics Committee (No. 025/2022). **Results:** Six particle size fractions were obtained. The highest powder retention was observed in the 180 µm sieve (44.74%), classifying the powder as semi-fine. Bulk density ranged from 0.39 to 0.44 g/mL, while tapped density ranged from 0.46 to 0.52 g/mL. The loss on drying value was 7.46 ± 0.03%, which is within the maximum permitted limit. Total ash content ranged from 9.82 to 11.26%. The pH ranged from 2.71 to 2.93, indicating an acidic character, likely associated with its chemical composition, including the presence of phenolic compounds. In the antiulcerogenic assay, the infusion at 5% significantly inhibited ulcer formation by 81.52%. However, the higher concentration (10%) was not able to inhibit ulcer formation in the model used. **Conclusion:** The results obtained were promising; however, further studies are required to ensure greater efficacy and safety regarding the use of infusions prepared from this species.

08.002 **Renin-Angiotensin System Modulators may alter the Monocytes Profile in COPD Patients**. Martins NRS, Freitas JVC, Paiva YMA, Medeiros VLD, Medeiros GB, Silva FS, Kennedy-Feitosa E. UFERSA-Mossoró, Morphophysiopharmacology Lab

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory disorder characterized by persistent airflow limitation, pulmonary emphysema, and chronic local and systemic inflammation. In addition to pulmonary impairment, the disease is associated with alterations in circulating immune cell populations, including monocytes. Monocytes are important contributors to COPD pathogenesis, participating in inflammatory responses and lung tissue remodeling. Recent evidence suggests that the renin–angiotensin system (RAS) can influence COPD pathophysiology through the modulation of inflammation. **Aim:** In this study we demonstrated that RAS modulators may influence the monocytes profile in COPD patients. **Methods:** Peripheral blood samples from 21 individuals were analyzed, including 12 participants without COPD and 9 with confirmed COPD. Participants were stratified according to COPD status and the use of renin–angiotensin system modulators (RASm) the divided into four groups: Non-COPD-No-RASm (Non-COPD patients not treated with RASm), Non-COPD-RASm (Non-COPD patients treated with RASm), COPD-No-RASm (COPD patients not treated with RASm), and COPD-RASm (COPD patients treated with RASm). Total leukocyte counts were performed in blood samples diluted with Türk's solution using a Neubauer chamber. For differential leukocyte analysis, peripheral blood smears were prepared on glass slides and stained using the May–Grünwald–Giemsa method, and monocyte percentages were determined by microscopic examination. Data were analyzed using two-way analysis of variance (two-way ANOVA) followed by post hoc multiple-comparison testing. Statistical significance was set at $p < 0.05$. **Results:** Two-way ANOVA showed an interaction between COPD status and RASm use on the percentage of circulating monocytes ($p = 0.0226$). A higher percentage of monocytes was observed in the COPD-No-RASm group compared with the Non-COPD-RASm group (mean difference = -3.971; 95% CI = -7.888 to -0.055; $p = 0.0465$). This pattern was less evident among participants using RASm. **Conclusion:** A significant interaction between COPD status and RASm use was observed regarding the percentage of circulating monocytes. These findings suggest a potential influence of RAS modulators on the monocyte response associated with COPD, highlighting the need for further studies to elucidate the underlying mechanisms and their clinical relevance.

08.003 *In vivo* and *In vitro* Study of the Acute Toxicity and Mechanisms Involved in the Antiulcerogenic Activity of the Compound 1-(4-chlorophenyl)-3-(1,3,4-thiadiazol-2-yl)thiourea (MS06). Rodrigues CVS, Costa TB, Andrade Junior MA, Fonseca MLP, Cavalcanti, MAT, De Moura RO, Dos Santos VL. UEPB, Lab Pharmacological Assays, Brazil, UEPB, Lab Drug Design and Synthesis, Brazil.

Introduction: Gastric ulcers are considered the most prevalent gastrointestinal disease, affecting approximately 10% of the world's population. The commonly used treatment is associated with many adverse effects. These factors have spurred research into alternatives for the treatment of gastric disorders. Thus, the compound 1-(4-chlorophenyl)-3-(1,3,4-thiadiazol-2-yl)thiourea (MS06) was developed using a bioisosteric strategy and modifications based on Topllis's decision tree, starting from a prototype compound that had already demonstrated gastroprotective activity. Objective: The overall objective of this study was to investigate the acute toxicity and possible mechanisms involved in the gastroprotective activity of compound MS06 *in vivo* and *in silico* . Methods: To this end, the acute single-dose toxicity, possible antisecretory mechanism, and the involvement of prostaglandins (PG) and ATP-dependent potassium channels (KATP) were evaluated *in vivo*; additionally, *in silico* , the mechanisms were investigated through molecular docking of MS06 with target structures involved in the regulation of gastric acid secretion and cytoprotection: H+/K+-ATPase, H2 receptor, M3 receptor, and EP2 receptor. The experimental protocols were approved by the Animal Ethics Committee (CEUA) of UEPB (opinion no. 036/2023). Results: In the toxicity assay, MS06 showed no signs of toxicity at a dose of 2000 mg/kg. In the pyloric ligation model, the compound at a dose of 12.5 mg/kg significantly reduced gastric volume and gastric content by 35% and 32%, respectively ($p<0.01$), and increased the pH of the gastric content from 2.6 to 4.1 ($p<0.01$), compared to the vehicle. In the ethanol model, pretreatment with indomethacin 10 mg/kg (a nonspecific COX inhibitor that reduces prostaglandin secretion) or glibenclamide 10 mg/kg (a KATP channel blocker) significantly reversed the gastroprotective effect exerted by MS06 ($p < 0.001$ and $p < 0.01$, respectively), indicating the involvement of prostaglandins and KATP in the compound's mechanism of action. In molecular docking, MS06 showed greater affinity for the M3 receptor (fitscore of 60.83) compared to the H2 receptor, EP2 receptor, and H+/K+-ATPase (fitscores of 52.51, 50.01, and 43.07, respectively). Molecular dynamics simulations demonstrated greater stability in the complexes formed with the H+/K+-ATPase (RMSD remained close to 0.5 nm) and the EP2 receptor (RMSD below 0.5 nm). Conclusion: These initial studies demonstrated that MS06 possesses gastroprotective potential, which may be related to a combination of mechanisms.

08.004 **N-Acylhydrazone Derivatives Promote Mild Relaxation of Rat Tracheal Smooth Muscle**. Santos VF[1], Lima FJB[2], De Moura RO[3], Ramos KRLP[1] [1]UEPB, Pharmacy Dept, Brazil, [2]UNIFACISA, Centro Universitário, Brazil, [3]UEPB, Lab Drug Design and Synthesis, Brazil.

Introduction: N-acylhydrazones have demonstrated promising biological activities. Among them, (E)-2-cyano-N'-(4-fluorobenzylidene) acetohydrazide (JR-13) and (E)-2-cyano-N'-(4-(dimethylamino)benzylidene) acetohydrazide (JR-15) exhibited anti-inflammatory activity in an animal model of lipopolysaccharide-induced acute lung injury (Ramos, KRLP. Chem Biol Interact., v. 420, 111677, 2025). However, their effects on airway smooth muscle contractility remain unknown. **Objectives:** To evaluate the potential relaxant effects of JR-13 and JR-15 on isolated rat tracheal smooth muscle. **Methods:** Wistar rats (n = 9) were euthanized by anesthetic overdose (ketamine 300 mg/kg, xylazine 30 mg/kg). Tracheal rings were excised and mounted in organ bath chambers containing Tyrode's solution (NaCl 136 mM, KCl 5 mM, MgCl2 0.98 mM, NaH2PO4 0.36 mM, NaHCO3 11.9 mM, CaCl2 2 mM, glucose 5.5 mM), maintained under a resting tension of 1 g at 37 °C and aerated with room air. After a stabilization period, KCl (80 mM) was added to assess tissue viability. The protocol consisted of precontraction with carbamylcholine (CCh, 1 µM), followed by cumulative concentration-response curves to JR-13 or JR-15 (0.01–300 µM). Verapamil (0.01–10 µM) was used as a positive control. Data are expressed as mean ± standard error of the mean (SEM). **Results:** A total of 17 tracheal segments were used, and KCl (80 mM) induced contractions of 0.559 ± 0.072 g (n = 17), confirming tissue viability. JR-13, JR-15, and verapamil induced concentration-dependent relaxation of CCh-precontracted tracheal rings. At the highest concentration tested (300 µM), JR-13 reduced CCh-induced contraction to 73.8 ± 3.7% (n = 6), whereas JR-15 reduced it to 79.9 ± 5.2% (n = 6). No significant difference was observed between the concentration- response curves of JR-13 and JR-15 ($p > 0.05$, two-way ANOVA). However, the maximal relaxant effects of both compounds were significantly lower than that of verapamil, which reduced contraction to 36.4 ± 15.4% (n = 5) at 10 µM ($p < 0.05$, one-way ANOVA followed by Dunnett's post hoc test). **Conclusion:** Despite the anti-inflammatory effects previously demonstrated in the airways, JR-13 and JR-15 produced only partial relaxation of CCh-precontracted tracheal rings. This effect was modest compared with that induced by the calcium channel blocker verapamil. Although these findings do not support a prominent bronchodilator action, they do not preclude further investigation of these compounds as potential therapeutic agents for airway diseases.

08.005 **Acute Bronchodilator Administration during Spirometry can Influence the Response in COPD Patients Treated with Renin-Angiotensin System Modulators**. Paiva YMA, Freitas JVC, Medeiros VLD, Medeiros GB, Martins NRS, Silva FS, Kennedy-Feitosa E UFERSA, Mossoró, Morphophysiopharmacology Lab

Introduction: Smoking is the leading risk factor for COPD, and hypertension — which affects more than 50% of this population — frequently coexists in smokers, making renin-angiotensin system modulators (RASm) among the most commonly prescribed drugs in these patients. Some RAS modulators accumulate bradykinin in the airways, a potent bronchoconstrictor that may modify airway smooth muscle tone and alter the spirometric bronchodilator response (BDR). Since post-bronchodilator FEV1/FVC is the cornerstone of COPD diagnosis, any pharmacological interference with BDR carries direct clinical implications. **Aim:** We investigated whether RASm use influences the FEV1/FVC bronchodilator response (BDR) during spirometry. **Methods:** Patients were allocated into non- COPD and COPD groups, stratified by pharmacological treatment: bronchodilators (BD) (Non-COPD or COPD-BD) , RASm (Non-COPD or COPD-RASm), or no medication (Non-COPD or COPD-NoMed). Spirometry was performed to confirm COPD diagnosis. Pre- and post-bronchodilator FEV1/FVC ratios were compared across groups using mixed-model interaction tests and Fisher's exact test (two-sided; $p<0.05$). **Results:** COPD-RASm showed a significant FEV1/FVC decrease after bronchodilation (pre-BD ≈0.67 to post-BD ≈0.51), greater than COPD-NoMed (≈0.63 to ≈0.60; p-int=0.016). COPD-BD showed a slight increase after bronchodilation (≈0.49 to ≈0.51). Non-COPD groups showed no relevant post-BD divergence. **Conclusion:** Acute bronchodilator administration during spirometry significantly alters FEV1/FVC in COPD patients using RASm, suggesting a pharmacological interaction between RASm and bronchodilators that may confound spirometric interpretation and overestimate disease severity.

08.006 **Preventive Effect of *Arthrospira platensis* on Oxidative and Inflammatory Changes in the Ileum of Rats Subjected to a Hypercaloric Diet**. Santos TJ[1,3], Claudino BFO[1],2, Silva JMA[1,2], Arruda RRA[1,2], Melo MB[1,3], Sousa Filho JEC[1,3], Barros BC[1,2], Barbosa YV[1,2], Costa BA[1,2,3], Diniz AFA[1,2] [1]UFPB, Lab Functional Pharmacology Prof. George Thomas, Institute of Research in Drugs and Medicines, Brazil. [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil. [3]UFPB. Dept Pharmaceutical Sciences, Health Sciences Center, Brazil.

Introduction: Chronic consumption of hypercaloric diets promotes metabolic alterations associated with increased production of reactive oxygen and nitrogen species, contributing to intestinal damage (Diniz, J. Funct. Foods, v.86, p.104715, 2021). The cyanobacterium *Arthrospira platensis* (AP) is notable for its high content of bioactive compounds, including phycocyanin, carotenoids, and phenolic compounds, which are associated with antioxidant and anti-inflammatory properties capable of modulating pathways related to oxidative stress and intestinal inflammation (Int. J. Food Sci. Technol., v.59, p.1197, 2024). **Objectives:** To evaluate the preventive effect of AP supplementation on nitrosative, oxidative, and inflammatory stress markers in the ileum of Wistar rats subjected to a hypercaloric diet. **Methods:** Male Wistar rats were randomly allocated into four experimental groups (n=5): standard diet (SD), hypercaloric diet (HCD), standard diet supplemented with AP (SD+AP25), and hypercaloric diet supplemented with *A. platensis* (HCD+AP25). Powdered *A. platensis* was suspended in 0.9% saline solution and administered daily by intragastric gavage at a dose of 25 mg/kg for eight consecutive weeks. At the end of the experimental period, animals were euthanized, and ileal segments were collected for biochemical and immunoenzymatic analyses. **Results:** Animals in the HD group exhibited impaired intestinal antioxidant defenses, evidenced by reduced activity of catalase (CAT) (72.88 ± 4.5) and glutathione peroxidase (GPx) (1.64 ± 0.2) compared with the control group (105.3 ± 4.7 and 6.21 ± 0.4, respectively), suggesting decreased capacity to neutralize reactive species in the ileum. In parallel, a marked increase in NOx (2654 ± 100) and nitrite levels (4.83 ± 0.2) was observed in HCD-fed rats compared with the control group (1615 ± 104 and 2.13 ± 0.1, respectively), indicating intensified nitrosative stress. Additionally, the HD group showed elevated levels of PGF2α (69.72 ± 2.4 vs. 21.40 ± 0.5 in the SD group), characterizing an intestinal inflammatory state associated with the hypercaloric diet. AP supplementation prevented these alterations by increasing CAT (108.8 ± 4.2) and GPx (5.37 ± 0.3) activities, while reducing NOx (737 ± 72.9), nitrite (2.9 ± 0.2), and prostaglandin F2α (PGF2α) (29.69 ± 2.2) levels, demonstrating a protective effect against HD-induced oxidative, nitrosative, and inflammatory stress. **Conclusion:** The results demonstrate that *Arthrospira platensis* supplementation attenuated hypercaloric diet-induced ileal damage by improving tissue antioxidant capacity and reducing markers of nitrosative stress and intestinal inflammation. These findings reinforce the therapeutic potential of AP as an adjuvant nutritional strategy for preventing intestinal alterations associated with chronic consumption of hypercaloric diets. All experimental protocols were approved by the CEUA/UFPB Ethics Committee (No. 6914241024). **Financial support:** CNPq.

08.007 *in silico* **Evaluation of the Pharmacokinetic and Toxicological Profile and Relaxant Effect of Free and β-Cyclodextrin-Complexed Farnesol** *in vitro*. Martins HRS[2], Souza ORB[1], Oliveira, MM[1], Silva PHS[2], Reis ML[1], Quintans JSS[3], Quintans-Júnor LJ[3], Oliveira AP[1], Santos RF[1], Oliveira RCM[1]. [1]UFPI, Center for Health Sciences, PPG Pharmacology, Brazil. [2]UFPI, Center for Research on Medicinal Plants, Brazil. [3]UFS, Lab Neurosciences and Pharmacological Assays (LANEF), Dept Physiology, PPG Health Sciences, Brazil.

Introduction: Asthma is a chronic lung disease characterized by airway inflammation, bronchoconstriction, and mucus hypersecretion, causing dyspnea, chest tightness, and cough. Control with corticosteroids has side effects. Thus, medicinal plants and their metabolites are investigating as sources for new drugs. Farnesol (an alcoholic sesquiterpene) has antioxidant, anti- inflammatory, and hepatoprotective activities. **Objective:** To investigate pharmacokinetic, toxicological, and *in silico* molecular interactions, as well as the *in vitro* spasmolytic effect of free farnesol and farnesol complexed with β-cyclodextrin (Fβ-CD) in isolated rat trachea. **Methods:** Physicochemical and pharmacokinetic parameters were analyzed using SwissADME, Drug-likeness, and ADME-Tox software, specifically PreADMET and GUSAR. Biological activities were evaluated using the online PASS (Way2Drug) and molecular docking via Molegro Virtual Docker. *In vitro* assays used Rattus norvegicus (180–250 g) and relaxation were evaluated in trachea pre-contracted with carbachol (CCh 10^{-6} M). At the tonic of contraction, the products were increased separately in cumulative concentrations (10^{-7}; M to 10^{-1} M). Emax and EC_{50} values were obtained by non-linear regression and t-test (GraphPad Prism 8.0). Approval by CEUA/UFPI (844/2024). **Results:** SwissADME indicated good oral bioavailability and cellular permeability of farnesol, favored by molecular weight, logP of 3.71 and low TPSA, without evidence of Lipinski's rule. ADME-Tox analyzes showed high absorption, good permeability, passage through the blood-brain barrier and low toxicity. Online PASS analysis revealed potential anti-inflammatory, antioxidant, and spasmolytic effects, and a probable involvement of potassium channels in the relaxing effect. Superficial docking with the KATP /SUR2B channel, farnesol (ΔGbind -107.544 kcal/mol) was more favorable than levcromakalim (ΔGbind -98.1493 kcal/mol), a stable interaction capable of modulating the channel, generating hyperpolarization of the smooth muscle cell membrane and bronchodilation. The results corroborate the *in vitro* data: free farnesol relaxed the muscles in a concentration-dependent manner (log EC_{50} -3.177 ± 0.81/Emax = 45.48 ± 1.53%), while Fβ-CD (log EC_{50} -5.44 ± 0.78/Emax = 71.90 ± 8.32%) demonstrated that complexation improved its physiological dispersion and interaction with cellular targets of tracheal smooth muscle. **Conclusion:** In the *in silico* studies, farnesol showed a favorable pharmacokinetic profile, low acute toxicity, potential anti-inflammatory, antioxidant, and spasmolytic activity, with predicted by the KATP target site. This pathway may be related to the relaxing effect observed *in vitro*, where Fβ-CD had a greater relaxation potential compared to free farnesol, evidencing a relevant pharmacological action that may be useful in the treatment of asthma. **Financial support** and **Acknowledgments:** CAPES, UFPI.

08.008 *In vivo* and *in silico* Antiulcerogenic Activity of Myrtenyl Ester Derived from (-)-Myrtenol Obtained by Biotransformation. Oliveira, GH[1], Viana, AFSC[1,2,3], Fernandes, HB[1,2], Martins, SCA[1], Pinheiro, CS[4], Reis, ML[1], Araújo, PBM[1,2], Silva, SA[3], Brito, MES[3], Kutyła, M[5], Stankevič, M[6], Trytek, M[5], Oliveira, RCM[1,2] [1]UFPI, Medicinal Plants Research Center (NPPM), Brazil, [2]UFPI, PPG Pharmacology, [3]UEMA, Brazil, [4]UFPI, PPG Renorbio, Brazil, [5]Maria Curie-Skłodowska, Lublin, Poland, [6]Maria Curie-Skłodowska University, Gliniana, Lublin, Poland.

Introduction: Gastric ulcer is a condition that affects the stomach lining and may extend into the submucosal and muscular layers, leading to discomfort and gastrointestinal bleeding. Complications related to gastroduodenal peptic ulcers occur up to five times more frequently in individuals who use nonsteroidal anti-inflammatory drugs (NSAIDs). Objective: This study aimed to evaluate the gastroprotective effect of myrtenyl laurate (ML), derived from the biotransformation of (-)-myrtenol by the mycelium of Cladosporium cladosporioides, using NSAID-induced gastric injury models and *in silico* analyses. Methods: *in silico* molecular docking studies were performed using AutoDock Vina 1.2.3 (2021). For the *in vivo* experiments, female Wistar rats (200–250 g, n = 6–7) maintained under controlled conditions with free access to food and water ad libitum were used. The animals were fasted for 18 h prior to the experiments and orally pretreated (p.o.) with vehicle (1% Tween 80 in distilled water), ML (6.25, 12.5, or 25 mg/kg), or pantoprazole (15 mg/kg). After 1 h, gastric lesions were induced with indomethacin (100 mg/kg, p.o.). Six hours later, the animals were euthanized, the stomachs were removed, and gastric lesion areas were quantified by planimetry using ImageJ software. The experimental protocols were approved by the Ethics Committee on the Use of Animals in Research of the Federal University Piauí (approval number 684/21). Results were expressed as mean ± SEM. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test, with $p < 0.05$ considered statistically significant. Results: In the *in vivo* study, ML (25 mg/kg) and pantoprazole (15 mg/kg) significantly reduced the gastric lesion area to 2.3 ± 1.8 mm^2 and 0.3 ± 0.1 mm^2, respectively, compared with the vehicle group (22.1 ± 3.8 mm^2). In molecular docking analyses demonstrated that ML exhibited affinity for the histamine H2 receptor and the proton pump, as evidenced by binding energies of - 5.869 and - 7.581 kcal/mol, respectively. Conclusion: ML demonstrated significant gastroprotective activity *in vivo* and, through *in silico* analyses, showed interactions with key proteins involved in the mechanisms underlying this effect. Acknowledgments: the authors acknowledge UFPI, NPPM, and the Department of Biophysics and Physiology of UFPI for their institutional and technical support.

08.009 **Relaxant Effect of Ethanolic Extracts from Branches and Leaves of *Machaerium acutifolium* Vogel on Isolated Rat Trachea**. Moraes RR, Silva PHS, Souza ORB, Oliveira MM, Chaves MH, Santos RF, Oliveira RCM UFPI, Center for Research on Medicinal Plants, PPG Pharmacology, Lab. of Natural Products, Brazil.

Introduction: Several disorders are associated with smooth muscle dysfunction, which can significantly impair quality of life. Medicinal plants represent an important source of bioactive compounds for the treatment of several diseases, including those associated with smooth muscle dysfunction. Among these, Machaerium acutifolium Vogel (Fabaceae), a species native to the Brazilian Cerrado, is traditionally used by indigenous communities in southeastern Pará for women's health conditions, including painful menstruation, as well as for the relief of stomach pain, suggesting a potential spasmolytic activity. **Objectives:** To evaluate the spasmolytic activity of ethanolic extracts from branches (Ma- EtOHg) and leaves (Ma-EtOHf) of M. acutifolium on isolated rat tracheal. **Methodology:** Male Rattus norvegicus rats (180-250 g) were used. Isolated tracheal rings were precontracted with carbachol (CCh, 10-6 M) or KCL (60 mM). Ma-EtOHg and Ma-EtOHf were cumulatively added to the organ bath (0.01-1000 µg/mL) during the tonic phase of contraction. Data were expressed as mean ± SEM and analyzed by nonlinear regression and Student's t-test, considering $p < 0.05$ as statistically significant. Experimental procedures were approved by the Ethics Committee for Animal Use of UFPI (CEUA/UFPI No. 629/2020). **Results:** Both extracts induced concentration-dependent relaxation. Against CCh-induced contractions, Ma-EtOHf was significantly more potent and effective (logEC50 = 1.125 ± 0.218; Emax = 100%) than Ma-EtOHg (logEC50 = 2.408 ± 0.208; Emax = 84.6 ± 13.0%). In KCl-induced contractions, both extracts produced complete relaxation (Emax = 100%), with similar potency for Ma-EtOHg (logEC50 = 1.002 ± 0.129) and Ma-EtOHf (logEC50 = 1.224 ± 0.129). The ability of both extracts to relax KCl-induced contractions suggesting a possible involvement of voltage- dependent calcium channels. **Conclusion:** Both extracts exhibited spasmolytic activity in isolated rat tracheal rings. Ma-EtOHf was more potent and effective against CCh-induced contractions, while both extracts showed similar relaxant effects against KCl-induced contractions, suggesting the involvement of calcium dependent mechanisms in their relaxant activity. **Financial support**: Federal University of Piauí (UFPI)

08.010 **Terpinolene as a Potential Antidiarrheal Agent: Evaluation of Acute Toxicity, Gastrointestinal Motility, and Mechanisms of Action in Mice**. Menezes PMF, Pessoa LF, Alves VP, Pessoa MMB, Pessôa MLS, Batista LM, UFPB, Brazil. UFPB, Gastrointestinal Pharmacology Lab, PGPNSB, Brazil

Introduction: Terpinolene is a monocyclic monoterpene widely found in several plant species and exhibits a variety of pharmacological effects, including anti-inflammatory and antioxidant activities. **Objectives:** To evaluate the acute toxicity of terpinolene, determine its median lethal dose (LD50), evaluate its antidiarrheal activity, its effects on gastrointestinal motility, and the mechanisms involved in these effects. **Methods:** Male Swiss mice (*Mus musculus*), weighing 28–35 g, were distributed into groups: negative control (2% tween 80), positive control (loperamide, 5 mg/kg), and terpinolene (10, 25, 50, 100, 200, 300, and 2000 mg/kg). Acute toxicity and behavioral analysis were evaluated (OECD. Acute Oral Toxicity-Acute Toxic. OECD Guideline For Testing Of Chemicals, 2001; Almeida, R.N. et al. Rev. Bras. Farmacogn., v.80, p.72, 1999). Antidiarrheal activity was evaluated using the castor oil-induced diarrhea model (Awouters C.J. et al. J. Pharm. Pharmacol. v.30, p.41, 1978). Gastric emptying was evaluated (Scarpignato, C.A. et al. Arch. Int. Pharmacodyn. Ther. v.246, p.286, 1980), and intestinal transit (Stickney, J.C. and Northup D.W. Proc. Soc. Exp. Biol. Med. v.101, p.582, 1959). Intraluminal fluid accumulation was evaluated using the castor oil-induced enteropooling model (Ezeja et al., Int. J. of Toxicol. Pharmacol Res., v.2, 2010). Adrenergic and muscarinic receptor participation was evaluated in antimotility mechanisms (Santos, FA; Rao, VSN. Eur. Jour. of Pharmacol. v.364, 1999; Capasso, R. Brit. J. of Pharmacol. v.134, 2001). Data were analyzed by ANOVA followed by Dunnett's test (mean ± standard deviation), followed by Tukey's post-test and Kruskal-Wallis test with $p < 0.05$. **Results:** Terpinolene (300 and 2000 mg/kg) did not promote behavioral changes, alterations in body weight progression, or mortality, indicating an LD50 >2500 mg/kg. It showed antidiarrheal activity at doses of 100 and 200 mg/kg, with diarrhea inhibition of 69% and 76% ($p <0.05$), respectively, compared to the negative control. Gastric emptying was significantly reduced by 88%, 85%, and 81% ($p <0.05$) at doses of 50, 100, and 200 mg/kg, respectively. In the intestinal transit test, terpinolene significantly reduced transit by 42%, 34%, 38%, and 35% ($p <0.05$) at doses of 25, 50, 100, and 200 mg/kg, respectively, compared to the control group. Terpinolene demonstrated involvement of adrenergic and muscarinic pathways and, at the dose of 100 mg/kg, reduced intestinal transit to 77% compared to the negative control. However, when associated with yohimbine, propranolol, and pilocarpine (1 mg/kg - i.p), this effect was reversed, increasing intestinal transit to 98%, 90%, and 86%, respectively. In the fluid accumulation evaluation, terpinolene (100 mg/kg) significantly reduced intestinal fluid volume by 27% ($p <0.05$), compared to the negative control. **Conclusion:** It can be inferred that terpinolene presents low acute toxicity, antidiarrheal activity, antisecretory and/or pro-absorptive activity, and effects on reducing gastrointestinal motility, involving adrenergic and muscarinic pathways. Animal Ethics Committee (CEUA- UFPB): 7877030524 and 2760060625 **Acknowledgments:** CNPq/UFPB/PgPNSB/IPeFarM

08.011 **Brown Propolis from *Mimosa tenuiflora* Prevents Airway Hyperreactivity through Multitarget Mechanisms in Ovalbumin-Induced Asthmatic Rats**. Lima CCM[1], Felício IM[2], Alves BFL[3], Souza MLB[1], Figueiredo IAD[2], Silva TMS[4], Picot, L[5]; Cavalcante FA[2,6] [1]UFPB, Pivic/UFPB, Brazil; [2]UFPB, CCS, PPgPNSB, Brazil; [3]Pibic/CNPq/UFPB; [4]UFPE, DQ, Brazil; [5]La Rochelle Université, LIENSs, France; [6]UFPB, CCS, DCB, Brazil

Introduction: Asthma is a chronic inflammatory disease characterized by airway remodeling, obstruction, and hyperresponsiveness. This heterogeneous condition affects around 300 million people worldwide, and at least one in ten patients does not respond satisfactorily to conventional management (Gina, 2026). In this context, natural products have emerged as complementary therapeutic agents, such as brown propolis (BP) from *Apis mellifera* bees (Ipaporanga, Ceará, Brazil). Its anti-inflammatory and antioxidant activities have been demonstrated, showing potential effects on the pathophysiological mechanisms of allergic asthma (Xu, W. Foods, v. 11, p. 2439, 2022). This study aimed to investigate the involvement of NO-, COX-, LOX-, and ROCK-related pathways in the protective effects of brown propolis on airway hyperreactivity in a rat model of allergic asthma. **Methodology:** Wistar rats were randomized into three groups (n = 5): control (CG), asthmatic (AG) and an asthmatic group treated with BP at 125 mg/kg (ABP125G). Asthma was induced over 21 days by ovalbumin sensitization and challenge, while control animals received saline. BP (125 mg/kg) was administered by intragastric gavage throughout the sensitization period. On day 22, tracheal rings were incubated with different inhibitors of enzymatic pathways: L-NAME (NOS inhibitor), indomethacin (COX inhibitor), zileuton (5-LOX inhibitor), or Y-27632 (ROCK inhibitor), followed by cumulative concentration-response curves to carbachol (CCh). Contractile reactivity was assessed by Emax and EC50 values. Statistical analyses were performed using ANOVA followed by Tukey's post-hoc test ($p < 0.05$). Experimental protocols were approved by the Animal Use Ethics Committee/UFPB (8719020621). **Results:** Inhibition of NOS, COX, and LOX pathways with L-NAME, indomethacin, and zileuton significantly reduced contractile efficacy in both AG and ABP125G. In AG, Emax decreased from 146.3 ± 5.6% to 107.9 ± 3.3%, 64.0 ± 5.8%, and 90.4 ± 6.7%, respectively, whereas in ABP125G, Emax decreased from 108.3 ± 8.1% to 43.1 ± 2.8%, 65.8 ± 6.0%, and 68.6 ± 11.2%, respectively ($p < 0.05$). Y-27632 produced the most pronounced effects, markedly reducing contractile efficacy in CG (Emax = 100.0% to 19.4 ± 3.2%), AG (Emax = 146.3 ± 5.6% to 59.7 ± 6.5%), and ABP125G (Emax = 108.3 ± 8.1% to 14.0 ± 5.7%). Unlike AG, the reduction in contractile efficacy induced by Y-27632 was accompanied by a reduction in potency, evidenced by increased EC50 values only in CG (9.6 ± 1.7 × 10-7 to 1.8 ± 0.3 × 10-5 M) and ABP125G (1,2 ± 0,2 × 10^{-}6 to 1.6 ± 0.5 × 10-5 M). **Conclusion:** These findings suggest that the protective effects of brown propolis against tracheal hyperreactivity are mediated by multitarget mechanisms involving NO-, COX-, LOX-, and ROCK-related pathways. **Financial support:** Pibic/CNPq/UFPB, PPgPNSB/CCS/UFPB, Capes.

08.012 **Association Between Catalase Activity and Pulmonary Function in Smokers and Former Smokers: The Modulatory Effect of the Renin-Angiotensin-System**. Medeiros GB, Freitas JLC, Paiva YMA, Medeiros VLD, Martins NRS, Amorim-Carmo B, Kennedy-Feitosa E, Silva FS UFERSA,Morphophysiopharmacology Lab. Brazil

Introduction: Chronic smoking promotes intense inflammation and oxidative stress, leading to progressive decline in pulmonary function. The classical axis of renin–angiotensin system (RAS) is an important way to induce inflammation and oxidative imbalance. Catalase activity is an antioxidant mechanism that can be used to recover the oxidative balance in the lungs. RAS- modulating drugs can be able to affect the catalase activity and modulate the redox status and impact in the lung function. **Objectives:** To evaluate the relationship between catalase activity and airflow limitation in smokers and former smokers undergoing treatment with RAS modulators. **Methods:** This study included 24 smokers and former smokers. Pulmonary function was assessed by spirometry according to SBPT standardization criteria (pre-bronchodilator FEV1/FVC below the lower limit of normal). Participants were stratified into two groups: users of RAS modulators (RASm) and non-users (Non-RASm). Catalase activity was quantified by spectrophotometry at 230 nm in plasma obtained from peripheral blood samples. Protein concentration was determined according to the Bradford method, and enzyme activity was expressed as U/mg of protein. Statistical analyses included Pearson's correlation and linear regression with slope comparison by Wald Z test, adopting a significance level of $p < 0.05$. **Results:** A negative correlation was observed between catalase activity and pre-bronchodilator FEV1/FVC ratio ($r = -0.53$; $p = 0.008$) among the 24 patients. However, stratification according to RASm use revealed distinct patterns. The Non-RASm group maintained a significant negative correlation ($r = -0.69$; $p = 0.009$). In contrast, this association was attenuated and no longer significant in the RASm group ($r = -0.45$; $p = 0.165$). Slope comparison confirmed statistically distinct profiles between the two groups ($p = 0.026$). **Conclusion:** Declining pulmonary function in smokers and former smokers is associated with a compensatory increase in catalase activity. However, the use of RAS modulators appears to modify this relationship. The divergent behavior observed between groups supports the hypothesis of a protective pleiotropic effect of these pharmacological agents, suggesting that treatment may be associated with attenuation of the overall oxidative burden.

08.013 **Evaluation of Acute Toxicity AND Antidiarrheal Activity of β-Pinene in Mice**. Pessoa LF, Menezes PMF, Alves VP, Pessoa MMB, Pessôa MLS,Batista LMUFPB, Gastrointestinal Pharmacology Lab, Brazil.

Introduction: β-pinene is a cyclic monoterpene found in the essential oils of plant species such as *Pinus* sp., for which antifungal and anti-inflammatory activities have already been described in the literature. However, there are no studies investigating its antidiarrheal activity. **Objective:** To evaluate the acute toxicity of β-pinene and its antidiarrheal activity, as well as its effects on gastrointestinal motility. **Methodology:** Male Swiss mice (*Mus musculus*), weighing 25–35 g, were distributed into groups: negative control (Tween 80 1%), positive control (Loperamide, 5 mg/kg, orally), and β-pinene at doses of 25, 50, 100, and 200 mg/kg. The methodology used to investigate the safety of β-pinene followed the acute toxicity assessment protocol (Almeida et al. Rev. Bras. Farmacogn. 80, 72, 1999; OECD. OECD Guideline Test. Chem. 423, 2001) at doses of 300 and 2000 mg/kg (p.o.), with observation for 14 days. Antidiarrheal activity was evaluated according to the castor oil-induced diarrhea model (Awouters C. J. et al. J. Pharm. Pharmacol. 30, 41–45, 1978). The effects of β-pinene on gastrointestinal motility were assessed through evaluation of gastric emptying (Scarpignato, C. A. et al. Arch. Int. Pharmacodyn. Ther. 246, 286–294, 1980) and the castor oil-induced intestinal transit model (Stickney, J. C. and Northup D. W. Proc. Soc. Exp. Biol. Med. 101, 582–583, 1959). Results were considered significant when $p < 0.05$ using ANOVA followed by Dunnett's/Tukey's post hoc test. **Results:** In the acute toxicity evaluation, the animals showed no behavioral changes or mortality at doses of 300 mg/kg and 2000 mg/kg. Furthermore, no alterations were observed in body weight progression, organ index, or food and water intake. Based on these findings, it can be inferred that the LD50 of β-pinene is greater than 2500 mg/kg, classifying it within category 5 of the Globally Harmonized System (GHS) as a substance with low toxicity. In the castor oil-induced diarrhea model, β-pinene at doses of 100 and 200 mg/kg showed diarrhea inhibition percentages of 58% ($p < 0.05$) and 65% ($p < 0.01$), respectively, when compared with the negative control group (Tween 80 1%). In the gastric emptying model, animals treated only with Tween 80 1% presented 87.6% gastric emptying, whereas groups treated with β-pinene at doses of 50, 100, and 200 mg/kg showed a significant reduction compared with the negative control group: 76.9% ($p < 0.05$), 76.4% ($p < 0.05$), and 64.6% ($p < 0.05$), respectively. In the intestinal transit model, groups treated with β-pinene significantly reduced ($p < 0.001$) the percentage of intestinal transit at all tested doses: 69%, 75%, 76.8%, and 74.3%, respectively, compared with the negative control group. **Conclusion:** Thus, β-pinene may be considered a low-toxicity substance that demonstrated antidiarrheal activity with effects on gastrointestinal motility, reducing both intestinal transit and gastric emptying. **Acknowledgments:** CNPq / UFPB / PgPNSB / IpeFarM. Animal Ethics Commitee (CEUA - UFPB): 2760060625

08.014 **Losartan does not Reduce the Risk of Respiratory Exacerbations in Hypertensive Smokers**. Costa GG, Santos JRA, Vidal TIR, Silva FS, Kennedy-Feitosa E Morphophysiopharmacology Lab, Federal University of the Semiarid Region (UFERSA), Mossoró, Brazil.

Introduction: Systemic arterial hypertension (SAH), when associated with smoking, induces a systemic pro-inflammatory state characterized by alterations in the leukocyte profile, increasing the risk of respiratory exacerbations. Antihypertensive treatment with losartan has been shown to exert additional effects, including the reduction of oxidative stress and inflammation, potentially decreasing the risk of respiratory exacerbations. Neutrophil-Lymphocyte ratio (NLR) has been used to indicate the risk of respiratory exacerbation. **Aim:** We investigated whether losartan treatment in hypertensive smokers patients impacts the leukocyte profile. **Methods:** Smokers with normal blood pressure (Smoker), non-smokers with hypertension receiving losartan treatment (Non-smoker+Losa), and hypertensive smokers receiving losartan treatment (Smoker+Losa) were enrolled in the study. Peripheral blood samples were collected, and blood smears were prepared and stained using the May–Grünwald–Giemsa method for total and differential leukocyte counts, focusing on neutrophils and lymphocytes per field. The neutrophil-to- lymphocyte ratio (NLR) was calculated as the number of neutrophils per field divided by the number of lymphocytes per field. Statistical significance was considered at $p < 0.05$. **Results:** The Smoker+Losa group showed an increased total leukocyte count (16.6 ± 4.0) compared with the Smoker ($p < 0.009$) and Non-smoker+Losa ($p < 0.03$) groups. The number of neutrophils per field in the Smoker+Losa group (71.25 ± 6.7) was higher than that observed in the Smoker (56.20 ± 3.1; $p < 0.05$) and Non-smoker+Losa (51.58 ± 2.3; $p < 0.05$) groups. No differences in lymphocyte counts were observed among the groups ($p > 0.05$). The neutrophil-to-lymphocyte ratio (NLR) in the Smoker+Losa group (2.96 ± 0.7) was higher than that of the Smoker (1.64 ± 0.1; $p < 0.05$) and Non-smoker+Losa (1.37 ± 0.2; $p < 0.05$) groups. **Conclusion:** These findings suggest that losartan use is not capable of attenuating the chronic systemic hyperinflammatory state observed in smokers, as it did not reduce NLR levels, thereby maintaining the leukocyte profile associated with an increased risk of respiratory exacerbations.

08.015 **Effect of LASSBio-468 on 5-fluorouracil-Induced Intestinal Mucositis in Mice**. Ferreira ABA[1], Monteiro CES[1], Franco AX[1], Silva BVL[1], Silva TML[1], Sales TMAL[2], Alicrim SAC[1], Monte AVO[1], Lopes AS[1], Souza MHLP[1], Soares PMG[1]
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Introduction: Intestinal mucositis is an important complication associated with 5-fluorouracil (5-FU)-based chemotherapy, characterized by inflammatory and histopathological alterations of the intestinal mucosa that may impair patients' quality of life and compromise treatment continuity. LASSBio-468 is a phthalimide analogue with anti-inflammatory properties related to the modulation of TNF-α and nitric oxide, representing a promising alternative for attenuating the effects of mucositis. **Objectives:** To evaluate the antioxidant and anti-inflammatory effects of LASSBio-468 in an experimental model of 5-fluorouracil-induced intestinal mucositis. **Methods:** The study was approved by the Animal Ethics Committee of the Federal University of Ceará (CEUA/UFC) under protocol no. 8941100323. Intestinal mucositis was induced in Swiss mice by intraperitoneal (i.p.) administration of 5-FU (450 mg/kg). Animals were allocated into the following groups: saline, 5-FU + dimethyl sulfoxide (DMSO), and 5-FU + LASSBio-468 (1, 10, and 50 mg/kg, orally). LASSBio-468 treatment was administered 30 min before induction and again at 24, 48, and 72 h after induction. Animals were then euthanized, and jejunum and ileum samples were collected for histopathological analysis, myeloperoxidase (MPO) activity, reduced glutathione (GSH) levels, nitrite levels, TNF-α levels, and NF-κBp65 and TNF-α gene expression. **Results:** Administration of 5-FU promoted villus shortening, crypt atrophy, cellular vacuolization, and inflammatory cell infiltration in the jejunum and ileum. Treatment with LASSBio-468 reduced histopathological alterations. MPO activity was reduced by 67.9% in the jejunum and 71.5% in the ileum, while TNF-α levels were reduced by 71.3% and 61.5%, respectively. GSH levels increased by 53.8% in the jejunum and 41.1% in the ileum, whereas nitrite levels decreased by 37.6% and 40.8%, respectively. Relative NF-κBp65 expression increased 4.6-fold in the 5-FU group and was significantly reduced following treatment with LASSBio-468. Likewise, TNF-α expression increased 5.6-fold in the 5-FU group compared with the saline group and was significantly reduced by treatment. **Conclusion:** LASSBio-468 attenuated 5-FU-induced intestinal mucositis by reducing histological alterations, inflammation, and oxidative stress. These effects appear to be related to modulation of the NF-κB/TNF-α pathway, highlighting the potential of this compound to attenuate chemotherapy-associated intestinal mucositis. This study was approved by the Animal Ethics Committee (CEUA) of the Federal

University of Ceará (UFC) under protocol no. 8941100323. **Financial support** was provided by the National Council for Scientific and Technological Development (CNPq).

08.016 **Lemon Gum Reduces Esophageal Inflammation and Oxidative Stress in Experimental Reflux Esophagitis**. Pimentel TFM[1], Teixeira LFLS[2], Silva KC[2], Ribeiro FOS[3], Freitas RA[4], Palumbo-Júnior A[5], Medeiros JVR[2], Souza MHLP[6], Cordeiro LMC[4], Silva DA[1], Nicolau LAD[2]. [1]UFDPar, Lab Inflammation and Translational Gastroenterology, Parnaíba, PI, Brazil. [2]UFDPar, PPG in Biotechnology, Parnaíba, PI, Brazil. [3] UFPR Dept Chemistry, PR, Brazil. [4] UFPR, BioPol, Dept Biochemistry and Molecular Biology, Curitiba, PR, Brazil. [5]UFC, Dept Physiology and Pharmacology, Fortaleza, CE, Brazil. [6]UFC Faculty of Medicine, , Fortaleza, CE, Brazil.

Introduction: Gastroesophageal reflux disease is associated with reflux- induced epithelial barrier disruption, oxidative imbalance and inflammatory cell recruitment, which together contribute to mucosal injury and disease persistence. Although acid suppression remains a central therapeutic approach, mucosal protection and epithelial repair require complementary strategies. In this context, bioadhesive polymers with barrier-forming and immunomodulatory properties have emerged as promising adjunctive candidates. Lemon gum (LG), an acidic arabinogalactan obtained from Citrus × latifolia exudate, is a structurally complex polysaccharide with potential affinity for the esophageal mucosa. **Objectives:** We evaluated whether LG prevents reflux esophagitis by reducing epithelial injury, inflammation and oxidative stress, and whether these effects are associated with mucin binding and epithelial repair. **Methods:** LG was characterized by GC-MS, HPSEC and 13C NMR. Reflux esophagitis was induced in Wistar rats by pylorus and forestomach ligation. Animals were orally pretreated with vehicle, LG (3, 30 or 90 mg/kg) or alginate; sham animals were used as controls. After 9 h, esophagi were collected for macroscopic analysis, MPO, GSH and MDA quantification, and histopathology. Erosion, inflammatory infiltrate, mast cells and dilated intercellular spaces (DIS) were scored or quantified. LG-mucin interactions were assessed by QCM-D, AFM and contact angle. FITC-LG adhesion was examined in human esophageal biopsies by confocal microscopy after washing. Cytotoxicity and scratch wound healing assays were performed in human esophageal epithelial cells. Data were analyzed by [insert exact statistical test]; $p<0.05$ was considered significant. **Results:** Reflux esophagitis increased mucosal injury, MPO activity, MDA levels, mast cell infiltration and DIS, while reducing GSH. LG, mainly at 30 mg/kg, significantly attenuated this inflammatory and oxidative profile. At this dose, LG decreased MPO activity, restored GSH, reduced MDA and improved both macroscopic and microscopic injury, with lower erosion and inflammatory scores, fewer mast cells and reduced DIS. The preventive index reached approximately 88%. In parallel, biophysical assays demonstrated stable LG adsorption to mucin, formation of a hydrated viscoelastic layer and increased mucosal affinity. Confocal microscopy further confirmed persistent FITC-LG adhesion to human esophageal epithelium after washing. *In vitro*, LG preserved cell viability and accelerated epithelial wound closure. **Conclusion:** LG prevented experimental reflux esophagitis through integrated anti- inflammatory, antioxidant, barrier-forming and pro-repair actions. These findings support citrus-derived arabinogalactan as a mucoadhesive biopolymer with translational potential for reflux-related esophageal injury.

08.017 **The Use of a Pressurized Metered Dose Inhaler with Spacer at the Pediatric Emergency Care Units**. Dorneles GL[1], Matos IF[2], Silva GS[1], Pires ARL[1], Castro PFS[1] [1]UEG, Biomedicine Program, Brazil; [2]UniEvangélica, Nursing Program, Brazil.

Introduction: Asthma is treated with inhaled corticosteroids and bronchodilators, the vast majority of which are delivered in inhaled devices, as these help to speed up the onset of action, reduce side effects, preserve lung function, and prevent changes in the structure of the airways, avoiding obstructions triggered after long years of the disease's action. The gaps in knowledge regarding the correct technique for handling inhalation devices are not only limited to patients living with asthma but also to health professionals and prescribers of inhalation therapy, which leads to misguided guidance for users. The aim was to evaluate the technique used by healthcare professionals at a pediatric emergency unit in the interior of Goiás, Brazil when using a pressurized metered dose inhaler (MDI) coupled with a spacer. **Methods:** A cross-sectional study was conducted with the participation of physicians, pharmacists, nurses, and nursing technicians. They answered a standardized questionnaire about the use of the MDI-spacer and handled it, simulating administration in children. Data was analyzed by SPSS Statistics Kruskal-Wallis test and Mann-Whitney post-test ($p<0.05$). Research Ethics Committee approval number: 5,836,421. **Results:** The results showed errors greater than 65% occurred for the steps: forced expiration, inhaling slowly and deeply, inspiratory pause, cleaning the spacer, and cleaning the oral cavity. The healthcare professionals who performed best on the use of MDI with spacer and mouthpiece and the use of MDI with spacer and mask, which mimics the use of the inhaler by children under 5 years of age on the removing the cap step were nursing technicians. **Conclusion:** Therefore, professionals showed difficulty in particularizing the differences in the use of MDI-spacer between children older and younger than 5 years old. **Financial support:** Universidade Estadual de Goiás (UEG).

08.018 **Eugenol Attenuates Pulmonary Parenchymal Damage in a Cigarette Smoke-Induced COPD Mouse Model.**
Santos JRA[1], Amorim-Carmo B[1], Costa GG[1], Oliveira MF[2], Silva FS[1], Kennedy-Feitosa E[1] [1]UFERSA, Morphophysiopharmacology Lab ; [2]UFERSA, Dept Animal Science

Introduction: Among non-communicable diseases, Chronic Obstructive Pulmonary Disease (COPD) stands out as a major contributor to worldwide morbidity and mortality, with cigarette smoke (CS) as its principal etiological factor. The pathophysiology involves smoke-triggered oxidative injury and inflammatory cascades that upregulate proteolytic enzymes, culminating in extracellular matrix breakdown and progressive loss of alveolar integrity. Given that available pharmacological approaches target symptom management without addressing tissue regeneration, novel therapeutic strategies remain urgently needed. Eugenol (EUG), a phenylpropanoid with well-documented anti- inflammatory properties and evidence of protection against acute pulmonary injury, represents a promising candidate. **Objective:** To investigate whether EUG modulates pulmonary parenchymal remodeling in a cigarette smoke CS-induced murine COPD model. **Methods:** Male C57BL/6 mice were allocated into six groups: Control (n=6), CS (n=5), CS+EUG 1 µg/ml (n=6), CS+EUG 3 µg/ml (n=6), CS+EUG 10 µg/ml (n=6), and CS+Dexamethasone (n=5). Animals underwent CS inhalation of smoke of 12 cigarettes three times daily for 60 days, followed by 60 days of treatment via inhaled EUG at designated concentrations or saline or intraperitoneal dexamethasone (0.4 mg/kg). Lungs were subsequently harvested for histological processing and morphometric quantification. Results are presented as mean ± SEM, with statistical significance set at $p<0.05$. **Results:** Gross examination revealed that CS exposure caused increased lung volume, hemorrhagic areas, and pigment deposition, all of which were visibly reduced following EUG treatment. Morphometric analysis demonstrated that EUG administration at all concentrations significantly decreased Airspace Diameter (AD) and Mean Linear Intercept (Lm), while increasing Alveolar Wall Area (AWA), reducing peribronchiolar collagen accumulation, and restoring bronchiolar epithelial height. **Conclusion:** These effects were independent of EUG concentration. Mean Septal Thickness (MST), Bronchoconstriction Index (BCI), and pigmented macrophage counts did not differ significantly between groups. Collectively, the findings support eugenol as a candidate agent for mitigating smoke-induced pulmonary architectural deterioration.

08.019 **The Role of IL-17 in Pulmonary Inflammation and pro-fibrotic Changes Induced by Experimental Gastroesophageal Reflux Disease**. Silva BVL[1]; Sales TMAL[2]; Ferreira ABA[1]; Silva TML[1]; Alicrim SAC[1]; Monteiro CES[1]; Franco AX[1]; Almeida VM[2]; Azevedo YG[2]; Melo BMS[2]; Daniel AML[1]; Alves JCF[2]; Riteau NDM[2]; Soares PMG[1]; Souza MHLP[1]. [1]UFC, Lab Gastrointestinal Physiopharmacology, Brasil; [2]USP, Immune Health Lab, Brasil.

Introduction: Gastroesophageal reflux disease (GERD) is associated with various extraesophageal manifestations, including inflammatory changes in lung tissue that may be linked to increased fibrosis. IL-17 plays a role in inflammatory processes and tissue remodeling in various lung diseases. However, there is no evidence to demonstrate its involvement in the pulmonary changes resulting from GERD. **Objectives:** To analyze the role of IL-17 in the development of inflammation and pulmonary fibrosis in an experimental model of GERD. **Methods:** Male C57BL/6 mice underwent surgical induction of GERD via pyloric substenosis and gastric fundus ligation; genetically modified mice (IL-17 KO) were also used. The animals were euthanized 3, 7, 14, 21, and 28 days after surgery. Pulmonary inflammation was identified through histology, assessment of myeloperoxidase (MPO) enzyme activity, and measurement of inflammatory cytokines (IL-17) by ELISA. Changes associated with pulmonary remodeling were analyzed using hydroxyproline, α-SMA, and Sirius Red staining. This study was approved by the Animal Ethics Committee (CEUA) of the Federal University of Ceará (UFC) and registered under CEUA No. 3392050625. **Results:** GERD induced progressive inflammatory changes throughout the experimental period. MPO activity increased significantly, peaking on day 7 (34.71 ± 3.95 U/mg, $p < 0.05$) compared to the sham group (3.39 ± 0.57 U/mg, $p < 0.05$), and remained elevated until day 28 (11.28 ± 0.88 U/mg). Histological analysis revealed alveolitis in the animals subjected to GERD. There was a significant increase in IL-17 levels on day 28 compared to the sham group (523.7 ± 34.3 vs. 296.7 ± 28.2; $p<0.05$). Elevated levels of hydroxyproline (64.05 ± 2.88 vs. 21.05 ± 9.81) and α-SMA expression (0.2929 ± 0.0075 vs. 0.2364 ± 0.0328) were observed on day 28 compared to the sham group. **Conclusion:** These findings suggest that GERD induces pulmonary inflammation, characterized by alveolitis, increased MPO activity, and elevated levels of IL-17. These changes appear to be related to those associated with pulmonary remodeling, demonstrating an initial pro-fibrotic profile. This study was approved by the Animal Ethics Committee (CEUA) of the Federal University of Ceará (UFC) under protocol no. 3392050625. Funding was provided by CAPES, CNPq, FUNCAP, and FAPESP.

08.020 **Refluxate Components Drive NETosis and Promote Experimental Reflux Esophagitis Trough PAD4-Dependent Mechanisms**. Gomes IAB[1]; da Silva GCP[2]; Ramos AS[3]; Pérez MM[3]; Sales TMAL[3]; Costa VF[3]; Araújo AVV[1]; Carvalho KS[1]; Medeiros JVR[1]; Saraiva EM[2]; Cunha FQ[3]; Nicolau LAD[1]. [1]UFDPar, PPG in Biotechnology, Brazil; [2]UFRJ, Dept Immunology, Brazil; [3]CRID-FMRP-USP, Brazil.

Introduction: Gastroesophageal reflux disease (GERD) results from exposure of the esophageal mucosa to gastric refluxate, leading to inflammation and tissue injury. Although neutrophils are detected in esophageal lesions, the role of neutrophil extracellular traps (NETs) in GERD remains unclear. **Objective:** To investigate whether refluxate components induce NETosis in human neutrophils and whether NETosis contributes to experimental GERD. **Methods:** Human neutrophils were stimulated with pepsin and bile salts. NET formation was assessed by PicoGreen, SYTOX Green and confocal microscopy. PAD4, calcium signaling, NLRP3 and gasdermin D inhibitors were used to investigate NETosis pathways. Reflux esophagitis was induced by pyloric stenosis and forestomach ligation. NET-targeted therapies (GSK484, disulfiram and DNase I) and neutrophil-specific PAD4-deficient (PAD4 ΔLy6G) mice were evaluated by histological, molecular and flow cytometric analyses. **Results:** Activated pepsin induced dose-dependent ROS production and NET formation, increasing SYTOX Green fluorescence from 2–4 · 10^6 UA in control- and HCl-treated neutrophils to 1.0 · 10^7;, 1.4 · 10^7; and 1.8 · 10^7; UA at 10, 50 and 100 µg/mL, respectively, exceeding inactive pepsin. Neutrophil death increased from 8–12% to 32%, 50% and 55%. All tested bile salts increased NET formation from 2.2 · 10^6 to 5.7–6.9 · 10^6 UA, whereas combined stimulation produced the greatest response (9.5 · 10^6 UA). Confocal microscopy confirmed NET formation by demonstrating extracellular DNA colocalized with neutrophil elastase. PAD4, calcium signaling, NLRP3 or gasdermin D inhibition reduced NET release (all $p < 0.05$). Reflux esophagitis increased MPO-DNA (1.922 vs. 8.996) and NE-DNA (0.577 vs. 3.088) while reducing DNase I (0.988 vs. 0.367) and DNase1L3 (1.494 vs. 0.584) compared with sham animals. Reflux reduced mucin content (PAS: 1.692 vs. 0.169), keratin (6.833 vs. 1.881) and epithelial thickness (6.440 vs. 2.355), while increasing dilated intercellular spaces (DIS: 2.2% vs. 7.7%), accompanied by increased inflammatory mediator production and inflammatory cell infiltration (all $p < 0.05$). GSK484, disulfiram and DNase I restored DNase levels, reduced NET accumulation, and attenuated esophageal injury. Similarly, PAD4 ΔLy6G mice exhibited reduced NET accumulation, preserved mucin content (PAS: 0.1949 vs. 0.6065), keratin thickness (2.895 vs. 5.829), epithelial thickness (6.825 vs. 8.661), and reduced DIS (7.0% vs. 5.5%) compared with PAD4fl/fl mice, confirming the contribution of neutrophil PAD4 to reflux-induced esophageal mucosal injury. **Conclusion:** Gastric reflux components induce NETosis through PAD4- and inflammasome-dependent mechanisms. Pharmacological inhibition of NETosis or neutrophil-specific PAD4 deletion attenuated esophageal mucosal injury, identifying NETosis as a potential therapeutic target in GERD. **Acknowledgments:**: Center for Research in Inflammatory Disease.

08.021 **Evaluation of the Subchronic Safety Profile and Anticolytic Activity of an N-acylhydrazone Derivative in an Animal Model.** Oliveira JEB[1], Araruna MEC[2], Santos VL[1], Moura RO[1] [1]UEPB, PPG in Pharmaceutical Sciences, Brazill, [2]UEPB, Pharmacological Testing Lab, Brazil

Inflammatory bowel diseases (IBDs) are part of a heterogeneous group of pathologies characterized by causing acute or chronic inflammation of the gastrointestinal tract (GIT) mucosa. Due to their prolonged clinical course and high recurrence rates, they represent a serious public health problem, impacting patients' quality of life. In light of current therapeutic limitations, the development of new, effective, and safe drugs becomes necessary. In this context, N-acylhydrazone derivatives, such as 2-cyano-N'-(3-ethoxy-4-hydroxybenzylidene)-acetohydrazide (JR-12), represent a class of organic compounds widely studied in medicinal chemistry. These compounds stand out for their structural versatility, enabling a wide spectrum of biological activities, such as anti-inflammatory and antioxidant properties, among others. Therefore, the aim of this study was to evaluate the subchronic safety and anticolitic activity of the compound JR-12. The repeated-dose toxicity study followed OECD Guideline 407, using male and female Swiss mice divided into six groups, which were treated orally for 28 days with JR-12 (10 or 20 mg/kg) or with saline + 5% dimethyl sulfoxide (DMSO) as a negative control vehicle. Body mass, relative organ weights (heart, kidneys, spleen, liver, and stomach), average water and food intake, macroscopic aspects, and hematological parameters were evaluated.The anti- inflammatory activity of JR-12 was investigated using the acute colitis model induced by 2,4,6-trinitrobenzenesulfonic acid (TNBS), in which Wistar rats were divided into six groups. After an eight-hour fast, they received 10 mg of TNBS dissolved in 0.25 mL of 50% v/v ethanol, administered rectally using a probe. Among the groups, the non-colitic group underwent only anesthesia and probe insertion procedures; the others were pre-treated with JR-12 (10 or 20 mg/kg), prednisolone, or vehicle, at 48, 24, and 1 hour before administration of the inflammatory agent. After induction of inflammation and euthanasia with a combination of 2% xylazine and 10% ketamine, ulcerative lesion area, inhibition percentage, lesion score, and the weight/length ratio of the excised colonic segment were evaluated. The results demonstrated a safe toxicological profile for JR-12, with no significant changes in the evaluated parameters ($p>0.05$). Moreover, the compound showed a therapeutic advantage over prednisolone by not presenting detectable immunosuppressive effects, unlike the corticosteroid. In the colitis induction assay, the derivative promoted a reduction in ulcerative lesions (87% and 92% inhibition for 10 and 20 mg/kg, respectively, $p<0.001$), as well as decreased lesion score and colon weight/length ratio, suggesting limitation of the inflammatory process, with less tissue edema and prevention of colonic shortening associated with fibrosis development. In conclusion, JR-12 presents a favorable toxicological profile and significant intestinal anti-inflammatory activity, supporting its potential as a drug candidate for IBDs.

08.022 **Investigation of the Gastroprotective Effect of a Formulation Based on Isoquercitrin Complexed with Gamma-Cyclodextrin: Role of the Nitric Oxide Pathway, Cytokines and Redox Homeostasis**. Barbosa TVGB[1], Rocha NA[1], Oliveira RCM[1], Sousa DP[2], Oliveira FA[1] [1]UFPI, Health Sciences Center, PPG Pharmacology, Brazil, [2]UFPB, Dept Pharmaceutical Sciences, Brazil

Introduction: Peptic ulcer disease remains a significant clinical challenge, often exacerbated by ethanol consumption and NSAID use. Isoquercitrin (ISO) is a flavonoid with recognized antioxidant properties and antinflammatory , but its therapeutic potential is hampered by low aqueous solubility. The development of a molecular inclusion complex with gamma-cyclodextrin (ISO/γ-CD) serves as a biotechnological strategy to enhance its solubility and bioavailability. **Objectives:** To evaluate the gastroprotective activity of ISO/γ-CD and investigate the participation of the nitric oxide (NO) pathway, pro-inflammatory cytokines, and antioxidant defenses in experimental models using rats. **Methods:** Male Wistar rats were pretreated with ISO/γ-CD (25, 50, or 100 mg/kg, p.o.) or vehicle. Gastric lesions were induced by absolute ethanol (1 mL/animal). The involvement of NO was assessed by pretreatment with L-NAME (20 mg/kg, i.p.). Tissue concentrations of TNF-α and IL-1β were determined by ELISA (R&D; Systems). In the pylorus ligation model, gastric secretion parameters (volume and pH) and adherent mucus were evaluated. Reduced glutathione (GSH) levels and superoxide dismutase (SOD) activity were measured via colorimetric assays. The protocol was approved by the local ethics committee CEUA/UFPI (859/2025). **Results:** In the ethanol model, ISO/γ-CD at 50 mg/kg was the most effective dose, reducing the gastric lesion area by 48.2% (7.36 ± 0.93 mm2) compared to the vehicle group (14.23 ± 1.38 mm 2; $p<0.001$). This protective effect was completely abolished by L-NAME, confirming dependency on the NO pathway. The formulation effectively restored mucosal GSH levels to approximately 2300 µmol/mg (compared to 1400 µmol/mg in the vehicle group) and promoted SOD superactivation (2.0 ± 0.2 U/mg protein), significantly exceeding the physiological levels of the Sham group (1.2 ± 0.1 U/mg).ELISA analysis showed that ISO/γ-CD significantly reduced TNF-α to approximately 130 pg/mL (vs. 220 pg/mL in vehicle) and IL-1β to 102 pg/mL (vs. 210 pg/mL in vehicle), returning both to baseline levels ($p<0.01$). In the pylorus ligation model, ISO/γ-CD did not alter the volume or pH of gastric juice but significantly increased the production of adherent mucus. **Conclusion:** The ISO/γ-CD formulation exerts a multi-target gastroprotective effect involving the modulation of redox homeostasis, reduction of pro-inflammatory cytokines, and activation of the nitric oxide pathway, without primary antisecretory mechanisms. These findings position the formulation as a promising strategy for treating gastric disorders. Keywords: Isoquercitrin; gastroprotection; γ-cyclodextrin **Financial support:** CAPES, UFPI

08.023 **Gastroprotective Activity of β-Pinene in Animal Models**. Alves VP, Pessoa MMB, Pessôa MLS, Menezes PMF, Pessoa LF, Batista LM UFPB, Gastrointestinal Pharmacology Lab, PGPNSB, Brazil.

Introduction: Peptic ulcer is an inflammatory disorder of the gastrointestinal mucosa. Current therapy is centered on the use of proton pump inhibitors, especially vonoprazan. However, this therapy has limitations, making the search for therapeutic alternatives necessary. In this context, natural products stand out due to their variety of bioactive molecules and widespread traditional use. β-pinene is a monoterpene present in essential oils, with anti-inflammatory and antioxidant activities described in the literature. **Objective:** To evaluate whether β-pinene has gastroprotective activity in different experimental models of gastric ulcer. **Methods:** Male Swiss mice (*Mus musculus*) aged 6 to 8 weeks, weighing 28–35 g, and male Wistar rats (Rattus norvegicus) aged 7 to 8 weeks, weighing 180–250 g, were used. Animals were maintained at 23 ± 2 °C under 12 h light/dark cycles. The following ulcer induction models were used: HCl/ethanol-induced ulcer (Mizui, T. Jpn. J. Pharmacol., v. 33, p. 939, 1983), stress-induced ulcer (Levine, R. J. Peptic Ulcer, p. 92, 1971), and nonsteroidal anti-inflammatory drug (NSAID)-induced ulcer (Puscas, I. Arzneimittelforschung, v. 47, p. 568, 1997). In rats, the absolute ethanol-induced ulcer model was used (Morimoto, Y. Jpn. J. Pharmacol., v. 57, p. 495, 1991). Data were expressed as mean ± standard deviation. One-way ANOVA followed by Dunnett's and Tukey's post-tests was used, with a minimum significance level of $p < 0.05$. **Results:** In the HCl/ethanol-induced ulcer model, carbenoxolone (100 mg/kg – positive control – p.o.) and β-pinene (25, 50, 100, and 200 mg/kg – p.o.) significantly reduced ($p < 0.001$) the ulcerative lesion index (ULI) by 57% (53 ± 3.7), 41% (71.8 ± 2.2), 49% (63.1 ± 1.1), 52% (58.8 ± 5.2), and 64% (44.4 ± 2.8), respectively, compared to the negative control group (1% Tween 80) (123 ± 8.3). In the stress-induced ulcer model, ranitidine (50 mg/kg – positive control – p.o.) and β-pinene (different doses) significantly reduced ($p < 0.001$) the ULI by 46% (42.5 ± 5.0), 13% (67.6 ± 4.7), 30% (55 ± 5.3), 48% (40.6 ± 4.4), and 45% (43 ± 4.0), respectively, compared to the negative control group (78 ± 2.8). In the NSAID-induced ulcer model, ranitidine and β-pinene (50, 100, and 200 mg/kg) significantly reduced ($p < 0.001$) the ULI by 40% (37.3 ± 5.2), 21% (49 ± 3.7), 48% (32.3 ± 2.8), and 47% (32.8 ± 4.9), respectively, compared to the negative control group (62 ± 4.6). In the absolute ethanol-induced ulcer model, animals pretreated with carbenoxolone (100 mg/kg) and β-pinene (different doses) showed a significant reduction ($p < 0.001$) in lesion area, with inhibition percentages of 81% (8.1 ± 0.5 mm^2), 54% (19.5 ± 1.7 mm^2), 71% (12.4 ± 2.0 mm^2), 88% (5.3 ± 0.8 mm^2), and 87% (5.5 ± 0.9 mm^2), respectively, compared to the negative control group (42.7 ± 3.3 mm^2). **Conclusion:** Thus, it can be inferred that β-pinene exhibits gastroprotective activity against different experimental models of gastric ulcer. **Acknowledgments:** CAPES/UFPB/PgPNSB/IPeFarM. Animal Ethics Committee (CEUA-UFPB): 6329300625.

08.024 **Fasudil, a Rho Kinase Inhibitor, Attenuates Intestinal Hypocontractility in an Experimental Model of Autism Spectrum Disorder: Preliminary Findings**. Longo B[1], Lima-Moura SA[1], Cury BJ[1], Santos MR[1], Cazarin CA[2], Willrich CH[1], Da Silva-Santos JE[1], Da Silva LM[1,2]. [1]UFSC, Dept Pharmacology, Brazil, [2]UFSC, Neuroscience Postgraduate Program, Brazil.

Introduction: Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that also affects the gastrointestinal tract, with motility disturbances such as diarrhea and constipation among the most common comorbidities. The RhoA/Rho kinase (ROCK) signaling pathway plays a key role in regulating intestinal motility by modulating gastrointestinal smooth muscle contraction. Under pathological conditions, dysregulation of RhoA/ROCK signaling may contribute to impaired intestinal motility. Furthermore, hyperactivation of this pathway has been associated with inflammation and tissue remodeling, which may impair intestinal neuromuscular function. Therefore, this study hypothesized that fasudil, a ROCK inhibitor, could improve motility disturbances in a valproic acid (VPA)-induced animal model of ASD. **Methods:** Pregnant female Swiss mice received a single intraperitoneal (i.p.) injection of VPA (350 mg/kg) or saline on gestational day 12.5. From postnatal day 27 to 37, male offspring prenatally exposed to VPA (n=6) were treated with fasudil (1, 3, or 10 mg/kg, i.p.) or vehicle (saline, 1 mL/kg, i.p.). Intestinal reactivity was evaluated in ileum and colon strips using isolated organ bath preparations. Concentration–response curves to carbachol (1 nM–300 μM) were generated in mice treated with fasudil or vehicle. In parallel, concentration–response curves in the presence of the ROCK inhibitor Y-27632 were obtained *in vitro* in control and VPA-exposed mice. Contractile responses to KCl (120 mM) and ACh (30 μM) were also evaluated. **Results:** VPA-vehicle group exhibited reduced carbachol-induced contractions in both the colon and ileum. Prolonged treatment with fasudil partially reversed colonic hypocontractility (1–10 mg/kg) and restored ileal contractions (1 and 3 mg/kg). Acute exposure to ROCK inhibitor Y-27632 reduced contractions in the colon of control mice and decreased ileal and colonic contractile responses in VPA-vehicle group. In addition, VPA-vehicle group showed reduced KCl-induced contractions and decreased ACh-induced phasic and tonic contractions in the colon, with no changes in ileal responses, contraction frequency, or amplitude compared with controls. Fasudil also reduced KCl-induced responses (3 and 10 mg/kg) and contraction frequency (1 mg/kg) in the colon. **Conclusion:** Prolonged treatment with fasudil attenuated colonic and ileal hypocontractility in VPA-exposed mice, possibly by inhibiting RhoA/ROCK-mediated intestinal remodeling associated with chronic inflammation, thereby improving responsiveness to contractile stimuli. Animal Ethics Approval Number: 8097040226\. **Financial support**: CNPq.

08.025 **Effect of Farnesol Complexed with β-Cyclodextrin in a Model of Bronchial Asthma Induced by Ovalbumin** *In vitro* **and** *in vivo*. Souza ORB[1], Oliveira MM[1], Silva RLT[1], Filho-Reis AC[1], Martins HRS[1], Reis ML[1], Sousa RWR[1,2], Ferreira PMP[1,2,3], Quintans, JSS[4], Quitans-Júnior LA[4], Oliveira AP[1], Almeida FRC[1], Santos, RF[1], Oliveira RCM[1] [1]UFPI, Health Sciences Center, PPG Pharmacology, Brazil. [2]UFPI, Lab Experimental Cancerology (LabCancer), Dept Biophysics and Physiology. [3]LOE-UFC, Lab Experimental Oncology, Dept Physiology and Pharmacology. [4]LANEF-UFS, Lab Neurosciences and Pharmacological Assays, Dept Physiology, PPG Health Sciences, Brazil.

Introduction: Asthma is a respiratory disease characterized by inflammation, hypersecretion, and bronchoconstriction. Several drugs are used, however, 10% of individuals remain without adequate control. Therefore, medicinal plants and phytochemicals with therapeutic potential stand out, such as farnesol, an alcoholic sesquiterpene with proven anti-inflammatory, antinociceptive, and hypotensive activities. **Objective:** To investigate the antiasthmatic activity of farnesol complexed with β-cyclodextrin (Fβ-CD) in an experimental model of ovalbumin (OVA) induced asthma, using *in vivo* and *in vitro* approaches. **Methodology:** Used were Male Wistar rats (180-220g; CEUA/UFPI 844/2024). Asthma induced was intraperitoneally with OVA and aluminum hydroxide on days 0, 7, and 14, followed by antigen challenge with OVA nebulization for 7 days. Tests were performed on asthmatic animals (GA), non-asthmatic controls, treated with dexamethasone (1 mg/kg) and Fβ-CD at different doses. Tracheal contractile reactivity was evaluated in animals previously treated with Fβ-CD 5, 25, and 100 mg/kg (p.o.), subjected to carbachol concentration-response curves (CCh 10^{-10} to 10^{-3} M). Bronchoalveolar lavage (BLV) was used for total and differential cell counts and quantification of TNF-α and IL-6. The antioxidant profile was evaluated in lung tissue for nitrite, malondialdehyde (MDA), and reduced glutathione (GSH) levels. The open field test was performed after the asthma induction process and treatments. Statistical analysis ANOVA followed by Tukey's test (*p<0.05)(GraphPad Prism 8.0). **Results:** Asthma induction was confirmed by the tracheal reactivity test in non-asthmatic animals (Emax = 160.34 ± 25.91%) and asthmatic animals (218.51 ± 19.64%*). Treatment with different doses of Fβ-CD 5 mg/kg (151.58 ± 20.20%), 25 mg/kg (107.86 ± 19.87%), and 100 mg/kg (145.07 ± 13.32%) significantly reduced this response; there was no significant difference compared to treatment with dexamethasone (154.62 ± 18.81%). Doses of Fβ-CD significantly reduced the total and differential leukocyte count in the LVB. These findings were corroborated by the reduction of TNF-α and IL-6 at doses of 25 and 100 mg/kg and in the dexamethasone group. Doses of 5 and 25 mg/kg promoted protection and restoration of nitrite, MDA, and GSH levels, indicating a reduction in oxidative stress. There was a significant reduction in locomotion in the asthmatic group compared to the non-asthmatic group, and those treated with dexamethasone, especially at the 5 mg/kg dose, showed attenuation of this parameter, suggesting modulation of neurobiological pathways of asthma. **Conclusion:** Fβ-CD demonstrated potential for the treatment of bronchial asthma, revealing its spasmolytic, anti-inflammatory, and protective effect against lung damage in asthmatic rats, with possible modulation of asthma neuroinflammation. **Financial support:** CAPES.

08.026 **Pharmacological Inhibition of the S100B/RAGE/NF-KB Pathway Attenuates the Inflammatory Response IN TNBS-Induced Colitis**. Silva TML[1], Sousa JJS[3], Almeida VPA[2], Sousa AK[2], Prudêncio RS[2], Furtado MGS[2], Costa ACC[2], Rodrigues VO[2], Rocha DML[2], Ferreira ABA[1], Silva BVL[1], Vale VS[3], Magalhães DA[2], Barbosa ALR[2] [1]UFC, Lab Gastrointestinal Physio-Pharmacology Studies, Brazil; [2]UFDPar, Lab Experimental Physiopharmacology, Brazil; [3]IFPI, Campus Parnaíba, Brazil

Introduction: Inflammatory bowel diseases (IBD), including ulcerative colitis and Crohn's disease, are chronic disorders characterized by persistent inflammation of the gastrointestinal tract. In the pathophysiology of IBD, enteric glial cells play an active role in modulating the intestinal inflammatory response through the secretion of the S100β protein, whose interaction with the RAGE receptor activates the NF-κB signaling pathway, promoting the production of pro-inflammatory mediators and oxidative stress, thereby contributing to the worsening of intestinal injury.** **Objectives:** ** **To investigate the impact of pharmacological inhibition of the S100β/RAGE /NF-κB pathway through pentamidine administration on the intestinal inflammatory response in a trinitrobenzenesulfonic acid (TNBS)-induced colitis model. **Methods:** Female Wistar rats (150–200 g) were used and distributed into groups of six animals. The animals received pentamidine isethionate (PNT; 4 mg/kg, i.p.), an S100β inhibitor, one hour before TNBS-induced colitis and in two additional administrations performed 24 and 48 hours after the first dose. Control groups received either 0.9% saline rectally or TNBS rectally. Seventy- two hours after induction, colon segments were collected for the evaluation of macroscopic and microscopic lesion scores, tissue wet weight, myeloperoxidase (MPO) activity, malondialdehyde (MDA) levels, reduced glutathione (GSH), nitrate/nitrite (NO3/NO2), and the pro-inflammatory cytokines TNF-α and IL-1β. The Animal Ethics Committee of the Parnaíba Delta Federal University (protocol no. 006/2021) approved experimental procedures. **Results:** The results demonstrated that S100β inhibition significantly reduced macroscopic and microscopic damage to the colonic mucosa, tissue wet weight, MPO activity, MDA levels, nitrate/nitrite levels, and TNF-α and IL-1β cytokine levels, while preserving GSH levels when compared with the TNBS group. **Conclusion:** It is concluded that the S100β protein contributes significantly to the inflammatory response in experimental colitis, suggesting the involvement of the S100β/RAGE /NF-κB pathway as a relevant mechanism in the pathogenesis of IBD.

08.027 **Evaluation of Bionutri AR-1®, a Biotechnological Nutraceutical Formulation Rich in α-and β-Glucans and Amino Acids, in Experimental Erosive Esophagitis**. Araujo AVV[1], Gomes IAB[1], Oliveira BC[1], Pimentel TFM[2], Monte MM[2], Santos BL[2], Rodrigues FSM[3], Gois MB[4], Medeiros JVR[1], Nicolau LAD[1] [1]UFDPar, PPG in Biotechnology, Brazil; [2]UFDPar, Lab of Inflammation and Translational Gastroenterology, Brazil; [3]Unifesp, Brazil. [4]UFR, Brazil.

Introduction: Gastroesophageal reflux disease (GERD) is a prevalent multifactorial disorder associated with substantial clinical burden and impaired quality of life. Although proton pump inhibitors (PPIs) remain the first-line treatment, a considerable proportion of patients experience incomplete symptom control, while alternative approaches, such as alginates, often provide limited benefit. These limitations highlight the need for adjunctive therapies targeting complementary mechanisms involved in esophageal injury. **Objective:** To investigate the esophagoprotective effects of Bionutri AR-1®, a biotechnological nutraceutical supplement rich in α- and β-glucans and supplemented with amino acids, in an experimental model of erosive esophagitis (EE). **Methods:** Acute EE was induced by pyloric stenosis combined with forestomach ligation. Animals were divided into eight groups: Sham, Vehicle, Alginate (1 mg/mL), Bionutri AR-1® (28-day supplementation; 300 mg/kg), single-dose Bionutri AR-1®, omeprazole (40 mg/kg), combined therapy (Bionutri AR-1® \+ omeprazole), and a glucan-free placebo (300 mg/kg). After 10 h, esophageal tissues were collected for macroscopic lesion assessment, wet weight determination as an edema marker, histopathological and histomorphometric analyses. Mucin-related parameters were evaluated by periodic acid–Schiff and Alcian blue staining, mucosal protection index, free mucin quantification, and MUC-2 expression. Inflammatory and oxidative stress biomarkers were also assessed. Complementary *in vitro* assays evaluated surface wettability by contact angle measurement and pepsin activity. **Results:** Vehicle-treated animals developed extensive esophageal ulceration, marked edema, and increased inflammatory and oxidative stress markers. In contrast, Bionutri AR-1® supplementation reduced macroscopic and microscopic lesions, preserved histological architecture, restored mucin content and organization, increased the mucosal protection index, and attenuated inflammatory and oxidative stress markers. *In vitro* assays demonstrated that Bionutri AR-1® increased surface wettability and reduced pepsin activity, suggesting beneficial effects on physicochemical properties. **Conclusion:** Bionutri AR-1® promoted esophagoprotection in experimental EE by reducing tissue damage, preserving mucus-associated parameters, attenuating inflammatory and oxidative stress markers, and improving esophageal surface physicochemical properties. *In vitro*, it increased surface wettability and reduced pepsin activity. These findings support further investigation of this nutraceutical as an adjunctive approach for GERD management, particularly in patients with incomplete responses to PPIs. **Acknowledgments:** Laboratory of Inflammation and Translational Gastroenterology. Animal Research Ethical Committee Number: Animal Ethics Committee of the Federal University of Delta do Parnaíba (UFDPar), No. 002/2024. **Financial support:** CAPES.

08.028 **Hesperetin Ameliorate TNBS-Induced Intestinal Inflammation: Role of Antioxidant System and Immunomodulation**. Pessoa MMB[1], Pessôa MLS[1], Alves VP1, Menezes PMF[1], Pessoa LV1, Araújo AA[2], Batista LM[1]
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Introduction: In recent years, many plant species and their isolated compounds, including flavonoids, have shown promising effects in the context of inflammatory bowel diseases in studies using animal models. Hesperetin is a flavonoid present in citrus fruits such as orange.. Thus, the present study aimed to evaluate the acute intestinal anti-inflammatory activity of carveol in animal models. **Methods:** For experimental procedures with animals, male Swiss mice (*Mus musculus*) weighing 25-30g were used. To evaluate intestinal anti-inflammatory activity of hesperetin, the animals were treated with Saline 0.9% (colitic group and non-colitic group), prednisolone 2 mg/kg (positive control) or hesperetin (25, 50, 100 and 200 mg/kg) the intestinal inflammatory protocol was used acute model of ulcerative colitis induced by trinitrobenzenesulfonic acid (TNBS) in mice and evaluation of the effects of hesperetin on the chronic relapsing phase of TNBS-induced Intestinal Inflammation in mice (Morris et al., Gastroenterology, v. 96, p. 795-803, 1989). The area of the ulcerative lesion was determined by the ulcerative lesion index (ILU). The antioxidant models evaluated were reduced glutathione (GSH) (Faure, Birkhäuser Basel, v.1 p. 237, 1995.), malondialdehyde (MDA), myeloperoxidase (MPO) (Krawisz, Gastroenterology, v. 87, p. 1344, 1984.) and superoxide dismutase (SOD) (Sun et al., Clin Chem. v. 34, p. 497, 1988). The cytokines evaluated were interleukin-1 beta (IL-1β), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α) and interleukin-10 (IL-10) (Kendall et al., Planta, v. 159, p. 505, 1983). The test was considered significant when $p < 0.05$. **Results:** According to the data analyzed, the oral administration of hesperetin protects the animals from reduced water and feed consumption. In the acute induction model of TNBS-induced intestinal inflammation, hesperetin at all doses (25, 50, 100 and 200 mg/kg) reduced ($p<0.05$) the macroscopic lesion score, ALU, weight/length ratio, and diarrheal index at all doses evaluated. In the sub-chronic protocol of ulcerative colitis with relapse, the most effective dose of hesperetin (100 mg/kg) reduced ($p<0.01$) the macroscopic lesion score, the ALU and the colonic weight/length ratio. From the acute and sub-chronic colitis protocols, it was observed that hesperetin (100 mg/kg) reduced ($p<0.001$) MDA and MPO levels and restored GSH and SOD levels. Furthermore, it reduced ($p<0.001$) the levels of IL-1β, TNF-α and IL-6, as well as restored ($p<0.01$) those of IL-10. **Conclusion:** Thus, the data suggest that hesperetin has intestinal anti-inflammatory activity in the acute and sub-chronic phase related to antioxidant and immunomodulatory activity, and that this activity is possibly related to cytoprotective mechanisms. **Keywords:** Natural Products. Hesperetin. Ulcerative Colitis. Intestinal Anti-Inflammatory Activity. **Acknowledgements**: CNPq / UFPB / PgPNSB / IpeFarM.

08.029 **Obesity Alters the Esophageal Mucosal Barrier in Diet-Induced Obese Mice**. Silva LMG[1], Sousa MKA[1], Alves ODC[5], Ribeiro TA[1], Freire PRP[1], Souza MFF[1], Silva FGO[1], Guimarães MB[1], Lopes BP[2], Vieira MESR[2], Mateus JS[3], Nascimento, JM[4], Fonsêca SGC[4], Soares PMG[2], Souza MHLP[2] [1]UFC, Lab Gastrointestinal Physiopharmacology, Graduate Program in Pharmacology, Brazil, [2]UFC, Lab Gastrointestinal Physiopharmacology, Brazil. [3]Estácio, Brazil. [4]UFC, Lab pharmaceutical technology, Brazil. [5]UFC, Lab Gastrointestinal Physiopharmacology, Graduate program in medical sciences, Brazil.

Introduction: Recent *in vitro* studies using cell cultures have demonstrated that adipose tissue in obesity can compromise the integrity of the esophageal epithelial barrier, leading to widening of the intercellular spaces, increased epithelial permeability, and activation of pathways related to cellular hypoxia. Furthermore, obese individuals exhibit structural and functional alterations in the esophageal epithelium even in the absence of gastroesophageal reflux. However, *in vivo* studies validating these experimental findings remain limited. **Objectives:** Accordingly, the aim of our study is to assess the impact of obesity on the integrity of the esophageal epithelial barrier in diet-induced obese mice. **Methods:** The study was approved by the Animal Ethics Committee of the Federal University of Ceará, under protocol no. 4111310724. Male Swiss mice (6 weeks old) were fed a modified diet (high-fat and high-carbohydrate chow) to induce obesity over 15 weeks chow, divided into control and obese groups. To assess body weight gain, the animals were weighed weekly. After the induction period, the animals were euthanized for assessment of body composition (bioimpedance) and biochemical parameters (glucose, triglycerides, and total cholesterol). Esophageal biopsies were obtained for detection of Hypoxia-Inducible Factor-1α (HIF-α) by Western blot, analysis of basal transepithelial electrical resistance (TER), and with a challenge solution (pH 0.5 + TDCA + pepsin) and analysis of fluorescein permeability using a Ussing chamber. **Results:** Animals fed the modified diet for 15 weeks showed a significant increase in body weight (34.16±3.06 vs. 30.86±1.94), BMI (6.3±0.1 vs. 5.7±0.1), and fat mass (49.0±2.5 vs. 28.4±4.2), as well as a reduction in fat-free mass (51.0±2.5 vs. 71.5±4.2), when compared to animals in the control group ($p<0.05$). In biochemical assays, obese animals exhibited a significant increase in glucose (158.1±5.7 vs. 116.6±10.6) and total cholesterol (224.8±4.2 vs. 183.6±7.4), but no significant difference in triglyceride levels ($p<0.05$). An increase ($p<0.05$) in HIF-1α levels was also observed in the esophageal epithelium of the obese group (0.51±0.05 vs. 0.09±0.01). In the analysis of esophageal mucosal integrity, there was no statistical difference in baseline TER between the groups ($p<0.05$); however, greater resistance was observed in the obese group after acid challenge (99.63±0.12 vs. 96.29±1.25), as well as a significant increase ($p<0.05$) in esophageal permeability (6,662±1,290 vs. 3,503±808.5), indicating an alteration in a parameter associated with barrier function. **Conclusion:** Our findings demonstrate that diet-induced obesity leads to alterations in the integrity of the esophageal epithelium, contributing to our understanding of the severity of esophageal manifestations observed in obese patients and the association between obesity and gastroesophageal reflux disease.

08.030 **Involvement of Prostaglandins in the Gastroprotective Effect of PHYTOL-βCD on Ethanol-Induced Gastric Lesions in Mice**. Sousa CFAJ[1], Amorim IF[2], Freitas FVS[2], Reis ML[2], Quintans-Junior LJ[3], Quintans JSS[3], Oliveira RCM[1,2]. [1]UFPI, PPG in Pharmacology; [2]UFPI, Research Center on Medicinal Plants; [3]UFS, Dept Physiology.

Introduction: Prostaglandins play a fundamental role in maintaining gastric mucosal integrity by stimulating mucus and bicarbonate secretion, preserving local blood flow, and contributing to tissue repair. Phytol complexed with β-cyclodextrin (Phytol-βCD) has demonstrated gastroprotective activity in experimental models of gastric injury. **Objective:** To evaluate the involvement of prostaglandins in the gastroprotective effect of Phytol-βCD in an ethanol-induced gastric lesion model in mice. **Methods:** To assess the participation of prostaglandins in the gastroprotective effect of Phytol-βCD, mice (n = 6/group) were pretreated with indomethacin (10 mg/kg, subcutaneously) 30 min before treatments. Animals then received vehicle (1% Tween 80 in saline, 10 mL/kg, orally), Phytol-βCD (25 mg/kg, orally), or misoprostol (50 μg/kg, orally). The 25 mg/kg dose was selected based on previous studies using an ethanol-induced gastric lesion model, in which doses of 6.25, 12.5, and 25 mg/kg were evaluated, with the latter showing the greatest gastroprotective effect. After 60 min, gastric lesions were induced by absolute ethanol administration (0.2 mL/animal, orally). Thirty minutes after lesion induction, the animals were euthanized and the stomachs collected. Ulcerated areas were determined by computerized planimetry using ImageJ software. Data were expressed as mean ± standard error of the mean and analyzed by one-way ANOVA followed by Tukey's test ($p < 0.05$). The study was approved by the Animal Ethics Committee under protocol number 823/2024-UFPI. **Results:** Mice in the vehicle group presented a gastric lesion area of 10.05 ± 2.94 mm^2. Treatment with Phytol-βCD significantly reduced this area to 3.04 ± 2.59 mm^2. However, prior administration of indomethacin increased the lesion area to 15.97 ± 3.99 mm^2, indicating loss of the previously observed effect. The misoprostol-treated group presented a lesion area of 12.07 ± 1.31 mm^2. These findings suggest that inhibition of endogenous prostaglandin synthesis impairs gastric mucosal protection, favoring the increase in lesions. **Conclusion:** Phytol-βCD exhibits a gastroprotective effect in an ethanol-induced gastric lesion model, which is reversed by indomethacin administration. These findings indicate that the protective action of Phytol-βCD depends, at least in part, on the participation of endogenous prostaglandins in maintaining gastric mucosal integrity.

08.031 **Farnesol Attenuates Duodenal Lesions and Intestinal Inflammation in Experimental Models**. Pessôa MLS, Pessoa MM, Alves VP, Pessoa LF, Menezes PMF, Batista, LM. UFPB, Graduate Program in Natural and Synthetic Bioactive Products, Brazil.

Introduction: Farnesol is an acyclic sesquiterpene alcohol widely distributed in the essential oils of plant species such as citronella (Cymbopogon nardus), lemongrass (Cymbopogon citratus), and chamomile (Matricaria chamomilla), as well as in mammalian tissues. It is recognized for its previously described pharmacological properties, including antioxidant, anti-inflammatory, and immunomodulatory activities, in addition to promising effects on the gastrointestinal tract, such as antidiarrheal and gastroprotective activities demonstrated by our research group. **Objectives:** To evaluate the antiulcerogenic activity of farnesol in duodenal ulcers, as well as its acute and chronic intestinal anti-inflammatory activity in animal models. **Methods:** Experimental models were performed using male Wistar rats (Rattus norvegicus) weighing 200–250 g and male Swiss mice (*Mus musculus*) aged six to eight weeks, weighing 20–30 g. The cysteamine hydrochloride-induced duodenal ulcer model was conducted according to the protocol described by Szabo (Am. J. Pathol., v. 93, p. 273, 1978). Intestinal anti-inflammatory activity was evaluated using both the acute and subchronic trinitrobenzenesulfonic acid (TNBS)-induced colitis models, as described by Morris (Gastroenterology, v. 96, p. 795, 1989). Parametric data were analyzed using one-way ANOVA followed by Dunnett's or Tukey's tests and expressed as mean ± SD. Non-parametric data were analyzed using the Kruskal–Wallis test followed by Dunn's post hoc test and expressed as median (minimum–maximum). Statistical significance was considered at $p < 0.05$ using GraphPad Prism 9.0 software. **Results:** In the cysteamine-induced duodenal ulcer model in rats, farnesol at doses of 25, 50, 100, and 200 mg/kg and lansoprazole (30 mg/kg) significantly reduced the ulcerative lesion area (ULA) ($p < 0.001$) compared with the negative control group (Tween 80 5%), showing lesion inhibition percentages of 58%, 77%, 95%, 96%, and 97%, respectively. In the acute ulcerative colitis model, farnesol at all tested doses (25, 50, 100, and 200 mg/kg, p.o.) significantly reduced ($p < 0.001$) the macroscopic lesion score, ulcerative lesion area (ULA), weight/length ratio, and diarrhea index. The intestinal anti-inflammatory effect was also evaluated in a subchronic ulcerative colitis relapse model, in which farnesol at its most effective dose (100 mg/kg) significantly reduced ($p < 0.001$) the macroscopic lesion score, ULA, and colon weight/length ratio. **Conclusions:** Farnesol exhibits anti-duodenal ulcer and intestinal anti-inflammatory activities in both the acute and subchronic phases of ulcerative colitis models in mice. Animal Ethics Committee (CEUA/UFPB): 4066081124. **Acknowledgments:** CNPq / UFPB / PgPNSB / IperFarm.

08.032 **Effect of *Akkermansia muciniphila* Supplementation on Intestinal Environment and Glucose Homeostasis in Male and Female Mice**. Ribeiro TA[2], Newman PP[1], Allen-Gregory E[1], Mims TS[3], Pierre JF3, Soares PMG[2], van der Merwe M[1] [1]University of Memphis, College of Health Sciences, United States, [2]UFC, Lab. of Gastrointestinal Physiopharmacology Studies, PPG Pharmacology, Brazil, [3]University of Wisconsin–Madison, Dept Food and Nutritional Sciences, USA

Introduction: Diet-induced obesity is characterized by chronic low-grade systemic inflammation (meta-inflammation), gut dysbiosis, and increased intestinal permeability, which contribute to metabolic dysfunction. *Akkermansia muciniphila* , a mucin-degrading gut commensal, has emerged as a promising next-generation probiotic because of its beneficial effects on intestinal barrier integrity, inflammation and improvement in glucose control. Previous studies suggest that *A. muciniphila* enhances mucus layer integrity and modulates the production of beneficial metabolites. However, the effects of lower-dose supplementation and sex-related differences remain unclear. **Objectives:** This study evaluated the sexually dimorphic effects of lower-dose *A. muciniphila* supplementation on adiposity, glucose tolerance, intestinal permeability and MUC2 levels, and inflammatory markers in high-fat fed male and female mice. **Methods:** Male and female C57BL/6 mice were randomly assigned to three groups: Control (normal chow), High-Fat Diet with 45% of lipids (HFD), and HFD supplemented with *A. muciniphila* (HF+AKK). Obesity was induced for 10 weeks. From week 6 onward, the HF+AKK group received daily oral gavage of *A. muciniphila* (3.36×10^7; CFU/200 µL glycerol-PBS) for four weeks, while the Control and HF groups received PBS. Body weight and food intake were monitored daily. Intestinal permeability was assessed using FITC-dextran after a run to fatigue test, and glucose tolerance was evaluated by GTT. Body composition was measured before euthanasia. Hepatic and colonic mRNA expression of IL-1β, TNF-α, and colonic MUC2 were quantified by qPCR. Data were analyzed using one-way or two-way ANOVA, with significance set at $p < 0.05$. All experimental procedures were approved by the Institutional Animal Care and Use Committee (IACUC) under Animal Research Protocol No. CY25-0012 A1. **Results:** HFD increased body weight and adiposity in male mice, but no significant differences were observed between HFD and HF+AKK groups. Male mice had significantly increased mesenteric fat and adipose tissue, and increased liver weight. Fasting blood glucose and glucose tolerance were not significantly improved by HFD+AKK, although sex-related variations were observed. Hepatic inflammation was not significantly altered in either sex. Intestinal permeability increased in HFD mice, and HFD+AKK did not significantly reverse this effect. However, HFD supplemented with *A. muciniphila* significantly restored colonic MUC2 expression ($p < 0.05$) and attenuated colonic inflammation in both sexes, particularly by reducing IL-1β expression ($p < 0.05$). **Conclusion:** Lower-dose *A. muciniphila* supplementation improved colonic barrier integrity and reduced local inflammatory signaling in high-fat fed mice, independent of changes in body weight or glucose tolerance.

08.033 *In vitro* and *In vivo* Evaluation of the Gastric Healing Effects of a Standardized *Citrus sinensis* (L.) Osbeck (Morosil®) Extract. Paz APS[1,2], Souza EMC[1], Ferreira RCS[1], Cardoso LP[1,2], Araújo BS[1], Ferreira DS[1], Kurogi KS[1], Lima IKC[1], Madeira LDPS[1], Mello VJ[1] [1]UFPA, Instituto de Ciências Biológicas, Lab Pesquisa, Ensino e Extensão em Análises Clínicas (LACPEE), Brazil; [2]PPG Farmacologia e Bioquímica

Introduction: Gastric ulcer is a multifactorial disease caused by an imbalance between aggressive factors (reactive oxygen species and acid-peptic secretion) and mucosal defenses (epithelial integrity, mucus secretion, and tissue regeneration). Its high prevalence and the adverse effects associated with conventional therapy justify the search for safer alternatives. Standardized Citrus sinensis (L.) Osbeck extract (ECS; Morosil®), widely used for weight loss, is rich in anthocyanins, hydroxycinnamic acids, flavanones, and ascorbic acid, which possess antioxidant and cytoprotective properties and may contribute to gastric mucosal protection and tissue repair. **Objectives:** Therefore, this work evaluated the gastric healing effects of ECS in *in vitro* and *in vivo* models and investigated possible mechanisms related to oxidative stress and gastric acidity. **Methods:** Cell migration was assessed by scratch assay in Vero cells treated with ECS (0.1 or 1 µg/ml), with wound closure monitored up to 48 h. *In vivo* healing was evaluated in Wistar rats with acetic acid-induced gastric ulcers treated orally with ECS (50, 100, 250, or 400 mg/kg) or omeprazole for 8 days. Based on dose-response findings, ECS 250 mg/kg was further evaluated in the pylorus ligation model. Oxidative stress markers, including malondialdehyde (MDA), nitrite, total glutathione (GSH), catalase (CAT), and superoxide dismutase (SOD), were measured in gastric tissue. Data were analyzed by ANOVA followed by Tukey's ($p<0.05$). **Results:** ECS at 1 µg/ml significantly increased cell migration from 4 h onward compared with the negative control ($p\leq0.0288$), with wound closure comparable to the positive control after 48 h, whereas 0.1 µg/ml was ineffective and, at 24 h, performed worse than the negative control. *In vivo*, all ECS doses significantly reduced ulcer area in acetic acid-induced lesions ($p\leq0.0039$), and 250 mg/kg showed the best response, comparable to omeprazole and without additional benefit at 400 mg/kg. ECS did not significantly modify gastric pH or total acidity, whereas omeprazole reduced acidity, indicating that ECS action was not related to acid secretion inhibition. In ulcerated tissue, ECS reduced MDA and nitrite levels ($p\leq0.0187$ and $p<0.0001$) and increased GSH and CAT activity ($p\leq0.0398$ and $p \leq 0.0444$); the 250 mg/kg dose showed superior effects to lower doses in some parameters and higher CAT activity than omeprazole, while SOD activity remained unchanged. **Conclusion:** Considering the lack of significant effects in the gastric acidity test, it is plausible that ECS promotes gastric healing *in vitro* and *in vivo* by combining antioxidant effects with enhanced mucosal defense rather than inhibiting acid secretion. The 250 mg/kg dose was the most effective, with no need to increase the dose. The observed effects suggest antioxidant modulation and may reflect the combined action of ECS bioactive constituents, reinforcing its potential as a complementary strategy for gastric ulcer treatment.

08.034 **The Gut After Sepsis: Persistent Intestinal Dysmotility and Sex-Related Differences**. Lima-Moura SA, da Silva-Santos JE UFSC, Lab Cardiovascular and Smooth Muscle Biology, Dept Pharmacology, SC, Brazil.

Introduction: During sepsis and septic shock, clinical and experimental evidence indicates that intestinal function is profoundly impaired, including alterations such as dysmotility, epithelial barrier disruption, impaired absorptive function, and gut dysbiosis. Here, we tested the hypothesis that sepsis-surviving rats develop persistent alterations in intestinal motility and investigated whether post-sepsis dysmotility differs between sexes. **Methods:** Female and male Swiss mice (3–4 months old) were anesthetized with isoflurane (3% in O2) and subjected to the cecal ligation and puncture (CLP) model of sepsis. Surviving animals evaluated at 15 and 30 days after surgery (S15 and S30 groups), along with age-matched control groups, were used to investigate whether the regulation of intestinal smooth muscle is altered after sepsis. *In vivo* measurements included sepsis score, blood glucose, fecal output, fecal water loss, and intestinal transit. For the *in vitro* analyses, the mice were euthanized under anesthesia, and segments of the ileum and colon (~1.5 cm) were mounted in organ baths. We evaluated intestinal damage, peristalsis, and contractile responses to acetylcholine (ACh) and electrical field stimulation (EFS). All differences described here were statistically significant ($p < 0.05$; ANOVA followed by Sidak's test). **Results:** The mortality rate induced by CLP was around 40–50%. Deaths occurred within the first 96 h, and all surviving animals presented severe sepsis scores, hypoglycemia, and weight loss at 24 h after CLP. The intestinal damage score was significantly higher in both male and female S15 and S30 groups. We observed increased fecal output in the male S30 group, despite reduced intestinal transit in both male and female S30 groups. Organ-bath experiments showed that peristaltic activity in ileal and colonic segments did not differ among the CT, S15, and S30 groups. Compared with their respective CT groups, KCl-induced contractions were reduced in the colon of both male and female mice in the S30 groups, whereas in the ileum only the S30 male group showed a similar reduction. Additionally, the phasic contractile response induced by 30 μM ACh in the ileum was reduced only in the female S30 group. In the colon, however, this response was reduced in both sexes at both post-sepsis time points, corresponding to an approximate reduction of 40% in males and 55% in females relative to their respective CT groups (46.9 ± 4.4 and 60.6 ± 6.7 g/g). Despite the reduced responses to exogenous ACh, EFS-induced contractions were enhanced in ileal S15 and colonic S15 and S30 preparations, in a sex-independent manner. **Conclusion:** Our study provides evidence that mice surviving experimental sepsis exhibit persistent gut dysmotility, accompanied by reduced contractile responses to KCl-induced depolarization and exogenous ACh. Increased neurally mediated contractions suggest a sustained imbalance in enteric neurotransmission. These alterations were observed in both male and female mice, varying according to intestinal segment and post-sepsis time point. Further studies are needed to clarify the underlying mechanisms and clinical implications.

08.035 **Effects of Bile Acids on Tracheal and Aortic Smooth Muscle Contractility in Isolated Rat Preparations**. Abdourahmane D, Sampaio MS, Magalhães PJC UFC, Lab Smooth Muscle Pharmacology, PPG Pharmacology, Brazil

Introduction: Pathological gastroesophageal reflux can lead to the microaspiration of bile acids (BA) into the airways and reach significant levels in the systemic circulation. In smooth muscle, BA exert effects through two main receptors: TGR5, a G-protein-coupled membrane receptor that activates the cAMP pathway, and FXR, a nuclear receptor. Although their involvement in esophageal contractility has been documented, their role in extra-esophageal tissues, notably the trachea and the aorta, remains poorly explored. This study aimed to characterize the effects of deoxycholic acid (DCA) and chenodeoxycholic acid (CDCA) on the contractility of these tissues in rats. **Objectives**: To investigate the effects of bile acids on tracheal and aortic smooth muscle contractility. Material and methods: Trachea and aorta from male Wistar rats were isolated and mounted in organ baths. Contractions were induced by potassium chloride (KCl, 60 mM) or by agonists (carbachol 3 µM for the trachea; phenylephrine 1 µM for the aorta). The effects of DCA (60 µM), CDCA (60 µM), obeticholic acid (FXR agonist, 10 µM), and oleanolic acid (TGR5 agonist, 100 µM) were evaluated during a 60-min exposure, using single-concentration protocols and concentration-response curves. The involvement of the adenylyl cyclase/cAMP pathway was explored using the adenylyl cyclase inhibitor MDL 12,330A, and the nitric oxide (NO)/cGMP pathway using the NO synthase (NOS) inhibitor L-NAME (aorta only). **Results:** Both DCA and CDCA induced a partial and progressive relaxation in both tissues. The effects of CDCA were qualitatively similar to those of DCA, but with a slightly lower potency, represented by a rightward shift of the curve. For both BA, relaxation was more pronounced when the contracting agent was carbachol or phenylephrine compared to KCl. Obeticholic acid produced a moderate and progressive relaxation throughout the exposure period. Oleanolic acid stood out with a rapid and pronounced peak relaxation within the first two to five minutes, followed by a partial recovery and stabilization. Inhibition of adenylyl cyclase with MDL 12,330A and inhibition of NOS with L-NAME (aorta) each resulted in a slight non-significant ($P > 0.05$) rightward shift of the curves. **Conclusion:** These preliminary results show that DCA and CDCA induce similar relaxation in tracheal and aortic smooth muscle, with CDCA being slightly less potent. Selective TGR5 and FXR agonists reproduce relaxing effects, suggesting a contribution of these receptors. However, the lack of significant effects from the partial inhibition of the cAMP and NO pathways indicates that the mechanism of extra-esophageal relaxation is not fully explained by these pathways. Keywords : bile acids; TGR5; FXR; smooth muscle; gastroesophageal reflux.

08.036 **Effects of Selective Agonists of Bile Acid Receptors TGR5 and FXR on the Contractility of Isolated Rat Esophagus**. Sampaio MS, Dairou A, Magalhães PJC UFC, Lab Smooth Muscle Pharmacology, PPG Pharmacology, Brazil

Introduction: Gastroesophageal reflux disease (GERD) is a disorder caused by the retrograde flow of gastric contents into the esophagus, producing symptoms such as heartburn, regurgitation, and mucosal irritation. In addition to gastric acid, this content may contain bile acids that, upon reaching the esophagus, potentiate tissue damage and contribute to complications. **Objectives:** In this study, the influence of bile acids on esophageal contractility was investigated, with a focus on the modulation of esophageal motor function. **Methods:** To this end, contractions of rat esophageal segments were recorded using a data acquisition system in the presence of agonists of the bile acid receptors FXR (Farnesoid X Receptor) and TGR5 (Takeda G-protein-coupled receptor 5). The esophageal segments were mounted in glass organ baths, allowing analysis of the contractile responses of the circular and longitudinal muscle layers. All experimental procedures were approved by the Animal Ethics Committee of the Federal University of Ceará (CEUA/UFC). **Results:** After 40 min with the lumen of the segments filled with Tyrode solution enriched with deoxycholic acid (DCA) or oleanolic acid (OlA), a TGR5 agonist, or obeticholic acid (ObA), an FXR agonist, the contractile responses induced by acetylcholine (ACh) or carbachol (CCh) were compared to those of segments exposed to control solution (Tyrode). In both muscle layers, pre-treatment with DCA reduced the contractile response to both CCh and ACh. OlA also reduced the response to CCh in both muscle orientations; however, unlike DCA, it increased esophageal contractility in response to ACh. ObA, in turn, produced no difference in contractile responses under any of the conditions evaluated. **Conclusion:** These results indicate that bile acids modulate esophageal contractility in distinct ways, depending on the receptor activated.

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08.037 **Effect of Kefir in Experimental Models of Gastroesophageal Reflux Disease: Changes in Gastric Juice and Effects on the Esophageal Mucosa**. Silva KC[1,3], Gomes IAB[1,3], Teixeira LFLS[1,3], Oliveira ACP[1,3], Souza HCA[1], Oliveira AP[3], Medeiros JVR[1,3], Rocha JA[1], Gois MB[2], Nicolau LAD[1,3]. [1]UFDPar, PPG in Biotechnology, Brazil. [2]UFR, PPG in Biosciences and Health, Brazil. [3]UFDPar, Lab Inflammation and Translational Gastroenterology, Brazil.

Introduction: Gastroesophageal reflux disease (GERD) is characterized by the reflux of gastroduodenal contents into the esophagus, causing mucosal injury and inflammation. Although proton pump inhibitors are the gold-standard therapy, refractory cases remain common, and these drugs do not directly target inflammation or pepsin activity, key mechanisms in GERD pathophysiology. kefir is a fermented dairy beverage with previously described gastroprotective effects. **Objectives:** To investigate the esophagoprotective effects of kefir in experimental models of GERD. **Methods:** Male rats were divided into four groups: Sham, reflux esophagitis (RE), RE + Alginate (1 mL, orally [p.o.]), and RE + Kefir (1 mL, p.o.). Treatments were administered for seven days before the surgical induction of RE by pyloric stenosis associated with gastric fundus ligation. After 10 h, esophageal tissues were collected for macroscopic analysis, wet weight measurement, histochemical staining with periodic acid–Schiff (PAS) and Alcian Blue (AB), histomorphometric and histopathological analyses, and determination of myeloperoxidase (MPO) and malondialdehyde (MDA) levels. Data were expressed as mean ± SEM and analyzed by one-way ANOVA followed by Bonferroni or Tukey's post hoc tests ($p < 0.05$). *in silico* molecular docking assays were performed to evaluate the interaction of nine kefir-derived peptides with pepsin, comparing them with the inhibitors Darunavir, Pepstatin, and Fosamprenavir. **Results:** Kefir pretreatment significantly reduced the macroscopic lesion area by 60% compared with the RE group (0.030 ± 0.008 vs. 0.075 ± 0.010 cm^2; $p < 0.05$). Esophageal edema was attenuated, with a reduction in wet weight (59.18 ± 5.29 vs. 114.4 ± 10.17 mg/cm; $p < 0.05$). Kefir also reduced MPO activity compared with the RE group (10.37 ± 1.06 vs. 27.01 ± 2.50 U/mg tissue; $p < 0.05$) and MDA levels (141.0 ± 11.36 vs. 501.2 ± 61.77 nmol/g; $p < 0.05$). Histochemical analyses demonstrated preservation of neutral mucins (PAS: 1.73 ± 0.11 vs. 1.16 ± 0.03 pixels/field) and sulfomucins (AB: 17.51 ± 0.83 vs. 7.22 ± 0.44 pixels/field; $p < 0.05$). Histomorphometric analysis showed preservation of keratin (32.86 ± 0.80 vs. 10.46 ± 0.30 μm) and epithelial thickness (22.74 ± 0.70 vs. 8.10 ± 0.33 μm), accompanied by reduced epithelial disorganization, edema, inflammatory infiltrate, and basal cell hyperplasia ($p < 0.05$). Molecular docking demonstrated that six kefir-derived peptides exhibited binding energies lower than -7.0 kcal/mol. Peptides 1 (-9.6 kcal/mol), 2 (-9.5 kcal/mol), and 3 (-9.6 kcal/mol) displayed higher binding affinity for pepsin than the reference inhibitors Pepstatin A (-8.2 kcal/mol), Darunavir (-8.0 kcal/mol), and Fosamprenavir (-7.4 kcal/mol). **Conclusion:** Kefir exerted protective effects on important mechanisms involved in GERD pathophysiology, highlighting its potential as a promising complementary therapeutic strategy. **Acknowledgments:**: Laboratory of Inflammation and Translational Gastroenterology. Animal Research Ethics Committee Approval Number: Federal University of Delta do Parnaíba (UFDPar), Protocol No. 001/2023. **Financial support**: CAPES.

08.038 *Arthrospira platensis* **Improves Intestinal Redox Homeostasis by Reducing Ileal $O_2^{\bullet-}$ and Increasing NRF2 Immunoreactivity in Hypercaloric Diet-Fed Wistar Rats**. Diniz AFA[1,2]; Claudino BFO[1,2], Santos TJ[1,5], Oliveira JCPL[2,3]; Fernandes GFS[3,4], Barbosa YV[1,2] Silva JMA[1,2], Arruda RRA[1,2], Melo MB[1,5], Sousa-Filho JEC[1,5], Cavalcanti BC[1,2], Medeiros IA[2,3], Veras RC[2,3], Silva BA[1,2,5] [1]UFPB, Lab Functional Pharmacology Prof. George Thomas, Institute of Research in Drugs and Medicines, Brazil; [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil; [3]UFPB, Lab. of Cardiovascular Pharmacology, PPG Natural and Synthetic Bioactive Products, Brazil; [4]UFPB, Center of Biotechnology, Dept. of Biotechnology, Brazil; [5]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil

Introduction: Obesity is associated with chronic low-grade inflammation, intestinal dysbiosis, and oxidative stress, contributing to gastrointestinal dysfunction. Excessive production of reactive oxygen species (ROS) disrupts intestinal homeostasis and impairs endogenous antioxidant defenses. Nuclear factor erythroid 2-related factor 2 (NRF2) is a key regulator of cellular antioxidant responses and redox balance. Previous studies from our group demonstrated that *Arthrospira platensis* (AP), a cyanobacterium rich in antioxidant bioactive compounds, prevents obesity-induced intestinal dysfunction and attenuates impaired intestinal reactivity in hypercaloric diet-fed rats (Diniz, Oxid. Med. Cell. Longev., v.2021, p.3260789, 2021; Diniz, J. Funct. Foods, v.115, p.106116, 2024). Therefore, this study evaluated the effects of AP supplementation on ROS production and NRF2 immunoreactivity in the ileum of rats subjected to a hypercaloric diet. **Objectives:** To evaluate the effect of AP supplementation on superoxide anion production and NRF2 immunoreactivity in the ileum of Wistar rats fed a hypercaloric diet. **Methods:** Male Wistar rats were allocated into four groups (n=5): standard diet (SD), standard diet supplemented with AP (25 mg/kg) (SD+AP25), hypercaloric diet (HCD), and hypercaloric diet supplemented with AP (25 mg/kg) (HCD+AP25). AP was suspended in saline (0.9% NaCl) and administered daily by intragastric gavage for eight weeks. After euthanasia, ileal sections were collected for superoxide anion ($O_2^{\bullet-}$) detection using dihydroethidium (DHE) fluorescence and NRF2 immunoreactivity analysis by immunofluorescence. Images were quantified using ImageJ and expressed as arbitrary units (AU). Data were analyzed by one-way ANOVA followed by Tukey's test ($p<0.05$). **Results:** HCD animals showed higher $O_2^{\bullet-}$ fluorescence (71.17 ± 4.10 AU) than SD animals (35.91 ± 1.19 AU), representing an increase of 98.2%. AP supplementation reduced $O_2^{\bullet-}$ levels in HCD+AP25 animals (58.85 ± 2.04 AU), corresponding to a decrease of 17.3% compared with HCD animals. Lower $O_2^{\bullet-}$ fluorescence was also observed in SD+AP25 animals (29.55 ± 2.12 AU). NRF2 immunoreactivity was markedly increased in AP-supplemented groups. In SD+AP25 animals, NRF2 fluorescence increased from 4.55 ± 1.76 AU to 52.23 ± 5.90 AU. Similarly, HCD+AP25 animals exhibited higher NRF2 fluorescence (27.99 ± 1.92 AU) than HCD animals (10.47 ± 1.89 AU). **Conclusion:**Hypercaloric diet induced oxidative imbalance in the ileum, evidenced by increased superoxide anion production. AP supplementation attenuated oxidative stress and enhanced NRF2 immunoreactivity, suggesting activation of antioxidant defense pathways and improvement of intestinal redox homeostasis. These findings indicate that NRF2 signaling may contribute to the intestinal protective effects of AP in experimental obesity. Animal Ethics Committee approval:CEUA/UFPB, protocol 6914241024. **Financial support**: CNPq.

08.039 **Modulation of the Heme/NADPH Oxidase Pathway During Ethanol- Induced Gastropathy in Mice**. Almeida ML[1], Oliveira AP[2], Moraes JA[3], Figueiredo-Junior AT[3], Góis MB[4], Oliveira ACP[2], Medeiros JVR[2], Nicolau LAD[1,2] [1]UFPI, Lab Inflammation and Translational Gastroenterology, Brazil; [2]UFDPar, Lab Inflammation and Translational Gastroenterology, Brazil; [3]UFRJ, Lab Redox Biology, Brazil; [4]UFR, Lab Morphology, Brazil.

Introduction: Ethanol-induced gastropathy is characterized by intense hemorrhagic lesions and oxidative stress in the gastric mucosa, mimicking ulcers associated with alcohol consumption in humans. Free heme and NADPH oxidase-derived reactive oxygen species synergistically enhance lipid peroxidation. Despite the clinical use of proton pump inhibitors, therapeutic limitations persist, encouraging the investigation of redox modulators such as diphenyleneiodonium (DPI). **Objectives:** To investigate the modulatory role of the heme/NADPH oxidase pathway in ethanol-induced gastropathy. **Methods:** Male Swiss mice were subjected to gastric lesions induced by 50% ethanol (orally, p.o.) and pretreated with DPI (10 µM, p.o.) or omeprazole (40 mg/kg, p.o.) with or without concomitant administration of heme (30 µM, p.o.). **Results:** Ethanol induced extensive gastric damage, increasing the lesion index (1.19 ± 0.17 mm^2) and lipid peroxidation, as evidenced by elevated malondialdehyde (MDA) levels (392.1 ± 27.72 nmol/g) and reduced glutathione (GSH) levels (111.7 ± 4.88 µg/g) and superoxide dismutase (SOD) activity (13.75 ± 0.90 U/µg). Co-administration of heme significantly aggravated these effects, increasing the lesion index (1.58 ± 0.21 mm^2), markedly raising MDA levels (713 ± 88.42 nmol/g), and promoting further antioxidant depletion (GSH: 65.74 ± 12 µg/g). In contrast, pretreatment with DPI, alone or combined with heme, exerted a significant gastroprotective effect, reducing the lesion index (0.57 ± 0.05 mm^2 and 0.54 ± 0.08 mm^2, respectively), restoring redox balance (GSH: up to 149.1 ± 7.72 µg/g; MDA:183.9 ± 15.47 nmol/g; SOD: 18.66 ± 1.40 U/µg), and preserving the histological integrity of the gastric mucosa. Histological analyses confirmed severe mucosal loss in the ethanol and heme groups (922 ± 24 µm), whereas DPI preserved mucosal thickness (1636 ± 49 µm), approaching saline control values (1903 ± 97.2 µm). Furthermore, ethanol and heme promoted intense depletion of gastric mucus, as evidenced by reductions in neutral glycoproteins and acidic and sulfated mucins, demonstrated by Periodic Acid-Schiff (PAS) and Alcian Blue staining (pH 2.5 and 1.0). These alterations were reversed by DPI pretreatment, similarly to omeprazole, contributing to preservation of the mucosal barrier. **Conclusion:** The heme/NADPH oxidase pathway plays a central role in ethanol-induced gastropathy, with heme acting as an amplifier of oxidative stress. DPI promoted gastroprotection by attenuating oxidative, histological, and mucus-related damage, highlighting redox modulation as a promising therapeutic strategy for oxidative stress-related gastric ulcers. **Acknowledgments:** Laboratory of Inflammation and Translational Gastroenterology (LIGAT). **Animal Research Ethics Committee Number:** Animal Ethics Committee of the Federal University of Delta do Parnaíba (CEUA/UFDPar), Protocol No. 006/2025. **Financial support:** CAPES, CNPq, and FAPEPI.

08.040 *Arthrospira platensis* Supplementation Attenuates Airway Remodeling in Asthmatic Rats. Oliveira GNM[1,2], Vieira MM[2], Silva JMA[2], Cavalcante-Silva LHA[3], Alves AF[2,4], Vasconcelos LHC[1,2,4] [1]UFPB, Lab Farmacologia Funcional Prof. George Thomas, Instituto de Pesquisa em Fármacos e Medicamentos, Brazil; [2]UFPB, PPG em Produtos Naturais e Sintéticos Bioativos, Brazil; [3]UFAL, Complexo de Ciências Médicas e Enfermagem, Brazil; [4]UFPB, Depto Ciências Biomédicas, Brazil.

Introduction: Asthma is a chronic immune-mediated inflammatory disease characterized by airflow obstruction. Allergic asthma involves Th2 response, which release IL-4 and IL-13, promoting airway remodeling and hyperresponsiveness. *Arthrospira platensis* (AP), an approved dietary supplement, has emerged as a promising alternative due to its anti-inflammatory properties. Objective: To investigate the effects of AP supplementation on inflammatory cytokines and lung parenchyma remodeling in asthmatic rats. Methods: Male Wistar rats (n = 7-12/group) were randomly assigned to a control group (CG), asthmatic group (AG), asthmatic groups supplemented with AP at 30 (AGAP30), 100 (AGAP100), or 300 mg/kg/day (AGAP300), and a dexamethasone-treated group (AGDEXA, 5 mg/kg). Asthma was induced by ovalbumin (OVA) over 21 days. Lung samples were processed for hematoxylin-eosin (HE), Masson's trichrome (MT), and immunohistochemical analyses using anti-α-smooth muscle actin (α-SMA) and anti-Rho kinase (ROCK) antibodies. IL-13 and IL-17 levels were quantified by ELISA. Data were expressed as mean ± SEM and analyzed statistically by one-way ANOVA followed by Tukey (p <0.05). Results: HE staining revealed marked inflammatory infiltration in AG and AGAP30 compared with CG, whereas AP at 100 and 300 mg/kg prevented this alteration, similarly to dexamethasone. MT analysis showed increased extracellular matrix deposition in AG (193.5±1.7 pixels/μm^2) and AGAP30 (172.8±1.8 pixels/μm^2) compared with CG (88.2±2.0 pixels/μm^2). This increase was prevented in AGAP100 (79.2±1.2 pixels/μm^2), AGAP300 (77.5±1.6 pixels/μm^2), and AGDEXA (77.2±1.1 pixels/μm^2). Likewise, α-SMA and ROCK immunolabeling were elevated in AG (116.0±1.9 and 102.2±1.2 pixels/μm^2, respectivelly) and AGAP30 (108.7±0.3 and 72.7±1.2 pixels/μm^2, respectivelly) compared with CG (75.7±1.6 and 28.8±1.1 pixels/μm^2, respectivelly), whereas AP at 100 (75.5±1.4 and 39.9±1.2 pixels/μm^2, respectivelly) and 300 mg/kg (65.5±1.3 and 26.5±1.6 pixels/μm^2, respectivelly) prevented these increases, with effects comparable to dexamethasone (63.3±0.6 and 29.7±1.5 pixels/μm^2, respectivelly). IL-13 levels were increased in AG (2.4±0.4 pg/mg) compared with CG (1.0±0.3 pg/mg), and this increase was prevented by AP100 (1.0±0.3 pg/mg). In contrast, IL-17 levels remained elevated in both AG (4.5±0.9 pg/mg) and AGAP100 (5.1±0.5 pg/mg) compared with CG (1.8±0.5 pg/mg). Conclusion: AP supplementation attenuated inflammatory and structural changes associated with experimental asthma, including extracellular matrix deposition, α-SMA and ROCK expression, and IL-13 production. These findings support a protective role of AP against airway remodeling, likely mediated by its anti-inflammatory effects.

08.041 **Experimental Acute Respiratory Distress Syndrome Model Induced by *E. coli* Lipopolysaccharide: Single and Repeated Dose in Wistar Kyoto and Spontaneously Hypertensive Rats**. Araújo LP, Ponce F, Rodrigues SF ICB-USP, Lab Vascular Nanopharmacology, Functional and Molecular Biology Graduate Program, Brazil

Introduction: Acute respiratory distress syndrome (ARDS) is characterized by hypoxemic respiratory failure as result of diffuse inflammatory lung injury, leading to increased alveolocapillary permeability, non-cardiogenic pulmonary edema, and impaired gas exchange. It is associated with high morbidity and mortality, and current treatment remains largely supportive, with no effective pharmacological therapies available. Experimental models are essential for the development of novel therapeutic strategies. Lipopolysaccharide (LPS) induced ARDS reproduces key features of the disease, although standardization of different severity levels remains challenging. Moreover, hypertension has been associated with increased ARDS severity and poorer clinical outcomes, although the mechanisms underlying this relationship remain elusive. **Objectives:** To establish and compare single and repeated dose LPS regimens for ARDS induction in Wistar Kyoto (WKY) rats and to evaluate the inflammatory response induced by LPS in spontaneously hypertensive rats (SHR). **Methods:** ARDS was induced by intratracheal (I.T.) administration of LPS from *E. coli*. WKY rats received either a single dose of LPS (5 mg/kg) and were analyzed 24 hours later or two doses of LPS (5 mg/kg, 24 h apart) and were analyzed 24 hours after the second shot. A single-dose LPS protocol (5 mg/kg) was also evaluated in SHR. Inflammatory responses were assessed by bronchoalveolar lavage fluid (BALF) analysis, hemogram, and clinical evaluation including motility and respiratory parameters**. **Results:** Both LPS regimens significantly increased inflammatory cell recruitment into the BALF compared with their respective SHAM groups (SHAM 1x: 1.1 ± 0.1 $\times 10^6$; LPS 1x: 23.4 ± 6.4 $\times 10^6$; SHAM 2x: 0.8 ± 0.3 $\times 10^6$; LPS 2x: 18.7 ± 6.2 $\times 10^6$ cells; $p < 0.05$), with no apparent significant difference between the single- and repeated-dose protocols. Likewise, LPS administration in SHR increased BALF inflammatory cell counts compared with control (SHAM SHR: 1.5 ± 0.5 $\times 10^6$; LPS SHR: 17.1 ± 0.6 $\times 10^6$ cells; $p < 0.05$). The greater number of leukocytes in BALF was mainly composed of neutrophils. LPS treatment significantly reduced the percentage of circulating lymphocytes in both WKY and SHR and increased circulating granulocyte percentages ($p < 0.05$), and significantly impaired the clinical score, reducing locomotion and enhancing respiratory rate, compared with their respective SHAM groups ($p < 0.05$). **Conclusion:** Intratracheal LPS administration successfully induced pulmonary inflammation and clinical manifestations consistent with ARDS in both WKY rats and SHR. A single LPS dose (5 mg/kg) was sufficient to establish a reproducible model of acute lung injury, as repeated LPS administration did not further increase pulmonary inflammatory or clinical parameters. Hypertension did not further impair the acute lung inflammation in SHR. **CEUA approval:** 3850260825\. FAPESP: 2023/05115-2.

08.042 **Endogenous 6-Nitrodopamine Release from Guinea Pig Trachea: A Novel Regulator of Airway Smooth Muscle Function**. Campos R, Ali K, Fuguhara V, Lorenzon F, Riffo- Vasquez Y, De Nucci G, Page CP Unicamp, Brazil, King's College London, United Kingdon, Unichristus, Brazil, USP, Brazil

Introduction: Asthma management still relies heavily on β2-adrenergic agonists. In human bronchi, adrenergic fibers are sparse and mainly supply the vascular bed, not the airway muscle itself which raises the question of what other endogenous signals might locally tune airway smooth muscle tone. One candidate is 6-nitrodopamine (6-ND), an epithelium-derived catecholamine shown to modulate contractility in seminal vesicles of rats and humans. Whether a similar epithelium-derived pathway operates in the airways remains unexplored. **Objectives:** The aim of this study was to determine whether 6-ND is released by guinea pig trachea could influence airway smooth muscle contractility. **Methods:** Guinea Pig Trachea (GPT) was isolated after euthanasia by an isoflurane overdose and suspended in 3-mL glass chambers with Krebs Henseleit Solution (KHS). Tissues were incubated with L-NAME (100μM); KHS samples were stored at -80°C for LC-MS/MS. For functional assays, trachea rings were mounted in 10-mL KHS baths and a concentration-response curves to 6-ND (100pM–300μM) were obtained under resting tension or precontraction with carbachol (1 μM) or histamine (30 μM). Tyrosine hydroxylase was detected by immunohistochemistry and FISH. **Results:** Guinea pig trachea released 6-ND at a concentration of 11.9 ± 8.1 ng/mL (n=5). The addition of L-NAME (100μM) strongly reduced, but did not abolish the basal release of 6-ND (1.4 ± 1.1 ng/mL, n=5). 6-ND promoted a concentration-dependent relaxation of GPT at resting tone (Emax: 9.97 ± 0.90 mN; pEC50: 4.60 ± 0.60; n=8). Salbutamol, a β2-adrenergic agonist, elicited a similar maximal relaxation (Emax: 9.55 ± 1.64 mN; n=6) but with markedly higher potency (pEC50: 7.16 ± 0.19). In addition, 6-ND promoted relaxation in trachea precontracted with either carbachol (Emax: 15.68 ± 1.73 mN; pEC50: 4.35 ± 0.02; n=5) or histamine (Emax: 13.35 ± 3.79 mN; pEC50: 4.39 ± 0.15; n=4). Tyrosine hydroxylase was positive in epithelium of guinea pig trachea. S100, a neuronal marker was positive in nerve fibers in guinea pig trachea. **Conclusion:** 6-ND is a new epithelium-derived signaling molecule in the airways, spontaneously released by isolated guinea-pig trachea and capable of relaxing tracheal smooth muscle. This identifies 6-ND as an endogenous catecholamine relevant to airway tone, suggesting a local, non-neuronal mechanism of bronchomotor tone complementing the classical adrenergic pathway and non adrenergic, non cholinergic pathways. **Acknowledgments:** Rafael Campos and Gilberto De Nucci thanks Fapesp Animal Research Ethical Committee Number (Certificates No.6482-1/2024- UNICAMP) **Financial support**: Rafael Campos (2022/08232-7 and 2023/15350-9) and Gilberto De Nucci (2019/16805-4) thanks FAPESP.

08.043 **Gastroprotective and Antispasmodic Effects of 1-(4-Chlorophenyl)-3-(1,3,4-thiadiazol-2-yl) thiourea (MS06) in Mice**. Lima FJB[1,2], Costa TB[1], Barbosa YV[1], Fonseca MLP[1], Silva LMQ[1], Cavalcanti, MAT[3], De Moura RO[3], Dos Santos VL[1]. [1]UEPB, Lab Pharmacological Assays, Brazil, [2]Centro Universitário UNIFACISA, Brazil, [3]UEPB, Lab Drug Design and Synthesis, Brazil.

Introduction: Thiourea and 1,3,4-thiadiazole derivatives have shown important biological activities, including anti-inflammatory and antimicrobial effects. Based on a prototype compound with antiulcerogenic activity, 1-(4-chlorophenyl)-3-(1,3,4-thiadiazol-2-yl)thiourea (MS06) was designed through bioisosteric modifications and the Topliss decision tree strategy. **Objectives:** To evaluate the gastroprotective effect of MS06 against ethanol-induced gastric lesions in mice and its antispasmodic effect on isolated gastric fundus strips. **Methods:** For the gastroprotective evaluation, animals received five different pretreatments: MS06 at doses of 12.5, 50, or 100 mg/kg, vehicle alone (Tween 80 5% v/v), or carbenoxolone 100 mg/kg as a positive control. All groups received absolute ethanol (0.2 mL, p.o.) and 1 h later the stomachs were then removed, opened, and the percentage of ulcerative lesion area (ULA) was measured. Myorelaxant evaluation employed gastric fundus strips from naive mice mounted in an organ bath system (Insight Ltda) containing Tyrode solution (pH 7.4) at 37 °C under a resting tension of 1 g. An initial contraction was induced by carbachol (CCh, 1 μM) in the absence of MS06, followed by repeated CCh-induced contractions in the presence of increasing concentrations of MS06 (10 nM–100 μM). **Results:** The ULA after ethanol administration in the vehicle group was 26.7 ± 5.3%, whereas pretreatment with carbenoxolone at 100 mg/kg or MS06 at doses of 12.5, 50, or 100 mg/kg significantly reduced ULA to 5.4 ± 0.9%, 6.2 ± 0.6%, 4.1 ± 0.7%, and 3.6 ± 1.1%, respectively ($p < 0.001$, one-way ANOVA followed by Tukey's post hoc test, n = 7/group). On isolated murine gastric fundus strips, MS06 inhibited CCh-induced contraction in a concentration-dependent manner, with an IC50 of 24.1 μM (95% CI: 14.6–39.9 μM, n = 5). This inhibitory effect was significantly greater than that produced by equivalent volumes of Tween 80 ($p < 0.001$, two-way ANOVA followed by Bonferroni's post hoc test). At 100 μM, MS06 reduced the CCh-induced contraction to 9.3 ± 3.1% of the reference response (n = 5), whereas an equivalent volume of Tween 80 maintained 86.0 ± 6.4% of the reference response (n = 4). **Conclusion:** MS06 showed gastroprotective effects against ethanol-induced gastric lesions and inhibited CCh-induced contractions in isolated gastric fundus strips. Although these findings are compatible with a potential antimuscarinic effect, additional studies are needed to confirm this mechanism. Nevertheless, the combined gastroprotective and antispasmodic activities support the potential of MS06 as a promising candidate for the treatment of gastrointestinal disorders.

08.044 **Myrtenyl Laurate reduces Inflammatory Markers in a Non-Surgical Model of Gastroesophageal Reflux Disease**. Viana, AFSC[1,2,3], Oliveira, GH[1], Fernandes, HB[1,2], Martins, SCA[1], Araujo, PBM[2], Gomes, EGS[3], Neto, ADC[3], Reis, ML[1] Guerra, SPL[4], Gonçalves, LMF[4], Kutyła, M[5], Stankevič, M[6], Trytek, M[5], Oliveira, RCM[1,2] [1]UFPI, Medicinal Plants Research Center (NPPM), Brazil, [2]UFPI, PPG Farmacology, Brazil, [3]UEMA, Campus Santa Inês, Brazil, [4]UFPI, Depto Morfologia, Brazil, [5]MCSU, Akademicka, Lublin, Poland, [6] MCSU, Gliniana, Lublin, Poland.

Introduction: Gastroesophageal reflux disease (GERD) is a digestive disorder characterized by the reflux of gastric contents, including acid, food, and fluids, from the stomach into the esophagus. Objectives: This study evaluated the effects of myrtenyl laurate (ML) in a non-surgical animal model of GERD. **Methods:** Myrtenyl laurate (ML) was synthesized through the esterification of myrtenol with saturated carboxylic acids of varying chain lengths using freeze-dried mycelium of Cladosporium cladosporioides 01 at Maria Curie-Skłodowska University. Female Swiss mice (25 g, 5 weeks old; n = 6/group) were maintained under controlled environmental conditions with a 12 h light/dark cycle. GERD was induced by alternate-day fasting for 4 weeks. Animals were subsequently treated orally (p.o.) for an additional 2 weeks while continuing the fasting protocol, receiving vehicle (1% Tween 80 in distilled water), ML (6.25, 12.5, or 25 mg/kg), or pantoprazole (15 mg/kg). A sham group consisted of non-induced and untreated animals. At the end of the 6-week experimental period, the animals were euthanized, and esophageal tissues were collected for histopathological (H&E) and immunohistochemical analyses of GERD-related inflammatory markers, including inducible nitric oxide synthase (iNOS) and tumor necrosis factor-alpha (TNF-α) (Cloud-Clone Corp.) (IM N-R, J. Investig. Med., v. 69, p. 1208, 2021). Quantitative analyses were performed using ImageJ software, and results were expressed as the percentage of immunopositive cells (mean ± SEM). Statistical analysis was conducted using one-way ANOVA followed by Tukey's post hoc test, with $p < 0.05$ considered statistically significant. **Results:** Histopathological analysis demonstrated that the vehicle group exhibited greater epithelial disruption and keratinocyte proliferation compared with the sham and ML 12.5 mg/kg groups. iNOS immunoreactivity was significantly elevated in the GERD vehicle group (17.8 ± 1.5% positive cells). Treatment with ML at doses of 6.25, 12.5, and 25 mg/kg significantly reduced iNOS expression (1.7 ± 1.5%, 6.9 ± 2.1%, and 7.3 ± 3.5%, respectively), similarly to pantoprazole treatment (5.0 ± 2.1%), compared with the vehicle group. The sham group exhibited 5.8 ± 2.5% positive cells. Likewise, TNF-α expression was significantly decreased in animals treated with ML (12.5 and 25 mg/kg) and pantoprazole (2.5 ± 1.8%) compared with the vehicle group (8.9 ± 2.8%). The sham group showed 3.5 ± 0.4% positive cells. **Conclusion:** These findings suggest that ML exerts significant anti-inflammatory effects in this experimental model of GERD, supporting its potential as a promising candidate for the development of novel therapeutic strategies for GERD treatment. Animal Research Ethics Committee: Approval no. 684/21-UFPI. **Financial support:** CNPq / CAPES / FAPEMA.

08.045 **Altered FEV1-FVC Coupling After Pharmacological Bronchodilation in COPD Patients Using Renin-Angiotensin System Modulators**. Silva FS, Paiva YMA, Medeiros VLD, Freitas JVC, Santos JRA, Medeiros GB, Kennedy-Feitosa E UFERSA-Mossoró, Morphophysiopharmacology Lab

Introduction: Chronic obstructive pulmonary disease (COPD) is defined by persistent post-bronchodilator (post-BD) airflow limitation, assessed by spirometry. While renin-angiotensin system modulators (RASm) have been associated with reduced mortality and potentially lower risk of exacerbations in COPD patients, evidence for improvements in spirometric parameters remains mixed and inconclusive. **Objectives:** To evaluate whether RASm (e.g., ACE inhibitors, AT1 receptor blockers) modify the post-BD relationship between forced expiratory volume in the first second (FEV1) and forced vital capacity (FVC) in COPD patients. **Methods:** Cross-sectional study enrolling 38 active and former smokers stratified by airflow obstruction into COPD(+) and COPD(–) according to the Brazilian Society of Pulmonology and Phthisiology (SBPT) criteria (post-BD FEV1/FVC < 0.70 or < the lower limit of normal). Individuals were further categorized into RASm and no-medication (NoMed) groups. Linear regression was fitted for post-BD FEV1 versus post-BD FVC within subgroups defined by medication use or COPD status. The FEV1–FVC relationships were compared using analysis of covariance (ANCOVA) with an FVC × group interaction term in GraphPad Prism (v. 8.0.2). A significant interaction P-value (P-int < 0.05) indicated slope heterogeneity between groups. **Results:** Post-BD FEV1 and FVC were strongly correlated in the full cohort ($P < 0.0001$; $R^2 = 0.87$; slope = 0.79), and medication use did not significantly modify the FEV1–FVC relationship (P-int = 0.5803). COPD status significantly changed the FEV1–FVC slope (P-int < 0.0001), with a lower slope in COPD(+) than COPD(–) individuals (0.49 vs. 0.82; $R^2 = 0.87$ vs. 0.96, respectively). No medication effect was observed in the COPD(–) group (P-int = 0.3249; slopes: NoMed = 0.80 vs. RASm = 0.89). In contrast, among COPD(+) patients, RASm use significantly accentuated the reduction in the FEV1–FVC slope (P-int = 0.0226; slopes: 0.36 vs. 0.59 for RASm and NoMed, respectively). **Conclusion:** RASm users with COPD appeared to have an altered coupling between FEV1 and FVC after pharmacological bronchodilation, a pattern not observed in non-COPD individuals and more pronounced than that observed in untreated COPD counterparts. As changes in recruited volume were not accompanied by proportional gains in airflow, these findings highlight a potential effect of RASm on post-BD spirometric dynamics and support further investigation into the interaction between the renin–angiotensin system and airway mechanics in COPD.

09. Natural Products and Toxinology

09.001 **Terpenes Enhance Antibiotic Activity Against Multidrug-Resistant** *Klebsiella pneumoniae*. Lourenço MS, Dantas IGP, da Silva AJA, Rodrigues EN, Bernardino PKC, Nascimento PHA, Bento AJM, Coutinho HDM, Oliveira-Tintino CDM, Araújo IM URCA, Brazil

Klebsiella pneumoniae is an important multidrug-resistant pathogen associated with healthcare-related infections. The growing prevalence of resistant strains has stimulated the search for adjuvant compounds capable of restoring antibiotic efficacy. Terpenes are natural products that may interfere with bacterial membranes and improve antimicrobial activity. To evaluate the antibacterial activity, antibiotic-modulating effect, and membrane permeability alterations induced by limonene, α-pinene, and isoeugenol against a multidrug-resistant strain of *Klebsiella pneumoniae*. Antibacterial activity was determined by broth microdilution. Antibiotic modulation assays were performed using subinhibitory concentrations of terpenes combined with gentamicin, polymyxin B, norfloxacin, and ceftazidime. Membrane permeability was assessed using the SYTOX Green fluorescence assay. Statistical analyses were performed using ANOVA followed by Bonferroni's post hoc test. None of the terpenes exhibited clinically relevant antibacterial activity alone (MIC ≥ 1024 µg/mL). However, all compounds modulated antibiotic activity. α-Pinene reduced the MIC of gentamicin from 50.79 to 40.31 µg/mL, polymyxin B from 512 to 256 µg/mL, norfloxacin from 40.31 to 32 µg/mL, and ceftazidime from 16 to 8 µg/mL. Isoeugenol showed the strongest modulatory effect, reducing gentamicin MIC from 50.79 to 12.69 µg/mL and polymyxin B MIC from 512 to 322.53 µg/mL. Limonene reduced the MICs of gentamicin, polymyxin B, and ceftazidime but increased the MIC of norfloxacin. Membrane permeability assays demonstrated increased fluorescence for all terpenes, with isoeugenol producing the highest effect (21%), followed by α-pinene (15%) and limonene (13%). The evaluated terpenes did not display significant intrinsic antibacterial activity but acted as effective antibiotic adjuvants against multidrug-resistant *K. pneumoniae*. The observed effects appear to be associated with increased bacterial membrane permeability, facilitating antibiotic action. Among the tested compounds, isoeugenol showed the most promising modulatory profile, supporting the potential use of terpenes as resistance-modifying agents in combination therapies.

09.003 Antioxidant Activity of *Commiphora leptophloeos*. Ferreira CES, Andrade IA, Fialho MLS, Gonçalo YA, Martins SO, Nóbrega VM, Oliveira MVM, Medeiros FD UFCG-Cuité, Center for Education and Health, Brazil.

Introduction: Brazil possesses one of the greatest biodiversities in the world, with emphasis on the Caatinga biome, characterized by the high diversity of plant species with broad pharmacological potential. In this context, the appreciation of phytotherapy in the country has been expanded through public policies that encourage the rational use of medicinal plants and the development of research in this field. Among the species of therapeutic interest, *Commiphora leptophloeos*, popularly known as Umburana de espinho, stands out and is used in traditional medicine for the treatment of inflammatory and infectious processes, as well as respiratory, gastrointestinal, and gynecological disorders. Therefore, studies investigating its chemical composition and biological potential are necessary. Objectives: To evaluate the antioxidant activity of the *Commiphora leptophloeos* extract. Methodology: The plant material was collected by pruning and subsequently subjected to drying in a forced-air circulation oven at 45°C for three days. After drying, the material was ground using a knife mill. The extraction process was carried out by maceration using ethanol/water (1:1 v/v) as the solvent. Subsequently, the extract was filtered and stored under refrigeration. The presence of secondary metabolites was investigated using qualitative methods. Antioxidant activity was determined by the ABTS and DPPH methods and expressed as µmol ascorbic acid equivalents/mL ± standard deviation. Results: Pharmacognostic characterization revealed the presence of alkaloids, saponins, and flavonoids, with a predominance of tannins and phenolic compounds. The antioxidant potential was evaluated by the ABTS and DPPH assays, which presented mean values of 0.015 ± 0.001 µmol AAE/mL and 0.002 ± 0.002 µmol AAE/mL, respectively, demonstrating the free radical scavenging capacity of the extract. This activity is frequently associated with the presence of phenolic compounds and tannins (Martins, LT. Remici., v. 4, p. 568-569, 2025), reinforcing the antioxidant potential of the species. Similarly, studies have demonstrated antioxidant activity by the DPPH assay in Umburana de espinho bark extracts associated with these secondary metabolites (Cordeiro, MLS. Oxid. Med. Cell. Longev., v. 2021, p. 8-9, 2021). Furthermore, a high capacity for ABTS radical neutralization was also observed (Araújo, JRF. Pharmaceuticals., v. 18, p. 5-6, 2025) in bark extracts, corroborating the results obtained in the present study. Conclusion: Thus, the findings reveal its relevance for pharmacological applications, contributing to the development of future formulations and new biological assays.

09.004 **Chemical and Biological Study of the Extract of *Cecropia pachystachya* Trec Collected in the Interior of the State of Ceara**. Pereira, LK[1], Santiago, MLA.[1], Costa MEP[1]., Silva, JBS[2], Morais SM[3], Maciel MHC[1], Moreira RF[1], Magalhães LC[1], Souza, EP[4], Pinto CCC[5]. [1]UNINTA, Faculdade de Medicina, [2]UFC, [3]UECE, Lab Química de Produtos Naturais, [4]UECE, Medicina, Depto Morfologia, Pós Graduação em Ciências Morfofuncionais, [5]UNINTA, Faculdade de Medicina, Lab Microbiologia

Interest in natural antioxidants has grown due to their potential to prevent chronic diseases associated with oxidative stress. Among plant-derived secondary metabolites, phenolic compounds stand out for their significant capacity to neutralize free radicals and are widely investigated for their biological properties. In this context, the present study aimed to characterize the phytochemistry and evaluate the antioxidant activity of the ethanolic extract from *Cecropia pachystachya* Trec. leaves (EEFCP). The plant material identified by herbarium specimen no. EAC0063215, consisted of 86 g of leaves, which were sun-dried for 29 days. Afterward, the leaves were ground and subjected to maceration extraction using 92.8° INPM hydrated ethyl alcohol as the solvent; the mixture was kept in a closed container for 25 days in a dry, well-ventilated area. Subsequently, the C. pachystachya ethanolic extract (EEFCP) was filtered using a funnel and cotton wool, and the solvent was completely evaporated to yield the crude extract. The EEFCP underwent phytochemical screening and antioxidant assays using DPPH and ABTS free radical scavenging methods, with quercetin serving as the positive control in both assays. In the DPPH assay, antioxidant activity was evaluated according to the methodology described by Carvalho et al. (2009), with modifications proposed by Penido et al. (2017). Samples were prepared in triplicate in methanol at concentrations of 3.125, 6.25, 12.5, 25.0, 50.0, and 100 µg/mL. Then, 2 mL of a 0.004% DPPH solution was added, using ethanol as the negative control. After incubation for 30 minutes protected from light, absorbance readings were taken at 517 nm using a UV-VIS spectrophotometer. The percentage of inhibition was calculated using the equation: IP% = [(DPPH absorbance - extract absorbance) / DPPH absorbance] × 100, and the 50% inhibitory concentration (IC_{50}) was determined via linear regression of the obtained data. For the ABTS assay, antioxidant activity was determined in flat-bottom 96-well plates using a BioTek ELISA reader (model ELX 800) with Gen5 V2.04.11 software, following the methodology described by Re et al. (1999). The ABTS + radical was prepared by mixing 5 mL of 7 mM ABTS solution with 88 µL of 140 mM potassium persulfate, followed by stirring and incubation at room temperature, protected from light, for 16 hours. Subsequently, 1 mL of this solution was diluted in 99 mL of ethanol. Into each microplate well, 300 µL of the ABTS solution and 3 µL of the extract sample (dissolved in methanol) were added. Sample and positive standard dilutions were prepared from a 20 mg/mL stock solution to achieve concentrations of 200, 100, 50, 25, 12.5, 6.25, 3.12, 1.56, and 0.78 µg/mL. Absorbance readings were taken at 630 nm using a UV-VIS spectrophotometer during a 10 minute incubation period. All solutions except the sample were used as a negative control, with values corresponding to the natural color of the extracts being subtracted. All analyses were performed in triplicate, and after data normalization, the IC_{50} was determined via non- linear regression using GraphPad Prism software (version 7.0). Phytochemical analysis revealed the presence of phenolic compounds, particularly flavonoids belonging to the flavonol and flavanone classes. In antioxidant assays, the extract exhibited free radical scavenging activity, with IC_{50} values of 11.98 ± 0.60 µg/mL for DPPH and 16.06 ± 0.08 µg/mL for ABTS, demonstrating antioxidant potential albeit lower than that of the quercetin standard. The results suggest that the observed antioxidant activity is linked to the phenolic compounds identified in the extract, highlighting the biological potential of *Cecropia pachystachya* Trec. as a natural source of antioxidants.

09.005 **Pharmacology Bioprospecting of the Brazilian Peppertree** (*Schinus terebinthifolia* **Raddi**)**: A Systematic Review**. Calado LP[1], Medeiros AD[2], Boeira LS[2], Alves MS[3], Oliveira Filho AA[1] [1]UFCG, Center for Health and Rural Technology, Brazil, [2]UEPB, Center for Applied Biological and Social Sciences, Brazil [3]UFCG, PPG of Health and Science Animal, Brazil

Introduction: Brazilian peppertree or red aroeira plant (*Schinus terebinthifolia* Raddi sin. Schinus terebinthifolius) it is a member of the Anacardiaceae family, with plant-based input rich in phenolic compounds, terpenoids, and tannins. The decoction made from its bark is widely used in traditional herbal medicine in Brazil. **Objectives:** Compile, analyze and appraise information regarding the pharmacological and therapeutic potential of the Brazilian peppertree. **Methods:** A rigorous systematic review was conducted in the databases, Pubmed®, SciELO® and CAPES periodicals, using the following terms and Boolean operators in the search: (*Schinus terebinthifolia* or *Schinus terebinthifolius*) and (pharmacological or anti-inflammatory or antimicrobial or antioxidant Or healing). The following were excluded review articles, monographs, theses, dissertations, *in sílico* studies, we also excluded publications not written in Portuguese or English, studies conducted for veterinary, food, or forestry purposes, and duplicate articles; including original studies published from 2020 to the present, whose aim objective was to describe and analyze therapeutic potentials of the *Schinus terebinthifolia* Raddi. **Results:** An initial total of 271 were identified; 45 were deemed eligible after a partial review of the title, and 34 were included after a full review. The reviewed material revealed numerous activities of clinical interest, as an antimicrobial, anti-inflammatory, and analgesic agent, with possible antiviral potential, notable for its antioxidant activity, as well as a candidate for cosmetic formulations. **Conclusion:** The raw material for the *Schinus terebinthifolia* Raddi, it has high therapeutic potential and is invaluable for making healthcare more accessible. It is of great value for drug development and formulation.

09.006 **Evaluation of the Effects of Hydralazine Derivatives on Vas Deferens Contractility**. Avelino CTS, Portácio LFS, Sousa BMS, Ferreira Santos C, Lima PSC, Wanderley MV, Uchôa RPM, Nascimento NRF UECE, Brasil

Introduction: Hydralazine is a vasodilator with a very limited indication as an antihypertensive agent due to its serious adverse effects. Twenty-nine hydralazine derivatives were synthesized for pharmacological screening to investigate their cardiovascular effects and actions on other tissues. **Objective:** To evaluate the effects of hydralazine derivatives on the contractility of electrically stimulated isolated vas deferens in order to investigate their potential antiadrenergic activity. **Methods:** All experimental protocols were approved by the Animal Ethics Committee of the State University of Ceará (CEUA/UECE) under protocol No. 31032.002804/2026-47. Both the right and left vas deferens were isolated from guinea pigs (*Cavia porcellus*; n = 3; 6 replicates). Tissue segments (1.5 cm in length) were mounted in organ baths for isometric contractility recording using isometric force transducers (PanLab TRI202, Barcelona, Spain). The tissues were maintained in Krebs–Henseleit solution and electrically stimulated through platinum electrodes (0.1 Hz, 10 ms pulse duration). The threshold stimulation intensity required to elicit contraction was determined for each preparation, after which stimulation was applied at an intensity 50% above the threshold. Hydralazine derivatives were added directly to the organ bath at different concentrations: 4Py (10^{-11} to 10^{-5} M), 3Et (10^{-11} to 10^{-5} M), or a single concentration (10^{-5} M) of OH, LOX, OCH_3, HBr, CN, and 2OH. Contractile responses were recorded using a data acquisition system with LabChart software and amplitude of the twitches were used as the primary endpoint. **Results:** The hydralazine derivatives evaluated did not produce significant changes in the contractility of isolated guinea pig vas deferens. The derivatives OH, LOX, OCH_3, HBr, CN, and 2OH produced only minor, non-significant changes (Δ = -0.10, -0.02, 0.03, -0.02, -0.10, and -0.10, respectively), maintaining a contractile profile similar to that observed before compound administration. Overall, the contractility recordings indicated low responsiveness of the vas deferens to the hydralazine derivatives at the concentrations tested. **Conclusion:** Under the experimental conditions employed, the hydralazine derivatives evaluated did not significantly alter the contractility of isolated guinea pig vas deferens. These findings suggest that the tested compounds do not exhibit antiadrenergic activity. They will subsequently be evaluated for their direct vasodilatory effects in blood vessels precontracted with the adrenergic agonist phenylephrine. **Acknowledgments:** The authors thank Prof. Helcio Silva dos Santos for providing the 29 hydralazine derivatives. **Financial support:** This research received no external funding. **References:** Brunton LL, Chabner BA, Knollmann BC. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 12th ed. Porto Alegre: AMGH; 2012.

09.007 **Effects of Dietary Flavonoids on Human Cognition: A Systematic Review**. Feitosa LFS[1], Azevedo ATF[1], Abreu DFP[2], Monteiro IO[1], Sousa PBC[1], Souza ADB[1], Silva JEB[1], Correia LCF[1], Silva VFB[123], Cruz YSES[123], Dantas DN[123], Vasconcelos KT1, Freitas GA[134], Sousa JMN[1,2], Santos NA[12345] [1]UFPB, Psychology Dpt, PGP Social Psychology Lab Perception, Neurosciencies, and Behavior, [2]UFPB, Psychology Dpt, PGP Cognitive Neuroscience and Behavior. Brazil.

Introduction: Flavonoids have gained importance as they are investigated as potential multimodal modulators of brain function, such as synaptic plasticity, regulation of neuroinflammation, and reduction of oxidative stress, presenting themselves as promising alternatives to overcome the pharmacotherapeutic limitations of unidimensional treatments in the preservation and restoration of cognition in neurodegeneration, aging, and psychiatric disorders. In humans, clinical trials indicate positive effects on working memory, verbal fluency, and processing speed. However, the findings are heterogeneous and frequently limited by a lack of pharmacokinetic control, short duration of intervention, and low statistical power. **Objectives**: To critically and translationally synthesize the literature on the effects of flavonoids on human cognition, particularly the molecular and pharmacokinetic mechanisms involved, their interactions with the gastrointestinal system, and the cognitive domains most frequently affected. Methods This study used a systematic literature review, including research on the impact of flavonoids on cognitive function, published in peer-reviewed journals in English, Portuguese, and Spanish, between 2016 and 2025. Studies using animal models, presenting incomplete or insufficient data, and articles that exclusively described research protocols were excluded. Searches were conducted in the Scopus, PubMed, and PsycInfo databases, specifically in August 2025. The search terms “Flavonoids OR Flavanols OR Isoflavones AND Cognition OR Cognitive Function” were used, with the platforms specifying that these descriptors should be present in the title and/or abstract of the article. In a total of 593 articles found, 26 studies were retained for the final sample. Results All selected articles were published in English. Regarding the sample size, they varied widely, ranging from 9 to 1,947 participants, encompassing children and young adults to the elderly, including healthy individuals and those with mild cognitive impairment, dementia, or schizophrenia. Thus, the studies suggest that flavan-3-ols, anthocyanins, and flavonols are most consistently associated with gains in memory, attention, and executive functions. However, the effects are heterogeneous, with variations in findings between age groups and within the non-healthy population, as well as differences in dose amounts, dietary sources, and cognitive domains assessed, generating inconsistent results**: Conclusion:** It is concluded that cognitive performance in response to flavonoids is highly dependent on the subclass, duration of the intervention, participant's baseline status, dosage, and cognitive task assessed. Therefore, the limitations found in the consistency of the results demonstrated the need for further studies with methodological standardization to elucidate the mechanisms and magnitude of the effects.

09.008 **Evaluation of the Antifungal Potential of 10 Essential Oils Obtained from Different Hop Cultivars** (*Humulus lupulus*) **against** *Candida albicans*. Silva-Filho AM[1], Silva VA[1], TAVARES IGS[1], Freire KRL[2], Abílio GMF[3] [1]UFPB, Centro de Ciências da Saúde, Brasil [2]UFPB, Centro de Biotecnologia - Depto Biologia Celular e Molecular, Brasil [3]UFPB, Centro de Ciências da Saúde - Depto Ciências Biomédicas, Brasil

Introduction: Although there are successful treatments on infections triggered by *Candida albicans* through using a wide range of available antifungals, there is an increase in emerging strains within this genus that present resistance, becoming difficult, above all, antibiotic therapy and prophylaxis against these infections. In this context, the literature shows that essential oils are a useful alternative to conventional antifungals, because they present low toxicity and lack of resistance. **Objectives:** Thereby, this study aimed to discover the antifungal properties of essential oils from hop cultivars (*Humulus lupulus*) against *Candida albicans* ATCC 90028, namely: Slade, Chinook, Sabro, Cascade, Sbrata, Luminosa, CGX Strata, M. Bavária, Galena and Amarillo. **Methods:** All procedures adopted were made in triplicate and followed the guidelines from the Clinical and Laboratory Standards Institute (2002). To determine the Minimum Inhibitory Concentration (MIC), 96-well plate microdilution was performed containing Sabouraud Dextrose broth, using nystatin as positive control and after incubation at 24 hours at 37 °C. The concentration of the specimen evaluated was from 15,62 to 2000 µg/mL. The Minimum Fungicidal Concentration (MFC) was determined by inoculating 50 µL on Sabouraud Dextrose agar by drop plate technique, using corresponding rates to the MIC and the two immediately higher concentrations and after incubation at 24 h and 37 °C. The subsequent steps consisted of visual reading to assess whether fungal growth had occurred. The MFC/MIC ratio was used to determine whether oil presented fungistatical activity (MFC/MIC ≥ 4) or fungicide (MFC/MIC < 4). **Results:** All tested oils show MIC from 500 to 2000 µg/mL. The M. Bavária oil exhibited MIC with moderated bioactivity (MIC between 126-500 µg/mL); mild bioactivity (MIC 501-1000 µg/mL) was observed for oils Chinook, Sabro, Sbrata, Luminosa, CGX Strata, Galena and Amarillo; and undefined bioactivity (MIC > 1000 µg/mL) was found for Slade and Cascade. MFC values ranged from 1000 µg/mL to concentrations greater than 2000 µg/mL. Sabro, Cascade, Luminosa and CGX Strata presented an MFC/MIC ratio equal to 1, while Sbrata, M. Bavária, Galena and Amarillo presented a ratio equal to 2, indicating fungicidal activity. For Slade and Chinook, the activity was considered undetermined. **Conclusion:** In light of the above, it is noteworthy that, except Slade and Cascade, all tested essential oils show antifungal activity, showing that different hop cultivars may be a therapeutic alternative to the use of antifungals for treatment of *Candida albicans* infections. Further studies are necessary for assessment their mechanisms of actions and potential toxic effects. Keywords: Antifungal, Candida, Humulus.

09.009 **Evaluation of the Antifungal Activity of** *Commiphora leptophloeos* **Extract**. Martins SO, Andrade IA, Ferreira CES, Fialho MLS, Gonçalo YA, Oliveira MVM, Nobrega VM, Pereira FO, Medeiros FD. UFCG, Cuité Campus, Center for Education and Health, Brazil.

Introduction: The Caatinga biome is exclusively Brazilian and presents a great diversity of medicinal plants. Given the increasing interest in herbal medicines, the species *Commiphora leptophloeos*, popularly known as "umburana-de-espinho", stands out as a potential phytotherapeutic candidate due to its traditional use in Northeastern Brazil and its medicinal properties. In addition, the species contains several bioactive secondary metabolites and has demonstrated potential antifungal activity. **Objective:** To evaluate the antifungal activity of the bark extract of *C. leptophloeos*. **Methodology:** Stem bark was collected and dried in an oven with air circulation at 45 °C for 72 hours. Subsequently, the material was ground using a knife mill to obtain the plant drug. The extract was prepared by maceration in a hydroalcoholic solution. Phytochemical characterization was performed using classical methods to identify the presence of the following secondary metabolites: alkaloids, phenolic compounds, flavonoids, saponins, and tannins. Antifungal activity was evaluated by determining the Minimum Inhibitory Concentration (MIC) and Minimum Fungicidal Concentration (MFC) using the broth microdilution technique against different fungal strains: *Microsporum canis* (ATCC and LM), *Nannizzia gypsea* (ATCC and LM), and *Trichophyton rubrum* (ATCC and LM). All assays were performed in duplicate to ensure reliability and reproducibility of the **Results:** Phytochemical analysis identified the presence of the following secondary metabolites: saponins, flavonoids, tannins, phenolic compounds, and alkaloids. Against M. canis (ATCC and LM), the extract showed an MIC of 512 µg/mL and an MFC of 1024 µg/mL. Similar results were observed for *N. gypsea* (ATCC and LM), with an MIC of 512 µg/mL and an MFC of 1024 µg/mL. For *T. rubrum* (ATCC), the extract also showed an MIC of 512 µg/mL and an MFC of 1024 µg/mL. However, no antifungal activity was observed against *T. rubrum* (LM). No previous studies have evaluated the activity of *C. leptophloeos* against dermatophyte. These findings highlight the novelty of the study and suggest the potential of the species as a promising antifungal alternative, particularly in the context of increasing fungal resistance. **Conclusion:** The tested extract demonstrated potential antifungal activity, although further studies are necessary to confirm its therapeutic efficacy.

09.010 **Potential Quorum Sensing Modulation by Ethyl Esters Derived from** *Pentaclethra macroloba* **Through Interaction with the LasR Receptor of** *Pseudomonas aeruginosa*. Lima AB[1], Castro MSM[2], Rodrigues ABL[3], Ramos RS[3], Oliveira FR[2], Nascimento AA[1,2]1Unifap, PPG Ciências da Saúde, Brasil, [2]Unifap, Lab Experimentação Animal, Brasil, [3]Unifap, LMQC, Brasil.

Introduction: Persistent endodontic infections are associated with resistant microorganisms and biofilm formation, requiring the investigation of new bioactive compounds. *Pentaclethra macroloba*Pentaclethra macroloba*Pentaclethra macroloba* is an Amazonian species rich in fatty acid ethyl esters with potential biological activity. In addition to direct antimicrobial effects, quorum sensing modulation has emerged as a promising antivirulence strategy against *Pseudomonas aeruginosa*. **Objectives:** To evaluate the chemical composition and the potential quorum sensing modulation of ethyl esters derived from *Pentaclethra macrolobaPentaclethra macrolobaPentaclethra macroloba* through molecular docking against the LasR receptor of *Pseudomonas aeruginosa*. **Methods:** The fixed oil of *Pentaclethra macrolobaPentaclethra macrolobaPentaclethra macroloba* was transesterified by enzymatic catalysis and analyzed by gas chromatography coupled to mass spectrometry (GC-MS). Molecular docking simulations were performed using DockThor against the LasR receptor (PDB: 4NG2). Pharmacokinetic and toxicological predictions were assessed using Discovery Studio v16.1. Data were analyzed descriptively. **Results:** GC-MS analysis demonstrated predominance of long-chain fatty acid ethyl esters, especially (E)-9-octadecenoic acid ethyl ester as the major constituent. However, docking simulations demonstrated high affinity between the identified compounds and the LasR receptor, with binding energies ranging from -7.563 to -10.352 kcal/mol, suggesting potential modulation of quorum sensing pathways associated with bacterial virulence and biofilm formation. **Conclusion:** Ethyl esters derived from *Pentaclethra macrolobaPentaclethra macrolobaPentaclethra macroloba* demonstrated relevant molecular interactions with the LasR receptor of *Pseudomonas aeruginosa*, indicating potential antivirulence activity through quorum sensing modulation. These findings support the biotechnological applicability of Amazonian bioactive compounds in the development of innovative intracanal formulations.

09.011 **Prospection of the Gastroprotective Activity of the Crude Ethanolic Extract from** *Sideroxylon Obtusifolium*. Sales AO, Lopes FG, Rodrigues CVS, Santos ELS, Farias AGC, Santos BRP, Morais FS, Lima FJB, Santos VL. UEPB, Lab Pharmacological Assays, Brazil. Centro Universitário Unifacisa, Brazil.

Introduction: Gastric ulcer is a common disease caused by factors like infection by Helicobacter pylori and the use of nonsteroidal anti-inflammatory drugs (NSAIDs), which can affect around 10% of the world's population. It is considered a recurring disease. The mostly utilized treatment has presented many adverse effects. Such factors have been stimulating the research with medicinal plants as an alternative to new effective medicines and with fewer adverse effects. The *Sideroxylon obtusifolium*, known as “quixabeira”, native brazilian species, with pharmacological activities already identified like, anti-inflammatory, healing, analgesic, and antioxidant. **Objectives:** To evaluate the acute toxicity and gastroprotective activity of the hydroalcoholic extract from the bark of *Sideroxylon obtusifolium* (EHASo). **Methods:** The HEASo was obtained by macerating the stem bark in 70% ethanol. The qualitative phytochemistry and the polyphenol content were determined by spectrophotometry. In the biological activity, male and female Swiss mice were used. Acute toxicity was performed according to OECD 401, and animals were treated with a dose of 2000 mg/kg. The gastroprotective activity was evaluated in the ethanol-induced ulcer model (animals were treated with doses of 125, 250, and 500 mg/kg), and in 0.5 cm strips of the gastric fundus pre-contracted with carbamylcholine. **Results:** The qualitative phytochemical analysis of HEASo revealed the presence of saponins, polyphenols, steroids, triterpenes, and flavonoids. The total polyphenol content was 261.8 mg/100 g of extract. In the acute toxicity study, HEASo at a dose of 2000 mg/kg caused no mortality or signs of toxicity; there were no changes in animal weight, and the organs showed no macroscopic alterations. In the ethanol-induced ulcer model, HEASo at doses of 250 and 500 mg/kg significantly inhibited the ulcerative lesion area (ULA) by 64.29% and 78.57%, respectively, compared to the control group. Regarding the addition of cumulative concentrations of HEASo (1 - 1000 µg/mL) to the stomach strips, only the 1000 µg/mL concentration statistically significantly reduced the contractile response to carbamylcholine to 56.8 ± 12.0% ($p<0.0\%$). **Conclusion:** These results suggest that *Sideroxylon obtusifolium* has therapeutic potential for the treatment of gastric ulcer as well as open perspectives for further studies to further explore the therapeutic potential of this species.

09.012 **Evaluation of the Impact of N-Tosylindole Exposure on the Progeny of *Caenorhabditis elegans***. Jesus LFS[1], Oliveira LMS[2], Cavalcanti SCH[2], Guimarães AD[2] [1]UFS-São Cristóvão, Dept Pharmacy, Brazil, [2]UFS-São Cristóvão, PPG in Pharmaceutical Sciences, Brazil

Introduction: Arboviruses transmitted by *Aedes aegypti* are a public health challenge. Intensive use of larvicides like temephos causes vector resistance and ecotoxicological impacts. N-tosylindole is a promising alternative in aquatic matrices, but its terrestrial safety requires investigation. The nematode *Caenorhabditis elegans* is a robust model to assess reproductive toxicity and transgenerational effects. **Objectives:** To evaluate the impact of chronic N-tosylindole exposure on the survival and reproduction of the *C. elegans* parental generation (P0), and to investigate transgenerational effects on progeny (F1) development. **Methods:** The *C. elegans* N2 strain was cultured on NGM with *Escherichia coli* OP50 at 20 °C. Synchronized L1 nematodes were chronically exposed to N-tosylindole (100, 200, and 400 µg/mL) for 48h. Tween 80 (1.0%) and M9 buffer were used as negative controls, and temephos (1 µg/mL) as the positive control. P0 survival was monitored daily until adulthood. Reproductive toxicity was assessed using egg-laying and hatching rates. For the transgenerational analysis, adult P0 worms were allowed to lay eggs on a fresh NGM medium for 4 hours, after which they were removed. The unexposed offspring (F1) were monitored every 24 hours to quantify larval development. At the L4 stage, sexual differentiation was assessed and adult egg production was quantified. Data were analyzed in GraphPad Prism, applying Kruskal-Wallis followed by Dunn's post-test for hatching rates, and Two-way ANOVA with Dunnett's post-test for developmental kinetics, considering $p < 0.05$ as statistically significant. **Results:** In the P0 generation, temephos induced 100% mortality within 24h, whereas N-tosylindole-exposed nematodes reached adulthood successfully. P0 embryonic viability (hatching rate) showed no significant difference versus the M9 control ($p > 0.05$). In the unexposed F1 progeny, the 96h follow-up revealed developmental kinetics identical to the control ($p > 0.05$). Almost all individuals reached maturity with normal hermaphroditic differentiation. Furthermore, the F1 generation maintained regular reproduction, comparable to controls ($p > 0.05$). **Conclusion:** Within the evaluated parameters, N-tosylindole showed a remarkable safety profile in *C. elegans*. Unlike temephos, it preserved parental survival and full transgenerational reproductive integrity. The absence of lethality and developmental toxicity in the progeny highlights this compound as an ecologically safe larvicide for non-target terrestrial organisms.

09.013 **Evaluation of the Antioxidant Activity of the Extract of** *Croton blanchetianus* **Baill**. Oliveira MVM, Ferreira CES, Fialho MLS, Martins SO, Nóbrega VM, Andrade IA, Gonçalo YA, Medeiros FD UFC-Cuité, Center for Education and Health, Brazil.

Introduction: *Croton blanchetianus*, popularly known as marmeleiro and belonging to the Euphorbiaceae family, is a Brazilian species native to the Caatinga biome, a biome rich in medicinal plants containing compounds with high bioactive potential, including antioxidant properties. Although oxidation is a physiological process, increased levels of reactive oxygen species can cause cellular damage and contribute to the development of several diseases, such as cardiovascular diseases (Deruy, ED. Antioxidants, v. 9, p. 864, 2020). Therefore, there is considerable scientific interest in antioxidant compounds capable of reducing these effects. Thus, investigating the antioxidant activity of the *C. blanchetianus* extract contributes to expanding knowledge of the Brazilian flora and to identifying new therapeutic options. **Objectives:** To evaluate the antioxidant activity of the *C. blanchetianus* extract. **Methodology:** Leaves of the studied species were collected, dried in a forced- air circulation oven at 40 °C for 48 hours, and ground using a knife mill. The *C. blanchetianus* leaf extract was obtained by hydroalcoholic maceration. The extract was subjected to qualitative phytochemical analysis and antioxidant assays using ABTS and DPPH. The radical solutions were prepared according to standardized methodologies, using ascorbic acid as the antioxidant standard. The samples were analyzed in triplicate, and the radical scavenging activity and Ascorbic Acid Equivalent (AAE) values of the extract were evaluated. **Results:** The phytochemical analysis of the *C. blanchetianus* leaf extract revealed the presence of phenolic compounds, tannins, alkaloids, saponins, and flavonoids, with phenolic compounds being the predominant constituents. In the antioxidant activity assays using the ABTS and DPPH methods, the C. blanchetianus extract presented values within the linear range of both methods, ensuring the reliability of the **Results:** Based on the ascorbic acid standard curve, the antioxidant activity was calculated as 0.012 ± 0.004 µmol of Ascorbic Acid Equivalents per mL (µmol AAE/mL) in the ABTS assay, indicating moderate radical scavenging efficiency. In the DPPH assay, the extract exhibited a radical scavenging activity of 0.005 ± 0.001 µmol AAE/mL, demonstrating its antioxidant activity. The literature highlights that phenolic compounds have high antioxidant potential, indicating that the extract's performance in the assay can be considered satisfactory (Bezerra, FWF. J Supercrit Fluids, v. 165, p. 104, 2020). Studies conducted with Croton blanchetianus corroborate its antioxidant potential, as evidenced by its ability to neutralize free radicals (Oliveira, AM. SAJB, v. 144, p. 238, 2022; Aquino, VVF. Actabra, v. 1, p. 7, 2017). **Conclusion:** The C. blanchetianus extract presented a relevant phytochemical profile and antioxidant activity in the ABTS assay. Therefore, the results highlight the potential of this species for biological and pharmacological applications.

09.014 **Chemical Characterization and** *in vitro* **Antifungal Activity of Galaxy Essential Oil against Candida spp**. Silva VA[1], Tavares IGS[1], Gonçalves GS[2], Bastos SJV[2], Freire KRL[3], Abílio, GMF[4] [1]UFPB, Centro de Ciências da Saúde, Brasil [2]UFPB, Centro de Biotecnologia, Brasil [3]UFPB, Centro de Biotecnologia, Depto Biologia Celular e Molecular, Brasil, [4]UFPB, Centro de Ciências da Saúde - Depto Ciências Biomédicas, Brasil

Introduction: Candidiasis is an opportunistic fungal infection predominantly caused by *Candida albicans*, followed by other species such as *Candida glabrata* and *Candida tropicalis*. Some antifungals, such as fluconazole, have less activity against these isolates. Essential oils obtained from hops (*Humulus lupulus*) emerge as a promising possibility for the treatment of candidiasis, since antimicrobial activity of hop-derived molecules is observed in the scientific literature. **Objectives:** In this scenario, the present study performed the chemical characterization and evaluated the *in vitro* antifungal activity of Galaxy hop essential oil against *C. albicans* ATCC 90028 and AMICO [05332023](tel:05332023), *C. glabrata* ATCC 90030 and *C. tropicalis* AMICO [04792017](tel:04792017). **Methodology:** The chemical characterization of the sample was performed by gas chromatography coupled to mass spectrometry, followed by comparison with international reference libraries. The Linear Retention Index calculation was used as a complementary validation method, aiming for greater reliability in characterization. Following the protocol proposed by the Clinical and Laboratory Standards Institute (2002), the Minimum Inhibitory Concentration (MIC) was determined using the Sabouraud Dextrose Broth microdilution technique in sterile plates, which were then incubated in an oven for 24 hours at 35°C. The MIC is considered to be the lowest concentration capable of visibly inhibiting fungal growth. From the results obtained, the contents of the wells corresponding to the MIC and the two immediately higher concentrations were seeded onto Petri dishes to determine the Minimum Fungicidal Concentration (MFC). These were then incubated at 35°C for 24 hours. The MFC is considered to be the lowest concentration capable of inhibiting the visible growth of the subculture. The MFC/MIC ratio was calculated to assess whether the substance has fungistatic (MFC/MIC ≥ 4) or fungicidal (MFC/MIC < 4) activity. **Results:** Chemical characterization of Galaxy oil reveals a profile rich in monoterpenes, with a predominance of 2-β-pinene (55.77%), in addition to the significant presence of sesquiterpenes, highlighting α-Humulene (13.9%) and Caryophyllene (9.43%). The Galaxy sample demonstrated undefined bioactivity (MIC > 1000 µg/mL) against *C. albicans* AMICO [05332023](tel:05332023), mild bioactivity (MIC between 501 and 1000 µg/mL) against *C. albicans* ATCC 90028, and moderate bioactivity (MIC between 126-500 µg/mL) against *C. glabrata* and *C. tropicalis*. MFC results ranged from 250 to 2000 µg/mL for the tested microorganisms. The sample showed fungicidal activity against *C. albicans*, while it also showed fungistatic activity against *C. glabrata* and *C. tropicalis*. **Conclusion:** It is evident that the sample has promising antifungal activity among the tested strains. Therefore, in order to verify its mechanism of action, further scientific investigations into essential oils obtained from different hop cultivars are suggested.

09.015 **Glycosylated withanolide from *Athenaea velutina* Suppresses the Inflammatory Response in Macrophages via Inhibition of NF-κB, JNK, and iNOS**. Da Silva LR[1], de Araújo KGR[1], Ribeiro MS[1], Rocha LM[1], Mendonça LS[2], Silva JGP[1], Procopio GS[1], Ferreira AGG[1], Pessoa ODL[2], Santos FA[1]. [1]UFC, Dept Physiology and Pharmacology, Natural Products Lab, Brazil. [2]UFC, Science Center, Dept Organic and Inorganic Chemistry, Brazil.

Introduction: Inflammatory response is a complex biological process essential for organism survival, activated in response to harmful stimuli such as pathogens, tissue injury, and chemical agents. Although initially protective, persistent inflammation may trigger a chronic inflammatory state capable of compromising tissue structural and functional integrity. In this context, macrophages play a central role by orchestrating inflammation through mediators that modulate multiple signaling pathways. *Athenaea velutina* (Sendtn.) D'Arcy, traditionally known as "jurubeba-de-morcego," is a Brazilian endemic Solanaceae species exhibiting anticancer, immunomodulatory, and anti-inflammatory activities associated with oxygenated steroidal withanolides in its composition. **Objective:** This study aimed to investigate the anti-inflammatory mechanisms of AV21 (1-O-acetyl-3-O-[α-L-rhamnopyranoside-(1→4)-β-D-glucopyranosyl]-27-dehydropubesnolide), a glycosylated withanolide isolated from *A. velutina*, in LPS-stimulated RAW 264.7 macrophages. **Methodology?** AV21 was isolated from the ethanolic leaf extract of *A. velutina* collected in Guaramiranga, Ceará, Brazil (SisGen no. ACBDA8A). RAW 264.7 macrophages were pretreated with AV21 (50, 100, and 200 μM) for 1 h prior to stimulation with LPS (1 μg/mL) for 24 h. Dexamethasone (10 μM) was used as a positive control, while cells treated only with vehicle (0.2% DMSO) served as the control group. The levels of TNF-α, IL-6, IL-1β, and IL-10 in the culture supernatants were quantified by ELISA. Protein expression of iNOS and COX-2 was evaluated after 24 h, whereas ERK1/2 and NF-κB activation were assessed after 60 min, and JNK activation after 15 min, all by Western blotting. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test. **Results:** AV21 at 50, 100, and 200 μM significantly ($p < 0.05$) reduced the levels of TNF-α by 38%, 44%, and 57%; IL-6 by 17%, 21%, and 26%; and IL-1β by 64%, 79%, and 86%, respectively, compared with the LPS-stimulated group. In contrast, IL-10 levels were markedly increased by 160%, 155%, and 162% at the same concentrations. AV21 at 50, 100, and 200 μM also significantly ($p < 0.05$) inhibited JNK phosphorylation by 33%, 62%, and 66%, and reduced iNOS expression by 35%, 51%, and 53%, respectively, while ERK1/2 phosphorylation remained unchanged. NF-κB p65 activation was also inhibited at all concentrations tested, however, COX-2 expression was not significantly affected. **Conclusion:** AV21 exhibits anti-inflammatory activity in macrophages by reducing pro-inflammatory mediator production, increasing IL-10 levels, and modulating NF-κB, JNK, and iNOS signaling, supporting its potential for the development of novel anti-inflammatory therapies.

09.016 **Extract from the Fruit of** *Sechium edule* **Induces Negative Inotropism, Vasorelaxation and Reduction of Blood Pressure in Rats**. Kistner MC[1], Peres VCA[1], Silva LKC[1], Soares JA[1], Brito DS[1,2], Rodrigues GA[1], Machado GI[1], Almeida JRGS[3], Silva DF[1,2] [1]UFBA, Brazi, [2]IGM-Fiocruz, PGBSMI, Brazil, [3]UNIVASF, Brazil

Introduction: Arterial hypertension is a major public health problem, associated with a high risk of cardiovascular events. The growing interest in complementary therapies has increased the investigation of natural products with antihypertensive potential. Although *Sechium edule* (chayote) is traditionally used to lower blood pressure, scientific evidence supporting its cardiovascular effects remains limited, warranting further investigation. **Objectives:** To investigate the vascular effects of the ethanolic extract of *Sechium edule* (EESE) on mesenteric arteries, the aorta, and atrial tissue from Wistar rats, as well as its hypotensive efficacy in normotensive and hypertensive animal models. **Methods:** Its cardiovascular effects were evaluated in isolated atrial tissue, mesenteric arteries, and aortic rings from Wistar rats to assess cardiac and vascular reactivity. In spontaneously hypertensive rats (SHR), the acute hypotensive effect of EESE (0.01–20 mg/kg) was determined by direct arterial blood pressure (ABP) recording, whereas acute effects were evaluated in SHR and normotensive Wistar rats, following a 7-day oral treatment (0.01 mg/kg) using the tail-cuff plethysmography method (indirect ABP recording). Protocol approved by the CEUA (6772070425). **Results:** The ethanolic extract of EESE presented phenolic compounds and terpenoids. In mesenteric arteries, EESE (0.01–600 µg/mL, cumulatively) did not induce vasorelaxation or alteration of basal tone. In aortic arteries, the extract (0.01–3 µg/mL) induced significantly greater concentration-dependent relaxation in the presence of functional endothelium (Emax: 25.8 ± 4.7) than in rings with dysfunctional endothelium (Emax: 7.8 ± 2.3). In addition, EESE did not affect KCl (80 mM)-induced vascular contractility or basal tone in endothelium-intact aortic rings. In isolated atria, EESE elicited a significant negative inotropic effect ($p < 0.05$), while chronotropic responses remained unchanged. *In vivo*, EESE administration reduced systolic blood pressure (SBP) by -9.69 ± 0.75 mmHg and diastolic blood pressure (DBP) by -6.67 ± 1.29 mmHg compared to the vehicle. Furthermore, oral treatment with EESE prevented the progression of hypertension. **Conclusion:** EESE demonstrated a vasorelaxant response in aortic arteries, as well as an antihypertensive effect in SHR rats, associated with a negative inotropic action, suggesting a possible direct action on cardiac tissue and large vessels.

09.017 **Natural Product-Based Protection Against Diabetic Lung Injury: Effects of *Spondias tuberosa* Arruda Extract**.
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Introduction: Diabetes mellitus (DM) is a chronic metabolic disorder characterized by the destruction or dysfunction of pancreatic β-cells, leading to persistent hyperglycemia and consequent morphofunctional alterations in several organ systems, including the respiratory system. Insulin therapy remains the conventional treatment for type 1 diabetes mellitus (T1DM), however, adverse effects associated with long-term insulin use may negatively affect patients' quality of life. In this context, natural products have emerged as promising complementary therapeutic strategies. **Objective:** This study aimed to evaluate the antidiabetogenic and histopathological effects of the fruit peel extract of *Spondias tuberosa* Arruda (ExSt) on the lungs of streptozotocin-induced diabetic rats. **Methods:** 44 male Wistar rats (CEUA/UFRN 319.056/2022) were allocated into five experimental groups: Control (CT), Diabetic (DM), Extract (EX), Diabetic Treated with Extract (DMEX), and Diabetic Treated with Insulin (DMIN). Diabetes was induced by a single intraperitoneal administration of streptozotocin (50 mg/kg). The fruits of *Spondias tuberosa* Arruda were collected in Olivedos, Paraíba, Brazil, and the hydroethanolic fruit peel extract (ExSt) was administered orally (500 mg/kg/day) for one week following diabetes induction. Clinical parameters (body weight, lung weight, water and food intake), blood glucose levels, histopathological scores, and digital pulmonary morphometry were evaluated. **Results:** The results demonstrated that treatment with ExSt did not reduce blood glucose levels, which remained at approximately 450 mg/dL, whereas insulin therapy significantly reduced glycemia to approximately 180 mg/dL ($p < 0.001$). Nevertheless, histological analysis revealed that treatment with either ExSt or insulin preserved alveolar architecture and significantly reduced inflammation, congestion, and fibrosis when compared with untreated diabetic animals. Morphometric analysis corroborated these findings, showing that ExSt prevented alveolar septal thickening and increased tissue area fraction. **Conclusion:** Therefore, although ExSt did not exhibit hypoglycemic activity in this experimental model, it effectively prevented diabetes- associated pulmonary injury through mechanisms that remain to be elucidated, suggesting its potential as an adjuvant therapeutic strategy for lung protection.

09.018 **Evaluation of the Anti-Inflammatory Activity of** *Cereus jamacaru* **DC.** (**Cactaceae**) **Roots**. Araújo PHL[1], Santos EE[2],Deus GO[1], Costa WK[3], Correia MTS[3], Souza TA[4], Abreu LS[5], Oliveira AM[2], Cibulski SP[2], Alves HS[1,2] [1]UEPB, CCBS, Dept. of Pharmacy, Brazil, [2]UEPB, PPG in Pharmaceutical Sciences (PPGCF), Brazil, [3]UFPE, CB, Dept. of Biochemistry, Lab Natural Products, Brazil, [4]UFPB, Institute of Research in Drugs and Medicines (IPeFarM), Brazil, [5]UFF, Institute of Chemistry, Brazil

Introduction: Historically, the roots of *Cereus jamacaru* DC. have been widely used in folk and traditional medicine due to their diverse therapeutic properties. These effects are attributed to the presence of a rich variety of bioactive compounds in their composition, including flavonoids, tannins, and other secondary metabolites, which contribute to their pharmacological activities and medicinal potential. However, despite the species' phytochemical richness, records regarding the biological activities of some of these compounds, especially saponins, remain limited, highlighting the need for further studies to validate and link this compound to specific therapeutic activities. **Objective:** This study evaluated *in vivo* anti- inflammatory activity of a root fraction from *C. jamacaru*. **Methodology:** The roots were dried, ground, and macerated (ethanol:water 7:3) to obtain the crude hydroethanolic extract. The methanol-water fraction (MWF) was obtained by vacuum liquid chromatography. The anti-inflammatory activity of the MWF from *C. jamacaru* was evaluated in male Swiss mice using experimental models of carrageenan-induced paw edema, carrageenan-induced peritonitis and air sac inflammation. The animals were divided into groups treated with the extract at varying concentrations (50, 100, and 200 mg/kg), a negative control using saline, and a positive control with dexamethasone or indomethacin. The parameters analyzed included edema formation, leukocyte migration, and the production of inflammatory mediators such as TNF-α and IL-1β. **Results:** Anti-inflammatory assays demonstrated that the *C. jamacaru* exhibited significant activity in all evaluated models. In carrageenan-induced paw edema, a reduction in edema of 39%, 45%, and 49.9% was observed at doses of 50, 100, and 200 mg/kg, respectively. In the carrageenan-induced peritonitis model, there was a dose-dependent decrease in leukocyte recruitment (32.4%, 53.3%, and 69.5%) and neutrophil recruitment (44.4%, 47.5%, and 62%), as well as a reduction in the levels of the pro-inflammatory cytokines IL-1β and TNF-α. In the air pocket model, reduced leukocyte migration by 48.2%, 53%, and 67.9% at the respective doses. **Conclusion:** The anti-inflammatory activity observed in the methanol-water fraction of *C. jamacaru* roots suggests that the saponins present in this species play a significant role in modulating the inflammatory response, supporting its traditional use in the treatment of inflammatory processes.

09.019 *Arthrospira platensis* **Prevents Uterine Hypercontractility Via Inhibition of Prostanoid and Nitric Oxide Pathways and Calcium Sensitization in a Wistar Female Rat Model of Primary Dysmenorrhea**. Sousa-Filho JEC[1], Silva JMA[1,2], Melo MB[1], Barbosa, YV[1,2], Santos TJ[1], Diniz AFA[1,2], Arruda RRA[1,2], Claudino BFO[1,2], Soares MFS2, Barros BC[1,2], Silva BA[1,2,3] [1]UFPB, Lab Functional Pharmacology Prof. George Thomas, Institute of Research in Drugs and Medicines, Brazil; [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil; [3]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil

Primary dysmenorrhea (PD) is characterized by menstrual pain with no pelvic disease, with its pathogenesis involving increased production of prostaglandins and free radicals that activate RhoA-kinase (ROCK), causing uterine hypercontractility. The pharmacotherapy for PD consists of non- steroidal anti-inflammatory drugs, contraceptives and antispasmodics, however, inefficacy and side effects encourage research into new therapies. In this context, emerges *Arthrospira platensis* (AP), also known as Spirulina platensis, a cyanobacterium rich in biocompounds with anti-inflammatory and antioxidant activities. Previous studies demonstrated the partial involvement of nitric oxide (NO) and prostanoids in the mechanism of AP in an PD experimental model. Therefore, this study investigated the interaction between NO and prostanoid pathways and the involvement of ROCK signaling in AP mechanism. Virgin Wistar female rats were randomly allocated into 3 groups: control (CG); primary dysmenorrhea (PD); and PD supplemented with AP (100 mg/kg) (PD + AP100, i.g.). AP powder was obtained from Infinity Pharma® (Hong Kong, China) and certified by Roval Compounding Pharmacy (Paraíba, Brazil; batch n. 405894). AP was administered daily for 8 weeks, while PD induction was performed by diethylstilbestrol injections (s.c.) during the last 10 days. Uterine reactivity was evaluated in isolated organs in the presence or absence of L-NAME (NO synthase inhibitor) + indomethacin (cyclooxygenase inhibitor) or Y-27632 (ROCK inhibitor). There was an increase in KCl Emax in the PD (250±10.7%) compared to the CG (100%), whereas AP fully prevented this increase in the PD + AP100 (95±12.4%), with no change in KCl potency among groups. Knowing the involvement of the prostanoid and NO pathways in the preventive effect of AP, the crosstalk between these pathways was investigated. The Emax of the PD + L-NAME + indomethacin (97.9 ± 2.10%) differed from the PD, without differing from CG. Meanwhile, the Emax of the PD + AP100 + L-NAME + indomethacin (91.4 ± 8.6%) also resembled the CG. Both groups showed no change in Emax when compared to the others, demonstrating the simultaneous participation of both pathways in the mechanism of AP. Continuing the investigation, the ROCK pathway was evaluated. The Emax of PD + Y-27632 (109 ± 4.84%) matched the CG, similarly to the Emax of PD + AP100 + Y-27632 (100 ± 8.65%), both also presenting pEC50 values similar to the other groups, showcasing the participation of ROCK in the preventive effect of AP in this experimental model of PD. In conclusion, AP prevents PD-induced uterine hypercontractility through coordinated modulation of prostanoid, NO, and RhoA/ROCK signaling pathways, thereby restoring uterine contractile homeostasis. These findings support the therapeutic potential of AP as a multi-target strategy for PD. Ethical approval: CEUA/UFPB (N. 1659111022). **Financial support:** CAPES, CNPq, FAPESQ.

09.020 **Evaluation of the Antifungal Activity of *Ximenia americana* Gel Against Dermatophytes**. Andrade IA, Ferreira CES, Fialho MLS, Gonçalo YA, Oliveira MVM, Martins SO, Nobrega VM, Pereira FO, Medeiros FD. UFCG-Cuité Campus, Center for Education and Health, Brazil.

Introduction: Climate change and extreme events, such as floods, have been associated with the increasing incidence of fungal infections and microbial resistance. In this context, the search for new natural therapeutic alternatives has intensified. The Caatinga stands out for its broad biodiversity and pharmacological potential of plant species, including Ximenia americana, which is widely used in folk medicine. Previous studies have demonstrated antioxidants (Almeida, MLB. Food Chem., v. 192, p. 1078-1082, 2016.), antibacterial (Carneiro, RS. SAJB., v. 151, p. 18-32, 2022.), and anti-inflammatory (Shettar, AK. SAJB., v. 111, p. 202-211, 2017.) properties of the species; however, investigations regarding its antifungal potential, especially in pharmaceutical formulations, remain limited. **Objective:** To evaluate the antifungal activity of a gel containing bark extract of X. americana against dermatophyte strains. **Methodology:** The gel formulation containing X. americana bark extract was evaluated against *Microsporum canis* (ATCC and LM) and *Trichophyton rubrum* (ATCC) strains using the broth microdilution technique to determine the Minimum Inhibitory Concentration (MIC) and Minimum Fungicidal Concentration (MFC). All assays were performed in duplicate to ensure reproducibility of the Results: The gel showed antifungal activity against all evaluated strains, with an MIC of 512 µg/mL, demonstrating a uniform fungistatic effect. *M. canis* (ATCC and LM) strains presented an MFC of 1024 µg/mL, while *T. rubrum* showed an MFC of 512 µg/mL, equivalent to the MIC, suggesting enhanced fungicidal activity against this strain. These findings demonstrate the potential of the gel as a therapeutic alternative for dermatophytoses, especially considering the increasing resistance to conventional antifungal agents. Furthermore, the results reinforce the relevance of prospecting medicinal species from the Caatinga for the development of new sustainable pharmaceutical products. Most previous studies focus on the phytochemical composition and general biological activities of *X. americana*, making this study relevant by demonstrating, for the first time, the antifungal potential of the gel formulation against dermatophytes. **Conclusion:** Therefore, the gel demonstrated promising antifungal potential against the tested dermatophytes, reinforcing the importance of the Caatinga as a source of bioactive compounds with potential pharmacological application in the development of new antifungal therapeutic alternatives. **Financial support:** CNPq, Ministry of Health.

09.021 **Pharmacological Evaluation of El Dorado Hop Oil: Chemical Characterization and Antifungal Activity Against Candida Species**. Tavares IGS[1], Silva VA[1], Gonçalves GS[2], Bastos SJV[2], Freire KRL[3], Abílio[1]UFPB, Health Sciences Center, Brazil [2]UFPB, Biotechnology Center, Brazil [3]UFPB, Biotechnology Center, Dept Cell and Molecular Biology, Brazil [4]UFPB, Health Sciences Center, Dept Biomedical Sciences, Brazil

Introduction: *Candida albicans* is an opportunistic fungus, primarily responsible for oral mucosal infections triggered by an imbalance in the microbiota, in addition to multiple predisposing factors associated with immune system weakening. Treatment with known antifungal drugs is effective; however, resistance mechanisms have grown exponentially among non-albicans species, including in intensive care units. **Objectives:** In this context, given the need for effective therapeutic alternatives, this study aimed to perform the chemical characterization and investigate the antifungal potential of the essential oil from the El Dorado cultivar of *Humulus lupulus*, through the determination of the Minimum Inhibitory Concentration (MIC) and Minimum Fungicidal Concentration (MFC) against *C. albicans* and non-albicans strains. **Methods:** For the present study, the phytochemical analysis of hop essential oil was obtained from the extraction of its American commercial variety, El Dorado, using gas chromatography coupled with mass spectrometry, followed by data comparison with international reference libraries. In addition, the MIC and MFC of the essential oil were determined for *C. albicans* ATCC 90028 and AMICO 05332023 strains, as well as *C. glabrata* ATCC 90030 and *C. tropicalis* AMICO 04792017. **Results:** Subsequently, the results of the phytochemical analysis obtained through the employed methodologies demonstrated that the major composition of the sample consisted of approximately 55% beta-myrcene and, likewise, 9.23% alpha-humulene, highlighting the bioactive profile of the oil against the tested strains. On the other hand, MIC analysis revealed 500 µg/mL for the tested sample against all strains, except for *C. albicans* AMICO 05332023, which presented an MIC of 1000 µg/mL. Therefore, based on the obtained data, moderate bioactivity (MIC between 126–500 µg/mL) was evidenced for most of the strains used. Furthermore, MFC observation indicated 2000 µg/mL for all strains, except for *C. albicans* ATCC 90028, which revealed an MFC of 1000 µg/mL. Thus, the tested sample exhibited fungicidal activity (MFC/MIC ≤ 4), since the MFC/MIC ratio was equal to or lower than 4 in all species. **Conclusion:** Therefore, the chemical characterization of El Dorado essential oil confirms the abundance of these monoterpenes and sesquiterpenes, as well as their crucial role in the bioactivity already documented in other microorganisms, with beta-myrcene being a potent agent with therapeutic properties. The determination of MIC and MFC confirmed the fungicidal action of the essential oil based on the MFC/MIC ratio ≤ 4. Further experiments investigating its mechanism of action on the microorganism, as well as *in vivo* studies, are of utmost importance.
Financial support: none

09.022 **Development of an Antioxidant Serum Containing Leaf Extract of *Eugenia uniflora* L.** Almeida, JBC, Silva, AP, Souza, SO, Guilherme, ACS, Sousa, JCR, Lima, CM UFS-Lagarto, Brasil.

Introduction: Aging is a natural and irreversible process associated with the accumulation of free radicals, unstable molecules that cause damage to biomolecules, favoring the onset of diseases, wrinkles, and skin lesions. In this context, the demand for anti-aging cosmetics and medicines has been increasing, especially among middle-aged and elderly individuals, aiming to prevent or reduce signs of aging, such as wrinkles, expression lines, and other skin alterations, thereby promoting better appearance and quality of life. **Objective:** To develop an antioxidant serum containing leaf extract of the Surinam cherry tree (*Eugenia uniflora* L.). **Methodology:** The hydroethanolic extract of *Eugenia uniflora* L. leaves was obtained by ultrasound and maceration methods. The extract was subjected to phytochemical screening and quantification of total flavonoids and phenolic compounds. Serum formulations containing 1, 5, 10, and 20% of the crude hydroethanolic extract were prepared and submitted to evaluation of antioxidant activity by the DPPH method, as were the extracts themselves. **Results:** The extraction yield by dynamic maceration was 9.88%, and 10.80% for ultrasound. Application of Student's t-test showed a significant difference between the yields, with $p < 0.05$. Phytochemical screening indicated the presence of flavonols, steroids, triterpenes, polyphenols, and saponins in the extracts. Metabolite quantification showed phenolic compound content of 18.7 ± 9.16 mg g-1 and flavonoid content of 35.2 ± 0.8 mg g-1 in the extract obtained by dynamic maceration, whereas the extract obtained by ultrasound presented 43.9 ± 2.5 mg g-1 of phenolic compounds and 87.6 ± 7.9 mg g-1 of flavonoids. Analysis of antioxidant activity by DPPH of the extracts demonstrated 94.34% inhibition for the extract obtained by ultrasound and 75.86% inhibition for the dynamic maceration extract. The ultrasound extract was chosen for serum preparation because it showed greater effectiveness. The antioxidant activity of the serums containing 1, 5, 10, and 20% of the extract was 19.13 ± 0.8%; 78.72 ± 1.12%; 95.95 ± 0.10%; and 96.10 ± 0.10% inhibition of DPPH, respectively. After statistical analysis of the results of the formulations, the formulation containing 10% extract was standardized as the reference, considering the absence of a significant difference compared with the formulation containing 20%. **Conclusion:** The serum containing *Eugenia uniflora* L. exhibits antioxidant activity and may represent a new alternative in the market for prevention of skin aging signs. **Acknowledgments:** Federal University of Sergipe (UFS) and the funding agency (COPES). Keywords: *Eugenia uniflora* L.; anti-aging; antioxidant activity; cosmetics.

09.023 *In vivo* and *in silico* Toxicological Evaluation of Brazilian Brown Propolis from *Mimosa tenuiflora*. Alves BFL[1], Felício IM[2], Souza MLB[1], Silva TMS[3], Silva JLV[4], Picot L[5], Cavalcante FA[2],[61]UFPB, PIBIC, Brazil; [2]UFPB, CCS, PPgPNSB, Brazil; [3]UFPE, DQ, Brazil; [4]FMO, Lab. of Functional Practice, Brazil; [5]La Rochelle Université, LIENSs, France; [6]UFPB, CCS, DCB, Brazil

Introduction: Toxicological studies represent an essential step in preclinical research. Advances in animal ethics guidelines have encouraged the use of complementary approaches such as computational pharmacology for preliminary safety assessment. Toxicity testing of natural products requires particular attention due to their complex chemical matrices, which may exhibit both pharmacological and toxic effects. In this context, brown propolis collected in Ipaporanga, Ceará, Northeastern Brazil is characterized by the presence of terpenes, specially triterpenes. Therefore, this study aimed to evaluate the toxicity of brown propolis from *Mimosa tenuiflora* produced by *Apis mellifera* bees in Ipaporanga (CE), using *in vivo* and *in silico* approaches. **Methods:** The *in vivo* toxicity study followed OECD Guideline 407. Wistar rats (n=30) received daily oral doses of 250 (BP250G) or 500 mg/kg (BP500G) of brown propolis or vehicle only (CG) for 28 days. Animals were monitored during the first 4 h after the initial administration and observed daily throughout the 28-day treatment period. Following treatment cessation, animals were further monitored for an additional 14 days to detect persistent or delayed toxic effects. Body weight and food intake were assessed throughout the 42-day experimental period. Following euthanasia, organs were weighed, and blood samples were collected for hematological and biochemical analyses. Data were analysed using GraphPad Prism®. Experimental procedures were approved by the Ethics Committee on Animal Use/UFPB (no. 8719020621). The *in silico* toxicological assessment was performed using the admetSAR 3.0 software to predict toxicity parameters for lupeol (L), lupeol acetate (LA) and β-amyrin (BA), the major terpenes of the brown propolis studied. **Results:** No adverse neurotoxic effects, behavioral changes, mortality, or alterations in body weight and food intake were observed. Hematological and biochemical parameters remained within normal ranges, except for increased serum alanine aminotransferase (ALT) levels in BP250G males (CG=36.0±2.7 U/L; BP250G=55.4±4.0 U/L; BP500G=33.6±1.5 U/L) and females (CG=36.0±1.6 U/L; BP250G=60.2±4.8 U/L; BP500G=32.8±2.0 U/L). However, since this alteration was not dose-dependent and was not accompanied by additional findings suggestive of hepatic toxicity, its toxicological relevance remains uncertain. These findings were consistent with *in silico* predictions, which indicated a favorable toxicological profile for lupeol, lupeol acetate and β-amyrin, with low probabilities of carcinogenicity (L=35.6%, LA=39.3%, BA=34.69%) and acute oral toxicity (L=17.29%, LA=14.09%, BA=11.7%), along with moderate probabilities of repeated-dose toxicity (L=64.4%, LA=61.2%, BA=58.6%). **Conclusion:** Taken together, the *in vivo* and *in silico* findings suggest a favorable safety profile of brown propolis from *Mimosa tenuiflora* and support its further pharmacological investigation.

09.024 **Analysis of the Toxicity of a Series of Acylhydrazone Derivatives of Isatin in the *Caenorhabditis elegans* Model**. Sousa LVBS[1], Almeida Filho GP[1], Lima TCBS[1], Carneiro CA[1], Campos CENS[1], Marreiro VS[1,3], Galdino FS[1,3], Costa MESM[1], Diniz MFFM[1,3], Janebro DI[1,3], Lima-Junior CG[3], Sousa FB[3] [1]UFPB, Lab Ensaios Toxicológicos, Brazil [3]UFPB, PPG Produtos Naturais, Brazil [3]UFPB, PPG Produtos Naturais, Brazil [3]UFPB, Lab Síntese Orgânica Medicinal da Paraíba, Brazil

Organic synthesis has become fundamental to the development of new drugs, enabling the creation of complex molecules with diverse therapeutic properties. In medicinal chemistry, heterocyclic compounds are particularly notable, as they are amenable to chemical modifications allowing for the Introduction: of functional groups for various purposes. Among these, isatin derivatives stand out as promising drug candidates, with various pharmacological activities reported in the literature. Preliminary toxicity studies are essential for the development of drug candidates, ensuring safety for human testing. In this context, the nematode *Caenorhabditis elegans* stands out as an *in vivo* animal model in toxicology due to its ease of cultivation, short life cycle, and high genetic homology with humans, which allows for the early identification of adverse effects. This study aimed to evaluate the toxicological profile of a series of isatin acylhydrazone derivatives—specifically compounds NAH1 and NAH3—using the *Caenorhabditis elegans* model, investigating potential changes in biological markers and comparing parameters such as embryotoxicity, motility, and pharyngeal activity. To this end, wild-type N2 strain *Caenorhabditis elegans* worms were maintained on solid medium supplemented with *E. coli* OP50 as a food source. Following synchronization of the individuals via alkaline lysis, the worms were exposed to the compounds at concentrations of 200, 1000, and 5000 µg/mL. Toxicological assessment included an egg-hatching assay after 24 hours of treatment, motility quantification via body bends, and analysis of pharyngeal pumping after 48 hours. Data were analyzed using one-way ANOVA followed by Tukey's post-hoc test, with significance set at $p < 0.05$. The results demonstrated that none of the tested concentrations of NAH1 and NAH3 induced significant toxicity regarding egg hatching, indicating an absence of embryotoxicity and the preservation of early larval development. In contrast, the motility assay revealed a significant increase in the frequency of body bends at a concentration of 1000 µg/mL for NAH1 and at concentrations of 200 and 1000 µg/mL for NAH3, suggesting possible neuromuscular dysfunction. Regarding pharyngeal pumping, NAH1 induced a significant increase at all concentrations—indicating probable metabolic modulation and the activation of physiological stress responses—whereas NAH3 did not alter this parameter, suggesting the maintenance of feeding homeostasis. It is concluded that the derivatives NAH1 and NAH3 exhibit a safe toxicological profile regarding embryonic development but display selective toxicity affecting physiological and behavioral parameters, with evidence of neurotoxicity and distinct metabolic responses. Therefore, the integrated use of behavioral assays in *Caenorhabditis elegans* proved essential for understanding the complexity of these compounds' interactions with the organism's neuromuscular system and physiology. Acknowledgments to UFPB, LASOM-PB, and LABETOX.

09.025 **Evaluation of the Antifungal Activity of the Extract of** *Combretum leprosum* **Mart. Against Dermatophytes**.
Nobrega VM, Andrade IA, Ferreira CES, Fialho MLS, Martins SO, Oliveira MVM, Almeida YA, Pereira FO, Medeiros FD
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Introduction: Climate change has been directly impacting the environment and human health, increasing the prevalence of dermatological diseases, including fungal infections, as well as raising the risk of fungal resistance development, limiting the effectiveness of conventional antifungal therapies. In this context, the search for therapeutic treatments derived from natural products has gained increasing prominence. In northeastern Brazil, a region predominantly covered by the Caatinga biome, the use of medicinal plants is a common practice due to the great biodiversity and pharmacological potential. An example is the species *Combretum leprosum*, popularly known as "mofumbo", widely used in folk medicine because of its broad range of pharmacological activities, including anti-inflammatory, antiproliferative, antioxidant, and antibacterial activities (Horinouchi, J. ETHNOPHARMACOL., v. 145, p. 311, 2013). **Objective:** To evaluate the antifungal activity of the bark extract of C. leprosum against different dermatophyte strains. **Methodology:** The bark extract was dried in an oven at 45 °C and pulverized using a knife mill. The antifungal activity was evaluated against the strains *Microsporum canis* (ATCC and LM), *Nannizia gypsea* (ATCC and LM), and *Trichophyton rubrum* (ATCC) using the broth microdilution technique to determine the Minimum Inhibitory Concentration (MIC) and the Minimum Fungicidal Concentration (MFC). Terbinafine was used as the reference antifungal drug (positive control), while dimethyl sulfoxide (DMSO) was used as the negative control. The assays were performed in duplicate to ensure greater reliability and precision of the **Results:** The bark extract of *C. leprosum* showed promising antifungal activity, with an MIC of 512 µg/mL, demonstrating its uniform inhibitory activity against these fungi. The strains of *N. gypsea* (ATCC and LM) showed an MFC of 1024 µg/mL, while the dermatophytes *M. canis* (ATCC and LM) and *T. rubrum* (ATCC) showed an MFC of 512 µg/mL, which was proportional to the minimum inhibitory concentration, suggesting enhanced fungicidal activity against these strains. However, studies regarding this plant remain scarce in the literature, increasing the need to further investigate the antifungal activity of this species against dermatophytes. **Conclusion:** Therefore, the bark extract of *C. leprosum* demonstrated good antifungal potential against the evaluated dermatophytes, maintaining balanced minimum concentrations. This further reinforces the importance of the Caatinga as a rich source of new therapeutic alternatives due to its broad biodiversity and the presence of plant species with pharmacological potential.

09.026 **Dermal Safety of Curcumin Hydrogel in Mice: Evaluation of Toxicity Following OECD 402 Guidelines**. Morais, MF[1], Falcão, ES[1], Oliveira, MX[2], Feitosa, JPA[2], Assreuy, AMS[1]. [1]UECE, Lab. of Physiopharmacology of Inflammation, PPG Physiological Science Brazil, [2]UFC, Lab. of Polymers Lab, PPG in Chemistry, Brazil.

Introduction: Curcumin is a polyphenol possessing anti-inflammatory, antioxidant, and antimicrobial properties, being widely investigated for its therapeutic potential in topical formulations. The growing preference for herbal medicines is associated with their efficacy, accessibility, availability, and lower occurrence of adverse effects when compared to conventional drugs. In this context, the evaluation of dermal toxicity is essential to ensure the safety of substances intended for topical use, allowing the identification of possible irritative or toxic effects on the skin. **Objectives:** This study aimed to evaluate the dermal toxicity of a curcumin hydrogel at a concentration of 440 µg mL^{-1}. (CH440) in mice following OECD 402 guidelines. **Methods:** Female mice (n=3/group) had their dorsal region shaved 24 h before the topical application of CH440 that was maintained under dressing for 24 h. After removal, the open field test was used to assess spontaneous locomotor activity and anxiety-like behavior, placing the animal in a closed arena and recording parameters such as locomotor activity and self-grooming. The Draize scale (0–4) assesses tissue irritation (erythema and edema), where 0 = no present and 4 = severe. The Grimace scale (0–2) evaluates pain-related facial expressions, where 0 = no present, 1 = moderate, and 2 = obvious. Both were used to quantify animal suffering over 14 days. At the end, hematological (total and differential leukocytes) and serum biochemical analyses were performed to evaluate hepatic (AST/ALT) and renal (creatinine) functions. Data were expressed as mean ± standard error of the mean (SEM) and analyzed by ANOVA, followed by Student's t-test. p <0.05 was considered for statistical significance. **Results:** Topical application of CH440 did not trigger signs of hyperemia, edema (0±0 vs 0±0 saline), pain, or suffering in the animals (0±0 vs 0±0 saline). No alterations were observed in the levels of serum AST (239.3±105.1 *vs* saline: 158±45.64 U/L), ALT (59.67±20.74 *vs*. saline: 42.33±9.8 U/L), and creatinine (0.25±0.014 *vs* saline 0.23±0.03 mg/dL), as well as in total leukocyte count (1025±375 *vs*. saline: 1000±200 cells/mm^3)and differential leukocyte count (20±14.14 *vs*. saline: 20±16%). Furthermore, no changes were observed in the animal's locomotor activity (2±0 *vs* saline: 1.6±0.6) and self-grooming behavior (70.7±10.35 *vs* 68.7±26.08) evaluated in the open field test. **Conclusion:** CH440 was shown to be safe for topical use at the concentration studied, not causing skin irritation, animal suffering, behavioral alterations, changes in defense cells, or alterations in renal and hepatic function markers. **Acknowledgments:** The authors are grateful to FUNCAP for the fellowship support.

09.027 **Nanoencapsulation of *Lippia microphylla* Essential Oil in Nanostructured Lipid Carriers (NLCs): Antifungal Activity and Cytotoxicity**. Moura DEG[1], Piancó MESV[2], Barreto JO[3], Silva LA[2], Lima LO[2], Nogueira PL[3], Alexandre HMS[2], Silva AL[2], Gonçalves JCR[2] [1]UFPB, Health Sciences Center, Dept Pharmaceutical Sciences, Undergraduate Program in Pharmacy, Brazil. [2]UFPB, Health Sciences Center, PPG in Bioactive Natural and Synthetic Products (PPgPNSB), Brazil. [3]UFPB, Health Sciences Center, PPG in Dentistry (PPGO), Brazil.

Introduction: The increasing resistance to conventional antifungal agents has compromised therapeutic efficacy, driving the search for new alternatives. In this context, *Lippia microphylla* Cham. essential oil (Lm- EO) exhibits antifungal potential; however, its application may be limited by characteristics such as low solubility and cytotoxicity. Nanoencapsulation in nanostructured lipid carriers (NLCs) represents a promising strategy to improve the properties of bioactive compounds and enhance their therapeutic activity. **Objective:** To evaluate the antifungal activity of Lm-EO, in its free and nanoencapsulated forms, against *Candida albicans*, as well as to investigate its possible mechanisms of action and cytotoxic effects on human cells. **Methods:** Free Lm-EO was evaluated for minimum inhibitory concentration (MIC), minimum fungicidal concentration (MFC), antibiofilm activity, and possible mechanisms of action using sorbitol and exogenous ergosterol assays. Biofilm activity was also assessed by confocal microscopy using propidium iodide staining. Cytotoxicity of free and nanoencapsulated Lm-EO was evaluated in human keratinocytes (HaCaT) using the MTT assay. NLCs containing Lm-EO were developed and characterized according to particle size, polydispersity index (PdI), and zeta potential, and subsequently evaluated for antifungal activity and cytotoxicity. **Results:** Free Lm-EO showed a MIC of 256 µg/mL and an MFC of 1024 µg/mL. MIC values remained unchanged in the presence of sorbitol, whereas a fourfold increase was observed in the presence of exogenous ergosterol, suggesting the involvement of the fungal cell membrane in the oil's mechanism of action. Lm-EO reduced *C. albicans* biofilm adherence by 66–86% at concentrations ranging from 256 to 2560 µg/mL, as confirmed by confocal microscopy with propidium iodide staining. NLCs containing Lm-EO were successfully developed using different lipid concentrations and surface functionalizations. The formulation functionalized with 5% Pluronic® exhibited a particle size of 122 nm and a PdI of 0.30. The NLC formulations showed antifungal activity against *C. albicans*, with MIC values ranging from 64 to 128 µg/mL, compared with 256 µg/mL for free Lm-EO. However, significant cytotoxicity persisted after nanoencapsulation, with residual HaCaT cell viability ranging from 3% to 7%, compared with less than 2% for free Lm-EO. **Conclusion:** Lm-EO exhibited antifungal and fungicidal activity against *C. albicans*, with results suggesting the involvement of the fungal cell membrane and ergosterol in its mechanism of action. Nanoencapsulation enhanced antifungal activity, with MIC values ranging from 64 to 128 µg/mL compared with 256 µg/mL for free Lm-EO. Despite a modest improvement in residual cell viability compared with the free oil, relevant cytotoxicity persisted after nanoencapsulation, limiting the therapeutic applicability of the formulations. Further studies are needed to optimize the nanoformulation and improve its safety profile.

09.028 **Evaluation of the Interaction Between Varespladib and Bothropstoxin-II Isolated from *Bothrops jararacussu* Venom on the Mouse Neuromuscular Junction**. Silva HF[1], Pereira ES[1], Ortolani PL[2], Fortes CL[2], Cavalcante WLG[1]
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Introduction: Snakebite envenomation is a major global public health issue, with the World Health Organization aiming for a 50% reduction in related deaths and disabilities by 2030. The current antivenom therapy has limitations, such as restricted effectiveness against local effects and high costs. Varespladib, a synthetic inhibitor of human phospholipases A2 (PLA2s), has emerged as potential complementary therapy, yet its interaction with Bothrops toxins remains poorly understood. **Objectives:** This study evaluated the effects of Varespladib on the neuromuscular blockade induced by Bothropstoxin-II (BthTX-II), a PLA2 isolated from *Bothrops jararacussu* venom. **Methods:** Phrenic nerve-diaphragm preparations from male Swiss mices were mounted in 12 mL organ baths containing Ringer Solution (35 °C), constantly aerated with carbogen (95% O_2 + 5% CO_2). The phrenic nerve was stimulated (0,5 ms, 0,2 Hz, 3 V) and contractions were recorded for 180 min. BthTX-II (13,976 µg/mL) was tested alone or pre-incubated (15 min) with varespladib at 1:1 and 1:5 mass ratios. At the end of the experiments, muscles were processed for histological study. Statistical analysis was performed using Student's t-test ($P < 0.05$, n=2-7). **Results:** BthTX-II induced a progressive time-dependent blockade promoting 88% inhibitions of twitches at 180 min ($P<0.05$ vs control). Varespladib, at both 1:1 and 1:5 ratios, partially attenuated the toxin-induced blockade by delaying the onset of paralysis. ($P<0.05$ vs control) Varespladib alone did not affect muscle contractions. **Conclusion:** These findings contribute to the potential of varespladib as an adjuvant to antivenom therapy in bothropics accidents. Furthermore, studying its interaction with BthTX-II contributes to understanding the toxin's mechanisms of action and points toward safer pharmacological alternatives for snakebite treatment. **Financial support:** This work was supported by UFMG, FUNED, FAPEMIG (APQ-00722-22), CNPq(404129/2025-0), and PRPQ. Approval by the Animal Research Ethical Committee was obtained. (2025/21).

09.029 **Evaluation of the Embryotoxic Effect of** *Bothrops lutzi* (**Miranda-Ribeiro, 1915**) **Venom**. Senna ESL, Novaes R, Braga JRM UFRB, Lab Reptiles and Amphibians, Cruz das Almas, Bahia, Brazil.

Introduction: Teratogenic agents are substances capable of inducing morphological and functional alterations during embryonic development. Experimental models using *Gallus gallus domesticus* embryos are widely employed for embryotoxicity assessment due to their morphophysiological similarities to mammalian embryos. **Objectives:** This study aimed to evaluate the possible embryotoxic effects of *Bothrops lutzi* snake venom (BltzV) using the in ovo chicken embryo model. **Methods:** Sixty fertile White Leghorn chicken eggs were distributed into experimental groups (n=10). Eggs were incubated for nine days (37.5 °C ± 0.5 °C; 70% humidity). On embryonic day 4 (ED4), the chorioallantoic membrane was exposed and 200 µL of BltzV (5 µg/mL) in serial dilutions was applied. The control group received 0.9% saline solution. Morphological alterations, embryonic heart rate, and biometric parameters were evaluated. For apoptosis analysis, embryos exposed to the highest venom concentrations were stained with Nile Blue Sulfate on ED6 and documented under a stereomicroscope. Data were analyzed using Student's t-test ($p<0.05$). **Results:** Embryos exposed to groups E1–E4 presented hyperemia and hemorrhagic spots. Significant alterations in heart rate and cephalocaudal length were observed in group E1. Significant differences in cardiac and hepatic masses were detected in groups E1–E3 compared to the control group. Severe morphological alterations were observed at concentration E5. Nile Blue staining revealed regions compatible with apoptosis, especially at higher venom concentrations, associated with lipid accumulation in embryonic tissues. **Conclusion:** *Bothrops lutzi* venom induced concentration-dependent embryotoxic effects, promoting morphological, hemodynamic, and tissue alterations in *Gallus gallus domesticus* embryos. The findings suggest cytotoxic and pro-apoptotic activity of the venom during embryonic development, reinforcing the importance of toxicological investigations involving snake venoms and their effects on cellular mechanisms associated with organogenesis.

09.030 **Biological Activity and Selectivity Profile of Balsam of Peru** (*Myroxylon balsamum*) **Oleoresin Against Clinically Relevant Microorganisms**. Lacerda AF[1,2], Oliveira-Filho JMD[1], Alves ARS[1,3], Souza PHO[2], Cunha DBL[2], Alves RV[2], Gadelha TS[2], Faheina-Martins GV[2], Vasconcelos U[23], Travassos RA[1,2,3]. [1]UFPB, Lab FarmacoBiotecnologia (FarmaBio), Brazil; [2]UFPB, Graduate Program in Cellular and Molecular Biology (PPgBCM), Brazil; [3]UFPB, Centro de Biotecnologia (CBiotec), Brazil.

Introduction: Antimicrobial resistance is a major global health threat, highlighting the need for new antimicrobial and antibiofilm agents. Natural products, including plant-derived oleoresins, are promising sources of bioactive compounds. **Objective:** This study evaluated the *in vitro* antimicrobial, antibiofilm, mechanistic, cytotoxic, and selectivity profiles of Balsam of Peru oleoresin. **Methodology:** Antimicrobial activity against *E. coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Staphylococcus aureus* ATCC 13150, and *Candida albicans* ATCC 76645 was assessed by broth microdilution to determine the Minimum Inhibitory Concentration (MIC). Biofilm inhibition was evaluated by crystal violet staining. A sorbitol protection assay was used to investigate possible interference with cell wall integrity. Cytotoxicity was assessed by the MTT assay in HEK-293 cells, and the selectivity index (SI) was calculated as IC_{50}/MIC. Experiments were performed in triplicate in at least three independent assays. Data were analyzed by one-way ANOVA followed by Bonferroni's post hoc test ($p < 0.05$). **Results:** The oleoresin showed selective antimicrobial activity, with the lowest MIC against *E. coli* (2 µg/mL), followed by *C. albicans* (8 µg/mL), *P. aeruginosa* (16 µg/mL), and *S. aureus* (128 µg/mL). Biofilm formation was inhibited in a concentration-dependent manner, with greater activity against Gram-negative strains and *C. albicans*. The sorbitol assay suggested that antimicrobial activity may involve impairment of cell wall integrity. The oleoresin showed concentration-dependent cytotoxicity in HEK-293 cells, with an IC_{50} of 557.3 µg/mL. SI values indicated low selectivity against *S. aureus* (4.35), high selectivity against *P. aeruginosa* (34.83) and *C. albicans* (69.66), and very high selectivity against *E. coli* (278.65). DMSO showed no intrinsic antimicrobial activity under the tested conditions. **Conclusion:** Balsam of Peru oleoresin exhibited relevant antimicrobial and antibiofilm activity, especially against *E. coli*, *C. albicans*, and *P. aeruginosa*. Its activity may be partly associated with cell wall damage, and the SI values suggest a favorable safety profile for most tested microorganisms. These findings support its potential as a natural source of antimicrobial and antibiofilm compounds, although further studies are needed to identify active constituents, confirm mechanisms of action, and assess therapeutic applicability in more complex models.

09.031 **Evaluation of the Genotoxicity and Antigenotoxicity of Natural and Aminated Red Angico Gum** (*Anadenanthera colubrina*) **in an** *In vivo* **Model of** *Drosophila melanogaster*. Sousa JS[1], Castro AJS[1], Araújo DD[1], Silva DA[2], Ribeiro FOS[2], Araújo AJ[1], Marinho-Filho JDB[1] [1]UFDPar, Lab Cultura de Células do Delta, Brasil; [2]UFDPar, Núcleo de Pesquisa em Biodiversidade e Biotecnologia, Brasil

Introduction: Natural gum polymers stand out as promising biomaterials for drug delivery systems and other applications, whether in their natural or modified form. Despite this, the polysaccharide from the exudate of the red angico (*Anadenanthera colubrina*) has been little explored. For its therapeutic use, rigorous safety evaluation is necessary, especially regarding genotoxic potential, since DNA alterations can induce carcinogenesis. In this context, the Somatic Mutation and Recombination Test (SMART) in *Drosophila melanogaster* emerges as an efficient and ethical method, serving as a viable alternative to mammalian models. **Objectives:** To evaluate the genotoxic and antigenotoxic potential of natural red angico gum (GAVN) and aminated red angico gum (GAVA) in somatic cells of D. melanogaster. **Methodology:** The gum was modified via two amination pathways (GAVA1 and GAVA2), using different volumes of ethylenediamine, 12 mL and 24 mL, respectively. The SMART assay was performed using 72-hour-old larvae from standard (ST) and high metabolic bioactivation (HB) crosses, treated with the gums at concentrations of 1000, 3000, and 6000 mg/mL. Distilled water and doxorubicin (DOX; 0.125 mg/mL) were used as negative and positive controls, respectively. For antigenotoxic activity, the gums were combined with DOX. The presence of mutant spots on the wings indicates changes in the hair pattern, suggesting DNA damage. These spots are associated with specific genetic events, allowing for the assessment of the compound's mutagenic and recombinogenic impact. Furthermore, the spots may be small, indicating late mutations, or large, indicating early mutations. **Results:** Those treated with GAVN showed no mutagenic effect in the ST cross; however, in the HB cross, a statistically significant increase in mutation frequency was observed, highlighting the need for cytochrome P450 metabolism to activate its mutagenic potential. Regarding antimutagenic activity, the results showed that GAVN has no protective effect against the chemotherapeutic agent. For GAVA1 and GAVA2, the results showed a significant increase in damage at all concentrations in both crosses, with a predominance of small single spots, pointing to mostly late mutations. In combination with DOX, none of the modified gums demonstrated a protective effect, maintaining damage frequencies statistically equivalent to those of DOX. **Conclusion:** It is concluded that both the natural and modified gums exhibit genotoxic potential under the conditions used, and this effect was accentuated by biometabolism in the natural gum. Furthermore, neither gum demonstrated the ability to modulate or attenuate the mutagenic effects of doxorubicin.

09.032 **The Esophagoprotective Effect of Spilanthol, an N-Alkylamide from *Acmella oleracea*, In Experimental Gastroesophageal Reflux Disease**. Santos BL[1], Monte MM[1], Oliveira ASS[2], Rodrigues MVN[2], Rodrigues RAF[2], Silva LMG[3], Souza MHLP[3], Sales TMAL[4], Rocha JA[5], Alves SKS[5], Nicolau LAD[1,5] [1]UFDPar, Lab Inflammation and Translational Gastroenterology, Brazil. [2]Unicamp, Multidisciplinary Center for Chemical, Biological and Agricultural Research, Brazil. [3]UFC, Lab Gastrointestinal Physio-Pharmacology Studies, Brazil. [4]USP, Ribeirão Preto Medical School, Brazil. [5]UFDPar, PPG in Biotechnology, Brazil.

Introduction: Gastroesophageal Reflux Disease (GERD) is a condition developed when the reflux of gastroduodenal contents causes troublesome symptoms and complications. Therapeutic alternatives must be considered, since there are reports of refractory events with the use of Proton Pump Inhibitors, a therapy considered the gold standard. Furthermore, these drugs do not have an evident response on the inflammatory condition, pepsin activity, and bile salts, which are considered important pharmacological targets in the context of GERD. Spilanthol, the main N-alkylamide present in Acmella oleracea (Jambu), has described anti-inflammatory properties and the ability to interact with proteases. **Objectives:** To investigate the esophagoprotective effects of spilanthol in experimental models of GERD. **Methodology:** Mice subjected to the surgical induction of chronic peptic esophagitis were distributed into experimental groups containing 8–10 animals per group and treated with spilanthol (10 mg/kg, p.o.) for seven days. Subsequently, macroscopic, histological, and functional parameters of the esophageal epithelial barrier were evaluated, including tissue wet weight, transepithelial electrical resistance (TEER) in a Ussing Chamber, and expression of the tight junction protein (ZO-1) by Western blotting. For histomorphological evaluation and analysis of esophageal mucus integrity, tissue samples were subjected to Periodic Acid-Schiff (PAS), Alcian Blue (AB) pH 2.5, and Toluidine Blue staining. Additionally, pepsin activity was evaluated *in vitro* by hemoglobin digestion assay, complemented by molecular docking analyses. **Results:** Treatment with spilanthol significantly reduced esophageal edema, evidenced by the decrease in wet weight. Microscopic analyses using PAS, AB, and Toluidine Blue revealed that spilanthol prevented mucus depletion and attenuated epithelial disorganization, promoting the preservation of the esophageal tissue architecture when compared to the untreated induced group. Furthermore, it restored the integrity of the epithelial barrier, promoting an increase in TEER and recovery of ZO-1 levels when compared to untreated animals with GERD. In the *in vitro* assays, spilanthol significantly inhibited the proteolytic activity of pepsin at different concentrations, an effect supported by *in silico* analyses, which demonstrated a favorable interaction of the compound with the enzyme's active site. **Conclusion:** Taken together, the results suggest that spilanthol exerts an esophagoprotective effect through mechanisms involving the preservation of epithelial barrier integrity, maintenance of mucus content, and inhibition of pepsin activity, supporting its potential for further preclinical and translational studies in GERD. **Acknowledgments:** Laboratory of Inflammation and Translational Gastroenterology. Animal Research Ethical Committee Number: Animal Ethics Committee of the Federal University of Delta do Parnaíba (UFDPar), No. 013/2022.

09.033 **Bioprospecting of Aqueous Extracts from *Pleurotus* spp. Mushrooms Cultivated on Agricultural Residues: Evaluation of Irritant Potential**. Dantas MEA[1,2], Alves AKL[1,2], Costa-Neto RC[5,2], Araújo ES[5,2], Brito JM[1,3], Nascimento JRS[1,3], Silva KKF[1,4], Barbora KMS[5,6], Araújo PL[5,6], Pereira FO[5,7], Dantas BB[1,7] [1]UFCG, Lab of the Curimataú Cancer Observatory (OCC), Brazil; [2]PIBIC/UFCG; [3]UFCG, PPGCNBiotec, Brazil; [4]UFPB, Renorbio, Brazil; [5]Lab of the Fungi Research Group, Brazil; [6]UFPB, PPGCN, Brazil; [7]UFCG, Education and Health Center, Brazil

Introduction: The genus Pleurotus comprises widely consumed edible mushrooms that stand out not only for their sensory characteristics but also for their nutritional composition and potential health benefits, meeting the growing interest in functional foods. Although considered culturally safe for oral ingestion, there is still a need to evaluate their potential irritants, since variations in cultivation conditions may modify the profile of produced metabolites, impacting consumption safety. Objectives To evaluate the irritant potential of aqueous extracts from mushrooms of the genus Pleurotus. Methods Mushroom species were cultivated on different agroindustrial waste materials by the FUNGI group. The aqueous extracts of Pleurotus djamor (P001A), prepared at a ratio of 1 g/10 mL (w/v), and of Pleurotus ostreatus (PO/A01), at a ratio of 1 g/20 mL (w/v), were subjected to ultrasonic bath extraction, followed by centrifugation and filtration (0.45 µm), yielding extracts of Pleurotus djamor cultivated on banana leaves (PD-B) or cajá residues (PD-C) and Pleurotus ostreatus cultivated on banana leaves (PO-B) or a blend of cajá and banana residues (PO-CB). During the HET-CAM (hen's egg test on chorioallantoic membrane) protocol, fertilized eggs of *Gallus gallus domesticus* were incubated until the 10th day, when the chorioallantoic membranes were exposed and the different extracts were applied. The vascular networks were recorded for 5 minutes and analyzed for the appearance of irritation signs — hemorrhage, hyperemia, and coagulation — used to calculate the mean irritation score (MSc). NaOH (0.1 N) and EtOH (99.9%) were used as positive controls, and NaCl (0.9%) as negative control. Results Pleurotus extracts were classified according to their MSc into: practically non-irritant (0.0-0.9), slight irritant (1.0-4.9), moderate (5.0-8.9), and severe (9.0-21.0). Banana leaf–cultivated extracts PD-B (MSc=4.83±3.09) and PO-B (MSc=3.25±1.09) induced discrete vascular reactions and were classified as slight irritants. Similarly, PD-C, produced on cajá residues (MSc=3.33±1.53), was also categorized as a slight irritant. In contrast, PO-CB, cultivated on cajá residues and banana leaves, induced only discrete hyperemia and was considered practically non-irritating (MSc=0.66±0.94), as well as 0.9% NaCl (MSc=0.58±0.80). Positive controls NaOH (MSc=19.0±0.0) and EtOH (MSc=18.58±0.38) induced intense vascular effects and were classified as severe irritants. **Conclusion:** Only PO-CB was classified as practically non- irritant, while PD-B, PO-B and PD-C exhibited slight irritability, suggesting that the fungal species and substrate influence the irritant potential. However, considering the oral use of these species, this effect tends to be attenuated by physiological barriers of the gastrointestinal tract. Nevertheless, further studies are required to assess additional toxicological parameters. **Financial support** CNPq, CAPES, FAPESQ.

09.034 **Lyophilized Hydroalcoholic Extract of *Spondias tuberosa* Arruda Leaves Reduces D-Galactose-Induced Oxidative Stress and Cellular Senescence-Associated β-galactosidase Activity in Endothelial Cells**. Pereira MEM[1], Gomes MLC[1,2], Albuquerque MN[1], Souza CMO[1,2], Fernandes GFS[1], Oliveira JCPL[1,2], Oliveira GD[5], Medeiros KCP6, Farias LRT[4], Langassner SMZ[4], Nascimento YM[2,5], Veras RC[1,2,3], Medeiros IA[1,2,3], Araújo IGA[1,2,3] [1]UFPB, Cardiovascular Pharmacology Lab, Institute for Drug and Medicine Research, Brazil. [2]UFPB, PPG in Bioactive Natural and Synthetic Products (PgPNSB), Health Sciences Center, Brazil. [3]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil. [4]UFRN, Pharmacognosy Lab, Brazil. [5]UFPB, Multi-User Lab for Characterization and Analysis, Brazil. 6UFRN, Dept Morphology, Brazil.

Introduction: Cellular senescence is characterized by irreversible cell cycle arrest, associated with intracellular alterations that contribute to age- related diseases, including cardiovascular disorders. The accumulation of senescent cells in the vascular endothelium is largely driven by oxidative stress, promoting endothelial dysfunction. In this context, natural products with antioxidant activity have demonstrated beneficial effects, and the search for compounds with antioxidant and anti-senescent properties has become relevant. The literature shows that fruit-bearing species such as *Spondias tuberosa* Arruda (umbuzeiro) present high levels of phenolic compounds with antioxidant potential. **Objectives:** This study evaluated the effects of the lyophilized hydroalcoholic extract of *Spondias tuberosa* Arruda leaves (EHLST) on human umbilical vein endothelial cells (HUVECs) subjected to D-galactose (D-gal)-induced cellular senescence. **Methods:** Nuclear Magnetic Resonance (NMR) analysis was performed to characterize the phytochemical components present in EHLST. For the pharmacological assays, HUVECs were challenged with D-gal (20 mg/mL) to induce senescence. EHLST (0.01; 0.05; 0.1; 0.5; and 1.0 µg/mL) was evaluated under basal conditions and in cells exposed to D-gal. Cell viability was assessed using the colorimetric MTT assay (3-[4,5-dimethyl-2-thiazolyl]-2,5-diphenyltetrazolium bromide), superoxide anion (O_2^-) production was measured using the fluorescent probe dihydroethidium (DHE), and the percentage of senescent cells was determined using the senescence-associated β-galactosidase (SA-β-gal) biomarker. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test, considering statistical significance when $p < 0,05$. **Results:** NMR analysis revealed signals compatible with phenolic compounds, including caffeic acid, rutin, and isoquercitrin. The cell viability assay confirmed the non-toxic profile of the extract, since under both basal and D-gal conditions, EHLST concentrations did not alter the percentage of viable cells. In the O_2^- production assay, EHLST did not significantly alter this parameter under basal conditions, except at the highest concentration tested, whereas in senescent HUVECs, EHLST significantly reduced the production of these anions ($p < 0,05$), which had been increased by D-gal exposure. The cellular senescence assay demonstrated that EHLST was unable to alter senescence under basal conditions; however, in senescent HUVECs induced by the D-gal model, it significantly reduced the proportion of senescent cells ($p < 0,05$). **Conclusion:** These findings provide preliminary evidence that EHLST reduces senescence-associated β-galactosidase activity, associated to antioxidant activity in a translational model of D-galactose-induced endothelial senescence. This suggests that EHLST may have therapeutic use in preventing disorders linked to aging.

09.035 **Brown Propolis from *Mimosa tenuiflora* Attenuates Oxidative Stress in a Rat Model of Allergic Asthma**. Souza MLB, Felício IM, Alves BFL, Figueiredo IAD, Golzio, AMFO, Silva TMS, Picot L, Cavalcante FA PPgPNSB/CCS/UFPB/Brazil, DPOA/CTDR/UFPB/Brazil, DQ/UFRPE/Brazil, , DCB/CCS/UFPB/Brazil La Rochelle Université/France

Introduction: Asthma is a chronic inflammatory disease of the airways in which an imbalance in oxidative stress strongly influences its pathophysiology, promoting the accumulation of free radicals and exacerbating inflammation. Propolis is mainly composed of plant resins collected by *Apis mellifera* honeybees, mixed with wax and bee secretions. Brazilian brown propolis exhibits anti-inflammatory, antibacterial, and antimutagenic activities (Felício, IM. Fito., v. 185, p. 106687, 2025). Therefore, the aim of this study was to evaluate the effects of brown propolis (BP) from *Mimosa tenuiflora* on oxidative stress in asthmatic Wistar rats. **Methods:** Wistar rats were randomized into three groups (n = 5): control (CG), asthmatic (AG) and an asthmatic group treated with BP at 125 mg/kg (BPAG125). Asthma was induced by ovalbumin sensitization and intranasal challenges, while controls received saline. Treatments were given orally during sensitization, and animals were euthanized on day 22. Tracheal reactivity was assessed in rings incubated with apocynin or tempol and exposed to carbachol (CCh). Lung homogenates were analyzed for oxidative stress markers: lipid peroxidation (TBARS-thiobarbituric acid reactive substances), nitrite (Griess), reduced glutathione (Ellman), and superoxide dismutase (SOD) activity (NBT-nitroblue tetrazolium). Experimental protocols were approved by the Animal Ethics Committee/UFPB (8719020621). **Results:** In the CG, the cumulative concentration-response curve to CCh was not significantly altered by apocynin or tempol, showing no differences in efficacy or potency. In AG, both apocynin and tempol significantly reduced the contractile efficacy (Emax = 146.3 ± 5.6% to 78.8 ± 5.6% and 102.1 ± 7.6%, respectively; $p < 0.05$), without affecting potency. In BPAG125, apocynin and tempol reduced both contractile efficacy (Emax = 108.3 ± 8.1% to 81.3 ± 15.0% and 45.8 ± 3.2%, respectively; $p < 0.05$) and potency (EC50 = 1.2 ± 0.2 × 10-6 M to 5.8 ± 1.7 × 10- 6 M and 3.8 ± 0.8 × 10-6 M, respectively; $p < 0.05$). In lung homogenates, AG showed increased malondialdehyde (MDA) levels (14.02 ± 1.05 mg/g) compared to CG (7.23 ± 0.50 mg/g) which was prevented in BPAG125 (7.38 ± 0.51 mg/g). Nitrite concentrations were elevated in AG (222.0 ± 23.70 µM/g) versus CG (127.10 ± 5.68 µM/g) but prevented in BPAG125 (141.7 ± 9.2 µM/g). GSH levels were reduced in AG (9.00 ± 0.87 µg/g) compared to CG (23.76 ± 0.35 µg/g) and BPAG125 prevented this reduction (23.54 ± 0.47 µg/g). SOD activity was lower in AG (20.14 ± 2.32 U/mg) relative to CG (49.51 ± 7.76 U/mg) but restored in BPAG125 (43.17 ± 4.76 U/mg). **Conclusion:** These findings suggest that the anti-asthmatic effects of BP from *Mimosa tenuiflora* are associated with attenuation of tracheal hyperresponsiveness and oxidative stress, possibly involving modulation of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase-dependent pathways.

09.036 **Bioactive Compounds from Cocoa Bean Shells Protect Human Keratinocytes against UVB-Induced Photodamage**. Santos LFS[1], Queiroz LL[1], Vidal DM[1], Lopes MTP[3], Lima MD[1], Freitas KM[4] [1]UESC, Dept of Chemistry, [3]UFMG, Pharmacology, Belo Horizonte/MG, [4]UESC, Health Science, PPGCS, Ilhéus, BA, Brasil.

Introduction: UVB radiation induces oxidative stress and inflammation in skin cells, contributing to photodamage. Cocoa bean shells (Theobroma cacao L.), an abundant and underutilized by-product of the cocoa industry, represent a sustainable source of bioactive phytochemicals with antioxidant and anti- inflammatory properties and potential photoprotective activity. **Objective:** This study investigated the photoprotective potential of bioactive compounds obtained from cocoa bean shells in human keratinocytes (HaCaT cells) exposed to UVB radiation. **Methods:** Cocoa bean shells (CBS) were roasted (110–130 °C), supplied by Chocosol®, were used in this study. The plant material was registered in SISGEN under number A5A4B69. Essential oil extraction was performed by steam hydrodistillation, while the extract was obtained by maceration in 70% ethanol. Phytochemical constituents and antioxidant activity were evaluated by DPPH assay. HaCaT cells were treated with the bioactive compounds and subsequently exposed to UVB radiation (30 mJ/cm^2; Cole-Parmer®, 15 W, 312 nm). Intracellular ROS production was quantified by flow cytometry using the DCFH-DA probe. In addition, COX-2 expression was assessed by immunocytochemistry, transmembrane transport activity was evaluated using the rhodamine 123 assay, pro-inflammatory protein release was determined by immunoassay, and cell death by Annexin V/propidium iodide (PI) staining followed by flow cytometry. **Results:** The hydrodistillation process yielded approximately 0.16 % (w/w) essential oil, while alcoholic maceration resulted 2.5 %. The bioactive compounds exhibited significant antioxidant activity and effectively reduced free radical production ($p < 0.001$); however, they did not affect keratinocyte viability following UVB exposure. Furthermore, the samples inhibited COX-2 expression and IL-8 release ($p < 0.05$) and significantly reduced the proportion of late apoptotic cells ($p < 0.05$). **Conclusion:** Bioactive compounds derived from cocoa bean shells (CBS) reduced UVB-induced oxidative stress and cellular damage in human keratinocytes, demonstrating promising *in vitro* photoprotective activity. The valorization of CBS also represents a sustainable strategy for the use of agro-industrial by-products with potential socioeconomic and environmental benefits. Reference: García, M. Am. J. Pathol., v. 177, pp. 865–872, 2010. Pratheeshkumar, P. Toxicol. Appl. Pharmacol., v. 280, pp. 127–137, 2014. Lim, J.S. J Supercrit Fluids, v. 221, p 1, 2025. **Financial support**. FAPESB.

09.037 **Biocompatibility and Molecular Changes in L929 Fibroblasts Induced by the Essential Oil of** *Pectis brevipedunculata* (**Gardner**) **Sch. Bip.** Lima GMSF[1], Lima RF[2], Reis ATF[3], Carvalho TGPM[4], Andrade LGS[5], Diniz Filho JFS[6], Barreto FS[7], Andrade MS[7], Rocha CQ[8], Carvalho RC[9], Dittz Junior D[10], Cartágenes MSS[2] [1]UFMA, LEED, Pharmacy Course, Brazil, [2]UFMA, LEED, PPGSAD, Brazil, [3]UFMA, LEED, PPGCS, Brazil, [4]UFMA, LEED, Renorbio, Brazil [5] UFMA, LQPN, Pharmacy Course, Brazil [6]UFMA, Bacabal Campus, Brazil [7],UFMA, PPGSAD, Brazil [8]UFMA, LQPN, PPGQUIM, Brazil [9]UFMA, Animal Facility, Brazil [10]UFPI, Dept Biochemistry and Pharmacology, Brazil

Introduction: The species *Pectis brevipedunculata* (Asteraceae), known as field rosemary, produces an essential oil rich in monoterpenes with potential biological activity. Given the search for new plant-based therapeutic alternatives, it is important to investigate its effects on cellular models as a first step toward future studies related to wound healing. **Objectives:** To evaluate the cytotoxicity and biochemical changes induced by *Pectis brevipedunculata* oil in L929 fibroblasts, providing preliminary evidence to support future investigations related to wound healing. **Methods:** L929 fibroblasts were cultured in DMEM (10% FBS, 37 °C, 5% CO_2) and treated with different concentrations (3.9 to 500 µg/mL) of *P. brevipedunculata* oil. *Helianthus annuus* (sunflower) oil was used as a control and tested at the same concentrations. Cell viability was assessed by the MTT assay after 72 h, and the IC_{50} was calculated from the MTT cell viability data by nonlinear regression using GraphPad Prism 10. Biochemical changes were investigated by Raman spectroscopy after 48 h of treatment. Raman spectra were obtained using a triple-beam Raman spectrometer (Horiba T64000) with a 532 nm laser (14 mW) and a 100× objective. Acquisitions were performed in the 700–1800 cm^{-1} range, with nine 20-second exposures at multiple points on the cell surface. Data preprocessing included removal of cosmic rays and correction for fluorescence background and glass substrate using fifth-order polynomial fitting with LabSpec6 software. **Results:** *P. brevipedunculata* oil exhibited concentration- dependent cytotoxicity, with an IC_{50} of 91.39 µg/mL. Sunflower oil showed no cytotoxicity and stimulated fibroblast proliferation. In Raman vibrational analysis, treatment with Pectis oil promoted more pronounced changes in L929 cells compared to sunflower oil. While sunflower oil induced an increase mainly in the band at ~1004 cm^{-1}, associated with phenylalanine, Pectis oil showed additional increases in the bands at ~1140, 1450, 1650, and 1675 cm^{-1}, related to vibrations of aromatic amino acid side chains, lipid and protein CH_2/CH_3 groups, as well as the amide I region and C=C stretching of unsaturated lipids. **Conclusion:** Pectis oil demonstrated concentration- dependent cytotoxicity and induced significant biochemical changes in L929 fibroblasts, as evidenced by alterations in Raman spectra consistent with changes in cellular biochemical composition. Further studies, including functional assays, are needed to elucidate its mechanisms of action and evaluate its potential relevance to wound healing. Keywords: *Pectis brevipedunculata*; Fibroblasts; Raman spectroscopy; Wound healing.

09.038 **Evaluation of Antioxidant Activity of Endophytic Fungi Extracts Isolated from *Lactuca sativa* by DPPH, FRAP and ABTS Assays**. Dantas A, Oliveira G, Fonseca YM UnB-Darcy Ribeiro, School of Health Sciences, Dept. of Pharmacy, Natural Products Lab, Brazil

Introduction: Endophytic fungi produce secondary metabolites with antioxidant potential, a promising alternative to synthetic antioxidants such as butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT), whose use is increasingly discouraged due to severe health risks such as toxicity and potential carcinogenic effects. Despite the growing interest in bioactive compounds, studies about the antioxidant activity of endophytic fungi isolated from *Lactuca sativa* remain scarce. **Objectives:** This study aimed to evaluate the antioxidant activity of crude extracts obtained from four endophytic fungal strains (F1, F2, F4R1, F4R2) isolated from *L. sativa* stems, using three complementary assays: DPPH and ABTS radical scavenging, and ferric-reducing antioxidant power (FRAP). **Methods:** Strains were cultivated by submerged fermentation (14 days, 28 °C,120 rpm) in potato dextrose broth (PDB), and secondary metabolites were extracted using ethyl acetate. Dried crude extracts were tested at concentrations ranging from 0.625 to 10 mg/mL against 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), absorbances measured at 518 nm and 734 nm, respectively. IC50 values were determined by nonlinear regression (four-parameter logistic curve, GraphPad Prism). Ferric-reducing power was measured at 595 nm and expressed as Trolox equivalents per mg extract (µg TE/mg). Data was analyzed by two-way ANOVA (concentration × strain), $p<0.05$. The highest F4R1 concentration (10 mg/mL, n=3) was excluded from the FRAP dataset as a technical outlier, resulting in n=57 (versus n=60 for DPPH/ABTS). **Results:** Two-way ANOVA confirmed significant effects of concentration and strain in all three assays ($p<0.0001$), with a significant concentration × strain interaction in DPPH and ABTS ($p<0.0001$), showing the four extracts did not respond uniformly to dilution. In DPPH, F1 and F2 showed the most reliable dose-dependent inhibition, with IC50 values of 6.38 mg/mL (R^2=0.977) and 5.94 mg/mL (R^2=0.978); for F4R1 and F4R2, a reliable IC50 could not be determined within the tested range. In ABTS, F1 and F2 again led, with IC50 values of 2.45 mg/mL (R^2=0.987) and 2.01 mg/mL (R^2=0.995), while neither F4R1 nor F4R2 yielded a reliable IC50. In FRAP, F1 showed the highest ferric-reducing capacity (~33 µg TE/mg at 10 mg/mL), while F2, despite strong radical-scavenging results, showed the lowest FRAP capacity of the four strains; F4R1 and F4R2 showed intermediate activity that rose and fell unevenly with concentration. **Conclusion:** F1 showed the most consistent antioxidant profile, combining efficient radical scavenging with the highest ferric-reducing capacity. F2 excelled in radical-scavenging assays but showed the weakest ferric-reducing performance, suggesting a mechanism-specific profile. F4R1 and F4R2 showed lower, less consistent activity, with radical-scavenging potency that could not be reliably quantified within the tested range. These variations among strains and assays highlights the need for multi-assay approaches to accurately characterize the antioxidant profiles of these endophythic fungal extracts.

09.039 **Evaluation of the Antioxidant Activity of the Plant Species** *Vitex gardneriana*. Gonçalo YA, Ferreira CES, Andrade IA, Fialho MLS, Martins SO, Nóbrega VM, Oliveira MVM, Medeiros FD. Gonçalo YA, Ferreira CES, Andrade IA, Fialho MLS, Martins SO, Nóbrega VM, Oliveira MVM, Medeiros FD. UFCG-Cuité, Center for Education and Health, Brazil.

Introduction: Oxidative stress results from an imbalance between the production of reactive species and the neutralization of free radicals in the human body, and the accumulation of these unstable molecules contributes to the development of several diseases, such as neurodegenerative disorders (Silva, VAR. Stud. Health Sci., v. 6, p. 4, 2025). From this perspective, among the medicinal species of the Caatinga biome, *Vitex gardneriana*, popularly known as Jaramataia, belongs to the Lamiaceae family, and previous studies have demonstrated antioxidant activity, considering the possible presence of secondary metabolites capable of combating these reactive species. **Objectives:** To evaluate the antioxidant activity of *Vitex gardneriana* extracts. Methodology The leaves of *Vitex gardneriana* were collected and subjected to drying in a forced-air circulation oven at 45°C for 72 hours. After drying, the plant material was ground using a knife mill. The extract was obtained by hydroalcoholic maceration. The presence of secondary metabolites in the extract was investigated using qualitative methods. Antioxidant activity was evaluated by the ABTS and DPPH methods and expressed as µmol ascorbic acid equivalent/mL ± standard deviation. **Results**: The phytochemical profile revealed the presence of alkaloids, phenolic compounds, saponins, and tannins in the extract. Antioxidant activity was confirmed, showing mean values of 0.015 ± 0.001 AAE/mL by the ABTS method and 0.007 ± 0.000 AAE/mL by the DPPH method. It is suggested that the antioxidant activity may be associated with the presence of the aforementioned phytochemical components, as demonstrated by previous studies (Silva, BS. Res. Soc. Dev., v. 11, p. 4, 2022), (Braz. J. of Develop., V. 6, p. 28807, 2020). **Conclusion:** Thus, *Vitex gardneriana* demonstrates bioactive potential, justifying further investigations in studies related to phytotherapeutic and pharmacological formulations with promising contributions to human health and the preservation of biomolecules.

09.040 **Protective Effects of *Spondias tuberosa* Arruda Fruit Peel Extract on Oxidative Stress and Senescence-Associated β-Galactosidase Activity in D-Galactose-Induced Endothelial Senescence Model**. Albuquerque MN[1], Gomes MLC[1,2], Pereira MEM[1], Souza CMO[1,2], Fernandes GFS[1], Oliveira JCPL[1,2], Oliveira GD[2,5], Medeiros KCP[6], Farias LRT[4], Langassner SMZ[4], Nascimento YM[2,5], Veras RC[1,2,3], Medeiros IA[1,2,3], Araújo IGA[1,2,3]. [1]UFPB, Cardiovascular Pharmacology Lab, Institute for Drug and Medicine Research, Brazil. [2]UFPB, PPG in Bioactive Natural and Synthetic Products (PgPNSB), Brazil. [3]UFPB, Dept Pharmaceutical Sciences, Brazil. [4]UFRN, Pharmacognosy Lab, Brazil. [5]UFPB, Multi-User Lab for Characterization and Analysis, Brazil. [6]UFRN, Dept Morphology, Brazil.

Introduction: Cellular senescence and oxidative stress are important mediators of aging. The development of age-related cardiovascular diseases is associated with endothelial senescence and vascular aging. Natural products with antioxidant properties have been identified as potential protective agents against cellular senescence. *Spondias tuberosa* Arruda is a symbolic tree of the Caatinga, a biome exclusive to northeastern Brazil, playing a fundamental role in the local economy, ecology, and culture. Its fruit, popularly known as "umbu", is rich in bioactive phenolic compounds and exhibits significant antioxidant activity. **Objective:** This study evaluated the effects of the lyophilized hydroalcoholic extract from the fruit peel of *Spondias tuberosa* Arruda (ST-FP) on oxidative stress, senescence-associated β-galactosidase (SA-β-Gal) activity, and cell viability in human umbilical vein endothelial cells (HUVECs) subjected to D-galactose-induced senescence. **Methods:** Proton nuclear magnetic resonance (^{1}H NMR) spectroscopy was used for the chemical characterization of secondary metabolites present in ST-FP. For the pharmacological assays, HUVECs were exposed to D-galactose (20 mg/mL). ST-FP (0.01, 0.05, 0.1, 0.5, and 1.0 µg/mL) was evaluated under basal conditions and in D-galactose-exposed cells. Cell viability was assessed using the MTT assay [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide]. Superoxide anion (O_2^-) production was measured using the fluorescent probe dihydroethidium (DHE), whereas SA-β-Gal activity was evaluated as a biomarker of cellular senescence. Statistical analyses were performed using one-way analysis of variance (ANOVA), followed by Tukey's post hoc test, with differences considered statistically significant at $p < 0.05$. **Results:** Chemical characterization by ^{1}H NMR revealed signals consistent with the presence of phenolic compounds. In the cell viability assays, ST-FP did not exhibit cytotoxicity at the concentrations evaluated. Analysis of O_2^- production demonstrated that cells exposed to D-galactose showed a significant increase in oxidative stress, whereas treatment with ST-FP reduced reactive oxygen species generation ($p < 0.05$), highlighting its antioxidant potential. Furthermore, in the SA-β-Gal assay, D-galactose increased the percentage of senescent cells, while ST-FP reduced cellular senescence ($p < 0.05$), suggesting a protective effect against endothelial senescence. **Conclusion:** These findings provide preliminary evidence that the ST-FP exhibits antioxidant activity and reduces senescence-associated β-galactosidase activity in an *in vitro* model of D-galactose-induced endothelial senescence. These effects are possibly associated with the phenolic compounds present in the extract. Collectively, the results indicate that ST-FP may represent a promising natural product for future investigations targeting endothelial senescence and vascular aging.

09.041 **Use of a Nanoencapsulated Formulation to Enhance the Antifungal Activity of Carvacrol Against Oral Candida albicans Isolates**. Silva PAE[1], Costa Neto RE[1], Bezerra JAF[2], Cardoso, ALMR[2], Xavier-Júnior FH[2], Guerra FQS[1], Chaves GM[3], Silva-Rocha WP[11]UFPB, Lab Micologia Clínica, Depto Ciências Farmacêuticas, Brasil, [2]UFPB, Lab Biotecnologia Farmacêutica, Depto Ciências Farmacêuticas, Brasil, [3]UFPE, Lab Micologia Médica, Depto Micologia, Brasil.

Introduction: Oral candidiasis is an opportunistic fungal infection frequently associated with the proliferation of yeasts of the *Candida genus*, with *C. albicans* being the most prevalent species. This microorganism can adhere to oral tissues, form biofilms, and develop resistance mechanisms against conventional antifungal agents, making infection management more challenging (Samaranayake, 2024). In this context, natural compounds have been investigated as alternative therapeutic approaches. Carvacrol, a phenolic monoterpene found in essential oils, exhibits well-documented antifungal activity; however, its clinical application may be limited by poor solubility and physicochemical instability. Nanoencapsulation and functionalization strategies have been proposed to enhance its biological performance. **Objective**: To evaluate the antifungal potential of carvacrol and investigate the influence of nanoencapsulation and functionalization on its activity against oral strains of *Candida albicans*. **Methods:** Lipid nanoparticles containing carvacrol were produced by the hot emulsification method followed by ultrasonication, using Precirol® ATO 5, medium-chain triglycerides, Tween® 80, and Span® 60. Fourteen Candida albicans strains were evaluated, including one reference strain (ATCC 90028) and thirteen clinical oral isolates. The antifungal activity of free and nanoencapsulated carvacrol was determined through Minimum Inhibitory Concentration (MIC) and Minimum Fungicidal Concentration (MFC) assays using the broth microdilution method according to the Clinical and Laboratory Standards Institute (CLSI) M27-A3 protocol. Tested concentrations ranged from 64 to 1024 µg/mL. Fungicidal activity was determined by the MFC/MIC ratio, with values ≤4 considered indicative of fungicidal action. **Results:** Both free carvacrol and the nanoformulation exhibited antifungal activity against all evaluated strains. For free carvacrol, MIC values ranged from 128 to 512 µg/mL, whereas MFC values ranged from 128 to 1024 µg/mL. The nanoformulation showed MIC values between 64 and 256 µg/mL and MFC values between 64 and 1024 µg/mL. A 50% reduction in MIC was observed after nanoencapsulation in the ATCC strain and in isolates LABM 90, 92, 96, 98, 99, and 100, demonstrating enhanced antifungal efficacy. All samples exhibited MFC/MIC ratios between 1 and 4, confirming fungicidal activity. Moreover, the nanoformulation presented an MFC/MIC ratio of 1 for most isolates, suggesting greater efficiency in fungal cell eradication. **Conclusion:** Carvacrol demonstrated significant antifungal activity against oral strains of *Candida albicans*. Nanoencapsulation enhanced this activity by reducing MIC values while maintaining fungicidal action against all tested isolates. These findings indicate that nanostructured delivery systems represent a promising strategy to optimize the antifungal performance of carvacrol and expand its potential application in the treatment of oral candidiasis.

09.042 **Healing Effect of Bioactive Polymeric Films Incorporating Gallic Acid and Ellagic Acid in Experimental Cutaneous Wounds**. Veloso RP[1,2], Amorim IF[2,3], Freitas FVS[2,3], Freitas Neto CAF[2,3], Martins HRS[2,3], Silva PHS[2,3], Moraes RR2,3, Santos LJC[1,2], Silva GFA[1,2], Souza LVSC[1,2], Reis ML[2,3], Carvalho ALM[1,2], Oliveira RCM[2,3,4]. [1]UFPI, Dermopharmacy Lab, [2]UFPI, Lab Gastrointestinal Pharmacology, [3]UFPI, PPGCF Graduate Program in Pharmaceutical Sciences, Brazil, [4]UFPI-NPPM, Medicinal Plants Research Center, Brazil [5]UFPI-PPGFarm, PPG in Pharmacology.

Introduction: Wound healing is a complex biological process involving coordinated cellular and molecular events to restore tissue integrity. In this context, biomaterials containing bioactive compounds have been extensively investigated as therapeutic alternatives to accelerate skin repair. Phenolic acids, especially gallic acid (GA) and ellagic acid (EA), have antioxidant, anti-inflammatory, and antimicrobial properties that may promote tissue regeneration. When incorporated into polymeric matrices, these compounds can enhance repair mechanisms, promoting a suitable environment for the recovery of damaged tissues. **Objective:** To evaluate the wound healing activity of carboxymethylcellulose and gum arabic polymer films containing gallic acid, ellagic acid, and the combination of both in an experimental surgical wound model in rats. **Methods:** Thirty adult male Wistar rats, weighing an average of 250 ± 50 g, were used and kept under controlled conditions of temperature, light, food, and hydration. The study was approved by the Animal Experimentation Ethics Committee of the Federal University of Piauí (CEEA/UFPI nº 864/2025). Full-thickness excisional skin wounds were created on the dorsal region of anesthetized animals using a sterile surgical biopsy punch. The animals were randomly distributed into five experimental groups (n=6): FAE (film containing 0.5% ellagic acid), FAG (film containing 0.5% gallic acid), FAEG (film containing a combination of ellagic and gallic acids, both at 0.5%), COLAG (treatment with collagenase ointment), and Sham (animals without induced skin lesions). In the FAE, FAG, and FAEG groups, the lesions were compared with the corresponding base film without active ingredients (FB). Wound healing activity was assessed over seven days through serial measurements of the lesions using a digital caliper. The length, width, and depth of the wounds were determined to calculate residual volume and monitor tissue regression. Additionally, hematological and biochemical analyses were performed to assess the safety of the formulations. **Results:** All treated groups showed crust formation and progressive regression of lesions throughout the experimental period. At the end of the seven days, a significant reduction in wound volume was observed in the FAE (18.97 ± 6.69 mm^3), FAG (31.08 ± 23.57 mm^3) and FAEG (20.65 ± 14.10 mm^3) groups, when compared to the base film without active ingredients (85.39 ± 31.87 mm^3). The results were statistically similar to those observed in the group treated with collagenase (14.43 ± 11.99 mm^3), demonstrating efficacy comparable to the reference treatment.**Conclusion:** Polymeric films containing gallic acid, ellagic acid, and their combination significantly accelerated the healing of cutaneous wounds in rats, showing efficacy similar to collagenase and a favorable safety profile. The results reinforce the therapeutic potential of these phenolic compounds incorporated into polymeric matrices as a promising strategy for the development of bioactive dressings for the treatment of skin wounds.

09.043 **Evaluation of the Antimicrobial Potential, Antibiofilm Activity, and Cytotoxic Effects of Andiroba Fixed Oil (*Carapa guianensis*) Against Clinically Relevant Microorganisms**. Azevedo KMS[1,3], Lacerda AF[1,2] Alves ARS[1,3], Souza PHO[2], Cunha DBL[2], Alves RV[2], Gadelha TS[2], Faheina-Martins GV[2], Vasconcelos U[2,3], Travassos RA[1,2,3] [1]UFPB, Lab FarmacoBiotecnologia (FarmaBio), Brazil; [2]UFPB, Graduate Program in Cellular and Molecular Biology (PPgBCM), Brazil; [3]UFPB, Centro de Biotecnologia (CBiotec), Brazil.

Introduction: Antimicrobial resistance is one of the major global public health challenges, compromising the effectiveness of conventional therapies and contributing to persistent and difficult-to-treat infections. In this context, plant-derived natural products have attracted scientific interest as potential sources of bioactive compounds with antimicrobial activity. Among these products, Andiroba fixed oil (*Carapa guianensis*), widely used in traditional Amazonian medicine, contains limonoids, terpenoids, and fatty acids with relevant biological properties. **Objectives:** This study aimed to evaluate the antimicrobial activity of Andiroba fixed oil against clinically relevant microorganisms, as well as its effects on microbial biofilms and its *in vitro* cytotoxicity profile. **Methods:** Antimicrobial activity was determined using the microdilution method against *E. coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Staphylococcus aureus* ATCC 13150, and *Candida albicans* ATCC 76645. Biofilm formation inhibition and mature biofilm eradication assays were performed using crystal violet staining. The putative mechanism of action was investigated using a sorbitol protection assay to assess possible effects on cell wall integrity. Cytotoxicity was evaluated by the MTT assay in HEK-293 cells. The selectivity index (SI) was calculated as the IC_{50}/MIC ratio. All experiments were performed in triplicate in at least three independent assays. Data were expressed as mean ± standard deviation (SD) and analyzed by one-way ANOVA followed by Bonferroni's post hoc test, with $p < 0.05$ considered statistically significant. **Results:** Andiroba fixed oil showed significant antimicrobial activity, with MIC values of 1 µg/mL for *E. coli* and *C. albicans*, 128 µg/mL for P. aeruginosa, and 64 µg/mL for *S. aureus*. It was particularly effective in reducing mature biofilm biomass. The sorbitol protection assay suggested a possible effect on microbial cell wall integrity. Furthermore, the Andiroba fixed oil showed cytotoxicity in HEK-293 cells, with an IC_{50} of 571.3 µg/mL. The selectivity index indicates low selectivity against *P. aeruginosa* and S. aureus (SI = 4.46 and 9, respectively) and very high selectivity against *C. albicans* and *E. coli* (SI = 571.3 for both). Vehicle control assays using DMSO showed no intrinsic antimicrobial activity under the experimental conditions, indicating that the observed biological effects observed were attributable to Andiroba oil rather than to the solvent system. **Conclusion:** Andiroba fixed oil demonstrated antimicrobial and antibiofilm activities associated with a concentration-dependent cytotoxicity profile, *in vitro*. These findings suggest that C. guianensis fixed oil may represent a promising source of bioactive compounds for the development of new antimicrobial strategies. **Financial support:** FAPESQ-PB

09.044 **Evaluation of the Antioxidant Activity of the Extract of** *Dysphania ambrosioides* **(L.)**. Fialho MLS, Ferreira CES, Andrade IA, Oliveira MVM, Martins SO, Nóbrega VM, Gonçalo YA, Medeiros FD. UFCG-Cuité, Center for Education and Health, Brazil.

Introduction: Reactive oxygen species are associated with the development of several diseases due to the cellular and molecular damage caused by oxidative stress. In this context, synthetic antioxidants are used to neutralize these reactive species. However, although widely used, they may have harmful effects on health, highlighting the need for safer and more effective natural alternatives (Luna, EM. Phytomed. Plus, v.2, p.100240, 2022). Among these potential alternatives, *Dysphania ambrosioides* (L.), popularly known as mastruz and belonging to the Amaranthaceae family, stands out. Found in the Caatinga biome, this species has a wide geographical distribution and ethnopharmacological relevance, being associated with antioxidant and anti-inflammatory activities with therapeutic potential (Ogunleye, GS. Ind Crops Prod, v.154, p.112723, 2020). **Objective:** To evaluate the antioxidant activity of *Dysphania ambrosioides* (L.) extract. **Methods:** To obtain the extract, the leaves were collected, dried in a forced-air circulation oven at 40 °C for 48 h, subjected to hydroalcoholic extraction by maceration for five days, and subsequently filtered. The presence of secondary metabolites was investigated using classical methods, and antioxidant activity was determined by the ABTS and DPPH methods, using ascorbic acid calibration curves expressed as µmol of ascorbic acid equivalents per milliliter (µmol AAE/mL) ± standard deviation. **Results:** In the qualitative phytochemical analysis, the leaf extract of *D. ambrosioides* (L.) showed the presence of alkaloids, phenolic compounds, and saponins. In the antioxidant activity assays, absorbance values of 0.007 ± 0.001 (µmol AAE/mL) by the ABTS method and 0.001 ± 0.000 (µmol AAE/mL) by the DPPH method were observed. The results demonstrated greater antioxidant activity detected by the ABTS assay compared with DPPH, highlighting differences in the response capacity of the methods employed. These findings corroborate studies described in the literature for *D. ambrosioides* (L.), whose antioxidant activity has already been demonstrated in different assays (Guleria, D. Prenap, v.10, p.100559, 2026). **Conclusion:** The extract of *D. ambrosioides* (L.) showed antioxidant activity detectable by the ABTS and DPPH methods, with greater antioxidant capacity measured by the ABTS method, in addition to a phytochemical profile characterized by the presence of alkaloids, phenolic compounds, and saponins, demonstrating biological potential and relevance for future phytochemical and pharmacological studies.

09.045 *Cissampelos sympodialis* **Extract Mitigates Oxidative Stress and Lung Remodeling in Cigarette Smoke-Induced Emphysema through Nrf2-Associated Mechanisms**. Barros-Moura MM[1,2], Queiroz-Neto RF[2], Silva FS[2], Oliveira MF[2], Kennedy-Feitosa E[2] [1]FMO - Olinda, PE, Brazil; [2]UFERSA, Morphophisiopharmacology Lab, Mossoro, Brazil

Introduction: Pulmonary emphysema is characterized by progressive alveolar destruction, oxidative stress, and lung remodeling caused by chronic cigarette smoke (CS) exposure. The nuclear factor erythroid 2-related factor 2 (Nrf2) is a key regulator of antioxidant defenses and plays an important role in protecting the lung against oxidative injury. *Cissampelos sympodialis* extract (ECsy) exhibits antioxidant properties and may protect against smoke-induced lung injury. **Objective:** To investigate whether ECsy attenuates oxidative imbalance and lung remodeling through Nrf2-associated mechanisms in a murine model of CS-induced emphysema. **Methods:** Male C57BL/6 mice were divided into three groups (n=7/group): Control, CS, and CS+100. The Control group was exposed to ambient air and treated with saline. The CS groups were exposed to smoke from 12 cigarettes/day for 60 days. After emphysema establishment, animals received saline (CS) or ECsy (100 mg/mL) by nebulization for an additional 60 days. Animals were euthanized on day 121, and the lungs were collected for analysis. ROS levels, SOD and CAT activities, and MDA concentration were measured in lung homogenates. Nrf2 expression was performed by immunohistochemistry. Lung remodeling was evaluated by mean linear intercept (Lm) and peribronchiolar collagen deposition. Statistical significance was considered at $p<0.05$. **Results:** The CS group showed increased ROS (333.5 ± 13.67), compared with the Control group (122.0 ± 16.7; $p<0.0001$). ECsy reduced ROS levels (58.0 ± 5.1; $p<0.0001$). The CS group showed increased SOD and CAT activities (132.1 ± 14.3 and 9.71 ± 0.63) compared with Control animals (49.3 ± 3.1 and 4.37 ± 0.3; $p<0.001$ and $p<0.0001$). ECsy reduced both parameters (88.8 ± 8.5 and 7.61 ± 0.42; $p<0.05$). The CS group showed increased MDA levels (330.7 ± 30.3) when compared with the Control group (158.9 ± 14.6; $p<0.0001$). ECsy decreased MDA levels (218.5 ± 15.7; $p<0.01$). The CS group showed decreased Nrf2 expression (56.5 ± 2.5) when compared with the Control group (92.6 ± 5.9; $p<0.0001$). ECsy increased Nrf2 expression (90.7 ± 3.6) when compared with the CS group (56.5 ± 2.5; $p<0.0001$). The CS group showed increased mean linear intercept (41.1 ± 1.0 µm) when compared with the Control group (25.29 ± 0.4 µm; $p<0.05$). ECsy decreased mean linear intercept (31.8 ± 1.0 µm) when compared with the CS group (41.1 ± 1.0 µm; $p<0.0001$). The CS group showed increased peribronchiolar collagen deposition (8.95 ± 1.2%) vs. Control group (2.84 ± 0.76%; $p<0.001$). ECsy decreased peribronchiolar collagen deposition (4.06 ± 0.8%) when compared with the CS group (8.95 ± 1.2%; $p<0.05$). **Conclusion:** ECsy reduced redox imbalance and lung remodeling in a cigarette smoke-induced emphysema model, effects that were associated with the restoration of Nrf2 expression and the reduction of oxidative and structural damage. Animal Research Ethics Committee Approval Number:16/2020.

09.046 **Evaluation of the Oxidative, Antioxidant, and Antimicrobial Activities of Isatin Acylhydrazone Derivatives**.
Almeida Filho GP[1], Rodrigues WDT[1], Sousa LVBS[1], Marreiro VS[1], Lima TCBS[1], Carneiro CA[1], Campos CENS[1], Galdino FS[1], Costa MESM[1], Sousa FB[2], Santos ESFR[3], Pessoa HLFP[1], Lima-Junior CG[2], Diniz MFFM[1], Janebro DI[1], [1]UFPB, Toxicological Testing Lab, PPG in Bioactive Natural and Synthetic Products, Brazil; UFPB, (PPgPNSB), Brazil [2]UFPB, Paraíba Lab Medicinal Organic Synthesis (LASOM), Brazil

Oxidative stress, characterized by an imbalance between the production of reactive oxygen species (ROS) and the capacity of endogenous antioxidant systems, plays a central role in the pathophysiology of several diseases. Simultaneously, the rise of bacterial resistance has become a major public health challenge, compromising the effectiveness of antimicrobial agents worldwide. In this context, isatin-derived compounds have attracted considerable attention due to their structural versatility and broad spectrum of biological activities, including antioxidant and antimicrobial properties. The present study aimed to investigate the oxidative, antioxidant, and antibacterial potential of isatin acylhydrazone derivatives (NAH1 and NAH3). Oxidative and antioxidant activities were evaluated *in vitro* using human erythrocytes from blood groups A+, B+, and O+. Methemoglobin (MetHb) formation was used as a biomarker of oxidative stress and quantified by spectrophotometry at wavelengths of 540 and 630 nm. Antioxidant capacity was assessed following oxidative stress induction with phenylhydrazine. Antibacterial activity was determined by the Minimum Inhibitory Concentration (MIC) assay using the broth microdilution method against Gram-positive and Gram-negative bacterial strains, including resistant isolates. Data were analyzed by analysis of variance (ANOVA) followed by Tukey's post hoc test, adopting a significance level of $p < 0.05$. The results demonstrated that NAH1 and NAH3 did not exhibit significant antibacterial activity against the tested strains, even at high concentrations (1024–4 µg/mL), indicating the absence of inhibitory effects under the evaluated experimental conditions. Furthermore, no significant increase in MetHb formation was observed, evidencing the lack of relevant pro-oxidant activity. Conversely, both compounds exhibited significant antioxidant activity, as demonstrated by the reduction of MetHb levels compared with the positive control, particularly in erythrocytes from blood groups B+ and O+, displaying a dose-dependent profile. In summary, although the isatin acylhydrazone derivatives did not demonstrate antibacterial efficacy under the tested conditions, the findings indicate a favorable redox safety profile associated with significant antioxidant potential. These results highlight the importance of further investigations using different biological models, especially in the context of oxidative stress-related diseases, contributing to the development of novel therapeutic candidates. Funding: National Council for Scientific and Technological Development (CNPq). **Acknowledgments:** Federal University of Paraíba (UFPB), LASOM-PB, and LABETOX.

09.047 **Preventive and Therapeutic Actions of *Spondias tuberosa* Arruda Extract on Diabetes-Associated Lung Injury**. Fernandes HEO[1], Albuquerque ECS[1], Pires LAB[1], Sena VNF[1], Felipe FD[1], Vieira RR2, Santos DD2, Araújo IGA3, Gil CD2, Medeiros KCP[1] [1]UFRN, PPG Structural and Functional Biology, Brazil, [2]Unifesp, Brazil, [3]UFPB, PPG in Bioactive Natural and Synthetic Products, Brazil

Diabetes mellitus (DM) is a chronic disease characterized by hyperglycemia, leading to systemic homeostatic disruptions, including damage to the respiratory system. Current therapies are associated with several adverse effects, highlighting the need for alternative therapeutic approaches. The extract of *Spondias tuberosa* Arruda (ExSt), a plant native to the Brazilian Caatinga biome, has demonstrated antioxidant, anti-inflammatory, and antidiabetic properties, representing a promising therapeutic alternative for diabetes management. **Objectives:** To evaluate the effect of hydroalcoholic extract of ExSt on metabolic parameters and lung morphology in streptozotocin (STZ)- induced diabetic rats. **Methods:** Forty male Wistar rats were divided into five experimental groups (CEUA/UNIFESP protocol: 5495290524): Control: healthy animals; Diabetic (DM); PRE/DM: preventive treatment; and TER/DM: therapeutic treatment. Diabetes was induced using streptozotocin (65 mg/kg, i.p.). ExSt (100 mg/kg, p.o.) was obtained from the fruit peels hydroalcoholic extraction and administered for seven consecutive weeks during both the pre- diabetic period and therapeutic treatment groups. Serum and lung samples were collected for preclinical, biochemical, and morphological analyses. **Results:** Preclinical analyses demonstrated that diabetic animals exhibited hyperglycemia, polydipsia, polyphagia, and significant weight loss compared with the control group. ExSt treatment significantly reduced water intake (PRE/DM: 21 ± 20.21mL; TER/DM: 19 ± 20.21 mL) compared with the excess observed in the DM group (DM: 28.3 ± 4.5 mL). ExSt treatment improved some biochemical and morphological parameters. ExSt significant reduction in LDL (PRE/DM: 11.2 ± 4.8 mg/dL; TER/DM: 13.4 ± 3.2 mg/dL and DM: 20.19 ± 9.5 mg/dL) and ALT levels (PRE/DM: 62 ± 20.21 mg/dL; TER/DM: 58 ± 20.21 mg/dL and DM: 85.2 ± 18.5 mg/dL), however, there was no significant reduction in glucose, triglycerides and cholesterol in the two treated groups. Morphological analysis of the lung revealed that ExSt increased the alveolar air space area (PRE/DM: 17010 ± 380 um 2 ; DM: 1299 ±360 um 2) in HE staining, reduced fibrosis accumulation (PRE/DM: 83± 12 u.a; TER/DM: 78±15 u.a; DM: 97 ±15 u.a) in Masson's trichrome staining. **Conclusion:** These findings demonstrate the potential of both preventive and therapeutic ExSt treatment as an alternative therapeutic strategy for diabetes mellitus, supporting the use of bioactive compounds derived from the diverse Brazilian flora. Furthermore, this study reinforces the therapeutic potential of Brazilian medicinal plants as valuable sources of bioactive compounds for the development of complementary strategies against diabetic complications, encouraging further investigations into natural products.

09.048 **Antimicrobial and Antibiofilm Potential of Jupati Oil** (*Raphia taedigera*)**: Cytotoxicity Profile and Selectivity Index Assessment**. Lacerda AF[1,3], Alves ARS[1,3], Souza PHO[2], Cunha DBL[2], Alves RV[2], Gadelha TS[2], Faheina-Martins GV[2], Vasconcelos U[2,3], Travassos RA[1,2,3]. [1]UFPB, Lab FarmacoBiotecnologia (FarmaBio), Brazil; [2]UFPB, Graduate Program in Cellular and Molecular Biology (PPgBCM), Brazil; [3]UFPB, Centro de Biotecnologia (CBiotec), Brazil.

Introduction: Antimicrobial resistance is one of the major global public health threats, aggravated by the formation of biofilms, which are structures that increase microbial tolerance and reduce the effectiveness of conventional treatments. In this context, natural products, such as plant-derived oils, stand out as promising sources of bioactive molecules with antimicrobial and antibiofilm potential. Therefore, this study aimed to evaluate the antimicrobial activity of Jupati oil against clinically relevant microorganisms, as well as to investigate its mechanisms of action, its interference with biofilm formation, and its cytotoxicity profile. **Methods**: Antimicrobial activity was determined using the microdilution method against *E. coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Staphylococcus aureus* ATCC 13150, and *Candida albicans* ATCC 76645. Biofilm inhibition assays were performed using crystal violet staining. The mechanism of action was investigated using sorbitol assays to evaluate possible effects on the cell wall. Cytotoxicity was assessed using the MTT assay in HEK-293 cells. The selectivity index (SI) was calculated as the IC_{50}/MIC ratio, using the IC_{50} obtained in HEK-293 cells and the MIC value determined for each microorganism. All experiments were performed in triplicate in at least three independent assays. Data were expressed as mean ± standard deviation (SD) and analyzed by one-way ANOVA followed by Bonferroni's post hoc test, with of $p < 0.05$ considered statistically significant. **Results:** Jupati oil showed significant antimicrobial activity, with MIC values of 1 µg/mL for *E. coli* and *C. albicans*, 2 µg/mL for *P. aeruginosa*, and 64 µg/mL for *S. aureus*. Strong inhibition of biofilm formation was observed. The sorbitol protection assay suggested a possible interaction with cell wall-related mechanisms. In addition, Jupati oil showed low cytotoxicity in HEK-293 cells, with IC_{50} values above 1000 µg/mL. The selectivity index indicates moderate high selectivity against *S. aureus* (SI = 15,6) and very high selectivity against *C. albicans*, *P. aeruginosa* and *E. coli* (SI ^{3} 100, for both). Vehicle control assays (DMSO) showed no intrinsic antimicrobial activity under the experimental conditions, indicating that the biological effects observed were attributable to Jupati oil rather than to the solvent system. **Conclusion:** Jupati oil demonstrated broad-spectrum antimicrobial and antibiofilm activity associated with low cytotoxicity *in vitro*, highlighting its potential as a promising source of compounds for the development of new antimicrobial strategies.

09.050 **Antifungal and Antibiofilm Activity of Nanoencapsulated Oregano** (*Origanum vulgare* L.) **Essential Oil against Clinically Relevant Yeasts**. Alves ARS[1], Pessoa JVA[1], Oliveira-Filho JMD[1], Azevedo KMS[1], Lacerda AF[1,2], Formiga ALD[3]; Santos LFA[3], Lima EO[3], Vasconcelos U[2,3], Júnior FHX[3], Travassos RA[1,2]. [1]UFPB, Lab FarmacoBiotecnologia (FarmaBio), Brazil; [2]UFPB, Graduate Program in Cellular and Molecular Biology, Brazil; [3]UFPB, Graduate Program in Bioactive Natural and Synthetic Products, Brazil.

Introduction: Antimicrobial resistance is a major global health challenge associated with recurrent and difficult-to-treat infections. *Origanum vulgare*, widely used in traditional medicine, produces an essential oil containing bioactive compounds with relevant. However, its instability and low aqueous solubility may limit its therapeutic applications. In this context, nanoencapsulation emerges as a strategy with the potential to improve the antimicrobial profile. **Objectives:** This study aimed to investigate whether nanoencapsulation enhances the antifungal and antibiofilm activities of oregano essential oil against clinically relevant yeasts and to explore the potential involvement of the fungal cell wall in its mechanism of action. **Methods:** The biological activities of free oregano essential oil (OEO) and OEO-loaded polymeric nanocapsules (NPCOEO) against the *Candida tropicalis* ATCC 13803, *Candida albicans* ATCC 10231, and *Cryptococcus neoformans* ATCC 66031. Antifungal activity was assessed using the broth microdilution method to determine the minimum inhibitory concentration (MIC). The potential involvement of the fungal cell wall was investigated using a sorbitol protection assay. Antibiofilm activity was assessed through tests for inhibition of biofilm formation and eradication of mature biofilms, using crystal violet. All experiments were performed in triplicate in at least three independent assays. Data were expressed as mean ± standard deviation (SD). **Results:** The MICs of free OEO against C. tropicalis, *C. albicans*, and *C. neoformans* were 512, 256, and 1024 µg/mL, respectively, whereas those of NPCOEO were 128, 64, and 256 µg/mL, respectively. Thus, nanoencapsulation decreased the MIC fourfold against all strains. The sorbitol assay increased the MIC for all strains tested, suggesting that the compound acts on the cell wall in the antifungal activity of NPCOEO. Susceptibility to the antibiofilm effects of NPCOEO varied among the strains, and active concentrations were generally higher than their respective MICs. At 4xMIC NPCOEO inhibited biofilm formation by 86.0% ± 5.4% for *C. tropicalis* and 80.1% ± 8.4% for *C. neoformans*, whereas *C. albicans* showed lower susceptibility. At the same concentration, NPCOEO reduced preformed biofilms of *C. tropicalis* and *C. neoformans* by 48.4% ± 3.2% and 63.7% ± 4.5%, respectively. No reduction in preformed *C. albicans* biofilms was observed at the concentrations tested. **Conclusion:** Nanoencapsulation enhanced the *in vitro* antimicrobial activity of oregano essential oil against all tested yeasts. NPCOEO also inhibited biofilm formation and reduced preformed biofilms, particularly those of *C. tropicalis* and *C. neoformans*. These findings support further investigation of NPCOEO as a potential complementary strategy for controlling clinically relevant yeasts and their biofilms.

09.051 **Renoprotective Action of Extract of *Spondias tuberosa* Arruda: Morphological Analysis in Experimental Diabetic Nephropathy**. Melo MEG[2] Sena VNF[1] Pires LAB[1] Felipe FD[2] Albuquerque[1] ECS Ladd FWL[3] Medeiros KCP[3] [1]UFRN, Center for Biosciences, Graduate Program in Biology Structure and Function, Brazil. [2]UFRN, Center for Biosciences, Brazil. [3]UFRN, Center for Biosciences, morphology Dept, Brazil.

Introduction: Diabetic nephropathy (DN) is a major microvascular complication of Diabetes Mellitus (DM), characterized by progressive structural renal damage and high morbidity. Due to the limitations and adverse effects of conventional therapies, medicinal plants have emerged as promising complementary therapeutic alternatives. *Spondias tuberosa* Arruda, popularly known as "umbu," is a native Brazilian species traditionally used in folk medicine to treat DM; however, its effects on renal morphology in DN have been insufficiently investigated. **Objectives:** To evaluate the renoprotective effects of the hydroalcoholic extract of *Spondias tuberosa* Arruda (ExSt) on renal morphological alterations using histopathological, stereological, and morphometric analyses in rats with streptozotocin-induced diabetic nephropathy. **Methods:** Forty-four male Wistar rats (CEUA: 319.056/2022) were used and distributed into the following groups: GC, normoglycemic animals; DM, hyperglycemic animals; EX, normoglycemic animals treated with ExSt; DMEX, hyperglycemic animals treated with ExSt; and DMIN, hyperglycemic animals treated with insulin. Treatment with ExSt (500 mg/kg, orally) and insulin (10 IU) was administered daily for 30 days following diabetes induction. Blood and renal tissue samples were collected for biochemical, histopathological, and stereological analyses. **Results:** The diabetic group exhibited marked renal injury, characterized by inflammation, hemorrhage, and tubular necrosis, as well as structural damage at both cortical and glomerular levels. Stereological analyses demonstrated a reduction in the total glomerular volume within the renal cortex, whereas morphometric analysis revealed an increase in the mean volume of individual glomeruli, indicating glomerular hypertrophy. Diabetic animals also exhibited glomerular basement membrane thickening and increased renal fibrosis. ExSt treatment, while showing no effect on glucose, urea, or creatinine levels, attenuated renal structural damage by reducing histopathological alterations, preserving cortical architecture, restoring mean glomerular volume toward normal values, decreasing glomerular basement membrane thickening and renal fibrosis. **Conclusion:** These findings suggest that the ExSt may attenuate renal structural damage associated with experimental diabetic nephropathy. Furthermore, this study contributes to the growing evidence supporting Brazilian medicinal plants as sources of bioactive compounds and encourages further investigations into their potential as complementary therapeutic approaches for diabetic nephropathy.

09.052 **Bioprospecting of Hydroalcoholic Extract from the Bark of a Native Caatinga Plant: Evaluation of Toxicity and Antiangiogenic Activity**. Brito JM[1,2], Dantas MEA[1], Alves AKL[1], Silva KKF[1,3], Nascimento JRS[1,2], Andrade IA[4], Medeiros FD[4,5], Dantas BB[4,5] [1]UFCG, Curimataú Cancer Observatory (OCC), Brazil; [2]UFCG, PPGCNBiotec, Brazil; [3]UFPB, Renorbio, Brazil; [4]UFCG, Pharmacognosy and Planetary Health Research Group, Brazil; [5]UFCG, Academic Health Unit, Center for Education and Health, Brazil

Introduction: Angiogenesis, a process characterized by the formation of new blood vessels and increased metabolic support for tissues, has been linked to a group of chronic conditions known as angiogenesis-dependent diseases. In this context, medicinal plants native to the Caatinga biome are emerging as potential agents for developing new therapeutic alternatives, particularly given that this biome remains underexplored pharmacologically. **Objective:** To evaluate the effect of the hydroalcoholic extract from Ximenia americana bark (EHXa) on the modulation of angiogenesis at a subtoxic concentration. Methods: EHXa toxicity (62.5–1000 µg/mL) was assessed using an acute toxicity assay on Artemia salina nauplii and a hemolysis assay on human erythrocytes. Irritation potential was determined via the Hen's Egg Test on the Chorioallantoic Membrane (HET-CAM) method, and anti-angiogenic activity was assessed using the chorioallantoic membrane (CAM) assay, both tests utilized a concentration of 125 µg/mL, which corresponded to the highest concentration showing no evidence of toxicity in preliminary assays. Vascular parameters were quantified using ImageJ software. Data were expressed as mean ± SEM and analyzed using ANOVA followed by Tukey's test and the t-test, with significance set at $p<0.05$. **Results:** EHXa exhibited low toxicity, with an LC50 of 901.6 ± 1.2 µg/mL against A. salina nauplii after 24h; no reduction in viability was observed up to a concentration of 125 µg/mL, with viability equivalent to 99.99 ± 1.6% of the negative control (0.9% NaCl; $p>0.05$). In the hemolysis assay, at the highest concentration evaluated (1000 µg/mL), the maximum percentage was 4.60 ± 0.3%, similar to the 1.16 ± 0.08% observed in the negative control (0.9% NaCl; $p>0.05$). Thus, 125 µg/mL was selected for the HET-CAM and CAM assays. EHXa induced mild vascular reactions, specifically hyperemia and hemorrhage, with a mean irritation score of 2.58 ± 0.92, classifying it as mildly irritating. It also modulated the angiogenesis process by reducing vascular diameter (97.33 ± 0.6%) and the number of branches (95.72 ± 0.6%) after 6h of treatment compared to baseline (100%; $p<0.05$); the positive control (dexamethasone 4 mg/mL) behaved similarly, reducing vascular diameter (80.65 ± 5.8%), the number of branches (100.96 ± 4.8%), and length (99.76 ± 2.9%) after 6h. **Conclusion:** The results provide preliminary evidence of the anti- angiogenic activity of EHXa at a subtoxic concentration. Although discreet, the observed effect on vascular parameters suggests biological activity that warrants further investigation through studies involving multiple concentrations, chemical characterization of the extract, and elucidation of the mechanisms of action. **Financial support:** CNPq, CAPES, FAPESQ-PB. Ethical approval: CEP/CES-UFCG (n° 6.728.938; CAAE: 77866323.3.0000.0154).

09.053 **Attenuation of UVA-Induced Cellular Senescence Activity and Reactive Oxygen Species Production by the Hydroalcoholic Extract of *Spondias tuberosa* Leaves in Immortalized Human Keratinocytes (HaCaT)**. Souza CMO[1,2], Gomes MLC[1,2], Pereira MEM[2], Albuquerque MN[2], Farias LRT[3], Langassner SMZ[3], Oliveira GD[1,4], Nascimento YM[1,4], Veras RC[1,2], Araujo IGA[1,2], Medeiros IA[1,2] [1]UFPB, PPG in Bioactive Natural and Synthetic Products (PgPNSB), Brazil, [2]UFPB, Cardiovascular Pharmacology Lab, Institute for Drug and Medicine Research, Brazil, [3]UFRN, Pharmacognosy Lab, Brazil, [4]UFPB, Multi-user Lab for Characterization and Analysis, Brazil.

Introduction: Ultraviolet A (UVA)-induced skin photoaging affects several skin cell types, including keratinocytes, fibroblasts, and melanocytes, and is strongly associated with oxidative stress and cellular senescence. Natural products have been investigated as potential agents for preventing and/or attenuating photoaging, particularly due to their antioxidant properties. *Spondias tuberosa* is a native species of the Brazilian semi-arid region that contains bioactive compounds with antioxidant activity, such as phenolics and flavonoids. Given the central role of oxidative stress in skin photoaging, cellular senescence, and the accumulation of UV-induced cellular damage, it is hypothesized that the hydroalcoholic extract of S. tuberosa leaves may exert protective effects by modulating these processes and attenuating alterations associated with photoaging. **Objectives:** To evaluate the anti-photoaging potential of the lyophilized hydroalcoholic extract of S. tuberosa leaves (EHFST-L) in an *in vitro* model of UVA-induced photoaging in HaCaT cells. **Methods:** Phytochemical characterization was conducted by ^{1}H NMR spectroscopy. HaCaT cells were cultured and exposed to UVA radiation for 40 min (13 J/cm^2). Experiments were performed in two groups: a baseline group consisting of non-irradiated HaCaT cells (control, CTL) treated or not with EHFST-L (0.01–1.0 µg/mL), and an irradiated group consisting of cells exposed to UVA radiation and treated or not with EHFST-L, with evaluations performed after 24 and 48 h. Cell viability was assessed using the MTT assay, reactive oxygen species (ROS) production by the dihydroethidium (DHE) fluorescence assay, and cellular senescence by senescence-associated β-galactosidase (SA-β-gal) activity. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test, with $p < 0.05$ considered statistically significant. **Results:** Chemical analysis revealed the presence of phenolic compounds, including flavonoids such as rutin and isoquercitrin, as well as phenolic acids such as caffeic acid. In the baseline group, EHFST-L did not significantly alter SA-β-gal activity, ROS levels, or cell viability. In the irradiated group, UVA exposure significantly increased SA-β-gal activity compared with CTL cells. Treatment with EHFST-L significantly reduced SA-β-gal activity at all tested concentrations ($p < 0.05$ vs. UVA), suggesting attenuation of cellular senescence. This effect was accompanied by reduced ROS production, without changes in cell viability. **Conclusion:** EHFST-L attenuated UVA-induced cellular senescence-associated β-galactosidase activity in HaCaT cells, possibly through modulation of oxidative stress. These findings suggest a potential protective effect of the extract against photoaging-related cellular alterations, although further studies are required to better elucidate the underlying mechanisms involved.

09.054 *Spondias tuberosa* **Arruda Extract Attenuates Pulmonary Oxidative Stress and Modulates NF-κB/P-JNK Signaling in Streptozotocin-Induced Diabetic Mice**. Albuquerque ECS[1], Pires LAB[1], Sena VNF[1], Donato FF[1], Albuquerque IA[2], Vieira RR[3], Santos DD[3], Gil CD[3], Medeiros KCP[1]. [1]UFRN, PPG Structural and Functional Biology, Brazil, [2]UFPB, Dept Pharmaceutical Sciences, Brazil [3]Unifesp, PPG Structural and Functional Biology, Brazil.

Introduction: Diabetes mellitus (DM) is a chronic metabolic disease characterized by persistent hyperglycemia resulting from impaired insulin secretion or reduced insulin action, leading to systemic toxicity and damage to several organs, including the lungs. Current diabetes therapy, particularly for type 1 diabetes mellitus, is based on the administration of exogenous insulin combined with antidiabetic agents. Although effective in glycemic control, these treatments may cause adverse effects, highlighting the need for the development of complementary and alternative therapies. *Spondias tuberosa* Arruda extract (ExSt), popularly known as “Umbuzeiro” and endemic to northeastern Brazil, has demonstrated antioxidant and anti-inflammatory properties in different metabolic disorders, including diabetes. **Objectives:** To evaluate the antioxidant and anti-inflammatory effects of *Spondias tuberosa* Arruda extract in an experimental model of streptozotocin-induced diabetes mellitus. **Methods:** Forty C57BL/6 mice approved by the CEUA/UNIFESP Ethics Committee (protocol no. 5495290524) were used in this study. Diabetes was induced by streptozotocin (65 mg/kg, intraperitoneally). Preventive and therapeutic treatment with ExSt (100 mg/kg, orally) was administered for seven weeks. The animals were divided into four experimental groups: control (CT), diabetic (DM), preventive treatment diabetic group (DMPRE), and therapeutic treatment diabetic group (DMTER). Serum and lung tissue samples were collected for analysis. **Results:** Oxidative stress evaluation demonstrated a significant reduction in fluorescence in the treated groups (DMPRE and DMTER) compared with the diabetic group, indicating lower oxidative stress levels. Immunohistochemical analysis revealed a significant decrease in catalase and CD68 density, especially in the DMTER group. Molecular analysis by Western blot showed that preventive treatment increased MMP-2 expression and reduced the inflammatory markers P-JNK and NF-κB, whereas therapeutic treatment reduced the expression of all evaluated markers. **Conclusion:** These findings demonstrate that ExSt was able to modulate enzymes associated with oxidative stress and inflammatory markers in the lung tissue of diabetic animals, highlighting its potential as a complementary therapy for the treatment of diabetes mellitus. CEUA/UNIFESP Ethics Committee (protocol no. 5495290524). This study was supported by the Brazilian Coordination for the Improvement of Higher Education Personnel (CAPES) - Finance Code 001

09.055 **Efficacy of *Cannabis sativa* L. Associated with Phonophoresis on Oxidative Stress in Skeletal Muscle of Rats**.
Santana RAN[1], Sousa DS[2], Lima MM[1], Nascimento VS[1], Azevedo IO[1], Santos LB[1], Oliveira ED[1], [1]UFS-PROBIO-Brasil, [2]UFS-Renorbio-Brasil

Musculoskeletal injuries are associated with oxidative stress and increased lipid peroxidation, contributing to tissue damage and impaired muscle recovery. *Cannabis sativa* L. compounds, especially THC and CBD, exhibit antioxidant and anti-inflammatory properties. In this context, pulsed therapeutic ultrasound (PTU) may enhance transdermal drug delivery through phonophoresis, improving the therapeutic effects of Full Spectrum formulations. Therefore, the aim of this study was to determine the effectiveness of topical administration of a hydrogel containing Cannabis sativa L. Full Spectrum oil associated with phonophoresis on oxidative stress-related variables in an experimental muscle injury model. Forty male Wistar rats weighing between 250 and 300 g were randomly divided into five groups (n = 8): control group (CTRL), muscle injury group (MI), pulsed therapeutic ultrasound group (PTU), pulsed therapeutic ultrasound associated with Full Spectrum gel group (PTU+CS), and topical Full Spectrum gel group (CS). Muscle injury was induced in the gastrocnemius muscle using a mechanical impact device consisting of a 0.459 kg mass released from a height of 18 cm, generating 0.811 J of energy. The animals were anesthetized with ketamine (90 mg/kg) and xylazine (25 mg/kg). Ninety-eight hours after injury induction, the animals were euthanized, and the gastrocnemius muscle was collected for biochemical analyses. Lipid peroxidation was evaluated by thiobarbituric acid reactive substances (TBARS) formation, while superoxide dismutase (SOD) and catalase (CAT) activities were determined by spectrophotometric methods. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test, considering $p < 0.05$. The physicochemical analysis of the gel demonstrated pH and density stability after freeze–thaw cycles. The MI group showed a significant increase in MDA levels (6.533 ± 1.059 nmol MDA/mg protein) compared to CTRL (1.580 ± 0.4092 nmol MDA/mg protein; $p < 0.05$). In contrast, the PTU+CS group demonstrated a significant reduction in MDA levels (0.5180 ± 0.1216 nmol MDA/mg protein; $p < 0.05$ vs MI). Treatment with the Full Spectrum gel, either alone or associated with ultrasound, significantly reduced SOD activity compared to the MI group. CAT activity also demonstrated a significant reduction in treated groups compared to untreated injured animals. These findings suggest that a hydrogel containing *Cannabis sativa* L. Full Spectrum extract, containing THC and CBD at a 1:1 ratio, associated or not with pulsed therapeutic ultrasound, may represent a promising strategy to reduce lipid peroxidation and modulate antioxidant responses in skeletal muscle injury.

09.056 **Topical Anti-Inflammatory Potential of Cannabigerol in Experimental Models of Cutaneous Inflammation** *in vivo* **and** *in vitro*. Silva NAA, Michelisa A, Sampaio EDSR, Christo EB, Lopes RV, Cabrini DA, Otuki MF UFPR, Dept Pharmacology, Graduate Program in Pharmacology, Brazil

Introduction: Cannabigerol (CBG) is a non-psychotropic phytocannabinoid with potential anti-inflammatory activity; however, its effects on inflammatory skin diseases remain poorly understood. In addition, its low systemic bioavailability suggests that topical formulations may represent a promising therapeutic strategy.

Objective: To evaluate the anti-inflammatory potential of CBG in experimental models of acute and chronic cutaneous inflammation, as well as its effects on cell proliferation and migration *in vitro*. **Methods:** In the acute model, male and female BALB/c mice (15–20 g) received topical application of TPA (2.5 µg/20 µL) to induce ear edema, followed by treatment with different doses of CBG (0.1, 0.3, or 1 mg/ear) or hydrocortisone (positive control, 20 mg/g). Ear thickness was evaluated after 6 and 24 h, followed by histological analysis. In the chronic model, animals received repeated TPA applications on alternate days for 9 days, with topical treatment starting on day 5. CBG was also tested in human keratinocytes (HaCaT) and murine fibroblasts (3T3) to evaluate cell viability, proliferation, and migration. **Results:** In the acute model, CBG at a dose of 1 mg/ear significantly reduced ear edema at 6 h, promoting a reduction of approximately 24.5 ± 7.0% compared to the control group, while hydrocortisone reduced edema by 74.0 ± 4.7%. The other doses did not significantly alter edema. After 24 h, CBG significantly reduced edema by 37.5 ± 7.0% and 32.1 ± 6.7% at doses of 0.3 and 1 mg/ear, respectively, whereas hydrocortisone inhibited edema by approximately 87.4 ± 5.7%. Histological analysis demonstrated a reduction in total ear thickness of approximately 38.5 ± 6.3% and 44.4 ± 5.5% with CBG at 0.3 and 1 mg/ear, respectively, in addition to a reduction in dermal inflammatory infiltrate of 59.5 ± 2.0% and 73.8 ± 2.7%, respectively, at the same doses. In contrast, in the chronic model, CBG significantly worsened ear edema from the seventh experimental day onward. Treatment with CBG at 0.3 mg/ear increased ear thickness by approximately 49.1 ± 22.9%, 41.7 ± 18.5%, and 27.9 ± 16.3% on days 7, 8, and 9, respectively. Likewise, the 1 mg/ear dose increased edema by 79.3 ± 34.8%, 99.9 ± 37.2%, and 44.2 ± 28.7% during the same periods, respectively. As expected, hydrocortisone reduced edema by approximately 73.3 ± 13.1% on day 7, 74.6 ± 11.9% on day 8, and 89.6 ± 9.4% on day 9. Evaluation of the analyzed organs (thymus, pancreas, and adrenal glands) showed that CBG did not induce alterations, unlike hydrocortisone. *In vitro* assays demonstrated that CBG induced cytotoxicity only at concentrations above 30 µM in both HaCaT and 3T3 cells. Direct treatment of these cells with non-toxic concentrations (0.1–10 µM) did not alter basal proliferation or cell migration. **Conclusion:** These preliminary results demonstrate that CBG exhibits topical anti-inflammatory activity in an acute model of cutaneous inflammation by reducing edema and dermal inflammatory infiltrate. However, in the chronic model, the compound aggravated the inflammatory response, indicating that its effects may vary depending on the pathophysiological context. Therefore, further studies are required to elucidate the mechanisms involved and define the therapeutic potential of CBG in inflammatory skin diseases.

09.057 **Evaluation of the Anti-Inflammatory Potential of an Oxygenated Withanolide Isolated from *Athenaea velutina* in LPS-Stimulated Macrophage Cells: Role of NO and IL-1beta**. Ribeiro MS[1], Da Silva LR[1], Rocha LM[1], Rocha KAD[2], Silva JGP[1], Procopio GS[1], Pessoa ODL[2], Santos FA[1]. [1]UFC, Faculty of Medicine, Dept Physiology and Pharmacology. [2]UFC, Science Center, Dept Organic and Inorganic Chemistry.

Introduction: *Athenaea velutina*, popularly known as "Jurubeba-de-morcego", is a Brazilian endemic plant belonging to the Solanaceae family. This species is known to contain compounds called withanolides, which are characterized by the presence of C28 steroidal δ- or γ-lactones in their chemical structure. These molecules exhibit several biological activities, including anti- inflammatory, antioxidant, and immunomodulatory effects. **Objective:** To evaluate the anti-inflammatory potential of a oxygenated withanolide (AV11), isolated from *A. velutina*, in lipopolysaccharide (LPS)-stimulated RAW 264.7 cells through nitric oxide (NO) and IL-1beta quantification. **Methods:** AV11 (27-dehydroxy-2,3-dihydro-24α,25α-epoxy-15-hydroxywithaferin A) was isolated from the hexane/ethyl acetate extract of *A. velutina* leaves collected in Guaramiranga, Ceará, Brazil (SisGen no. ACBDA8A). RAW 264.7 macrophages were cultured in DMEM supplemented with 10% fetal bovine serum and antibiotics at 37 °C and 5% CO_2. Cell viability was assessed by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay after treatment with AV11 (5–200 µM) for 24 h. For anti-inflammatory evaluation, cells were pretreated with AV11 (25–100 µM) for 1 h and stimulated with LPS (1 µg/mL) for 24 h. Nitrite production was determined by the Griess reaction, and IL-1beta levels were measured by ELISA according to the manufacturer's instructions. Dexamethasone (10 µM) was used as a positive control, and vehicle-treated cells (0.2% DMSO) served as controls. **Results:** AV11 at concentrations ranging from 0.78 to 100 µM did not affect RAW 264.7 cell viability compared with the control group, whereas treatment with 200 µM AV11 reduced cell viability by 48.8%. AV11 at 25, 50, and 100 µM (18.93 ± 3.04, 8.79 ± 1.36, and 6.52 ± 0.40 µM nitrite/mL, respectively) significantly ($p < 0.05$) reduced nitrite production in LPS-stimulated macrophages compared with the control group (39.20 ± 4.78 µM nitrite/mL). Likewise, AV11 at 25, 50, and 100 µM significantly ($p < 0.05$) reduced IL-1beta levels by 48.5%, 68.2%, and 86.1%, respectively, compared with the LPS-stimulated group (14.37 ± 1.52 pg/mL). The positive control, dexamethasone (10 µM), significantly ($p < 0.05$) reduced nitrite and IL-1beta levels by 48.4% and 51.9%, respectively. **Conclusion:** AV-11 demonstrated potential anti-inflammatory activity by reducing NO and IL-1beta levels, indicating its potential for further studies investigating the mechanisms underlying its anti-inflammatory effects.

09.058 **Multisystemic Effects of *Hovenia dulcis* in a Complex Animal Model of Metabolic Syndrome: A Multitarget Perspective**. Higashijima AN[1], Bezerra CS[1], Santa Clara-Amorim RC[1], Ribeiro RRM[1], Silva GR[1], Marcon MV[2], Barboza LN[3], Souza P[4], Sari MHM[5], Farago PV[2], Lívero FADR[1] [1]UFPR, Graduate Program in Pharmacology, Curitiba, Brazil; [2]UEPG, Graduate Program in Pharmaceutical Sciences, Ponta Grossa, Brazil; [3]UNIVEL, Biochemistry Lab, Cascavel, Brazil; [4]Univali, Graduate Program in Pharmaceutical Sciences, Itajaí, Brazil; [5]UFPR, Graduate Program in Pharmaceutical Sciences, Curitiba, Brazil

Introduction: Metabolic syndrome (MS) comprises a cluster of interrelated comorbidities. Due to its complexity, management relies on polypharmacy, while the lack of representative animal models limits new therapy development. Medicinal plants emerge as an alternative to the "one drug, one target" paradigm, owing to metabolites acting on multiple pathological pathways. Hovenia dulcis Thunb. (Japanese raisin tree) peduncles are traditionally used as a hepatoprotective agent after excessive alcohol intake. Although no studies have specifically investigated its use in MS, the reported preclinical hypolipidemic and antidiabetic effects suggest this species as a candidate for MS treatment. **Objectives:** Evaluate the systemic effects of the ethanol-soluble fraction of H. dulcis peduncles (HD) in a multitarget animal model of MS. **Methods:** Male spontaneously hypertensive rats received a cholesterol-enriched diet (0.5%) ad libitum and fructose (20%, ~50 mL/day) for 7 weeks (CEUA/UFPR no. 1656/2025). During the final 3 weeks, animals were randomized (n = 5-6) and treated daily by gavage with vehicle (negative control; C-), HD (30, 100, or 300 mg/kg), or simvastatin (2.5 mg/kg) plus enalapril (15 mg/kg) (positive control). Male Wistar rats receiving filtered water served as the basal group. Blood pressure (tail-cuff), oral glucose tolerance test (OGTT), morphometric indices, serum biochemistry, organ weights, and hepatic lipids were assessed. **Results:** The model induced dyslipidemia, hyperglycemia, hepatic, cardiac, and renal alterations. HD showed a hormetic dose-response curve, with the 30 mg/kg dose producing the most prominent effects. HD30 improved lipid, glycemic, and inflammatory parameters, normalizing serum total cholesterol, VLDL, LDL, HDL, triglycerides, and OGTT glucose levels, while partially restoring fasting glucose, IL-6, and TNF-α. Cardioprotective effects included complete restoration of systolic and diastolic blood pressure and relative heart weight. HD30 also normalized ALT, γ-GT, and relative liver weight, while partially reducing AST and hepatic lipid content. In addition, HD30 exerted nephroprotective effects, normalizing creatinine and relative kidney weight, while partially reducing urea levels. Finally, HD30 markedly reduced the abdominal obesity index, atherogenic index of plasma, and cardiac risk ratio, important indicators of cardiovascular and metabolic protection. At 100 and 300 mg/kg, effects were weaker and mostly partial: systolic blood pressure normalization was lost (comparable to C-), while diastolic blood pressure, relative heart weight, and HDL were only partially restored, and ALT and AST were not reduced at 100 mg/kg, confirming the inverted-U profile. **Conclusion:** These findings demonstrate the pharmacological potential of HD across multiple axes of MS pathophysiology. **Financial support:** The authors thank the Coordination for the Improvement of Higher Education Personnel (CAPES - 88887.004084/2024) for providing fellowships.

09.059 **Caulerpin Modulates the Calcineurin-NFAT Signaling AXIS and Attenuates T-Cell Activation in Human Peripheral Blood Mononuclear Cells**. Santos-Junior SS, Dos Santos JSP, Correia AGV, Oliveira VS, Silva DKC, Souza CVC, Santos-Filho OA, Martinez ST, Soares MBP, Meira CS Fiocruz-BA, Salvador, UNEB, Salvador, SENAI CIMATEC-BA, Salvador, UFRJ-RJ, Rio de Janeiro FURG-RS, Rio Grande do Sul.

Introduction: The calcineurin-NFAT signaling pathway is a central regulator of T-cell activation, proliferation, and effector function. Persistent activation of this pathway contributes to the pathogenesis of several inflammatory and autoimmune diseases. Although calcineurin inhibitors such as cyclosporine and tacrolimus are clinically effective, their long-term use is associated with significant toxicity. Caulerpin, a marine bisindole alkaloid isolated from algae of the genus Caulerpa, has demonstrated anti-inflammatory properties in experimental models; however, its effects on human lymphocyte signaling pathways remain poorly understood. **Objectives:** To investigate the immunomodulatory effects of caulerpin on human PBMCs and its impact on the calcineurin-NFAT signaling pathway. **Methods:** Human PBMCs were stimulated with phytohemagglutinin (PHA) and treated with different concentrations of caulerpin. Cell viability was assessed using the MTT assay and propidium iodide staining by flow cytometry. Cell proliferation was assessed using the sulforhodamine B assay. The levels of pro-inflammatory cytokines was assessed by ELISA. The cell cycle and immunophenotyping were analyzed by flow cytometry. Calcineurin enzymatic activity was determined by a colorimetric assay. Gene expression analysis was performed by real-time quantitative PCR. *in silico* molecular docking studies were conducted to evaluate the interaction between caulerpin and calcineurin. Statistical significance was defined as $p \leq 0.05$. **Results:** Caulerpin did not affect PBMC viability at the tested concentrations, maintaining viability above 92%. However, it significantly reduced PHA-induced lymphocyte proliferation, reaching a maximum inhibition of 79%, and promoted cell-cycle arrest in the G1 phase, increasing the proportion of cells in this phase from 70.8% to 89.3%. Functional analyses revealed marked reductions in IL-2- and IFN-γ-producing T cell populations, with CD3+IFN-γ+ and CD3+IL-2+ populations decreasing by approximately 64% and 42%, respectively, indicating suppression of Th1- and Tc1-associated responses. Furthermore, caulerpin inhibited calcineurin activity and downregulated key components of the calcineurin-NFAT pathway, including CALM2/3, PPP3C isoforms, NFAT1/2/4, and NFAT-regulated genes involved in T-cell activation, such as IL2, IFNG, IL2RA, CD28, and CCL5. Genes associated with TCR, PI3K/AKT, and inflammatory signaling were also significantly downregulated. Molecular docking analyses demonstrated favorable interactions between caulerpin and calcineurin, with a ChemPLP score of 69.46, supporting a potential direct inhibitory mechanism. **Conclusion:** These results highlight caulerpin as a promising marine-derived immunomodulatory molecule and a potential lead compound for the development of new therapies targeting immune-mediated inflammatory diseases.

09.060 **Protective Effects of *Agaricus blazei* Polysaccharides on Cell Viability and Mitochondrial Membrane Potential in Human Renal Tubular Cells Subjected to Hypoxia-Reoxygenation**. Lima EQ[1], Ribeiro MENP[2], Menezes RRPPB[3], Queiroz MGR[3], Aragão DA[3], Magalhães EP[3], Sousa VQ[4], Sampaio TL[3], Martins AMC[1] [1]PPG in Pharmacology, UFC, Brazil. [2]PPG in Chemistry, UFC, Brazil. [3]PPG in Pharmaceutical Sciences, UFC, Brazil. [4]Undergraduate Program in Pharmacy, UFC, Brazil.

Acute Kidney Injury (AKI) is a major health condition that can be caused by multuple factors, including ischemic/reperfusion injury, often related to the transport of kidneys for transplantation. Ischemia refers to the loss of bloodflow, while reperfusion is the rapid restoration of oxygen supply. This pathogenesis is associated with oxidative stress induction, leading to cell death through several mechanisms, like the disruption of the mitochondrial membrane potential and triggering programmed cell death. Natural compounds have been investigated as sources of bioactive molecules with antioxidant and cytoprotective potential. *Agaricus blazei Murril*l has attracted attention due to its antioxidant effects attributed to β-D-glucans, a class of polysaccharides. This study aimed to evaluate the effects of this *A. blazei Murrill* polysaccharides (AbMP) on cell viability and mitochondrial function in human renal tubular cells (HK-2) subjected to an *in vitro* model of ischemia- reperfusion (hypoxia-reoxygenation) injury. For this purpose, HK-2 cells were seeded into 24-well plates, incubated overnight, and culture medium was replaced with glucose-, pyruvate-, and fetal bovine serum-free DMEM. The plates were then maintained under hypoxic conditions in an anaerobic chamber at 37°C for 12 h, followed by complete medium and oxygen restoration. After 4h, the cells were treated with 50 µg/mL or 100 µg/mL of AbMP. Aerobic cells served as controls. After 24h of treatment, the cells were detached, centrifuged, washed, and stained with 7-AAD/Annexin V or Rhodamine 123 fluorochromes. Finally, the samples were analyzed in triplicate using a BD FACSCalibur™ flow cytometer. Statistical analysis was performed using GraphPad Prism 6 with one-way ANOVA followed by Bonferroni's post hoc test. Results were expressed as mean ± SEM, and a p-value < 0.05 was considered statistically significant. Rhodamine 123 results were evaluated by Relative Fluorescence Intensity (RFI), using the control group as the reference (1.0). Cells subjected to I/R showed a significant increase in the population stained only with Annexin V (13.30 ± 0.3%) compared with the control group (7.36 ± 0.5%). In contrast, post-treatment with 50 µg/mL AbMP reduced the percentage of Annexin V-positive cells (9.91 ± 0.3%), with a more pronounced effect observed at 100 µg/mL (7.13 ± 0.3%). Double-positive cells, consistent with late apoptosis or secondary necrosis, increased after I/R (9.80 ± 0.3% vs. 5.77 ± 0.4% of control group), and was reduced in the group treated with 100 µg/mL AbMP (5.75 ± 0.2%). Rhodamine 123 staining showed that treated cells (50 µg/mL = 0.88; 100 µg/mL = 1.2) displayed relative fluorescence intensities closer to the control group (1.0) than untreated I/R cells (0.80), suggesting preservation of mitochondrial transmembrane potential following AbMP treatment. These findings suggest apoptotic pathways may contribute to the cell death process induced by hypoxia-reoxygenation. Moreover, AbMP treatment promoted cellular and mitochondrial parameters closer to those observed in the aerobic control group, indicating a potential cytoprotective effect, although further studies are needed.

09.061 **Molecular Docking of Crotamine with the LDL Receptor: an Investigation of Animal Metabolism Regulation**.
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Introduction: Crotamine is a cationic polypeptide from *Crotalus durissus terrificus* venom, structurally similar to human β-defensins. Beyond its cell- penetrating peptide (CPP) activity, it reduces total cholesterol, LDL, triglycerides and white adipose tissue (WAT), while increasing HDL, basal metabolism, brown adipose tissue (BAT) and thermogenic biomarkers (UCP1, PGC- 1α, PRDM16). Although its interaction with voltage-gated potassium channels (Kv1.3) is well documented, its metabolic mechanisms remain incompletely elucidated. Since the LDL receptor (LDLR) is critical for lipid supply to BAT thermogenesis and mitochondrial/lysosomal integrity, crotamine may interact with LDLR domains to exert its metabolic effects. **Objectives:** To evaluate *in silico* the interaction of crotamine with molecular targets (LDLR and Kv) involved in metabolic modulation. **Methods:** 3D structures (< 3 Å) were retrieved from PDB: crotamine (1Z99), LDLR (1LDL, R1 domain; 2LGP, R4-R5 domains) and Kv channel (7EJ1). Complexes were modeled using ColabFold v1.5.5 (AlphaFold-Multimer), and 200 ns molecular dynamics (MD) simulations were run on OpenMM 8.0 (CHARMM36m, TIP3P, 0.15 M NaCl, NPT 300 K/1 atm, Langevin integrator, 4 fs timestep). Trajectories were analyzed with MDTraj for potential energy, RMSD, radius of gyration (Rg), RMSF and hydrogen bonds, with VMD visualization. **Results:** The Kv1.3 channel complex (positive control) showed stable energy but high structural mobility (RMSD 25-30 Å; Rg > 45 Å), with a robust hydrogen bond network (~25 - 35 simultaneous interactions), suggesting sustained but dynamic affinity. The R1 domain complex showed low affinity: RMSD reached 12.5 - 17.5 Å, Rg peaked at 22 Å after 75 ns, and hydrogen bonds were weak and transient (1 - 4), with complete absence between 90 - 120 ns. The R4-R5 domains complex exhibited the most stable profile: RMSD stabilized at 5 - 9 Å, Rg remained constant at ~18 Å, RMSF was low (< 0.4 nm) and hydrogen bonds were consistent and uninterrupted (14 - 18 simultaneous interactions). **Conclusion:** These findings identify the R4-R5 domains of LDLR as a promising molecular target for crotamine, supporting their role in mediating its metabolic and thermogenic effects and opening new avenues for obesity-related therapeutic development. **Financial support:** FAPESP, CNPq, CAPES.

09.062 **Investigation by MTT Assay and Raman Spectroscopy of the Effects of *Caryocar brasiliense* Oil on the Viability of L929 Fibroblasts**. Lima RF[1], Reis ATF[2], Lima GMSF[3], de Lima RF[2], Carvalho TGPM[4], Barreto FS[5], Diniz Filho JFS[7], Dos Santos CC[7], Dittz Junior D[8], Garcia JBS[1], Carvalho RC[6], Andrade MS[5], Cartagenes MSS[1] [1]UFMA, LEED, PPGSAD, Brazil; [2]UFMA, LEED, PPGCS, Brazil; [3]UFMA, LEED, Pharmacy Course, Brazil; [4]UFMA, LEED, Renorbio, Brazil; [5]UFMA, PPGSAD, Brazil; [6]UFMA, Animal Facility, Brazil; [7]UFMA, Vibrational and Impedance Spectroscopy Lab, Brazil; [8]UFPI, Dept Biochemistry and Pharmacology, Brazil

Introduction: Wound healing restores tissue integrity after injury, involving inflammation, proliferation, and remodeling phases. Fibroblasts are essential for forming granulation tissue and extracellular matrix. Disruptions in this process can lead to inefficient healing or fibrosis, impacting health. In this context, plant metabolites emerge as promising alternatives due to their therapeutic potential. **Objectives:** To evaluate the cytotoxicity and biochemical alterations induced by *Caryocar brasiliense* oil in fibroblasts for its application in wound healing. **Methods:** L929 cells were cultured in DMEM (10% FBS, 37 °C, 5% CO_2). In the initial screening and dose-response curve, cells (1×10^4/well in 96-well plates) were exposed to concentrations ranging from 10 to 500 µL of *Helianthus annuus* (sunflower) and *C. brasiliense* (pequi) oils for 72 hours. Metabolic activity was assessed using the MTT assay (577 nm, Epoch spectrophotometer). Data were analyzed using GraphPad Prism 10 (One-way ANOVA, Dunnett's test), $p < 0.0001$. Molecular analysis was performed using a triple Raman spectrometer (T64000, Horiba) in single mode (532 nm laser, 14 mW), collecting spectra in the 650–1800 cm^{-1} region at multiple cellular points. Preprocessing was carried out in LabSpec 6, including cosmic ray removal and baseline subtraction. **Results:** The MTT assay demonstrated no significant cytotoxicity under all conditions, with IC_{50} values greater than 500 µg/mL. At the molecular level, Raman spectroscopy revealed crucial data on cellular integrity. Amide I (1657 and 1685 cm^{-1}) and Amide III (1231 and 1267 cm^{-1}) bands maintained their conformational profiles, indicating absence of structural toxicity or protein denaturation, thus preserving translational cellular activity. Markers showed that *C. brasiliense* oil contributes to phospholipid bilayer protection (bands at 1300 and 1445 cm^{-1}), remaining stable and equivalent to control, demonstrating no plasma membrane lysis. Therefore, *C. brasiliense* oil maintained a molecular profile similar to control, without alterations in proteins or lipids. However, H. annuus oil induced a slight increase in the phenylalanine band (1004 cm^{-1}), suggesting increased metabolic activity or protein reorganization, reinforcing the biological safety of both oils. Preservation of nucleic acid bands (787 and 1518 cm^{-1}), related to phosphate backbone of purine bases (adenine and guanine), confirmed a non-genotoxic profile, with no fragmentation or degradation of nucleic acids. **Conclusion:** *C. brasiliense* oil does not exhibit cytotoxic effects, and Raman spectroscopy confirms its high fidelity as a cytoprotective agent, maintaining membrane homeostasis and genomic stability. The oil is safe for tissue repair formulations, providing molecular support to cells during wound healing.

Keywords: *Caryocar brasiliense*; Fibroblasts; Raman Spectroscopy; Wound Healing

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09.063 **Effect of Hydroalcoholic Extract of** *Piper klotzschianum* (**Kunth**) **C. DC. on the Evaluation of Anti-Inflammatory Activity in Mice**. Silva MT[1], Silva JM[2], Nunes ERS[3], Sales MR[3], Lima JVJS[3], Jesus RA[2], Nascimento ACS[3], Aragão JMD[3], Ramos LS[3], Santos GJ[3], Fabricante JR[1] Gois AM[1], Camargo EA[3], Moraes VRS[2], Santos JR[3] [1]UFS, PPG Ciências Naturais, Brasil, [2]UFS, PPG Química, Brasil, [3]UFS, PPG Ciências Fisiológicas, Brasil.

Introduction: Inflammation is a physiological response triggered by tissue injury. Although currently available anti-inflammatory drugs are effective, their prolonged use may be associated with adverse effects. The traditional use of medicinal plants represents an important source for the discovery of novel therapeutic agents. In this context, *Piper klotzschianum* (Kunth) C.DC. has been traditionally used to treat inflammatory disorders; however, experimental evidence supporting its anti-inflammatory activity remains limited. **Objective:** To evaluate the anti-inflammatory activity of the hydroethanolic extract of *Piper klotzschianum* (HEPK) in mice subjected to 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced ear edema. **Methods:** Swiss mice (*Mus musculus*) of both sexes (25–30 g) were randomly assigned to five groups (n = 14/group): (1) TPA; (2) HEPK (0.3 mg/ear); (3) HEPK (1.0 mg/ear); (4) HEPK (3.0 mg/ear); and (5) dexamethasone (DEXA). 20 µL de TPA (1 µg/ear) was topically applied to the right ear, while acetone was applied to the left ear as the control. Five minutes later, groups 2, 3 and 4 received 10 µL of HEPK at doses of 0.3, 1.0, or 3.0 mg/ear, respectively, whereas group 5 received 20 µL of dexamethasone (0.05 mg/ear). Anti-inflammatory activity was assessed by measuring ear edema and myeloperoxidase (MPO) activity. Data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test, with statistical significance set at $p < 0.05$. All experimental procedures were approved by the Animal Ethics Committee of the Federal University of Sergipe (protocol no. 5464090925). **Results:** HEPK significantly reduced ear edema at all tested doses (0.3, 1.0, and 3.0 mg/ear) compared with the TPA group ($p < 0.0001$ for all comparisons). However, dexamethasone produced a significantly greater reduction in ear edema than HEPK ($p = 0.0470$, $p = 0.0376$, and $p = 0.0012$ for the 0.3, 1.0, and 3.0 mg/ear doses, respectively). Likewise, MPO activity, a marker of neutrophil infiltration, was significantly reduced at all HEPK doses compared with the TPA group ($p < 0.0001$ for all comparisons). Nevertheless, dexamethasone produced a significantly greater reduction in MPO activity than HEPK ($p = 0.0187$, $p = 0.0071$, and $p = 0.0041$ for the 0.3, 1.0, and 3.0 mg/ear doses, respectively). As expected, dexamethasone also significantly reduced both ear edema and MPO activity compared with the TPA group ($p < 0.0001$ and $p = 0.0069$, respectively). **Conclusion:** The hydroethanolic extract of *Piper klotzschianum* exhibited promising anti-inflammatory activity, as demonstrated by significant reductions in ear edema and MPO activity compared with the TPA group. Although dexamethasone showed greater efficacy, all tested doses of HEPK produced consistent anti-inflammatory effects, highlighting its potential as a source of bioactive compounds for the development of novel anti-inflammatory agents. **Keywords:** Inflammation; Hydroethanolic extract; Medicinal plants.

09.064 **Gel Containing Naringin Combined with Phonophoresis Reduces Inflammatory and Oxidative Biomarkers After Musculoskeletal Injury**. Nascimento VS[1], Santana CBL[1], Sousa DS[2], Oliveira ED[1]. [1]UFS, Programa de Pós-Graduação em Biotecnologia (PROBIO), Brasil. [2]UFS, Rede Nordeste de Biotecnologia (Renorbio), Brasil.

Introduction: Skeletal muscle injuries are common in both daily routines and during exercise. Understanding the local inflammatory cascade and regeneration mechanisms is fundamental to optimizing and accelerating the muscle repair process. Research indicates that natural compounds with antioxidant properties can attenuate the damage caused by the inflammatory process. **Objectives:** This study aimed to evaluate the effects of a gel with naringin complexed in β-cyclodextrin combined with phonophoresis on inflammatory and oxidative biomarkers after musculoskeletal injury in rats. The animals were equally divided into five groups (n = 40): control (CTR), muscle injury (MI), therapeutic ultrasound (UST), gel with naringin complexed in β-cyclodextrin (NAR), and therapeutic ultrasound associated with gel with naringin complexed in β-cyclodextrin (UST + NAR). The injury was induced in the gastrocnemius muscle by mechanical impact, and treatment was performed at intervals of 2, 12, 24, 48, 72, and 96 hours after the injury. After 98 hours, the animals were sacrificed, and the injured muscle was collected for biochemical and histological analyses. **Results:** Regarding oxidative damage, quantified by malondialdehyde (MDA) formation and activation of superoxide dismutase (SOD) and catalase (CAT) enzymes, all treated groups showed a reduction compared to the MI group, with the UST + NAR group showing the best **Results:** Histological analysis revealed intense cellular infiltrate and centralized nuclei in the MI group, while the treated groups demonstrated a more evident structural recovery. **Conclusion:** The association of NAR with therapeutic ultrasound proved promising in attenuating the inflammatory response and modulating the cellular redox state. These results highlight the effectiveness of NAR as an antioxidant agent in topical formulations, especially when combined with UST (phonophoresis), opening new possibilities for the development of natural compounds aimed at treating muscle injuries and inflammatory disorders.

09.065 **Investigation of the Toxicological Profile of Surfactants Used in Nanoformulations in an** *in vivo* *Caenorhabditis elegans* **Model**. Pacheco PGS[1], Silva VGO[2], Fagundes LS[2], Sá MEB[2], Poderoso VM[2], Araujo DS[2], Lisboa JS[1], Souza JB[1], Trancoso CT[1], Cândido-Santos JH[4], Araujo ZS[3], Barreto MS[2], Silva AS[1], Guimarães AG[5], Lira AAM[5]. [1]UFS-São Cristóvão, PPG in Pharmaceutical Sciences, Brazil, [2]UFS-São Cristóvão, Dept Pharmacy, Lab. of Clinical and Experimental Pharmacology, Brazil, [3]UFS, Campus Lagarto, PPG in Applied Health Sciences, Brazil, [4]UFS-São Cristóvão, PPG in Health Sciences, Brazil, 5UFS, Dept Pharmacy, Brazil

Introduction: The development of pharmaceutical technologies, particularly nanoformulations, has gained prominence for improving the physicochemical properties of active ingredients, thereby enhancing their stability, solubility, and therapeutic efficacy. However, the impact of these technologies on living organisms is hampered by gaps in our understanding, such as the biocompatibility and bioaccumulation of the surfactants used. To evaluate these aspects, the alternative model *Caenorhabditis elegans* has been used because it exhibits behavioral responses to chemical compounds, making it useful for assessing toxicity biomarkers, in addition to allowing the verification of lethality. **Objective:** To evaluate the toxicological aspects of different surfactants in the *C. elegans* animal model. **Methods:** After synchronization at the L1 larval stage, approximately 40–50 nematodes were placed in Petri dishes containing Nemathoid Growth Medium (NGM) and *E. coli* OP50, and then exposed to the surfactants Tween® 20, Tween® 80, Cremophor 40®, Propylene Glycol, Olivem® 300, Polyvinyl Alcohol (PVA), and Polaxamer 407, all at a concentration of 10% (v/v), and to the control (M9 buffer). The experiment was conducted in triplicate and in a blinded manner. After 24, 48, and 72 hours of exposure, the proportion of live individuals was assessed, and at 44 hours of exposure, pharyngeal beating was measured in n=30 worms per group, based on the average of three 10-second cycles, and expressed as beats per minute; in parallel, the worm's body size was recorded and subsequently analyzed using ImageJ software, totaling n=10 individuals per group; For statistical analysis of the behavioral results and proportion of survivors, GradPad Prism 8 software was used, applying one-way ANOVA and two- way ANOVA tests, followed by Bonferroni and Dunnet post-hoc tests, respective to the experiments, comparing the surfactant groups to the control group. **Results:** A statistically significant difference was observed in pharyngeal beating ($p<0.05$) for both Tween (20 and 80), Cremophor 40 ($p<0.005$), and Olivem 300 ($p<0.005$); likewise, there was a difference in body size for Tween 20 and 80 ($p<0.0005$ and $p<0.05$, respectively) and Olivem 300 ($p<0.0005$). Finally, there was no statistically significant difference in the proportion of viable cells between the groups. **Conclusion:** These results contribute to the discussion regarding the selection of surfactants for specific formulations, with an emphasis on safety profiles in addition to physicochemical parameters. **Acknowledgments:** The authors acknowledge the Federal University of Sergipe (UFS) and the National Council for Scientific and Technological Development (CNPq) for their support.

09.066 **Methyl Cinnamate Attenuates Epithelial-to-Mesenchymal Transition via Endoplasmic Reticulum Stress in TGF-β1-activated Alveolar Epithelial Cells**. Ferreira EGA, Barros ABB, Fidelix MSP, Silva GRS, Santana JR, Silva JP, Barreto E UFAL, Lab Biologia Celular

Introduction: Fibrosis is a primary driver of mortality, contributing to nearly 45% of all deaths in industrialised nations. It is characterised by excessive production of extracellular matrix components that destroy normal tissue architecture and cause organ failure. During fibrogenesis, epithelial-to-mesenchymal transition (EMT) polarises epithelial cells, which acquire mesenchymal characteristics and increase the production of extracellular matrix components, promoting tissue remodelling and organ dysfunction. Several studies demonstrate that endoplasmic reticulum (ER) stress-mediated epithelial-mesenchymal transition (EMT) is involved in the process of fibrosis in different tissues. In this scenario, compounds capable of modulating TEM via ER stress may represent promising antifibrotic strategies. Methyl cinnamate is found in various medicinal plants and exhibits multiple biological activities, including antioxidant and anti-inflammatory effects; however, its ER stress-mediated EMT has not been investigated to date. Here, we explored the effects of methyl cinnamate (MC) on transforming growth factor (TGF)-β-induced endoplasmic reticulum stress in mediating EMT in alveolar epithelial cells. **Methods:** A549 cells were maintained in DMEM supplemented with 10% FBS, 1% penicillin/streptomycin, and 2 mM L-glutamine at 37°C in 5% CO_2. MC cytotoxicity (1–30 μM) was assessed using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) viability assay. EMT was induced with TGF-β1 (10 ng/mL) and ER stress was induced with thapsigargin (0.5 μM) in the presence or absence of MC (10 μM) or salubrinal (20 μM) for 24 h. Morphological changes were assessed by microscopy and morphometric analysis. Immunofluorescence was used to assess mesenchymal marker expression (α-SMA). Data were analyzed using one-way ANOVA and Tukey's test ($p < 0.05$). **Results:** MC did not affect cell viability. TGF-β1 induced EMT-associated morphological alterations, characterised by reduced roundness and circularity by 48%, increased α-SMA expression, and enhanced cell migration 80%. Thapsigargin (TG) also induced morphological changes via ER stress induction. Treatment with MC (10 μM) attenuated these effects by reducing α-SMA expression, partially restoring epithelial morphology, and decreasing cell migration at 24 h 35%. Notably, MC mitigated TG-induced morphological alterations and TGF-β1-induced migration similarly to salubrinal, a well-established ER stress inhibitor, suggesting the involvement of shared ER stress-related mechanisms. **Conclusion:** These findings demonstrate that methyl cinnamate attenuates TGF-β1-induced morphological and EMT-related phenotype changes in A549 cells, possibly through modulation of ER stress, supporting its potential as an antifibrotic agent.

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09.067 From Popular Use to Scientific Evidence: Safety and Bioactivity of *Baccharis dracunculifolia* DC. Bezerra CS[1], De Paula MS[1], Lowen NV[2], Higashijima AN[1], Santa-Clara RC[1], Silva GR[3], Lívero FAR[1] [1]UFPR, Cardiometabolic Pharmacology Lab, PPG Pharmacology, Brazil, [2]UFPR, Cardiometabolic Pharmacology Lab, Pharmacy Course, Brazil. [3]Unipar, Lab Preclinical Research of Natural Products, PPG Animal Science with Emphasis on Bioactive Products, Brazil.

Introduction: *Baccharis dracunculifolia* DC. is a medicinal plant rich in flavonoids, terpenes, and phenolic acids. Although the plant is widely recognized for its antioxidant and anti-inflammatory properties, represents the main botanical source of Brazilian green propolis, and has well-documented pharmacological potential, evidence regarding its toxicological safety remains limited.

Objective: To evaluate the toxicity of the hydroethanolic extract of *B. dracunculifolia* using integrated *in vitro* and *in vivo* approaches. Additionally, antioxidant and anti-inflammatory activities were also investigated. Methods: Total phenolic and flavonoid contents were determined using the Folin–Ciocalteu and aluminum chloride methods, respectively. Antioxidant activity was evaluated using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) and Ferric Reducing Antioxidant Power (FRAP) assays. Anti-inflammatory activity was investigated through hemolysis inhibition, macrophage spreading, and phagocytosis assays. Cytotoxicity was analyzed in NIH/3T3 fibroblasts using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. Acute oral toxicity of the extract was assessed in female Wistar rats according to OECD guideline 423. Biochemical, hematological, and histopathological analyses were performed. Results: Treatment with the hydroethanolic extract of *B. dracunculifolia* showed concentration-dependent phenolic content and moderate antioxidant activity. Anti-inflammatory activity increased in a concentration-dependent manner, with the highest hemolysis inhibition observed at 600 µg/mL. Cytotoxicity analysis demonstrated cell viability above 70%. *In vivo*, no mortality, behavioral changes, alterations in relative organ weight, body weight, or hematological parameters were observed. Serum triglyceride and creatinine levels showed a significant reduction in treated groups, whereas aspartate aminotransferase (AST), alanine aminotransferase (ALT), cholesterol, and urea concentrations remained unchanged. Histopathological analysis confirmed the absence of liver, kidney, and heart alterations related to plant administration. Conclusion: Treatment with *B. dracunculifolia* extract demonstrated safety associated with antioxidant and anti-inflammatory activities. The absence of toxicological alterations supports its potential as a safe bioactive ingredient for nutraceutical formulations. However, additional studies evaluating chronic exposure and genotoxicity are still required. Funding: COPG/UNIPAR, CNPq – 306919/2021-4, and Fundação Araucária/SETI (CP 20/2018 and 014/2020). Ethical approval: CEUA/UNIPAR No. 1003/2022.

09.068 **Effect of Orange** (*Citrus sinensis*) **Free Oil on Stearic Acid-Induced Lipid Accumulation in** *Caenorhabditis elegans*. Araújo ZS[1], Pacheco PGS[2], Barreto MS[2], Santos AS[2], Lisboa JS[2], Silva VGO[3], Sá MEB[3], Guimarães AG[1,2,3]
[1]UFS-Lagarto, Graduate Program in Applied Health Sciences (PPGCAS), Brazil, [2]UFS-São Cristóvão, Graduate Program in Pharmaceutical Sciences (PPGCF), Brazil, [3]UFS-São Cristóvão, Dept Pharmacy (DFA), Brazil.

Introduction: Disorders associated with excessive lipid accumulation represent a serious global public health problem; dysregulation of this metabolism is linked to obesity, dyslipidemia, and metabolic syndrome. (Dakal, TC. Lipids Health Dis., vol. 24, p. 61, 2025; Zhang, H. Metab. Clin. Exp., vol. 160, p. 155999, 2024). In this context, natural compounds have been extensively investigated as potential therapeutic alternatives due to their biological properties (Nainu, F. Heliyon, v. 9, p. e16919, 2023). Orange oil (*Citrus sinensis*), rich in compounds such as d-limonene, exhibits potential anti-obesogenic activity in mammals through the activation of the AMP-activated protein kinase (AMPK) signaling pathway (Liao, JT. Nutrients, vol. 15, p. 267, 2023); this signaling pathway is also found in the alternative experimental model *C. elegans*. (Apfeld, J. Genes Dev., p. 3004, 2004) **Objective:** To evaluate the effect of orange essential oil on lipid accumulation in *C. elegans* subjected to stearic acid induction. **Methods:** *C. elegans* N2 strain animals were maintained in Nematode Growth Medium (NGM) seeded with *E. coli* OP50 and subjected for one week to medium supplemented with stearic acid to induce lipid accumulation, combined with treatment with different concentrations of free orange oil (5 µM, 25 µM, 50 µM, 100 µM, and 200 µM). Lipid content was assessed by staining with Oil Red O, followed by imaging under bright-field microscopy, and quantitative analysis of the images using ImageJ software. The assays were conducted in duplicate, and the data were analyzed using GraphPad Prism® 10, employing appropriate statistical tests with a significance level of $p > 0.05$. **Results:** The treatment significantly reduced lipid accumulation at all tested concentrations ($p < 0.001$) compared to the control, with peak efficacy observed at the 100 µM dose. In the morphometric assessment of body size, a significant reduction in nematode dimensions was observed at all administered doses (p ranging from < 0.05 to < 0.0001). **Conclusion:** The results suggest that orange free oil has the potential to modulate lipid metabolism in *C. elegans*, demonstrating promising activity for future research into metabolic disorders. Supported by the Coordination for the Improvement of Higher Education Personnel (CAPES) and Maratá. The use of *C. elegans* does not require approval by the Animal Ethics Committee (CEUA).

09.069 **Uvaol Mitigates TGF-β1-Induced Activation of Human Hepatic Stellate Cells Through Anti-Inflammatory and Antioxidant Mechanisms**. Barros ABB[1], Ferreira EGA[1], Fidelix MSP[1], Pereira JP[1], Lagente V[2], Barreto E[1] [1]UFAL, Lab Cell Biology, Brazil. [2]UMR991-INSERM, Université de Rennes 1, Rennes, France.

Introduction: Liver fibrosis is a progressive wound-healing response that can ultimately lead to cirrhosis and hepatocellular carcinoma. In this condition, hepatic stellate cells (HSCs) play a central role in fibrosis progression and modulation of the inflammatory response. Upon exposure to fibrogenic mediators, such as transforming growth factor-β1 (TGF-β1), HSCs increase the production of inflammatory and profibrotic factors that contribute to tissue remodelling. Despite the clinical relevance of liver fibrosis, there are currently no approved antifibrotic therapies for human use. Uvaol is a bioactive pentacyclic triterpenoid isolated from olive trees (Olea europaea) that exhibits anti-inflammatory properties in different experimental models. The present study investigated the effects of uvaol on TGF-β1-induced oxidative stress, inflammatory response, and profibrotic gene expression in human hepatic stellate cells. **Methods:** The human hepatic stellate cell line LX-2 was cultured at 37 °C in a humidified atmosphere containing 5% CO2 using Dulbecco's Modified Eagle Medium (DMEM) supplemented with 5% fetal bovine serum (FBS) and 1% penicillin/streptomycin. Cell viability was assessed by MTT assay after 24 h of exposure to uvaol (1–100 μM). Intracellular reactive oxygen species (ROS) generation and cytokine gene expression were evaluated in TGF-β1-stimulated LX-2 cells using flow cytometry with the DCFH-DA probe and quantitative PCR (qPCR), respectively. Data were analysed by one-way ANOVA followed by Tukey's post hoc test ($P < 0.05$). **Results:** Uvaol at concentrations of 1, 3, and 10 μM did not affect LX-2 cell viability, whereas concentrations of 30 and 100 μM reduced viability by 27.5% and 45.4%, respectively. Stimulation with TGF-β1 induced a 3.3-fold increase in ROS generation compared with vehicle-treated cells. Uvaol significantly attenuated this response, reducing ROS levels by 21% and 34% at concentrations of 1 and 10 μM, respectively. TGF-β1 also markedly increased the expression of inflammatory genes, including IL-1β (3.5-fold), IL-6 (2.66-fold), and CCL2 (2.4-fold), as well as profibrotic genes, including COL1A2 (3.1-fold), ACTA2 (5.9-fold), PDGFβ (3.5-fold), and MMP2 (5.8-fold). Treatment with uvaol (10 μM) significantly reduced the expression of IL-1β (40%), IL-6 (38%), CCL2 (45%), COL1A2 (38%), ACTA2 (40%), PDGF-β (23%), and MMP2 (56%). **Conclusion:** Uvaol attenuated TGF-β1-induced oxidative stress, inflammatory response, and profibrotic gene expression in human stellate cells. These findings highlight the potential of uvaol as a promising candidate for the development of novel therapeutic strategies targeting liver fibrosis.

09.070 **Antioxidant and Cytoprotective Action of** *Cenostigma pyramidale* (**TUL.) Gagnon & G. P. Lewis in HaCaT Cells Exposed to Lipopolysaccharide**. Santos AF[1], Albuquerque, MCS[1], Silva GNB[2], Silva BM[2], Sobral R[2], Sette-de-Souza PH[1], Santos HLS[2], Correia ACC[1,3]. [1]UPE, PPG Saúde e Desenvolvimento Socioambiental, Brazil, [2]UPE, PPG Biologia Celular e Molecular aplicada, Brazil. [3]UPE, Curso de Licenciatura em Ciências Biológicas, Brazil.

Introduction: *Cenostigma pyramidale* (Tul.) Gagnon & G.P. Lewis, popularly known as catingueira, is a native species of the Caatinga biome widely used in traditional medicine for the treatment of coughs, pain, and inflammatory processes. The bark and leaves of the species have significant phytochemical potential, being described by the presence of phenolic compounds, flavonoids, and tannins, secondary metabolites associated with important biological activities, including antioxidant, anti-inflammatory, antimicrobial, gastroprotective, healing, and cytotoxic actions. **Objectives:** To perform phytochemical screening of the hydroethanolic extract of *Cenostigma pyramidale* bark (Cp-HE) and evaluate its antioxidant, cytotoxic and anti-inflammatory potential. **Methods:** The botanical material was collected at the UPE Campus in Arcoverde, Pernambuco, Brazil. A voucher specimen was deposited at the Herbarium of Parque das Dunas, Rio Grande do Norte, Brazil (No. 5286). The project was registered in SISGEN under No: A511611. The crude hydroethanolic bark extract (Cp-HE) (70:30; v/v) was obtained by ultrasound-assisted extraction (20 min/25 °C), followed by rotary evaporation (40 °C, 55 rpm). Total phenolic compounds in Cp-HE were quantified using the Folin–Ciocalteu method, while total flavonoid content was determined by the aluminum chloride colorimetric assay. Antioxidant activity was evaluated using DPPH and ABTS assays. Cytotoxic potential was assessed through the MTT assay, morphological analysis, and trypan blue exclusion assay in HaCaT cells exposed to increasing concentrations (1–729 µg/mL) of Cp-HE. For the anti-inflammatory assay, cells were exposed to lipopolysaccharide (LPS) for 24 h and subsequently treated with different concentrations of Cp-HE (1, 3, 9, 27 and 81 µg/mL). The anti- inflammatory potential was determined using the MTT assay. **Results:** Cp-HE showed high levels of total phenolic compounds (266.71 µg GAE/g) and total flavonoids (202.91 µg QE/g). These findings corroborate its strong antioxidant activity in the DPPH and ABTS assays, with IC_{50} values of 0.155 ± 0.009 µg/mL and 0.310 ± 0.108 µg/mL, respectively. The ascorbic acid equivalent antioxidant capacity (AAEAC) values were 0.04 ± 0.02 mM AAE/100 g, while the Trolox equivalent antioxidant capacity (TEAC) was 0.012 ± 0.06 mM TE/100 g. The extract did not exhibit cytotoxicity in HaCaT cells after 24 h of exposure at any of the tested concentrations. This absence of toxicity was confirmed by MTT, trypan blue exclusion, and morphological analyses. Furthermore, the concentration of 81 µg/mL of Cp-HE exerted a protective effect on HaCaT cells subjected to LPS-induced stress, suggesting a potential anti-inflammatory effect. **Conclusion:** *Cenostigma pyramidale* exhibits relevant antioxidant and cytoprotective properties, reinforcing its promising potential as a therapeutic alternative for the management of cutaneous inflammatory processes.

09.071 **Antidiabetic Potential of Cocoa Bean Shell Extract** (*Theobroma cacao* L.)**: Phytochemical Profile, α-Glucosidase Inhibition, and GLP-1 Modulation**. Martins CBR, Freire GA, Xavier Filho RR, Silveira MS, Canuto KM, Wurlitzer NJ, Frederico MJS UFC, Faculty of Medicine, Dept Physiology and Pharmacology, Center for Research and Development of Medicines, Lab Biochemistry and Pharmacology, Graduate Program in Pharmacology, Fortaleza, Ceará, Brazil; UFC, Center for Agricultural Sciences, Dept Food Engineering, Graduate Program in Food Science and Technology, Fortaleza, Ceará, Brazil; EMBRAPA, Brazilian Agricultural Research Corporation, Tropical Agroindustry, Fortaleza, Ceará, Brazil.

Type 2 diabetes mellitus (T2DM) affects approximately 537 million adults worldwide, requiring therapeutic strategies capable of mitigating postprandial hyperglycemia. This study investigated the antidiabetic potential of the aqueous extract of cocoa bean shell (AECBS), an agro-industrial byproduct, through phytochemical characterization and biological assays involving enzymatic and incretin modulation. Chemical screening by ^{1}H NMR and UPLC-PDA- ESI-QDa revealed a complex matrix rich in methylxanthines (theobromine and caffeine), amino acids (arginine and leucine), and phenolic compounds, including catechin, epicatechin, and rosmarinic acid. AECBS exhibited inhibitory activity against α-glucosidase, with an IC_{50} of 0.042 ± 0.01 mg/mL, significantly lower than that of the reference drug acarbose (IC_{50} of 0.393 ± 0.03 mg/mL). At a concentration of 1.0 mg/mL, the extract achieved 97.77% enzymatic inhibition. In cell viability (MTT) assays, concentrations ranging from 0.01 to 100 µg/mL increased metabolic activity, suggesting a cytoprotective effect. Furthermore, ex vivo treatment with 1000 µg/mL AECBS significantly increased GLP-1 secretion in colon fragments, surpassing the stimulation induced by glucose alone. These results indicate that AECBS exerts a dual action, suggesting a possible delay in carbohydrate digestion and absorption, to be further confirmed in *in vivo* models, while simultaneously stimulating the incretin axis. Overall, the aqueous extract of cocoa bean shell demonstrates potential as a bioactive matrix for future studies aimed at the development of functional ingredients or nutraceuticals associated with postprandial glycemic control. **Financial support:** CAPES and EMBRAPA

09.072 **Chemical Characterization by LC/MS and the Lipid-Lowering Potential of the Aqueous Extract of** *Helianthus annuus* **L. Seeds in** *Caenorhabditis elegans*. Barreto MS[1], Araújo ZS[2], Pacheco PGS[1], Souza JB[1], Lisboa JS[1], Silva AS[1], Sá MEB[3], Santos VR[1], Oliveira DP[1], Cavalcante MD[1], Borges LP[1], Guimarães AG[1] [1]UFS, Graduate Program in Pharmaceutical Sciences, São Cristovão, Brazil, [2]UFS, Graduate Program in Health Sciences, Lagarto, Brazil, [3]UFS, Dept Pharmacy, Lab Clinical and Experimental Pharmacology (LAFACE), Brazil

Introduction: *Helianthus annuus* L., commonly known as the sunflower, is a plant widely used for oil production in the food and cosmetics industries and as a biofuel. Sunflower seeds contain phenolic compounds such as flavonoids and phenolic acids, particularly chlorogenic acid, which exhibit antioxidant and lipid-lowering properties. **Objectives:** This study investigates the phytochemical profile and lipid-lowering properties of the aqueous extract of sunflower seeds in a *Caenorhabditis elegans* model induced to accumulate lipids. **Methods:** The aqueous extract of sunflower seeds was obtained by maceration (2 h, room temperature) followed by freeze-drying. The aqueous extract was characterized using liquid chromatography coupled with mass spectrometry (LC/MS) on a C18 column in both positive and negative ionization modes. For the *in vivo* test, *C. elegans* were synchronized and transferred to Nematode growth medium (NGM) containing *E. coli* OP50. When they reached the L4 stage, the worms were transferred to new plates containing E. coli, 500 mg/mL stearic acid, the reproduction inhibitor (FuDr) at 50 µM, and the treatments. The treatments consisted of a blank, 100 µg/mL, and 200 µg/mL of the extract. Toxicity was evaluated in a previous experiment, which demonstrated the safety of concentrations of 100 and 200 mg/mL for behavioral parameters such as body size, motility (swimming and body bends), and worm survival. After 5 days of exposure, the worms' intracellular lipid content was stained with Oil Red O solution, and images were captured and analyzed in Image J. Ten worms per group were quantified. The statistical analysis consisted of an ANOVA test followed by Tukey's post-hoc test. A p-value of <0.05 was considered statistically significant. **Results:** LC/MS characterization identified chlorogenic acid (5-CQA) as the major compound in the extract. Regarding the results of the *C. elegans* tests, quantification yielded an average lipid percentage of 44.07% for the control group, differing significantly from the 100 µg/mL group (m = 32.53%, 95% CI 3.93–19. 15, p=0.0013) and the 200 µg/mL group (m=34.48%, 95% CI 2.19–17.40, p=0.0072). **Conclusion:** The aqueous sunflower extract showed potential to reduce lipid accumulation in the tested model, which may be due to the presence of chlorogenic acid and other compounds acting synergistically. Further research is needed to investigate the likely mechanism of action involved in this effect, as well as to compare the effects of the extract with those of clinically used drugs. **Acknowledgments:** We thank the Coordination for the Improvement of Higher Education Personnel (CAPES/Brazil).

09.073 **Evaluation of the Effects of Lauric Acid on Senescence in Human Umbilical Vein Endothelial Cells (HUVECs)**. Assis TFM[1], Gonçalves TAF[2], Oliveira JCPL[2], Queiroz TM[1] [1]CAV/UFPE; [2]CCS/UFPB

Introduction: Cardiovascular diseases are associated with increased reactive oxygen species (ROS) production, which contributes to endothelial dysfunction and cellular senescence. Nutritional compounds with antioxidant properties have therefore emerged as potential strategies for protecting vascular function. **Objective:** This study investigated the effects of lauric acid (LA), the predominant medium-chain fatty acid in coconut oil, on angiotensin II (Ang II)-induced senescence in human umbilical vein endothelial cells (HUVECs). **Methods:** HUVECs were allocated into control (CTL), Ang II (1 μM), and LA-treated groups (0.5, 1, 5, and 10 μM), evaluated under basal conditions and following Ang II exposure for 24 h. Cell viability was assessed by the MTT assay, intracellular superoxide anion ($O_2^{\bullet -}$) production by dihydroethidium (DHE), and cellular senescence by senescence-associated β-galactosidase (SA-β-gal) activity. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test, and differences were considered statistically significant when $p < 0.05$. **Results:** LA showed no cytotoxicity under basal conditions at any concentration tested. Ang II significantly reduced cell viability compared with CTL, whereas LA at 0.5, 1, 5, and 10 μM significantly improved viability relative to Ang II alone. Under basal conditions, LA produced effects on $O_2^{\bullet -}$ production, reducing superoxide levels at 0.5 μM, showing no significant effect at 1 μM, and increasing $O_2^{\bullet -}$ at 5 and 10 μM. In Ang II-exposed cells, however, LA reduced $O_2^{\bullet -}$ production at 0.5, 5, and 10 μM. Ang II also significantly increased SA-β-gal activity compared with CTL, while LA at 1, 5, and 10 μM attenuated this response. **Conclusion:** Overall, LA improved cell viability and attenuated Ang II-induced endothelial senescence, with the most consistent protective effects observed at 1–10 μM. These findings support the potential of LA as a modulator of endothelial dysfunction and warrant further investigation into the molecular mechanisms underlying its effects.

09.074 **Cardiotoxicity of Snake Venoms and Toxins Assessed Using Cockroach** (*Nauphoeta cinerea*) **Semi-isolated Heart Preparations**. Oliveira IN[1], Silva AB[1], Oliveira RS[1], Dias DRC[2], Guimarães MP[3], Vinadé L[4], Dal Belo CA[1,3], Silva Júnior NJ[5], Hyslop S[1] [1]Unicamp, Faculty of Medical Sciences, Dept Pharmacology, Pharmacology Graduate Program, Brazil; [2]UFES, Dept Statistics, Brazil; [3]Unifesp-Osasco, Paulista School of Politics, Economics and Business, Multidisciplinary Dept, Campus, Brazil; [4]Unipampa, São Gabriel Campus, Brazil; [5]PUC-GO, Graduate Program in Environmental and Health Sciences, Brazil.

Introduction: Snake venom biological activities have traditionally been assessed in vertebrates, but the use of invertebrates as alternative models offers advantages such as low maintenance costs, easy handling, and reduced ethical concerns. The lobster cockroach *Nauphoeta cinerea* has been used to study pesticides and toad venoms, but its suitability for evaluating snake venoms and their toxins remains poorly explored. **Objective:** To examine the cardiotoxicity of *Bothrops*, *Crotalus*, *Lachesis* and *Micrurus* snake venoms and toxins in cockroach semi-isolated heart preparations. **Methods:** Cockroach semi-isolated heart preparations were prepared as described (Rosa et al., 2023, J Exp Biol 226, jeb245239; Ferreira et al., 2024, Pestic Biochem Physiol 205, 106167). Changes in heart rate (mean±SD) were monitored for 1 h and analyzed using one-way ANOVA followed by the Bonferroni test ($p<0.05$ compared to saline controls; Prism software v.5, GraphPad). **Results:** Basal (control, 0.9% saline) heart rate was 72±1 beats/min (bpm) (n=10). *Micrurus surinamensis* venom (600 µg) showed no cardiotoxicity after 1 h (72±2 bpm; n=10), whereas *M. d. carinicauda* (300 µg) and M. spixii (600 µg) caused bradycardia leading to cardiac arrest in 2.5±1.3 min and 8.5±2.6 min, respectively ($p<0.05$, n=10). Among Bothrops venoms, *B. jararacussu*, *B. moojeni* and *B. neuwiedi* were the most potent, causing cardiac arrest in 2.8±0.7, 6.5±4.5 and 2.2±1.2 min, respectively, at 300 µg, and 0.8±1.0, 0.9±0.3 and 2.7±1.6 min, respectively, at 600 µg ($p<0.05$, n=5); *B. alternatus*, *B. atrox* and *B. jararaca* venoms (600 mg) were less potent (cardiac arrest in 23.9±6.0, 2.8±0.8 and 3.8±1.5 min, respectively; n=5). *Lachesis muta muta* produced cardiac arrest only at 600 µg (9.7±5.6 min, n=5). At a dose of 600 mg, *Crotalus durissus terrificus* venom increased heart rate (102±12 bpm, $p<0.05$, n=5), while those of *C. d. cascavella* (86±21 bpm; n=5) and *C. d. collilineatus* (72±1 bpm, n=5) did not affect heart rate. Alpha-bungarotoxin (10 mg) and b-bungarotoxin (100 mg) caused bradycardia without cardiac arrest (54±3 bpm and 56±6 bpm, respectively, after 1 h; n=5). PLA_2 toxins from *B. moojeni* were cardiotoxic: Moojeni toxin I (100 µg) caused irreversible cardiac arrest in 9±7 min (n=5) and Moojeni toxin II produced cardiac arrest in 27±14 and 20±10 min at 30 µg and 100 µg, respectively (n=5). Bothropstoxin I (from *B. jararacussu*) caused cardiac arrest at 30 mg and 100 mg (15±5 and 15±13 min, respectively; n=5), whereas Bothropstoxin II (100 mg) caused bradycardia (44±3 bpm, $p<0.05$, n=5) without cardiac arrest. **Conclusion:** The cockroach semi-isolated heart showed variable sensitivity to snake venoms and toxins. This preparation may be useful for screening snake venoms and toxins, and could replace vertebrates as part of the 3R principles.

09.075 **Antiproliferative Activity and** *In vitro* **Mechanisms of Casearin J on a Triple-Negative Breast Cancer Model**. Almeida ML[1], Barbosa SLM[1], Sousa RCL[1], Sousa RWR[1], Negreiros HA[3], Silva LRA[3], Zalewski S[2], Camargo JGS[2], Carvalho FA[2], Santos AG[2], Castro JMC[3], Dittz D[3], Ferreira PMP[1],[4] [1]UFPI, Lab Experimental Cancerology (LabCancer), Dept Biophysics and Physiology; [2]Unesp, Lab Pharmacognosy, Faculty of Pharmaceutical Sciences; [3]UFPI, Dept Biochemistry and Pharmacology; [4]UFC, Lab Experimental Oncology (Loe), Dept Physiology and Pharmacology, Brazil

Introduction: Triple-negative breast cancer (TNBC) is an aggressive subtype characterized by the absence of estrogen, progesterone, and HER-2 receptors, with high molecular heterogeneity, early recurrence, and limited therapeutic options. Given its resistance to conventional chemotherapy, natural compounds emerge as promising alternatives. In this context, *Casearia sylvestris* Sw. (Salicaceae), stands out for the pharmacological potential of clerodane diterpenes, as casearin J (Cas J). **Objectives:** To evaluate the antiproliferative action of Cas J upon breast cancer cell lines and to characterize its effects on the murine TNBC line 4-T1. Methods Leaves of C. sylvestris (SisGen #A33EA7A, SISBIO 33429-1) were subjected to ethanolic extraction, partitioned with ethyl acetate, and analyzed by chromatography and mass spectrometry. Tumor breast lines (4-T1, MCF-7 and MDA-MB-231), as well as healthy mammary cells (MCF-10) were exposed to Cas J (0.34-44.47 μM) for 72 h and cytotoxicity and the selectivity index (SI) were analyzed by Alamar Blue™. Afterwards, additional assays were performed using 4-T1 cells: trypan blue exclusion assay, cell migration assay, colony formation assay, morphological analysis by light and fluorescence microscopy using propidium iodide and acridine orange, micronucleus assay with cytokinesis block, quantification of intracellular reactive oxygen species (ROS) using the fluorescent probe DCFH, and cell viability after co-treatment with N-acetylcysteine (NAC). **Results:** Cas J exhibited cytotoxicity against the 4-T1, MCF-7, and MDA-MB-231 cells, with IC50 values of 1.44, 1.33, and 9.99 μM, respectively, and selectivity (SI > 2) for 4-T1 (7.50) and MCF-7 (8.10) lines when compared to MCF-10 cells. In 4-T1 cells, Cas J induced concentration-dependent morphological changes and apoptosis-related features, including shrinkage, karyorrhexis and pyknosis, reduced cell viability, increased the population of apoptotic cells, and showed *in vitro* low clastogenic effects ($p < 0.05$). ROS levels increased at the highest concentration only (44.47 μM), with partial attenuation of the cytotoxic effect by NAC. Casearin J inhibited cell migration at non-cytotoxic concentrations (0.02-0.18 μM) and reduced colony formation at 0.90 μM ($p < 0.05$). **Conclusion:** Casearin J demonstrated higher selectivity cytotoxicity on TNBC, inducing apoptotic death of 4-T1 cells, and inhibits colony formation and cellular migration at concentrations up to 100 times lower than IC50, emerging as a promising molecule for the development of new therapeutic agents. **Financial support** CNPq/CAPES/FAPEPI.

09.076 **p-Coumaric Acid Suppresses IL-1β-Induced ICAM-1 and CXCL8 Expression in Human Alveolar Epithelial Cells** Fidelix MSP, Barros ABB, Ferreira EGA, Silva GRS, Silva JP, Barreto E. UFAL, Lab Biologia Celular

Introduction: Natural products such as p-coumaric acid (p-CA) have demonstrated anti-inflammatory properties and are considered promising candidates for the development of novel therapeutic agents with low toxicity. In previous studies (Souza et al. 2021), we demonstrated that p-CA reduces neutrophil recruitment in a murine model of lipopolysaccharide (LPS)-induced acute lung injury. However, the cellular and molecular mechanisms underlying these pharmacological effects remain poorly understood. Therefore, the present study investigated the effects of p-CA on human alveolar epithelial cells, with particular emphasis on the expression of the pro-inflammatory mediators CXCL8 and intercellular adhesion molecule-1 (ICAM-1), both of which play key roles in inflammatory cell recruitment. **Methods:** Human alveolar epithelial A549 cells were cultured in DMEM supplemented with 10% foetal bovine serum (FBS), 1% penicillin/streptomycin, and 2 mM L-glutamine at 37°C in a humidified atmosphere containing 5% CO_2. Cytotoxicity of p-CA (1, 5, 10, 30, 50, and 100 µM) was assessed using the MTT assay. Cells were pre-treated with p-CA (10 µM) for 1 h before stimulation with IL-1β (1 ng/mL) for 6 h. ICAM-1 and CXCL8 mRNA expression levels were quantified by qPCR. Data was analysed by one-way ANOVA followed by Tukey's post hoc test ($p < 0.05$). **Results:** p-CA showed no cytotoxic effects at concentrations up to 50 µM. Pre-treatment with p-CA significantly reduced IL-1β-induced ICAM-1 and CXCL8 mRNA expression in A549 cells by 40% and 12%, respectively. **Conclusion:** p-Coumaric acid attenuates the inflammatory activation of alveolar epithelial cells by suppressing ICAM-1 and CXCL8 gene expression while exhibiting low cytotoxicity. These findings are consistent with our previous *in vivo* observations and support the therapeutic potential of p-CA for neutrophil-driven acute lung inflammation.

09.077 **Biological Evaluation of** *Borreria verticillata*, *Monteverdia rigida* **and** *Sarcomphalus joazeiro* **and their Potential for the Development of Phytocosmetics in** *Aloe vera* **Gel**. Silva GNB[1], Ferreira EF[2], Pereira JBM[2], Santos HLS[1], Nascimento GILA[1], Silva BM[1], Sobral R[1], Santos AF[3], Correia ACC[3], Falcão REA[3], Albuquerque PBSA[1],[31]UPE, PPG Biologia Celular e Molecular Aplicada, Brazil, [2]UPE, Curso de Licenciatura em Ciências Biológicas, Brazil, [3]UPE, PPG Saúde e Desenvolvimento Socioambiental, Brazil.

Introduction: Photoaging, accelerated skin damage caused by solar radiation, is largely originated by oxidative stress derived from free radicals. In this context, the Brazilian biome: "Caatinga" has a rich flora as a promising source of bioactive compounds, as the region's water and thermal stress conditions induce the adaptive synthesis of secondary metabolites. Based on traditional use of plants in the Castainho quilombola community, the species *Borreria verticillata*, Monteverdia rigida and Sarcomphalus joazeiro were selected for the investigation of their biological potential, aiming to develop an innovative phytocosmetic. **Objectives:** Determine the phenolic content, antioxidant activity and *in vitro* cytotoxicity of leaf extracts of *B. vercillata* and S. joazeiro, and the bark of M. rigida, to incorporate the most promising extract into a gel-based formulation of *Aloe barbadensis*. **Methodology:** The selection of these species resulted from a previous ethnobotanical survey, carried out through interviews in a project approved by the Research Ethics Committee (CAAE nº 24906014.9.0000.5207). The extract of the bark of M. rigida and leaves of *B. verticillata* and S. joazeiro were obtained by ultrasonic bath (BU; 10 minutes) and sonication (SO; 30, 45 and 60 min), using 99%; 70% and 50% (v/v) ethanol, totaling 36 extracts. These were subjected to quantification of total phenolics content by the Folin-Ciocalteu method. The data was analyzed to select the most optimized extractive profile. Antioxidant activity was determined by the DPPH radical method (from a range of 1.0 to 500.0 µg/mL), with DPPH and ethanol as reaction's control, and the cytotoxic potential was estimated by the MTT assay in fibroblasts of the L929 lineage (1.2 to 625.0 µg/mL). Triton-X-100 was used as positive control. The results were expressed by mean ± standard deviation, in triplicate, and analyzed over test t or analysis of variance (ANOVA), followed by Dunnett's post-test. **Results:** The ethanolic extracts of *B. verticillata* (BU), M. rigida (SO, 45 min) and S. joazeiro (SO, 60 min) presented the highest phenolic contents and were selected for the assays. The antioxidant activity assay presented IC50 values of 3,04; 2,09 and 37,6 µg/mL respectively, while the control (ascorbic acid) demonstrated an IC50 value of 2,9 µg/mL. Furthermore, the cytotoxicity assay demonstrated that cell viability was maintained above 70% at all concentrations tested. **Conclusion:** The data confirms that the method, solvent and extraction period are crucial variables in the phenolic yield. M. rigida extract stood out with superior antioxidant performance than the standard control. The low cytotoxicity observed for all ethanolic extracts reiterates the safety of their use. Finally, the extract with most optimized bioactive performance will be selected, after completion of the remaining biological tests, to be incorporated into an Aloe vera-based gel, continuing the development of the formulation.

09.078 *Arthrospira platensis* **Prevents Hypercaloric Diet-Induced Hepatic Histological and Oxidative Damage in Wistar rats**. Claudino BFO[1,2], Diniz AFA[1,2], Arruda RRA[1,2], Silva JMA[1,2], Melo MB[1], Sousa-Filho JEC[1], Santos TJ[1], Barros BC[1,2], Alves AF[2,3], Silva BA[1,2,4]. [1]UFPB, Lab Functional Pharmacology Prof. George Thomas, Institute of Research in Drugs and Medicines, Brazil [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil [3]UFPB, Dept Biomedical Sciences, Health Sciences Center, Brazil [4]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil

Introduction: Obesity is a chronic metabolic disorder resulting from an imbalance between energy intake and expenditure. As adipose tissue expands, its capacity to store excess energy becomes impaired, leading to systemic metabolic dysfunction, increased release of free fatty acids, and enhanced lipid flux to the liver. Given the global rise, there is growing interest in natural products with fewer adverse effects for the prevention and treatment of obesity-related comorbidities. In this context, *Arthrospira platensis* (AP) has emerged as a filamentous cyanobacterium with antioxidant, anti-inflammatory, and hepatoprotective properties. **Objectives:** This study evaluated the preventive effects of AP supplementation (25 mg/kg) on histological alterations, nitrosative stress markers [NOx (nitrate + nitrite) and nitrite], and the activity of antioxidant enzymes catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GPx) in the liver of male Wistar rats fed a hypercaloric diet. **Methods:** Male Wistar rats were randomly allocated into three groups: standard diet (SD), hypercaloric diet (HCD), and hypercaloric diet supplemented with AP (25 mg/kg) (HCD + AP25). Diets and supplementation were administered simultaneously for eight weeks. Powdered AP was suspended in saline (0.9% NaCl) and the suspension was administered daily by intragastric gavage. After euthanasia, liver samples were collected for analysis. Hepatic nitrite and NOx levels were determined by the Griess reaction, while antioxidant enzyme activities (CAT, SOD, and GPx) were assessed by spectrophotometric assays. **Results:** Histological analysis revealed preserved hepatic parenchyma in the SD group, whereas the HCD group developed hepatic steatosis characterized by intense vacuolization and cellular disorganization. AP supplementation markedly prevented these alterations, preserving liver architecture similarly to the SD group. In parallel, HCD significantly reduced SOD (1.22 ± 0.07 U/mg protein), CAT (61.03 ± 4.37 nmol/min/mL), and GPx (3.01 ± 0.47 nmol/min/mL) activities compared with SD (1.59 ± 0.07, 86.34 ± 2.44, and 9.54 ± 0.35, respectively). AP supplementation prevented these reductions (1.82 ± 0.03, 100.9 ± 3.23, and 16.85 ± 0.54, respectively). Regarding nitrosative stress, HCD increased NOx levels (1380 ± 112 vs. 664 ± 83.6 µM/g protein in SD) and nitrite levels (3.98 ± 0.4 vs. 2.08 ± 0.6 µM/g tissue in SD). AP supplementation partially attenuated NOx elevation (1023 ± 38.6) and completely normalized nitrite levels (2.68 ± 0.4). **Conclusion:** AP supplementation exerted a marked hepatoprotective effect by preventing hepatic steatosis, preserving liver histoarchitecture, restoring antioxidant enzyme activity, and attenuating nitrosative stress induced by a hypercaloric diet. These findings reinforce the therapeutic potential of AP in preventing hepatic metabolic and oxidative disturbances associated with obesity. **Financial support:** CNPq. **Ethical approval: CEUA/UFPB 6914241024.

09.079 **Varespladib Reverses Neuromuscular Blockade induced by Crotoxin in Mouse Phrenic Nerve-Diaphragm Preparations**. Pereira ES[1], Silva HF[1], Ortolani PL[2], Fortes CL[2], Cavalcante WLG[1] ICB-UFMG, Dept. Pharmacology, Brazil. [2]FUNED, CPD, Brazil.

Introduction: Snakebite envenoming is recognized by the World Health Organization as a neglected disease that primarily affects economically vulnerable populations. Despite the effectiveness of antivenom therapy, its limited availability and associated adverse reactions highlight the need for complementary treatments. In this context, Varespladib, a synthetic low-molecular-weight compound, has emerged as a promising agent due to its ability to neutralize snake venom toxins. **Objective:** To evaluate the ability of varespladib to reverse the neuromuscular blockade induced by Crotoxin (CTX), isolated from the venom of *Crotalus durissus terrificus*, using mouse phrenic nerve–diaphragm neuromuscular preparations. **Methods:** Phrenic nerve-diaphragm preparations from male Swiss mice were mounted in 12 mL organ baths containing Ringer solution, aerated with carbogen at 35°C. Myographic recordings were obtained under indirect electrical stimulation (0.5 ms, 0.2 Hz, 3 V) and contractions were recorded for 180 minutes. Three protocols were conducted: (a) CTX (5 µg/mL) followed by varespladib (5 µg/mL) at 10, 30, or 60 min (n=4-7); (b) CTX with washing at 30 or 60 min (n=5-8); (c) CTX, washing (30/60 min), followed by varespladib (n=3-7). Morphological analysis assessed tissue integrity and myonecrosis index (n=4-5). The data (mean) were analyzed by Student's t-test and ANOVA ($p<0.05$). **Results**: CTX caused an irreversible blockade, promoting 96% inhibition of twitches at 180 min ($p<0.01$ vs. control). Varespladib prevented the blockade when administered 10 minutes after CTX ($p>0.05$ vs. control), showing partial effects at 30 and 60 minutes with 42% and 33% inhibition, respectively ($p<0.01$ vs. control). Washing performed 30 minutes after CTX exposure prevented blockade progression, maintaining 50% contractile activity, while at 60 minutes the blockade was irreversible ($p<0.01$ vs. control). Varespladib administered after washing promoted the reverse of blockade (100% recovery) at both 30 and 60 minutes ($p>0.05$ vs. control). **Conclusion**: Varespladib prevented and reversed CTX-induced blockade without causing direct muscular effects, demonstrating its potential as a complementary or first-aid therapy in snakebite envenomations. Financial Support: FAPEMIG (APQ-00722-22), CNPq (404129/2025-0) and PRPQ. Approval by the Animal Research Ethical Committee was obtained (CEUA 25/2021).

09.080 **Green Synthesis and Characterization of Silver Nanoparticles from *Tocoyena bullata*: antioxidant, cytotoxic, and wound-healing activities**. Santos HLS[1], Santos AF[2], Araújo AAB[2], Almeida, ERM[2], Silva GNB[1], Silva BM[1], Sobral R[1], Costa CACB[3], Sette-de-Souza PH[2], Freitas JD[3], Correia ACC[2], Albuquerque PBSA[1,2]. [1]UPE, PPG Biologia Celular e Molecular aplicada, Brazil, [2]UPE, PPG Saúde e Desenvolvimento Socioambiental, Brazil, [3]IFAL, Lab Síntese, Análise Química e Caracterização de Materiais, Brazil.

Introduction: The green biosynthesis of silver nanoparticles using phenolic extracts represents a sustainable alternative for the development of wound- healing agents, tissue regeneration through bioactive compounds associated with AgNPs. **Objectives:** This study reports the biosynthesis, characterization, cytotoxicity and wound healing activity of silver nanoparticles (AgNPs) using the extract of Tocoyena bullata (Tb-aq). **Methods:** Synthesis was performed with 30 mL of Tb-aq (adjusted to pH 10 with NaOH 0.1 mol/L), 25 mL of $AgNO_3$ (0.01 mol/L), at 3 °C for 10 min. AThe AgNPs were characterized by Ultraviolet–Visible spectroscopy (UV–Vis), Fourier Transform Infrared Spectroscopy (ATR-FTIR), thermal analyses (TGA/DSC), Dynamic Light Scattering (DLS), and Zeta potential measurements. The antioxidant potential of Tb-aq was evaluated using DPPH and ABTS assays. The cytotoxicity of Tb-aq and AgNPs was assessed in L929 and HaCaT cells through MTT assays, morphological analysis, and trypan blue exclusion tests (1–729 µg/mL). Wound-healing properties were evaluated using the scratch wound-healing assay at 6, 12, and 24 h. **Results:** The FTIR-ATR spectrum showed bands at 3328.6 cm^{-1} (O–H stretching) and 1639.1 cm^{-1} (C=C stretching vibrations), consistent with the presence of functional groups in phenolic compounds and flavonoids, respectively. Antioxidant assays confirmed the presence of the aforementioned compounds at levels of 44.33 ± 0.34 mg GAE/g (phenolic compounds) and 658 ± 16.37 mg QE/g (flavonoids), with IC_{50} values of 82.10 ± 10.87 µg/mL and 15.45 ± 0.53 µg/mL for DPPH and ABTS+ radical scavenging, respectively. The AgNPs exhibited a Zeta potential of -13.06 ± 0.56 mV, indicating good electrostatic stabilization, and an average size of 34.84 ± 0.81 nm (PDI of 0.35 ± 0.005), suggesting that the silver colloidal solution with Tb-aq was stable and free from significant aggregation. Tb-aq (1–729 µg/mL) did not affect cell viability at the tested concentrations in either cell line, whereas the AgNPs showed IC_{50} values of 47.41 ± 2.40 µg/mL (L929) and 65.3 ± 3.29 µg/mL (HaCaT) in the MTT assay, and 41.7 ± 2.4 µg/mL (L929) and 64.2 ± 5.9 µg/mL (HaCaT) in the trypan blue exclusion test. Significant morphological changes in L929 cells were observed from 81 µg/mL onward, while in HaCaT cells the changes were moderate at 81 µg/mL and more pronounced at 243 µg/mL. In the *in vitro* wound-healing assay, Tb-aq promoted increased cell migration in L929 fibroblasts and HaCaT keratinocytes compared to the control group. AgNPs (9 µg/mL) enhanced this effect, increasing cell migration by 14.04% and 16.65% (6 h), 16.36% and 25.72% (12 h), and 16.96% and 25.4% (24 h) in L929 and HaCaT cells, respectively. **Conclusion:** This study, therefore, reveals that Tb-aq functionalized AgNPs possess good colloidal stability and *in vitro* healing potential, which highlights their applicability as a promising therapeutic agent for the treatment of cutaneous wounds.

09.081 **Validation of Leaf Infusions of *Moringa oleifera* Lamarck in the Prevention of Hypertension and Platelet Aggregation**. Portela JVF[1,3,5] ; Silva ND[1,2,3]; Portela EP[1,2,3]; Rêgo AF[2,3]; Albuquerque BA[1,2,3]; Rocha VA[1,2,3]; Oliveira AP[1,2,3,4]. [1]UFPI, Graduate Program in Pharmacology, Brazil; [2]UFPI, Lab Cardiovascular Pharmacology, Brazil; [3]UFPI, Center for Research on Medicinal Plants, Brazil; [4]UFPI, Dept Biophysics and Physiology, Brazil; [5] UFPI, Graduate Program in Biotechnology – Renorbio, Brazil.

Introduction: Cardiovascular diseases are the leading cause of global mortality, with arterial hypertension (AH) and exacerbated platelet aggregation being critical risk factors for thromboembolic events and atherosclerosis *Moringa oleifera* Lamarck is rich in phytochemicals such as flavonoids, glucosinolates, and alkaloids with antioxidant and cardioprotective properties. **Objectives:** To evaluate the prophylactic effects of a 3% *M. oleifera* leaf infusion (InMO 3%) on AH prevention and platelet aggregation in Wistar rats. **Methods:** In MO 3% was prepared with 3 g of leaf powder in 100 mL boiling water, steeped for 2 hours and stored at -20 °C. Male Wistar rats (CEUA/UFPI 275/16) received InMO 3% (0.5 mL·100 g^{-1}, p.o.) for 14 days. Hypertension was induced by L-NAME (100 $mg \cdot kg^{-1} \cdot day^{-1}$, p.o.) for 7 days, with prophylactic treatment starting simultaneously on day 8. SBP and heart rate were monitored by tail plethysmography. Platelet aggregation was induced by ADP (20 μM) and measured by turbidimetry, with mechanistic investigation using sodium nitroprusside (SNP, 10 μM), calmidazolium (10 μM), and ticagrelor (90 $mg \cdot kg^{-1}$). Biochemical, oxidative stress (MDA, SOD, GSH, MPO), and histopathological analyses were performed. Data analyzed by ANOVA/Tukey ($p<0.05$). **Results:** InMO 3% reduced baseline SBP by 15.92 mmHg. In the L-NAME model, it prevented AH onset, reducing SBP by 24.93 mmHg versus the untreated hypertensive group (~120 mmHg), also preventing tachycardia. Biochemically, blood glucose fell 27.07%; total cholesterol (70.67±5.61 mg/dL), LDL (19.07±7.59 mg/dL), VLDL (8.00±1.27 mg/dL), and triglycerides (37.50±4.63 mg/dL) decreased, while HDL rose to 45.50±2.75 mg/dL. Atherogenic index reduced to 0.26±0.04. Cardiac MDA decreased from 287.91 to 115.19±0.07 $nmol \cdot g^{-1}$; SOD increased from 89.99 to 176.85±3.10 μg/μg; GSH rose to 227.10±7.08 mg/g. Histopathology showed reduced vasculitis and necrosis. Platelet aggregation was inhibited by 75.24% (InMO alone) and 75.20% (L-NAME group), via P2Y12 receptor and calmodulin/nitric oxide pathway. **Conclusion:** InMO 3% acts prophylactically against AH and platelet aggregation, likely through oxidative stress modulation, increased nitric oxide bioavailability, and purinergic receptor interaction. Keywords: *Moringa oleifera* Lamarck; Systemic arterial Hypertension; Bioactive compounds. Bioaccessibility; Cardioprotective. **Financial support:** CAPES, CNPq, FAPEPI, UFPI.

09.082 **Anti-Aging Effect of *Spondias tuberosa* Arruda Fruit Peel Extract in a Model of Cellular Photoaging in Immortalized Human Keratinocyte Cells**. Gomes MLC[1,2,3], Pereira MEM[1,3], Albuquerque MN[1,3], Oliveira JCPL[1,2,3], Souza CMO[1,2,3], Fernandes GFS[1], Lima VS[1,2,3], Farias LRT[4], Langassner SMZ[4], Oliveira GD[2,5], Nascimento YM[2,5], Medeiros KCP[6], Veras RC[1,3], Araújo IGA[1,2,3], Medeiros IA[1,2,3]. [1]UFPB, Cardiovascular Pharmacology Lab, Institute for Drug and Medicine Research, Brazil. [2]UFPB, PPG in Bioactive Natural and Synthetic Products (PgPNSB), Health Sciences Center, Brazil. [3]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil. [4]UFRN, PharmacognosyLab, Brazil. [5]UFPB, Multi-User Lab for Characterization and Analysis, Brazil. [6]UFRN, Dept Morphology, Brazil.

Introduction: Cutaneous photoaging is a multifactorial process resulting from chronic exposure to UV radiation, especially UVA, which induces oxidative stress, DNA damage, and inflammation. In this context, natural products rich in antioxidant metabolites, such as -*Spondias tuberosa*- Arruda (umbu tree), an endemic species of the Caatinga biome with great socioeconomic importance, show potential for modulating cellular senescence. **Objective:** This study evaluated the effect of a lyophilized hydroalcoholic extract from the fruit peel of -*Spondias tuberosa* Arruda (LEHCST) in a model of UVA radiation-induced senescence in immortalized human keratinocyte (HaCaT) cells. **Methods:** Chemical characterization was performed by nuclear magnetic resonance (NMR), allowing the identification of secondary metabolites. A UVA radiation-induced senescence model (6, 13, and 19 J/cm^2 corresponding to 20, 40, and 60 minutes of exposure, respectively) was standardized in HaCaT cells using assays for cell viability, superoxide anion production, and cellular senescence, with evaluations performed immediately and at 24 and 48 hours post-radiation. Subsequently, the effect of LEHCST was investigated using two experimental groups: Basal (CTL: non-irradiated cells treated with LEHCST at concentrations of 0.01, 0.05, 0.1, 0.5, and 1.0 µg/mL) and UVA (CTL, UVA 40 min, and UVA 40 min treated with LEHCST at the same concentrations) for 24 and 48 hours to evaluate the aforementioned parameters. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test, and differences were considered statistically significant when $p < 0.05$. **Results:** NMR characterization revealed the presence of phenolic compounds and flavonoids in the extract. Exposure of HaCaT cells to UVA radiation for 40 minutes (13 J/cm^2), with evaluations at 24 and 48 hours, was established as the most suitable experimental condition, as it induced oxidative stress and senescence without causing significant cell damage. In the basal group, LEHCST did not alter cell viability, superoxide anion production, or senescence. In contrast, in the UVA-induced model, all extract concentrations demonstrated antioxidant and anti-senescent activities ($p < 0.05$), evidenced by a significant reduction in superoxide anion production and in the percentage of senescent cells. **Conclusion:** These results demonstrate that LEHCST exerted a protective effect against UVA-induced senescence-associated β-galactosidase activity in HaCaT cells, possibly related to its antioxidant activity. These novel findings highlight the extract's potential as a promising agent for the prevention of cutaneous photoaging. Further studies are needed to elucidate its mechanisms of action.

09.083 **Does Cannabidiol Associated with Pulsed Therapeutic Ultrasound Potentiate Antioxidant Responses in Skeletal Muscle Injury?** Sousa DS, Dos Santos LB, Santana RAN, Lima MM, Azevedo IO, Nascimento VS, Oliveira ED UFS

Musculoskeletal injuries represent conditions of high clinical relevance, capable of generating kinesiological and functional alterations associated with oxidative stress and exacerbated inflammatory processes. These events involve changes in cellular signaling, increased production of reactive oxygen species, lipid peroxidation, and pro-inflammatory mediators. In this context, cannabidiol (CBD), a bioactive compound present in *Cannabis sativa* L., emerges as a potential therapeutic resource due to its antioxidant and anti- inflammatory properties. Furthermore, pulsed therapeutic ultrasound (PTU) may enhance transdermal drug delivery through phonophoresis, potentially favoring the therapeutic effects of full-spectrum formulations. Therefore, this study aimed to evaluate the *in silico* physicochemical properties of CBD and determine the efficacy of topical administration of a CBD-rich C. sativa L. hydrogel, isolated or associated with phonophoresis, on oxidative stress variables in an experimental model of muscle injury. The *in silico* evaluation was performed using SwissADME, PreADMET, and AutoDock Vina to analyze bioavailability, skin permeability, toxicity, and molecular interactions between CBD and antioxidant enzymes, including catalase (CAT) and superoxide dismutase (SOD). The *in vivo* analysis included forty male Wistar rats (250–300 g), randomly distributed into five groups (n = 8): control (CTRL), muscle injury (MI), pulsed therapeutic ultrasound (PTU), PTU associated with full-spectrum gel (PHONO), and topical CBD-rich gel (TOP). Muscle injury was induced in the gastrocnemius muscle using a mechanical impact device generating 0.811 J of energy. Ninety-eight hours after injury induction, the animals were euthanized and the gastrocnemius muscle was collected for biochemical analyses. Lipid peroxidation was evaluated by thiobarbituric acid reactive substances (TBARS), while SOD and CAT activities were determined by spectrophotometric methods. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test ($p < 0.05$). Bioinformatics analyses demonstrated that CBD presented high lipophilicity, adequate bioavailability, favorable skin permeability, and low toxicological potential. Molecular docking revealed stable and energetically favorable interactions between CBD and CAT and SOD, with binding affinities ranging from -7.7 to -9.2 kcal/mol and -6.1 to -7.0 kcal/mol, respectively. Physicochemical analysis of the hydrogel demonstrated pH and density stability after freeze–thaw cycles. The MI group showed increased MDA levels (7.17 ± 2.33 nmolMDA/mg protein) compared with CTRL (1.58 ± 0.82 nmolMDA/mg protein; $p < 0.0001$), whereas PHONO markedly reduced MDA (0.36 ± 0.44 nmolMDA/mg protein; $p < 0.0001$). MI also increased SOD activity (3.86 ± 0.12 U/mg protein), which was reduced by PHONO (0.77 ± 0.19) and TOP (0.92 ± 0.12 U/mg protein; both $p < 0.0001$). Similarly, CAT activity decreased from 1.55 ± 0.08 U/µg protein in MI to 0.32 ± 0.04 in PHONO and 0.48 ± 0.10 U/µg protein in TOP (both $p < 0.0001$). The lower activities of these antioxidant enzymes may reflect reduced intracellular oxidative challenge and, consequently, a lower requirement for compensatory enzymatic antioxidant activity following treatment, rather than impairment of antioxidant defenses. These findings suggest that the CBD-rich hydrogel, associated or not with pulsed therapeutic ultrasound, may reduce lipid peroxidation and modulate intracellular antioxidant responses in skeletal muscle injury.

09.084 **Evaluation of the Effects of Mentha x villosa Ethanolic Extract on the Vascular Reactivity of Rat Aorta**. Alves SML[1], Silva KT[1], Oliveira SKM[1], Ferreira JG[1], Silva MEF[1], Silva MCC[1], Tavares, JF, Araújo AV[1] [1] UFPE-Centro Acadêmico de Vitória (CAV), Brazil [2]UFPB, Brazil

Introduction: Cardiovascular diseases are the leading cause of death in Brazil and worldwide and Systemic Arterial Hypertension (SAH) is the main risk factor. Despite therapeutic advances, blood pressure control remains a challenge, leading many patients to use complementary therapies, such as the use of medicinal plants. **Aim:** To evaluate the cardiovascular effects and mechanisms of action of the ethanolic extract of the aerial parts of *Mentha x villosa* (MVEtPA). **Methods:** Vascular reactivity experiments were made in aortic rings from Wistar rats. Concentration-effect curves were performed on rings with and without endothelium and in preparations pre-contracted with phenylephrine, KCl 20 or 80 mmol/L. Data are expressed as mean ± standard error mean. Difference among groups were assessed by Student's t-test. It was used GraphPad Prism Software and difference was considered when $p < 0.05$. **Results:** MVEtPA induced relaxation in a concentration-dependent manner in rings with (Emax= 102 ± 2.2%, pCE50= 2.84 ± 0.11; n= 7), or without endothelium (Emax= 109 ± 4.6%, pCE50= 2.94 ± 0.01; n= 7). There was no difference between the relaxation induced by MVEtPA in rings pre-contracted with KCl 20 mmol/L (Emax= 112.5 ± 4.3%, pCE50 = 3.48 ± 0.01; n= 4) and KCl 80 mmol/L (Emax= 113.8 ± 5.7%, pCE50= 3.2 ± 0.07; n= 5). **Conclusion:** MVEtPA showed vasorelaxant activity in an endothelium-independent way. The data suggests a possible participation of calcium channels. More studies are needed to further elucidate its mechanism of action. CEUA: 116/2025

09.085 **Evaluation of the Genotoxicity and/or Antigenotoxicity of Natural and Amination-Modified Cashew Gum, through the Somatic Mutation and Recombination Test in *Drosophila melanogaster* Wings**. Castro AJS[1], Machado FS[1], Ribeiro IS[2,3], Paula RCM[3], Araújo AJ[1], Marinho-Filho JDB[1]. [1]UFDpar, Lab Cultura de Células do Delta-PPGBIOTEC- Brasil; [2]IFPI-Brasil; [3]UFC- Brasil

Introduction: Polysaccharide gums are widely distributed renewable resources in nature, and can be extracted from plants, animals, and microorganisms. These polymers have been studied due to their physicochemical properties and the possibility of structural modifications, which broaden their potential applications in pharmacology. In this context, they can be used as excipients in controlled drug release systems, contributing to the protection of active ingredients, increasing bioavailability, and improving therapeutic adherence. The gum extracted from cashew exudate (*Anacardium occidentale*) is a branched heteropolysaccharide composed of β-D-galactose, α-D-glucose, arabinose, rhamnose, and glucuronic acid. Despite its promising properties, cashew gum is still underexplored, making it necessary to deepen studies related to the biological activities of these polysaccharides. **Objective:** To evaluate the mutagenic and antimutagenic potential of natural cashew gum (GCN) and aminated cashew gum (GCA). **Methodology:** For this purpose, the Somatic Mutation And Recombination Test (SMART) was used in *Drosophila melanogaster*, in which 72 -hour-old larvae, resulting from standard (ST) and high metabolic bioactivation (HB) crosses, were treated with the following concentrations of gums (1000 mg/mL, 3000 mg/mL, 6000 mg/mL). Doxorubicin (DOX) was used as a positive control (0.125 mg/mL). The evaluation of antimutagenic activity used the same concentrations of gums in association with DOX. **Results:** GCN showed a significant increase in the number of mutant spots only at the highest concentration, in both the ST and HB crosses. In the ST cross, the frequency of twin spots and the total number of spots increased, while in the HB cross, the increase in mutant spots occurred only in the frequency of small single spots. When associated with DOX, the results show that GCN, at the tested concentrations, did not modulate the mutagenic effects of DOX in either cross. In those treated with GCA, there was a significant increase in the number of mutant spots at all concentrations in the HB cross. When associated with DOX, GCA showed no significant difference at any concentration compared to the positive control. **Conclusion:** Thus, under the experimental conditions, GCN exhibits mutagenic effects at high concentrations and showed no difference in relation to biometabolism. However, GCA exhibits mutagenic effects when metabolized by P450. We can also conclude that neither gum modulates the mutagenic effects of doxorubicin.

09.086 **The Triterpene Friedelin Attenuates TGF-β-Induced EMT in NCI-H292 Lung Cancer Cells and Upregulates TIMP3 Expression**. Almeida JH[1], Bodin A[2], Victoni T[23], Barreto EO[1], Lagente V[2], Ferro JNS[1] [1]UFAL, Lab Biologia Celular, Maceió, AL, Brasil. [2]Université de Rennes, Inserm, Inrae, NuMeCan (Nutrition, Métabolismes et Cancer), Rennes, France. [3]Université de Lyon, VetAgro Sup, Lyon, France.

Epithelial-mesenchymal transition (EMT) is a crucial process in tumor progression, invasion, and metastasis in lung cancer. Transforming growth factor-beta (TGF-β) is a primary driver of EMT, promoting stromal remodeling and loss of cell adhesion. The triterpene Friedelin (FD) is a natural product isolated from plants such as *Maytenus ilicifolia* and *Clusia nemorosa*. It has gained interest due to its anti-inflammatory, antiproliferative and antitumor properties, but its potential role in modulating EMT remains to be elucidated. This study aimed to evaluate the modulatory potential of friedelin on TGF-β-induced EMT in the NCI-H292 lung carcinoma cell line. Initially, EMT induction was standardized by exposing cells to TGF-β (5, 10, or 25 ng/mL) for 48h. Morphological alterations consistent with EMT were observed at 10 and 25 ng/mL, and 25 ng/mL was selected for subsequent experiments. In addition, cell viability was assessed by ATP assay following treatment with FD (10-100 μM), and no significant cytotoxicity was observed at any concentration tested. NCI-H292 cells were then stimulated with TGF-β and treated with FD (FD10 or FD30 μM). Cell morphology was assessed using Giemsa staining and quantitative morphometric analysis (circularity, roundness, and aspect ratio). Gene expression of epithelial (E-cad), mesenchymal (N-cad), and metalloproteinase/inhibitor markers (MMP2, TIMP1, TIMP2, and TIMP3) was determined by qPCR. TGF-β successfully induced a mesenchymal phenotype, significantly altering all morphometric parameters and strongly upregulating N-cad and MMP2 expression (approximately 70-fold). Treatment with FD10 exerted a prominent protective effect, maintaining epithelial morphological characteristics ($p<0.05$). Mechanistically, this morphological preservation correlated with a significant and upregulation of TIMP3, even under TGF-β stimulation. Interestingly, N-cad and MMP2 mRNA levels remained elevated in the FD10 group, suggesting that the initial transcriptional EMT signal was not interrupted. In contrast, treatment with FD30 provided a more modest preservation of epithelial morphology and was accompanied by a reduction in N-cad expression. Friedelin attenuates the morphological transition associated with TGF-β-induced EMT in NCI-H292 cells. This effect does not appear to occur through suppression of the primary EMT transcriptional program, given the persistence of N-cad expression, but may instead involve restoration of proteolytic control through TIMP3 upregulation, limiting cellular remodeling. The distinct responses observed between FD concentrations suggest the involvement of different molecular mechanisms. Previous studies have shown that pentacyclic triterpenes can inhibit the canonical TGF-β/SMAD signaling pathway, while MUC4 silencing has been associated with EMT suppression in NCI H292 cells. Therefore, both pathways emerge as potential molecular targets of friedelin and warrant further investigation. To validate the functional impact of these findings on tumor progression, migration and invasion assays will be performed to determine whether TIMP3 upregulation effectively impairs the invasive potential of these cells.

09.087 *in silico* Characterization of Babassu Oil Constituents as Cyclooxygenase Ligands. Marques MA, da Silveira Cruz-Machado S, Quilenda JC, Nascimento Neto DE, Soares WRA UESB, Dept Health II, Lab Biomedical Sciences and Innovation, Graduate Program in Nursing and Health, Brazil

Introduction: From an ethnopharmacological perspective, the use of babassu oil (Attalea speciosa) in treating cutaneous and gastric lesions suggests anti-inflammatory properties. While its major components (Fatty acids [FAs], tocopherols, and vitamins) are known, their specific bioactive potential remain poorly explored. Nevertheless, they are presumed to modulate cyclooxygenases (COX-1/COX-2), blocking prostaglandin production. This study aimed to identify the major constituents of babassu oil, evaluate their pharmacokinetic and toxicological profiles, and investigate their molecular affinity for COX enzymes *in silico* . Methods: Babassu oil was obtained by cold pressing (Jacobina, BA, Brazil) and analyzed via gas chromatography. Identified FAs and reference NSAIDs (Bromfenac and Diclofenac), obtained from the IUPHAR/BPS database, were optimized for *in silico* predictions. Molecular docking simulation targeting human COX-1 (PDB ID: 6Y3C) and COX-2 (PDB ID: 5IKQ) was performed via AutoDock Vina, with protocol validation via redocking (RMSD), and ADMET predictions through SwissADME. Ligand–receptor interactions within catalytic pockets were mapped using Discovery Studio. Results: The main FAs identified: Lauric Acid (LA, 50.45%), Oleic Acid (OA, 13.23%), Myristic Acid (MA, 12.38%), Capric Acid (CA, 9.12%), Palmitic Acid (PA, 7.37%), and Stearic Acid (SA, 4.94%), complied with Lipinski's Rule of Five (zero violations), exhibiting ideal skin permeability and no cardiotoxicity. *in silico* docking showed potential binding of the FAs to COX-1 (LA: -5.4, OA: -6.6, MA: -6.1, CA: -5.2, PA: -6.1, SA: -6.6 kcal/mol), and COX-2 (LA: -5.3, OA: -5.1, MA: -5.8, CA: -5.3, PA: -5.1, SA: -6.0 kcal/mol) comparable to bromphenac (COX-1: -7.3 versus COX-2: -6.2 kcal/mol) or diclofenac (COX1: -6.6 versus COX2: -5.7 kcal/mol), commercial approved non-selective COX inhibitors. Although OA exhibited the greatest binding selectivity between the cyclooxygenases, the remaining FAs showed similar energies when comparing COX-1 versus COX-2. Unlike the approved drugs, which are known to present hepatotoxicity, these FAs showed no predictive hepatotoxic potential. All fatty acids interacted with active site residues via hydrophobic interactions and hydrogen bonds, with SA establishing the greatest number of key interactions. Conclusion: Babassu oil contains anti-inflammatory phytocomplexes with favorable ADMET profiles. *in silico* binding energies of FAs to cyclooxygenases were comparable to approved drugs. Altogether, this study elucidates molecular targets underlying the anti-inflammatory properties of babassu oil, providing a computational foundation to support its traditional ethnopharmacological use and future viability for dermaceuticals and drug development. This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES).

09.088 **Antioxidant Effect of Extract of *Spondias tuberosa* Arruda in Experimental Diabetic Nephropathy**. Sena VNF[1], Pires LAB[1], Donato FF[2], Albuquerque ECS[1], Araújo IGA[5], Vilar NF[4], Araújo RF[3], Medeiros KCP[3] [1]UFRN, Center for Biosciences, PPG in Biology Structure and Function, Brazil. [2]UFRN, Center for Biosciences, Brazil. [3]UFRN, Center for Biosciences, Morphology Dept, Brazil. [4]UFRN, Center for Biosciences, PPG in Health Sciences, Brazil. [5]UFPB, Health Sciences Center, PPG in Bioactive Natural and Synthetic Products, Brazil.

Introduction: Oxidative stress plays a central role in the pathophysiology of diabetic nephropathy (DN), contributing to renal injury and disease progression in Diabetes Mellitus (DM). Due to the limitations and adverse effects of conventional therapies, medicinal plants have gained attention as potential complementary treatments. *Spondias tuberosa* Arruda ("umbu"), traditionally used in folk medicine for diabetes treatment, remains poorly investigated regarding its effects on renal oxidative stress in DN. **Objectives:** To evaluate the antioxidant activity of the hydroalcoholic extract of *Spondias tuberosa* Arruda (ExSt) on renal oxidative stress in rats with experimental diabetic nephropathy, through immunohistochemical analyses and quantification of reactive oxygen species by immunofluorescence and spectrophotometry. **Methods:** A total of 44 male Wistar rats were used (CEUA: 319.056/2022) and allocated into the following experimental groups: GC, normoglycemic animals; DM, hyperglycemic animals; EX, normoglycemic animals treated with ExSt; DMEX, hyperglycemic animals treated with ExSt; and DMIN, hyperglycemic animals treated with insulin. ExSt treatment (500 mg/kg, orally) and insulin administration (10 IU, intraperitoneally) were performed daily for 30 days after diabetes induction. Renal reactive oxygen species (ROS) production was evaluated using a fluorescent probe, and fluorescence intensity was quantified with ImageJ software. Nitric oxide (NO) and superoxide dismutase (SOD) levels were determined in renal tissue homogenates. In addition, immunohistochemical analyses were performed to evaluate the expression of SOD and caspase-3 (CASP-3) in renal tissue. **Results:** Diabetic animals exhibited marked oxidative stress and renal tissue damage, evidenced by increased ROS fluorescence intensity, elevated nitric oxide (NO) levels, and increased caspase-3 (CASP-3) immunoexpression, confirming the deleterious effects of diabetes on renal tissue. In contrast, diabetic animals treated with ExSt showed reduced ROS fluorescence intensity and lower NO levels, indicating attenuation of oxidative stress. A reduction in CASP-3 expression and increased superoxide dismutase (SOD) immunoreactivity were also observed in renal tissue after ExSt treatment, suggesting decreased cellular damage and increased antioxidant defense mechanisms. **Conclusion:** These findings suggest that ExSt possesses relevant antioxidant activity and may contribute to renal protection in experimental diabetic nephropathy. Furthermore, this study reinforces the therapeutic potential of Brazilian medicinal plants as valuable sources of bioactive compounds for the development of complementary strategies against diabetic complications, encouraging further investigations into natural products for nephroprotective therapies.

09.089 **Hepatoprotective Effect of *Spondias tuberosa* Arruda Extract in Experimental Diabetes and Isolated Hepatocyte Cell Line: Involvement of Oxidative Stress and the PI3K/AKT Pathway**. Pires, LAB[1], Sena, VNF[1], Felipe, FD[2], Vilar, NF[2], Araújo Júnior, RF[2], Vieira, RR[3], Gil, CD[3], Santos, DD[3], Medeiros, IA4, Gonçalves, IGA4, Medeiros, KCP[2] [1]UFRN, Biosciences Center, Graduate Program in Structural and Functional Biology, Brazil, [2]UFRN, Biosciences Center, Dept Morphology, Brazil; [3]Unifesp-EPM, Lab Morphological Sciences and Inflammation, Brazil; [4]UFPB, PPG in Bioactive Natural and Synthetic Products, Brazil

Introduction: Type 1 Diabetes Mellitus (T1DM) is characterized by autoimmune destruction of pancreatic beta cells, resulting in hyperglycemia and metabolic alterations associated with oxidative stress and liver damage. **Objective:** To evaluate the hepatoprotective effects of the hydroalcoholic extract obtained from the fruit peel of *Spondias tuberosa* Arruda (ExSt) in an experimental model of streptozotocin-induced diabetes and its effects on HepG2 cell viabilit. **Methods:** Forty male C57BL/6 mice were used for the experimental T1DM model (CEUA/UNIFESP No. 5495290524) and distributed into the following groups: control (CT), diabetic (DM), therapeutic diabetic (DMTER), and preventive diabetic (DMPRE). Diabetes was induced with streptozotocin (65 mg/kg, i.p.), and ExSt was orally administered (100 mg/kg) for seven weeks. For the *in vitro* evaluation, HepG2 hepatocytes were cultured in DMEM medium. Clinical, biochemical, morphometric, oxidative stress, immunohistochemical and cellular liver analyses were performed. HepG2 cell viability under hyperglycemic conditions was assessed using the MTT assay. **Results:** Diabetic animals (DM) exhibited marked weight loss, polydipsia, polyphagia, and liver injury. Treatment with ExSt (100 mg/kg) partially improved these parameters, significantly reducing water intake and serum ALT levels. Histopathological analysis demonstrated that ExSt attenuated diabetes-induced hepatic damage by reducing necrosis and inflammatory infiltrate, while mitigating hydropic degeneration observed in untreated diabetic animals. Moreover, ExSt decreased tissue reactive oxygen species fluorescence and increased the immunohistochemical expression SOD-1, PI3Kp110β, and AKT-1 ($p<0.05$). TThe MTT assay demonstrated increased HepG2 cell viability under hyperglycemic conditions following ExSt treatment. **Conclusion:** The findings suggest a hepatoprotective effect of ExSt in experimental diabetes, associated with reduced oxidative stress and increased expression of PI3Kp110β and AKT-1. These results reinforce the therapeutic potential of *Spondias tuberosa* as a source of bioactive compounds for the management of T1DM-associated liver complications. However, further studies are required to elucidate the underlying molecular mechanisms.

09.090 **Antioxidant Effects of Annatto Compounds during Aging: Involvement of the Nrf2 and p38MAPK Pathways in Human Mononuclear Cells**. Pádua BC[1,2], Barros e Silva JC[1], Borsato DF[1], Franco FN[1], Chaves MM[1] [1]ICB-UFMG, Biochemistry Lab Aging and Correlated Diseases, Graduate Program in Biochemistry and Immunology, Brazil. [2]CEFET- Curvelo-MG, Dept General Education, Brazil.

Introduction: Aging is characterized by the progressive decline of physiological functions, mainly driven by increased production of reactive oxygen species (ROS) and reactive nitrogen species (RNS). Excessive physiological production of these molecules promotes cumulative oxidative damage, which may result in functional decline of tissues and organs, as they contribute to the development of inflammatory and degenerative diseases. Antioxidants capable of neutralizing or modulating the deleterious effects of reactive species have been widely investigated due to their critical role in attenuating oxidative stress and preventing a broad range of associated disorders. In this context, carotenoids have emerged as prominent bioactive compounds because of their well-established redox properties. Among the natural sources of these compounds, annatto (*Bixa orellana*), rich in geranylgeraniol and tocotrienols, has been described as a potent antioxidant with potential modulatory effects on cellular signaling pathways. However, the mechanisms through which these compounds act during the aging process remain unclear. **Objective:** To investigate, *in vitro*, the antioxidant effects of annatto compounds, as well as their ability to modulate the Nrf2 and p38MAPK pathways in human mononuclear cells from different age groups. **Methodology:** Sixty individuals of both sexes were selected and divided into three age groups (20–39, 40–59, and 60–80 years). Exclusion criteria included smoking, infection, inflammation, lymphoproliferative disorders, atherosclerosis, heart failure, or the use of medications directly affecting immune function. After isolation of mononuclear cells and incubation with 70 mM annatto and/or 150 mM H_2O_2, assays were performed to analyze reactive species production and cellular signaling. This study was approved by the Research Ethics Committee of UFMG (CAAE: 86014525.5.0000.5149). **Results:** Annatto compounds reduced ROS levels under both basal and oxidative conditions in all age groups, particularly in older donors. These compounds also modulated reactive nitrogen species by increasing nitric oxide (NO) levels and reducing peroxynitrite ($ONOO^-$), resulting in a favorable $NO/ONOO^-$ ratio indicative of an antioxidant environment. Inhibition assays revealed that although p38MAPK contributes to redox regulation, the antioxidant effects of annatto are mainly mediated through Nrf2 activation, as confirmed by increased levels of phosphorylated Nrf2 (p-Nrf2), particularly in individuals over 40 years of age. **Conclusion:** Annatto compounds exert age-dependent antioxidant effects, mainly through activation of the Nrf2 signaling pathway, highlighting their potential as a therapeutic strategy against aging-associated oxidative stress.

09.091 **Chalcones Counteract Ketamine-Induced Behavioral, Cognitive, and Neurochemical Alterations in a Schizophrenia-Like Model**. Dalmagro AP[1,2], Reginatto ABCM[3], Riffel IM[3], Valachinski AW[1,4], Lehmkuhl RA[1,5], Buzzi FC[1], Souza MM[1]. [1]Univali, PPG in Pharmaceutical Sciences. [2]FURB, Dept Pharmaceutical Sciences. [3]Univali, BSc Biomedicine. [4]Univali, BSc Psychology. [5]Univali, BSc Biological Sciences.

Introduction: Schizophrenia is a complex psychiatric disorder characterized by positive symptoms, such as delusions and hallucinations, as well as negative and cognitive symptoms. Although currently available antipsychotics are primarily effective in controlling positive symptoms, they show limited efficacy against negative and cognitive symptoms and may cause significant adverse effects. Chalcones are naturally occurring or synthetic compounds with neuropharmacological potential, including effects on oxidative and inflammatory processes and neurotransmitter systems involved in psychiatric disorders. **Objective:** To evaluate the antipsychotic potential of five chalcones in mice subjected to a ketamine-induced schizophrenia-like model. **Methods:** Three-month-old female Swiss mice weighing 25–30 g were subjected to a ketamine-induced schizophrenia-like model (10 mg/kg, i.p.). The animals were assigned to the vehicle, naïve, CH1, CH2, CH3, CH4, CH5, and haloperidol groups. Chalcones were administered intraperitoneally at 10 mg/kg, while haloperidol (1 mg/kg, i.p.) was used as the positive control. Following model induction, the animals were evaluated in the open-field test (OFT), climbing test (CT), stereotypy test, inhibitory avoidance test (IAT), elevated plus-maze test (EPM), catalepsy test, and tail suspension test (TST). The prefrontal córtex (PFC) and striatum (S) were dissected for dopamine and glutamate quantification. CEUA/UNIVALI approved the experimental protocol; protocol no. 021/2020. **Results:** Ketamine induced hyperlocomotion and increased exploratory activity in the OFT ($p<0.01$), altered climbing and stereotyped behaviors ($p<0.05$), impaired memory performance ($p<0.001$), and induced anxiety-like behavior in the EPM ($p<0.05$). In the OFT, animals treated with chalcones 1 and 3 showed fewer crossings ($p<0.001$). Exploratory activity was reduced in animals treated with chalcones 1, 3, 4, and 5 ($p<0.001$) and chalcone 2 ($p<0.01$). The ketamine-induced memory deficit was reversed in all chalcone-treated groups ($p<0.05$). Animals treated with chalcones 1 and 4 showed a higher frequency of entries into the open arms of the EPM ($p<0.05$). Catalepsy was observed only in animals treated with chalcone 4 or haloperidol ($p<0.001$). Neurochemical analysis showed that ketamine increased dopamine levels in the S ($p<0.001$) and PFC ($p<0.01$), as well as glutamate levels in both brain regions ($p<0.01$). Treatment with all chalcones reduced striatal dopamine levels, with more pronounced effects in animals receiving chalcones 4 and 5 ($p<0.001$). In the PFC, dopamine levels were reduced in all chalcone-treated groups ($p<0.05$). Regarding glutamate, animals treated with chalcones 1, 3, and 4 showed reduced levels in the S ($p<0.05$), whereas reduced glutamate levels in the PFC were observed in animals treated with chalcones 2 and 4 ($p<0.01$) and chalcone 3 ($p<0.05$). **Conclusion:** Taken together, the findings indicate that the evaluated chalcones have antipsychotic potential, with effects on ketamine-induced behavioral, cognitive, and neurochemical alterations. Further studies are needed to identify the most promising compounds and clarify their mechanisms of action.

09.092 **P1G10 Proteolytic Fraction of** *Vasconcellea cundinamarcensis* **Latex Induces Analgesia through Activation of the PI3Kγ/NOS/NO/KATP Signaling Pathway in neuropathic mice**. Machado DPD Araújo BS Cota MES Freitas KM Romero TRL Lopes MTP. ICB-UFMG, Dept Pharmacology, PPG in Biological Sciences: Physiology and Pharmacology, Brazil

Introduction: The P1G10 proteolytic fraction from the fruit latex of *Vasconcellea cundinamarcensis* shows evidence of antitumor/antimetastatic activity against breast tumor in a 4 applications model, in the presence or absence of Paclitaxel (PTX). This chemotherapeutic agent is known to induce neuropathic pain and neurotoxicity. Furthermore, in the 4 applications model, we observed an improvement in the clinical signs of female Balb/C mice. Since anti-inflammatory activity is also described for P1G10, we propose its possible analgesic activity against PTX-induced neuropathy. **Objectives:** The aim of this study was to evaluate the analgesic potential of P1G10 in neuropathic pain and the role of the nitrergic system in this process. **Methods:** Female BALB/c mice were induced to develop neuropathy through the administration of PTX (8 mg/kg - four days, *i. p.*). To assess nociception, we used the Randall and Sellito test. To evaluate the nitrergic system, a pathway common to many analgesic systems, we used inhibitors of components of the PI3Kγ pathway and an ATP-sensitive potassium channel blocker. The results are presented as the mean and standard error of the mean. The data obtained were submitted to analysis of variance (ANOVA) followed by the Bonferroni test, they were considered statistically significant values of $p < 0,05$. CEUA 161/2023, UFMG. **Results**: It was observed that P1G10 was able to increase the nociceptive threshold of neuropathic animals. When testing the participation of the pathway PI3K/NOS/NO/KATP. A reduction in the nociceptive threshold in the inhibition of PI3Kγ and soluble guanylate cyclase, indicating the participation of this pathway in the analgesic process. A reduction in the nociceptive threshold was also observed in the inhibition of the three isoforms of nitric oxide synthase (neuronal, inductive e endothelial), indicating that NO participates in analgesia. And a reduction in the nociceptive threshold was observed when blocking the channel for ATP-sensitive potassium, a common analgesic mechanism for this pathway, showing that P1G10 analgesia goes through the entire process of PI3K/NOS/NO/KATP. **Conclusions:** The results demonstrate that P1G10 can reverse PTX-induced neuropathic pain, and the PI3k/NOS/NO/GCs pathway, which can activate ATP-sensitive potassium channels, participates in the analgesic process of this substance. **Financial support:** FAPEMIG, APQ 01758-22 and BPD-00941-22

09.093 **Esophagoprotective Effect of *Arthrospira platensis* in Experimental Erosive Esophagitis: Contribution of Antioxidant Activity Following Simulated Gastrointestinal Digestion**. Ferreira JL[1], Lopes ALF[1], Silva KC[1], Fernandes TMP[1], Oliveira AP[1], Gomes IAB[1], Rodrigues FSM[2], Medeiros JVR[1], Nicolau LAD[1]. [1]UFDPar, Lab Inflammation and Translational Gastroenterology, Brazil, [2]Unifesp, Lab Autonomic and Cardiovascular Pharmacology.

Introduction: Gastroesophageal reflux disease (GERD) is a chronic inflammatory disorder characterized by reflux-induced esophageal injury. Although proton pump inhibitors remain the standard therapy, incomplete symptom control and concerns regarding long-term use have stimulated the search for complementary therapeutic approaches. *Arthrospira platensis* (Spirulina) is a cyanobacterium rich in bioactive compounds with antioxidant and anti-inflammatory properties that may contribute to esophageal protection. **Objective:** To evaluate the esophagoprotective effects of *Arthrospira platensis* in experimental erosive esophagitis and to investigate its antioxidant activity under simulated gastrointestinal digestion conditions using the INFOGEST static *in vitro* digestion protocol. **Methods:** Male Wistar rats (250–290 g) were allocated into four groups: Sham, erosive esophagitis (EE), Spirulina (500 mg/kg/day, p.o.) + EE, and alginate + EE. Animals received Spirulina supplementation for two months before surgical induction of EE. Ten hours after surgery, esophageal tissues were collected for macroscopic evaluation, wet weight determination, myeloperoxidase (MPO) activity, malondialdehyde (MDA) levels, histomorphometric analyses, and histochemical staining with periodic acid-Schiff (PAS) and Alcian Blue. Antioxidant activity of Spirulina extracts was evaluated by 2, 2-diphenyl-1-picrylhydrazyl (DPPH) and 3-ethylbenzothiazoline- 6-sulfonic acid (ABTS) assays before and after simulated gastrointestinal digestion using the INFOGEST static *in vitro* digestion model. **Results:** EE induced extensive esophageal lesions, increased tissue edema, elevated MPO activity and MDA levels, and promoted histological alterations associated with mucosal injury. Pretreatment with *Arthrospira platensis* significantly reduced macroscopic damage, esophageal wet weight, MPO activity and lipid peroxidation. Histological analyses demonstrated preservation of epithelial architecture, while PAS and Alcian Blue staining revealed maintenance of mucin content and the protective mucus layer. In antioxidant assays, Spirulina subjected to simulated gastrointestinal digestion exhibited greater DPPH and ABTS radical scavenging activity than non-digested preparations, suggesting enhanced bioaccessibility of antioxidant compounds after digestion. These findings were accompanied by attenuation of oxidative stress markers *in vivo*. **Conclusion:** Long-term supplementation with *Arthrospira platensis* protected the esophageal mucosa against reflux-induced injury, reducing inflammation and oxidative stress while preserving epithelial and mucus barrier integrity. The enhanced antioxidant activity observed after simulated gastrointestinal digestion supports the bioaccessibility of Spirulina-derived antioxidant compounds and may contribute to its esophagoprotective effects.

09.094 **Antimicrobial and Antibiofilm Activity of Polymeric Nanocapsules Loaded with Oregano** (*Origanum vulgare* L.) **Essential Oil against Gram-Negative Bacteria**. Alves ARS[1], Oliveira-Filho JMD[1], Pessoa JVA[1], Azevedo KMS[1], Formiga ALD[3], Lacerda AF[1,2], Santos LFA[3], Lima EO[3], Vasconcelos U[2,3], Júnior FHX[3], Travassos RA[1,2] [1]UFPB, Laboratório de FarmacoBiotecnologia (FarmaBio), Brazil; [2]UFPB, Graduate Program in Cellular and Molecular Biology (PPgBCM), Brazil; [3]UFPB, Graduate Program in Bioactive Natural and Synthetic Products (PPgPNSB), Brazil.

Introduction: Antimicrobial resistance and biofilm formation pose major challenges to the effective control of bacterial infections. In this context, nanostructured delivery systems may enhance the stability, bioavailability, and antimicrobial efficacy of bioactive compounds. Therefore, this study aimed to produce and characterize polymeric nanocapsules containing oregano essential oil (NPCOEO) and evaluate their antimicrobial and antibiofilm activities against Gram-negative bacteria. **Methods:** NPCOEO were prepared using the nanoprecipitation method and characterized in terms of particle size, polydispersity index (PDI), zeta potential, Fourier-transform infrared spectroscopy (FTIR), OEO content, encapsulation efficiency, and physicochemical stability over 30 days. *E. coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Klebsiella pneumoniae* ATCC 13883, and *Salmonella enterica* serovar Typhimurium ATCC 14028 were tested. The antimicrobial activities of free and nanoencapsulated oregano essential oil (OEO) were assessed using the broth microdilution method to determine the minimum inhibitory concentration (MIC). The potential involvement of the cell wall was investigated using a sorbitol protection assay. Antibiofilm activity was assessed by crystal violet staining in assays evaluating the inhibition of biofilm formation and the eradication of mature biofilms. All experiments were performed in triplicate in at least three independent assays. Data were expressed as mean ± standard deviation (SD). **Results:** NPCOEO had a mean particle size of 247.4 ± 2.8 nm, a PDI of 0.101 ± 0.016, and zeta potential of -25.06 ± 0.57 mV, indicating a homogeneous particle distribution. The OEO content was 19.41 ± 0.59 mg/mL, with encapsulation efficiency greater than 99.99%. The physicochemical parameters remained stable throughout the 30-day evaluation period. The MICs of free OEO against *E. coli*, *P. aeruginosa*, *K. pneumoniae*, and *S. Typhimurium* were 1,024, 1,024, 256, and 256 µg/mL, respectively, whereas those of NPCOEO were 256, 512, 512, and 256 µg/mL, respectively. Thus, nanoencapsulation decreased the MIC fourfold against *E. coli* and twofold against *P. aeruginosa*, did not alter the MIC against S. Typhimurium, and increased it twofold against *K. pneumoniae*. In the presence of sorbitol, increased MICs were observed against *E. coli* and S. Typhimurium, suggesting that alterations in the bacterial cell envelope may contribute to the antimicrobial activity of NPCOEO. At the highest concentrations tested, NPCOEO inhibited biofilm formation by up to 99.8% for *K. pneumoniae* and 96.3% for *P. aeruginosa*. It also reduced preformed biofilms by up to 78.6% for *E. coli*, 67.5% for *P. aeruginosa*, and 62.3% for *K. pneumoniae*. **Conclusion:** NPCOEO exhibited suitable physicochemical properties, high encapsulation efficiency, and stability throughout the 30-day evaluation period. Nanoencapsulation enhanced the antimicrobial activity of OEO against *E. coli* and *P. aeruginosa* and provided relevant activity against biofilm formation and preformed biofilms. These findings support NPCOEO as a promising formulation for further investigation as a complementary strategy for controlling Gram-negative bacteria and their biofilms.

09.095 **Glucomannan from *Acrocomia corumbaensis* Attenuates Inflammation and Preserves the Mucus Barrier in DSS-Induced Colitis**. Brito MSC[1], Taporoski AK[2], Rech KS[1], Santos LBS[1], Martins FG[1], Gois MB[3], Cordeiro LMC[2], Werner MFP[1] [1]UFPR, Pharmacology and [2]Biochemistry and Molecular Biology, [3]UFR, Faculty of Health Sciences

Introduction: Ulcerative colitis (UC) is a chronic inflammatory disease characterized by weight loss, abdominal pain, diarrhea and hematochezia. The polysaccharide from bocaiuva pulp (BFS), an acetylated glucomannan (Man:Glc 4.3:1; 24% acetylation; Mw=1.82×10^5 g/mol), showed mucosal protection via physical barrier formation in an ethanol-induced gastric ulcer model. Thus, this study investigated BFS in an UC model. **Methods:** For 7 days, UC was induced in female and male C57BL/6 mice with 3% DSS and animals were orally treated with vehicle (water) or BFS (100 mg/kg). Weight loss, hematochezia and stool consistency were monitored daily to calculate the disease activity index (DAI). Then, animals were euthanized and colons were excised for histology and cytokine analysis. **Results:** DSS reduced body weight (females: 13%; males: 11%) and increased DAI, peaking at day 8 (6.5±0.6; 6.1±0.3 scores). DSS decreased colon length (females: 18% males: 21%) relative to controls (8.6±0.2; 9.7±0.2 cm). BFS did not prevent these UC signs. DSS increased submucosal (females: 218%; males: 142%) and muscular layer thickness (females: 68%) and reduced female mucosal thickness (28%) relative to controls (31.4±4.1; 31.5±3.2; 56.6±6.6 µm; 278.1±20.3). BFS reduced submucosal thickness (35%) and increased mucosal thickness (39%) in females. Crypt depth and width decreased with DSS (females: 53%, 43%; males: 42%, 25%) relative to controls (112.9±3.1, 34.5±1.1; 129.5±3.5, 32.6±0.7 µm), but increased with BFS (118%, 58%; 52%, 32%). Enterocyte height decreased with DSS (females: 17%; males: 29%) relative to controls (20.4±0.7; 21.3±0.1 µm) but increased with BFS (15%; 28%). Histological scores increased with DSS (females: 75%; males: 50%) relative to controls (2.0 scores) and decreased with BFS (42%; 33%). MPO increased with DSS (females: 122%; males: 123%) relative to controls (9.6±0.8; 11.7±1.2 O.D./mg of protein) and decreased with BFS (46%; 74%). DSS elevated IL-1β, TNF-α, IFN-γ in females (1022%, 130%, 132%) and IL-1β in males (170%) relative to controls (1.4±1.4, 0.4±0.1, 0.5±0.1; 1.8±0.5 µg/mg of protein) and BFS reduced all cytokines (70%, 68%, 67%; 51%). DSS reduced acid and neutral mucins (females: 37%, 35%; males: 59%, 63%) and MUC-2 (81%; 56%) relative to controls (172743±8756, 153027±13946, 186923±20224; 135245±17754, 101578±97642; 58493±31796 pixels/field), while BFS increased these (62%, 84%; 115%, 195%; 415%, 113%). **Conclusion:** BFS did not prevent clinical signs but preserved the mucus barrier and exerted anti-inflammatory effects.

09.096 **Decrease of the Postprandial Hyperglycemia in Patients with Type 2 Diabetes by Raw Cinnamon in the Form of Hard Gelatin Capsules or Powder Dissolved in Water**. Welker AF, Moreira FD, Gallassi AD, Moreira DC, Reis CEG, UnB

Introduction: Contradictory claims about the efficacy of several medicinal plants to promote glycemic control in patients with type 2 diabetes mellitus (T2DM) have been explained by divergences in the administration form and by extrapolation of data obtained from healthy individuals. It is not known whether the antidiabetic effects of traditional herbal medicines are influenced by gelatin capsules. This randomized crossover trial aimed to evaluate the acute effect of a single dose of raw cinnamon consumed orally either dissolved in water as a beverage or as ordinary hard gelatin capsules on postprandial hyperglycemia (>140 mg/dL; >7.8 mmol/L) in T2DM patients elicited by a nutritionally-balanced meal providing 50 g of complex carbohydrates. Methods Fasting T2DM patients (n = 19) randomly ingested a standardized meal in five experimental sessions, one alone (Control) and the other after prior intake of 3 or 6 g of crude cinnamon in the form of hard gelatin capsules or powder dissolved in water. Blood glucose was measured at fasting and at 0.25, 0.5, 0.75, 1, 1.5 and 2 hours postprandially. After each breakfast, its palatability scores for visual appeal, smell and pleasantness of taste were assessed, as well as the taste intensity sweetness, saltiness, bitterness, sourness and creaminess. Results The intake of raw cinnamon dissolved in water, independently of the dose, decreased the meal-induced large glucose spike (peak-rise of +87 mg/dL and Δ1-hour glycemia of +79 mg/dL) and the hyperglycemic blood glucose peak. When cinnamon was taken as capsules, these anti-hyperglycemic effects were lost or significantly diminished. Raw cinnamon intake did not change time-to-peak or the 2-h post-meal glycaemia, but flattened the glycemic curve (lower iAUC) without changing the shape that is typical of T2DM patients. Conclusions This cinnamon's antihyperglycemic action confirms its acarbose-like property to inhibit the activities of the carbohydrate-digesting enzymes α-amylases/α-glucosidases, which is in accordance with its exceptionally high content of raw insoluble fiber. The efficacy of using raw cinnamon as a diabetes treatment strategy seems to require its intake at a specific time before/concomitantly the main hyperglycemic daily meals. Trial registration: Registro Brasileiro de Ensaios Clínicos (ReBEC), number RBR-98tx28b.

09.097 *In vitro* and *in vivo* Neuropharmacological Evaluation of Guarana and Mate Aqueous Extracts. Falconi-Souto A, Piristrello BS, Marques AA, Chaves VSOG, Lago JHG, Mendes FR. UFABC

Introduction: Guarana (*Paullinia cupana*, PC) and mate (*Ilex paraguariensis*, IP) are Brazilian plants rich in caffeine and popularly used as stimulants, anti-stress, for memory improvement and other uses related to adaptogen activity. Our goal was to evaluate the effect of this species on target enzymes and animal models of memory and depression. Methods: Extracts of IP leaves and PC seeds were prepared using 10% of the powders in hot water. The main chemical classes were evaluated by nuclear magnetic resonance. *In vitro* acetylcholinesterase (AChE) inhibition was determined based on Ellman's method using acetylthiocholine iodide as substrate, while the inhibition of tyrosine was evaluated using L-DOPA as substrate. The *in vitro* inhibitory activity of total monoamine oxidase (MAO) was first measured in rat brain homogenate and then each isoform was evaluated using recombinant human MAO-A and MAO-B purified enzymes and kynuramine as substrate. In behavioral studies, groups of eight animals (3-months male C57BL/6 mice) were treated orally with water, IP or PC (50 and 300 mg/kg) and submitted to the following tests: Morris water maze (MWM), passive avoidance test (PAT) and tail suspension test (TST). Scopolamine (1 mg/kg, i.p.) was used to induce amnesia in the memory tests. Plasmatic levels of corticosterone and the levels of dopamine and serotonin from mice's cortex were determined by ELISA following the manufacturer's protocol. The project was registered at the National System for Genetic Heritage and Associated Traditional Knowledge Management (protocols #A415A1E and #AC4A3DC) and approved by the Ethic Committee on Animal Use of ABC (protocol #1962031224). Results: Phenolic acids and alkaloids were identified in both extracts, including the presence of caffeine. The IC50 of AChE was 665.8 (IP) and 163.3 µg/ml (PC) and for tyrosinase was 130.1 (IP) and 108.3 µg/ml (PC). IP and PC induced 55.8 and 68.6% of inhibition of MAO total at 1 mg/ml, respectively. Assays with purified isoforms of MAO revealed that IP and PC extracts are not selective, inhibiting both isoforms in a similar way. In the behavioral study, scopolamine induced deficits on MWM and PAT ($p<0.05$), but IP and PC did not prevent memory impairment. PC at both doses and IP at the higher dose reduced the immobilization time on TST ($p<0.05$). There was an increase in corticosterone level of mice after the TST stress in control animals compared to non-stressed mice (83.3±11.3 vs 139.5±10.0), but IP and PC did not reverse this effect. There was no difference among groups on the brain levels of dopamine and serotonin. No other differences were observed. Conclusion: The results showed moderate *in vitro* inhibitory activity of IP and PC on AChE, tyrosinase and MAO and antidepressant-like effect on TST, but this effect may be due to the caffeine stimulant effect.

09.098 **Oral Supplementation with** *Pennisetum glaucum* (L.) **Mitigates Multi-Organic Dysfunction in HPV16-Transgenic Mice**. Lima LAS, Oliveira PA, Hajri L, Bastos MMSM, Medeiros R, Ghodbane S, Ammari M, Faustino-Rocha AI, Gil da Costa RM [1]UFMA, PPG in Adult Health, Brazil. [2]University of Trás-os-Montes and Alto Douro, Centre for the Research and Technology of Agro-Environmental and Biological Sciences, Portugal. [3]University of Tunis El Manar, Higher Institute of Applied Biological Sciences of Tunis, Tunisia. [4]University of Porto, Lab for Process Engineering, Environment, Biotechnology and Energy, Portugal. [5]Research Center of IPO-Porto, Molecular Oncology and Viral Pathology Group, Portugal.

Introduction: Human papillomavirus (HPV)-induced cancers are frequently associated with oxidative stress, and cachexia. *Pennisetum glaucum* (L.) is a fast-growing cereal cultivated mainly in tropical regions. **Objectives:** To evaluate the effects of oral *Pennisetum glaucum* supplementation in HPV16-transgenic mice. **Methods:** The experimental groups included (1) wildtype (WT) mice with standard diet, (2) WT mice with 36% Pennisetum, (3) transgenic mice with standard diet, (4) transgenic mice with 29% Pennisetum, and (5) transgenic mice with 36% Pennisetum (n=5/group). The seeds were incorporated into the diet at 29% and 36%. During 4 weeks, body weight, food and water intake, and humane endpoints were recorded. Body condition, posture, coat and grooming, mucosae, eyes, ears, and whiskers, response to external stimuli, mental status, body temperature, respiratory rate, presence of papillomas, and faeces appearance were evaluated. At sacrifice, blood and tissue samples were collected for analysis. The activity of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GR), glutathione S-transferase (GST), reduced glutathione (GSH), oxidized glutathione (GSSG), oxygen reactive species (ROS), thiobarbituric acid reactive substances (TBARS), and carbonyls were evaluated as markers of oxidative stress. Continuous data were compared among groups using analysis of variance (ANOVA) followed by post hoc Tukey's test. Histological data were examined using the Chi-squared test. **Results:** Oral millet supplementation was safe and well tolerated by WT and transgenic mice, with no adverse effects on animal welfare. In HPV16-transgenic mice, supplementation improved health status, reduced serum glucose levels, enhanced antioxidant responses, and decreased the severity of HPV-induced skin and organ lesions, but no significant differences were found between the 29% and 36% doses. **Conclusion:** *Pennisetum glaucum* was safe under the experimental conditions and showed potential as a functional food to reduce systemic complications associated with HPV-induced disease.

09.099 **Preliminary Evaluation of Cytotoxicity and Survival Rate After Beta-Myrcene and Gamma Terpinene Treatment in Experimental Sepsis**. Silva GHO, Previato CFA, Rocha EMT, Cuman RKN UEM

Sepsis is a clinical syndrome in which infection triggers an uncontrolled systemic inflammatory response, leading to organic dysfunction, septic shock, and death. Thus, sepsis is the one of the greatest challenges for septic patient management, whereas they presented high morbidity and mortality. This study aimed to evaluate the cytotoxicity and survival rate of beta-myrcene (MYR) and gamma-terpinene (TPN) in an experimental sepsis model. Cytotoxicity was assessed by MTT assay in leukocytes exposed to MYR or TPN at concentrations of 3, 10, 30, and 90 µg/mL for 90 minutes performed in three independent experiments. Survival rate was evaluated over 7 days in C57BL/6 mice (n=10) subjected to cecal ligation and puncture (CLP), treated orally with MYR or TPN at 100 or 200 mg/kg one hour before surgery and once daily thereafter, by gavage. Data were analyzed using GraphPad Prism® software (version 8.0) and expressed as mean ± standard error of the mean (SEM). Data were submitted to analysis of variance (ANOVA) followed by Tukey's post hoc test, with $p<0.05$ considered statistically significant. Survival rate was calculated using the Kaplan-Meier method. All compounds exhibited no cytotoxic activity at any tested concentration, maintaining cell viability above 90%. Regarding survival, the Sham group maintained 100% survival throughout the study, confirming the validity of the sepsis model, while the CLP group reached 30% survival at day 7. MYR at 100 mg/kg maintained 100% survival, while MYR 200 mg/kg and TPN 200 mg/kg reached 80%, and TPN 100 mg/kg reached 90% survival. All treated groups showed significantly higher survival rates compared to CLP ($p<0.05$). These findings indicate that MYR and TPN have no cytotoxicity and improve survival in experimental sepsis, suggesting their potential as adjuvant therapeutic strategies. However, further studies are needed to elucidate the mechanisms underlying these effects, particularly regarding the modulation of inflammatory mediators and cell signaling pathways involved in sepsis progression. Ethics Committee approval: No. 4628291021. **Financial support:** CAPES e CNPq. Enable GingerCannot connect to Ginger Check your internet connection or reload the browserDisable Ginger?How to use GingerRephraseRephrase with Ginger (Ctrl+Alt+E)Edit in GingerGinger is checking your text for mistakes...Disable Ginger in this text fieldDisable Ginger on this website×

09. 100 **Cytotoxic Activity of Sediment-Associated Bacteria Isolated from the Parnaíba Delta EPA, Northeastern Brazil.** Garcia IAA[1], Dias LFS[1], Trindade MAC[1], Lacerda JC[1], Silva JYG[2], Florêncio KGD[2], Wilke DV[2], Guimarães LA[1]
[1]UFPI, Senador Helvídio Nunes de Barros Campus, School of Medicine, Picos, Piaui, Brazil; [2]UFC, School of Medicine, Dept Physiology and Pharmacology, Drug Research and Development Center, Fortaleza, Ceara, Brazil.

Introduction: Sediments from coastal and estuarine ecosystems are recognized as reservoirs of microbial diversity and an important source of microorganisms capable of producing bioactive metabolites with potential pharmaceutical applications. Although the Parnaíba Delta Environmental Protection Area (EPA) represents one of the most important coastal ecosystems in Northeastern Brazil, the biotechnological potential of its sediment-associated bacteria remains poorly explored. **Objectives:** To investigate the cytotoxic activity of crude extracts produced by sediment-associated bacteria recovered from sites within the Parnaíba Delta EPA, including Coqueiro Beach (Piauí) and the margins of the Delta (Maranhão). **Methods:** Sediment samples collected during low tide from Coqueiro Beach and sites within the Parnaíba Delta EPA were processed using desiccation and heat-treatment approaches followed by cultivation on seawater agar (SWA) and A1 media supplemented with cycloheximide to inhibit fungal growth. Plates were incubated at 24–26°C, and individual colonies were purified through successive subculturing on A1 agar. Purified isolates were cultivated in A1 liquid medium (50 mL) for 7–10 days under agitation (150 rpm, 26–28°C). Aliquots (150–200 µL) of the resulting cultures were spread onto A1 agar plates and incubated for an additional 7–10 days. Solid cultures were then harvested and extracted with ethyl acetate (50 mL) in three extraction cycles assisted by ultrasonic bath (20 min), followed by filtration and solvent evaporation under reduced pressure. Crude extracts were evaluated for cytotoxic activity in human colorectal cancer cells (HCT-116) using the sulforhodamine B (SRB) assay at 50 µg/mL after 72 h of incubation. **Results:** Of the 44 bacterial isolates obtained, 27 crude extracts were evaluated for cytotoxic activity. Eight extracts (29.6%) exhibited greater than 75% inhibition of cell proliferation in the SRB assay and were therefore considered active. The most active extracts were BRD-011 and BRD-012, which produced nearly complete inhibition of cell proliferation. Additional active extracts included BRD-014 (89.3%), BRD-006 (87.2%), BRD-003 (86.6%), BRD-004 (86.4%), BRD-002 (85.9%), and BRD-010 (83.3%). Notably, six of the eight active extracts were obtained from isolates recovered from the Parnaíba Delta EPA, including the two most active extracts (BRD-011 and BRD-012). **Conclusion:** Sediment-associated bacteria from the Parnaíba Delta and Coqueiro Beach represent a promising source of cytotoxic metabolites. The predominance of active extracts among isolates recovered from the Parnaíba Delta EPA highlights the biotechnological potential of this understudied ecosystem. These findings reinforce the importance of exploring coastal microbial diversity as a source of bioactive compounds with potential pharmaceutical applications.

09. 101 **Exploring the Analgesic and Anti-Inflammatory Potential of *Oxyuranus scutellatus* Snake Venom**. Giorgi R[1], Corrêa RCD[1], Camilo MEP[1], Spencer P[2], Gonçalves LRC[1], Zychar BC[1], Chacur M4 [1]IBu, Lab Pathophysiology, PPG in Toxinology, Brazil; [2]Nuclear and Energy Research Institute, Brazil; [3]ICB-USP, Dept Anatomy, Brazil.

Introduction: The venom of the snake *Oxyuranus scutellatus* (vOs), commonly known as the coastal taipan, is considered one of the most neurotoxic venoms in the world and causes severe systemic reactions. However, it does not induce significant local effects such as pain or edema. Literature has demonstrated that snake venoms with neurotoxic activity may contain molecules with analgesic (antinociceptive) properties. In this sense, previous results obtained by our group showed that orally administered (p.o.) vOs induces antinociceptive effects in rats. However, it remains unknown whether vOs possesses anti-inflammatory properties that could contribute to its antinociceptive effects. **Objectives:** In this study, we investigated the analgesic profile of vOs in carrageenan (Cg)-induced hyperalgesia in rats. In addition, we evaluated its potential anti-inflammatory activity. **Methods:** The analgesic profile of vOs was evaluated in carrageenan (Cg)-induced hyperalgesia (200 µg/paw) in rats subjected to the paw pressure test. A dose of 1 µg/kg of vOs (p.o.), previously established as the most effective dose for inducing analgesia in inflammatory pain, was used. Both the duration of the analgesic effect of vOs and its ability to inhibit established hyperalgesia were assessed. Hyperalgesia was measured at the peak of the Cg response, 3 h after intraplantar (i.pl.) administration. The anti-inflammatory activity of vOs (1 µg/kg, p.o.) was assessed by measuring rat paw thickness before and after i.pl. injection of Cg (500 µg/paw). In addition, the effect of vOs on leukocyte-endothelial interactions was investigated by intravital microscopy using the microcirculation of the rat spermatic fascia following intrascrotal injection of Cg (150µg/100µL). The parameters analyzed included leukocyte rolling, adhesion, and migration. Oral administration of sterile saline was used as a control group in all evaluations. **Results:** The obtained data demonstrated that vOs (1 µg/kg) not only induced analgesia when administered 4 h before Cg injection, but also reversed hyperalgesia when treatment was performed 1 h after the irritant injection. Regarding the inflammatory parameters, vOs at a dose of 1 µg/kg inhibited edema at both the third and fifth hours after Cg administration. In addition, analysis of leukocyte-endothelial interactions showed that vOs increased leukocyte rolling while significantly reducing leukocyte adhesion and migration in the inflamed area. **Conclusion:** Our results demonstrate for the first time that, during acute inflammatory processes, vOs not only induces analgesia but also exhibits anti-inflammatory activity. These findings suggest that the venom of *Oxyuranus scutellatus* may represent a promising source of therapeutic molecules for the treatment of pain and inflammation.

09. 102 **Toxicity and Genotoxicity Evaluation of the Aqueous Extract of** *Mimosa tenuiflora* (**Willd.**) **Poir.** (**Fabaceae**) **in Mice**. Santana JI[1], Dorvigny BM[2], Carvalho MEO[1], Silva TG[2], Aguilar CN[3], Chagas CA[5], Martins RD[5], Ximenes RM[2]
[1]UFPE, PPG in Biological Sciences, Brazil, [2]UFPE, Dept Antibiotics, Brazil, [3]Universidad Autónoma de Coahuila, School of Chemistry, Mexico, [5]UFPE, Academic Center of Vitoria, Brazil.

Mimosa tenuiflora (Willd.) Poir. (Fabaceae) is a tree species widely distributed throughout Central and South America. In addition to its ritual use by various Indigenous communities in Northeastern Brazil, its bark has long been employed in traditional medicine as an anti-inflammatory and to promote wound healing. This species has been reported to exhibit antimicrobial, antioxidant, anti-inflammatory, and wound-healing activities, which have been attributed to the presence of phenolic compounds, terpenoids, and alkaloids. Nevertheless, despite its therapeutic potential and extensive history of traditional use, studies assessing its toxicological safety remain scarce. Therefore, the present study aimed to evaluate the acute and subacute toxicity, as well as the genotoxic potential, of the aqueous extract of M. tenuiflora in mice. This study was approved by the Animal Ethics Committee of UFPE (CEUA No. 101/23) and conducted in accordance with OECD guidelines. The plant material was collected in Pesqueira, Pernambuco, Brazil, and the aqueous extract was prepared by infusion. Acute toxicity was evaluated in male mice following the administration of a single dose of 2,000 mg/kg, with a 14-day observation period. Subacute toxicity was assessed in male and female mice receiving daily doses of 100, 300, or 1,000 mg/kg over 28 days. Clinical signs, body weight, food intake, and hematological and biochemical parameters were monitored. Genotoxicity was evaluated using the comet assay and the micronucleus test. Data from the treated groups were compared with those of the control group using Student's t-test or ANOVA, with a significance level set at $p < 0.05$. No mortality was observed during the experimental period; therefore, the LD_{50} was estimated to be greater than 2,000 mg/kg. In the acute toxicity study, a reduction in food intake and a decrease in hematocrit levels were observed in the treated group. In the subacute toxicity study, body weight reduction was observed in both sexes. In male mice, all treated groups exhibited decreased food intake and increased urea levels, while an increase in white blood cell count was detected in the group receiving 300 mg/kg. In female mice, a reduction in albumin levels was observed in the group treated with 300 mg/kg. The results of the comet assay and micronucleus test revealed no significant DNA damage or chromosomal alterations in any of the groups. Overall, the aqueous extract of *Mimosa tenuiflora* exhibited low toxicity and showed no evidence of genotoxicity in mice. Although some alterations were observed in the biochemical and hematological analyses, these findings were not indicative of systemic toxicity.

Nevertheless, further studies are warranted to provide a more comprehensive safety assessment. The *in vivo* toxicological evaluation of medicinal plant extracts is essential to support their safe use in traditional medicine.

09. 103 **Low Molecular Weight Heparin Improves Mouse Muscle Regeneration after Damage Induced by Bothrops Venom**. Elias SC[3], Souza PDN[1], Machado MM[1], Strauch MA[1,2], Melo PA[1]. [1]ICB-UFRJ, Lab Farmacologia das Toxinas, PPG em Farmacologia e Química Medicinal, Rio de Janeiro, RJ, Brazil; [2]ICBS-UFRRJ, Depto Ciências Fisiológicas, Seropédica, Brazil; 3FF-UFF,-Depto Farmácia e Administração Farmacêutica, Niterói, RJ, Brazil

Introduction:-We examined the effect of treatment with fractionated heparin and polyvalent antivenom on the regeneration of mouse *Extensor digitorum longus* (EDL) muscle after damage by *Bothrops jararacussu* venom injection. Methods- The mice received i.v. treatment, with either low molecular weight heparin (LMWH) or polyvalent antivenom (PAV) 15 minutes and 4 hours after the venom injection. Twenty-one days later, the muscles were dissected and examined by different protocols. Results- The contractile properties were preserved by LMWH treatment, as well as the protein distribution analyzed by western blotting, which showed a decrease of myosin heavy chains in the muscle that received only the venom. On the other hand, when processed on electron microscopy, the regenerated muscle that received only the venom showed myofibrillar disarray and the treatments with LMWH resulted in well preserved and organized myofibrils. LMW treatment did not change the control bleeding time and antagonized this intensity, as well as the inflammatory reaction induced by *Bothrops jararacussu* venom injection. Conclusion-Overall, these data show that fractionated heparin antagonized Bothrops venom myotoxicity, preserved muscle function, architecture and improved regeneration. Key words: Low Molecular Weight Heparin; Skeletal muscle; Muscle Damage and Regeneration; *Bothrops jararacussu* Venom

09. 104 **Gastroprotective Effect of** *Plectranthus gandris* **Decoction Against Ethanol-Induced Gastric Lesions in Mice: Involvement of Antioxidant Activity**. Santos FA[1], Rocha LM[1], Procopio GS[1], Silva JGP[1], Ribeiro MS[1], de Araújo KGR[1], da Silva LR[1], Fontes GCCAB[1], de Souza GS[2], da Silva MEF[2], Pessoa ODL[2]. [1]UFC, Dept Physiology and Pharmacology, Natural Products Lab, Brazil, [2]UFC, Dept Organic and Inorganic Chemistry, Brazil

Introduction: Gastric ulcer is a widespread gastrointestinal disorder affecting millions of people worldwide and results from an imbalance between gastric defensive mechanisms and aggressive factors. Ethanol-induced gastric lesions are associated with free radical generation, lipid peroxidation, and inflammation. Due to the limitations and side effects of conventional therapies, natural products have been investigated as alternative gastroprotective agents. The genus Plectranthus is widely used in folk medicine, particularly for gastrointestinal and hepatic disorders. Among the species cultivated in the Francisco José de Abreu Matos Medicinal Plant Garden at UFC, *P. grandis* ("boldo grande") is used for research and community purposes. **Objectives:** This study aimed to investigate the gastroprotective and antioxidant effects of *P. grandis* decoction (PGD) in mice. **Methods:** Fresh *P. grandis* leaves (1.2 kg), collected in September from the Francisco José de Abreu Matos Medicinal Plant Garden, were boiled in distilled water for 15 min, yielding 20.5 g of extract after freeze-drying. A voucher specimen (No. 28377) was deposited at the Prisco Bezerra Herbarium, UFC. Male Swiss mice (25–30 g, n=8) received vehicle (saline), PGD (50, 100, or 200 mg/kg), or N-acetylcysteine (NAC, 200 mg/kg) orally. After 60 min, absolute ethanol (99.5%, 0.2 mL, p.o.) was administered, and animals were euthanized 30 min later. A normal group without ethanol treatment was included. Gastric lesions were quantified by planimetry using ImageJ software. Gastric homogenates were analysed for malondialdehyde (MDA), reduced glutathione (GSH), catalase (CAT), and superoxide dismutase (SOD). Data were expressed as mean ± SEM and analysed by one-way ANOVA followed by Tukey's test ($p<0.05$). This study was approved by CEUA-UFC (no. 3093050625). **Results:** Mice that received ethanol (vehicle) showed an area of gastric lesion of 16.67 ± 1.23 mm2. PGD 50, 100, and 200mg/kg significantly reduced the area of gastric lesion by 55.4, 64.9, and 77.6%, respectively, compared with the vehicle group. In the NAC group, the area of gastric lesion was reduced by 60.5%. Ethanol-induced increases in MDA level (by 178.7%) and significantly decreased the levels of GSH (by 49.0%), as well as reduced the activity of SOD and CAT by 37.8 and 47.5%, respectively, when compared to the normal group. PGD (50, 100, 200mg/kg) reduced MDA by 62.5, 68.5, and 75.1%, respectively, when compared to the vehicle group. PGD (50, 100, 200 mg/kg) inhibited the decrease of GSH level by 103.5, 118.3, and 138.9% and increased the activity of SOD by 29.7, 35.2, and 41.0% and of CAT by 44.8, 54.5, and 60.6%. NAC (200mg/kg) reduced MDA, prevented the decrease of GSH level, and increased the activity of SOD and CAT. **Conclusion:** These findings demonstrate the gastroprotective effect of the *P. grandis* decoction and provide scientific support for its traditional medicinal use. In addition, its antioxidant activity participates in the gastroprotection mechanism.

09. 105 **Octyl Gallate Exhibits Antiplatelet Activity and Promotes Synergic Antithrombotic Effects in Rats When Associated with Enoxiparin**. Oliveira JCPL[1], Ramalho, RC[1,4], Fernandes GFS[1,2], Medeiros IA[1,3,4], Veras RC[1,4], [1]UFPB, Lab Cardiovascular Pharmacology, Brazil. [2]UFPB, Biotechnology Center, Brazil. [3]UFPB, PPG in Bioactive Natural and Synthetic Products, Brazil. [4]UFPB, Dept Pharmaceutical Sciences, Health Sciences Center, Brazil.

Introduction: Octyl gallate (OG) is a phenolic compound derived from gallic acid that exhibits anti-inflammatory and ATP-antagonist activities, with low toxicity. However, no studies of this molecule on the hemostatic system have been described in the literature. **Objectives:** This study aimed to evaluate the antiplatelet, anticoagulant, and antithrombotic activities of OG in rat plasma, both *in vitro* and *in vivo*. **Methods:** Thrombus formation time, aggregometry, and clotting tests were performed to evaluate the hemostatic effect of OG. **Results:** Aggregometry demonstrated, for the first time, the antiplatelet action of octyl gallate (Emax = 37.59 ± 1.49% and EC50 = 0,68 ± 0,04 µmol L-1) when aggregation was stimulated with ADP. However, the gallic acid derivative did not affect prothrombin time (PT) or activated partial thromboplastin time (aPTT) during *in vitro* plasma incubation. In view of these findings, the antithrombotic action of octyl gallate was evaluated in animals that received it intravenously. Treatment with OG 10 mg.kg-1 increased the time to carotid obstruction by FeCl3-stimulated thrombus (time = 1,619 ± 40 s) and, surprisingly, the combination of OG 5 mg.kg-1 with enoxiparin 5 mg.kg-1 (anticoagulant) increased the time to obstruction (time = 3,627 ± 19 s) more than the individual treatments (at doses of 5 mg.kg-1), indicating the synergism of these effects. In addition, in animals treated with octyl gallate in combination with enoxaparin, the estimated thrombus weight and thrombus area relative to the carotid artery were lower. It was also observed that OG treatment reduced platelet aggregation, while PT and TTPa were unchanged. However, the combination of OG 5 mg.kg-1 with enoxiparin 5 mg.kg-1 increased TTPa relative to both the control and the group treated with enoxiparin 5 mg.kg-1 alone. **Conclusion:** These results highlight the therapeutic potential of octyl gallate as an antithrombotic agent and its possible usefulness in combination with other anticoagulants for the treatment of thrombotic disorders. We thank the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and the Conselho de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) for **Financial support** throughout the project's execution.

09. 106 **Effect of the Volatile Fraction of** *Thymus vulgaris* **L. (thyme) Essential Oil and Thymol on Cell Viability of Fibroblasts and Lung Tumor Cells**. Kanunfre CC[1], Santos JG[2], Verde LL[1] [1]UEPG,Dept General Biology, Ponta Grossa, PR, Brazil; [2]Unicentro, Dept Biological Sciences, Guarapuava, PR, Brazil.

Introduction: Essential oils (EOs) are a rich source of volatile compounds with diverse pharmacological activities. However, studies specifically focusing on the biological effects of their volatile fraction (vapor phase) remain limited. **Objective:** The present study aimed to evaluate the effects of the volatile fraction of thyme essential oil (VFTEO) and the volatile fraction of thymol (VFTY) on the viability of human lung carcinoma cells (A549 and H292) and fibroblasts (MRC-5). **Methods:** *Thymus vulgaris* L. essential oil was purchased from Ferquima Ltda. Based on the EO density (915 mg/mL) and the molecular weight of thymol, stock solutions were prepared at 100 mg/mL. The EO and thymol were dissolved in a vehicle solution containing ethanol and propylene glycol (75:25, v/v), and saline solution was used for dilution to the concentrations tested. As an experimental strategy, cells were seeded in the eight central wells of 24-well culture plates and exposed for 24, 48, or 72 h to the volatile fraction generated from different concentrations of EO or thymol. Concentrations of 62.5–1000 µg/mL/well for EO and 31.5–500 µg/mL/well for thymol were added to the remaining 16 cell-free peripheral wells. Cytotoxicity was assessed using the MTT reduction assay and the sulforhodamine B (SRB) assay, allowing determination of the concentration capable of generating sufficient vapor to reduce cell viability by 50% (ICV50). In addition, the effects of VFTEO and VFTY on A549 cells were evaluated by flow cytometric analysis of cell cycle distribution using propidium iodide (PI) staining. **Results:** GC/MS analysis of thyme EO identified thymol (41.84%) and *p* -cymene (32.67%) as the major constituents. Both VFTEO and VFTY exhibited dose-dependent cytotoxicity in all three cell lines. After 48 h of exposure, A549 cells were more responsive than H292 cells to both treatments. For VFTEO, the ICV50 values obtained for A549 cells were 305.2 ± 97.6 µg/mL/well in the MTT assay and 320.5 ± 47.0 µg/mL/well in the SRB assay. For H292 cells, the corresponding values were 648.0 ± 282.6 and 659.6 ± 196.9 µg/mL/well, respectively. In contrast, VFTY exhibited greater cytotoxicity, with ICV50 values for A549 cells of 155.1 ± 55.0 µg/mL/well in the MTT assay and 132.0 ± 65.4 µg/mL/well in the SRB assay. For H292 cells, the respective values were 137.9 ± 34.1 and 157.0 ± 15.2 µg/mL/well. Among the treatments evaluated, only VFTY demonstrated lower toxicity toward non-tumor MRC-5 cells, presenting a selectivity index (SI) equal to or greater than 2 after 48 h of exposure. Furthermore, both VFTEO and VFTY induced cell cycle arrest in A549 cells, characterized by an increased proportion of cells in the G0/G1 phase. **Conclusion:** These findings demonstrate that both VFTEO and VFTY reduce the viability of A549 and H292 lung carcinoma cells. However, considering its selectivity index, the VFTY appears to be a promising complementary therapeutic approach for lung cancer. This is particularly relevant because volatile compounds may be delivered directly to lung tissue through inhalation. **Financial support:** Fundação Araucária, CAPES.

10. Cancer Pharmacology

10.001 **The lncRNA H19 in Lung Adenocarcinoma (LUAD): an *in silico* Prognostic, EMT-Pathway and Driver-Mutation Profile**. Soares IF[1,2], Mota JA[1,3], Scandolara TB[1], Sales SLA1,3,Manso MP[4], Melo VB[5], Gress LSB[2,3], Macêdo SMN[1], Oliveira KAF[1], Xavier EEP[1,6], Bastos RS[1,3], Fernandes MCR[1,7], Maranhão SS[1], Pessoa C[1,3], Furtado CLM[5] [1]UFC, Experimental Oncology Lab, Drug Research and Development Center, Brazil, [2]UNIFOR, Center for Health Sciences – CCS, Brazil, [3]UFC,Dept Physiology and Pharmacology, Graduate Program in Pharmacology, Brazil, [4]INCA, Cellular and Gene Immunotherapy Lab, Brazil, [5] UFMG, Dept Genetics, Ecology and Evolution, Institute of Biological Sciences, Brazil, [6]UFC, Faculty of Pharmacy, Brazil, [7]UFC, Graduate Program in Translational Medicine, Brazil.

Introduction: H19, an imprinted long non-coding RNA, is reported to be dysregulated in multiple tumors (with both oncogenic and tumor-suppressive roles), to mediate epithelial-mesenchymal transition (EMT), and, in non-small-cell lung cancer (NSCLC), to promote resistance to cisplatin and EGFR- tyrosine-kinase inhibitors, with serum exosomal H19 elevated in resistant patients (Pan & Zhou, 2020). Building on our group's prior pan-cancer profiling (32 TCGA cohorts), where lung tumors were enriched for high H19 and the LUAD line A549 expressed high H19 *in vitro*, we investigated the LUAD- specific *in silico* profile of H19. **Objectives:** To describe, using public web platforms, the prognostic and molecular-context profile of H19 in LUAD, as a basis for planned *in vitro* validation. **Methods:** All analyses were *in silico* on public data. In GSCA (TCGA LUAD): differential expression (tumor vs paired normal); pathway activity from reverse-phase protein arrays (TCPA/RPPA) comparing tumors with high vs low H19 (median split); and survival (Cox proportional-hazards and log-rank; OS/PFS/DSS/DFI). In cBioPortal (LUAD TCGA PanCancer Atlas): H19 mRNA expression compared between driver-mutant and wild- type groups for TP53, EGFR and KRAS (Mann-Whitney; Benjamini-Hochberg q). In GEPIA2: Pearson co-expression of H19 with candidate ferroptosis and autophagy effector genes in LUAD tumors. **Results:** H19 showed a non-significant trend toward higher expression in LUAD versus normal lung. High H19 was associated with worse overall (HR=1.36, p=0.039), progression-free (HR=1.44, p=0.003), disease-specific (HR=1.51, p=0.032) and disease-free (HR=1.85, p=0.004) survival, and with activation of the EMT pathway (LUAD FDR=1x10-3; EMT activation also significant in eight further cancer types). H19 was higher in TP53-mutant than wild-type LUAD (p=0.015, q=0.057; single cohort, preliminary), without association with EGFR or KRAS status. Co-expression of H19 with ferroptosis and autophagy effector genes was not significant. **Conclusion:** In LUAD, H19 expression is associated with an EMT-activated, poorer-prognosis and TP53-mutant enriched profile, supporting its association with an aggressive disease and consistent with literature reports of H19-mediated therapy resistance in NSCLC. All findings are associative, derived from public cohorts on single platforms, and the TP53 association is borderline and not replicated in independent cohorts owing to limited lncRNA coverage. We plan to validate these associations *in vitro*, including H19 modulation and drug-response assays in H19-high (A549) versus H19-low/negative (NCI-H460) NSCLC lines.

10.002 **Enantioselective Antiproliferative Activity of Homoisoflavonoids from *Urginea depressa* against Non-Small Cell Lung Cancer Cell Lines with High Selectivity over non-Tumorigenic Cells**. Feijó Neto JR[1]; Pereira JVM[1,3] ; Vieira Neto JdB[1,3]; Castro CM[1]; Desiderio GA[1,3]; Falcão JS[2]; Silva MVO[2]; Costa PRR[2]; Caleffi GS[2]; Pessoa CÓ[1,3]. [1]UFC, Lab. de Oncologia Experimental, Brazil; [2]UFRJ, Lab. de Química Bioorgânica (LQB), Brazil; [3]UFC, PPG Pharmacology, Brazil.

Introduction: Lung cancer remains among Brazil's five most common cancers (INCA, 2025), with non-small cell lung cancer (NSCLC) the predominant subtype and a major therapeutic challenge due to resistance to conventional treatments. Standard therapies, including chemotherapy and radiotherapy, often cause severe adverse effects, highlighting the need for selective antineoplastics. Natural products such as homoisoflavonoids show promise. A homoisoflavonoid from *Urginea depressa* demonstrated potent antiproliferative activity in various cancer cell lines, but its precise mechanism remains unclear (Dai et al., 2013). **Objective:** To evaluate the antiproliferative potential of a homoisoflavonoid's enantiomeric forms, (R), (S), and racemic mixture (RM), against NSCLC cell lines and to examine cellular alterations by flow cytometry. **Methodology:** Cytotoxicity of (R), (S), and RM was assessed by MTT assay, with paclitaxel as positive control, after 24 h and 72 h exposures. IC50 values were determined in four NSCLC lines: A549, NCI-H460, NCI-H1975, and HCC827. Selectivity was evaluated using non-tumor lung fibroblasts (MRC-5) and peripheral blood mononuclear cells (PBMCs) from healthy donors under ethical approval. Flow cytometry in NCI-H460 and HCC827 analyzed plasma membrane integrity with DAPI and cell cycle after 24 h treatment with the (S)-enantiomer. **Results:** The (S)-enantiomer showed the highest antiproliferative potency at 72 h, with IC50s of 1.97 µM (HCC827), 0.72 µM (NCI-H460), 0.82 µM (A549), and 0.86 µM (NCI-H1975). The (R)-enantiomer and RM were much less active, with IC50s >5.0 µM in all cancer lines. The (S)-enantiomer exhibited high selectivity (SI > 25) versus MRC-5 and PBMCs. Flow cytometry after 24 h treatment with 0.5 µM (S) did not markedly affect membrane integrity and induced G2/M cell cycle arrest, consistent with antimitotic activity. **Conclusions:** The (S)-enantiomer of the *Urginea depressa* homoisoflavonoid has potent, selective antiproliferative activity against NSCLC cell lines and induces G2/M arrest. These results support homoisoflavonoids as a scaffold for developing new lung cancer therapeutics. Keywords: Lung cancer; antineoplastic; homoisoflavonoids. **Acknowledgements:** Supported by INCTBIO2, PRONON, Brazilian Ministry of Health, FINEP, CNPq, CAPES, and FUNCAP.

10.003 **Evaluation of Apoptotic Mechanisms Associated with *Solanum jabrense* Agra & M. Nee Extract in MCF-7 Cells**. Gomes KNC[1], Alexandre HMS[2], Abreu-Junior AR[2], Santana PVS[2], Marques KKG[2], Pereira ERM[2], Souza RRM[2], Ramalho IGS[2], Santos PBG[1], Araújo YKO[1], Silva AL[2], Agra MF[3], Tavares JF[2], Sobral MV[2],Gonçalves JCR[2]. [1]UFPB, Health Sciences Center, Pharmacy, Brazil. [2]UFPB, Health Sciences Center, PPG in Bioactive Natural and Synthetic Products, Brazil. [3]UFPB,Biotechnology Center, Brazil.

Introduction: Breast cancer is the most prevalent neoplasm among women worldwide. Although chemotherapy remains one of the main therapeutic approaches, its effectiveness is often limited by tumor resistance and toxicity to healthy cells. In this context, natural products have been investigated as potential sources of selective antitumor compounds. *Solanum jabrense*, a plant native to Northeastern Brazil, is rich in bioactive metabolites, especially alkaloids, with promising antitumor activity in breast adenocarcinoma cell lines. **Objectives:** This study aimed to investigate, *in vitro*, the apoptotic mechanisms involved in the antitumor effects induced by the hydroethanolic fraction of S. jabrense (FSJ) in MCF-7 breast adenocarcinoma cells. **Methods:** Aerial parts (leaves and branches) of S. jabrense were collected in Matureia-PB, Brazil (SisGen #AD609FD). Part of the material was used to prepare a voucher specimen deposited in the Lauro Pires Xavier Herbarium (JPB) at the Federal University of Paraíba (UFPB). MCF-7 cells were treated with FSJ at concentrations of 17 and 35 µg/mL. Cell death was evaluated using AO/PI dual staining analyzed by confocal microscopy and Annexin V-FITC/PI assays quantified by flow cytometry. These techniques allowed differentiation between apoptosis and necrosis, as well as the identification of morphological and biochemical apoptotic markers. Statistical analyses were performed using standard error of the mean (SEM), followed by one-way ANOVA and Tukey's post hoc test ($p < 0.05$). **Results:** FSJ treatment for 48 h promoted a marked and concentration-dependent increase in apoptosis in MCF-7 cells. In the AO/PI assay, early apoptotic cells reached 96.37 ± 6.6% at 35 µg/mL and 87.54 ± 3.8% at 17 µg/mL, while necrosis remained low (maximum 1.06%), indicating selective programmed cell death. Flow cytometry confirmed these findings, with early apoptosis reaching 68.8 ± 2.9% and total apoptosis 72.65 ± 10.16% at 35 µg/mL, compared to 1.73% in the control group. Positive Annexin V staining confirmed phosphatidylserine externalization. **Conclusion:** FSJ predominantly induced apoptosis in MCF-7 cells in a concentration- dependent manner, confirming apoptosis as the main mechanism involved in its antitumor effects and reinforcing its potential as a selective antitumor agent.

10.004 **AMTAC-06 Induces ROS-Associated Cytotoxicity in HCT-116 Colorectal Cancer Cells**. Santana JP[1], Duarte SS[2], Souza RRM[2], Januário VHS[1], Rodrigues JS[1], Queiroga LM[2], Farias APGM[2], Ramalho IGS[2], Lyra GB[2], Gouveia RG[2], Silva JM[3], Moura RO[4], Gonçalves JCR[2], Sobral MV[2] [1]UFPB, Health Sciences Center, Pharmacy, Brazil. [2]UFPB, Health Sciences Center, PPG in Bioactive Natural and Synthetic Products, Brazil. [3]UFPE, PPG in Pharmaceutical Sciences, Brazil. [4]UEPB, Dept Pharmacy, Drug Development and Synthesis Lab, Brazil.

Introduction: Cancer comprises a heterogeneous group of diseases characterized by uncontrolled cell proliferation, invasive capacity, and metastatic potential. Despite advances in antineoplastic therapies, cancer treatment still presents important limitations, including systemic toxicity, low selectivity, and tumor resistance, highlighting the need for novel bioactive molecules with improved antitumor potential. Acridine derivatives have attracted considerable interest due to their relevant pharmacological properties, especially their antitumor activity associated with DNA interaction, oxidative stress induction, and modulation of cell death pathways. Previous studies demonstrated that the spiro-acridinic derivative (E)-1'-((4-chlorobenzylidene)amino)-5'-oxo-1',5'-dihydro-10H- spiro[acridine-9,2'-pyrrole]-4'-carbonitrile (AMTAC-06) exhibited cytotoxic activity against HCT-116 (colorectal carcinoma), HL-60 (promyelocytic leukemia), and MCF-7 (breast adenocarcinoma) tumor cell lines, induced apoptosis in HCT-116 cells, and promoted antitumor effects in an Ehrlich carcinoma mouse model. **Objectives:** This study aimed to evaluate the cytotoxic activity of AMTAC-06 against HCT-116 colorectal cancer cells and investigate the involvement of oxidative stress in its mechanism of action. Methods: Cytotoxicity was evaluated against HCT-116 cells by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay after 72 h of treatment with AMTAC-06 (3.12–200 μM) to determine the half- maximal inhibitory concentration (IC50) value. Intracellular reactive oxygen species (ROS) production was assessed by flow cytometry using the 2',7'-dichlorodihydrofluorescein diacetate (DCFH-DA) fluorescent probe. Additionally, the cytotoxicity of AMTAC-06 was evaluated in the absence and presence of the antioxidant N-acetylcysteine (NAC). All experiments were performed in triplicate in three independent experiments. Data were expressed as mean ± SEM and analyzed by one-way ANOVA followed by Tukey's test. **Results:** AMTAC-06 exhibited cytotoxic activity against HCT-116 cells, with an IC50 value of 15.68 ± 1.16 μM. The DCFH-DA assay demonstrated increased ROS levels following treatment with the compound. After 30 min of exposure to AMTAC-06 at 15 and 30 μM (corresponding to the IC50 and twice its value), the percentage of DCFH-labeled cells increased by 21 ± 1.45% and 14 ± 4.06%, respectively. After 1 h this value increased by approximately 90 ± 1.36% and 85 ± 2.61% at concentrations of 15 and 30 μM, respectively. Moreover, pretreatment with NAC (5 mM) reduced AMTAC-06-induced cytotoxicity by approximately 24% and 23% at 15 and 30 μM, respectively. **Conclusion:** AMTAC-06 exhibited cytotoxic activity against HCT-116 colorectal cancer cells. Additionally, increased ROS production and partial reversal of cytotoxicity by NAC suggest that oxidative stress is involved, at least in part, in the cytotoxic mechanism induced by this acridine derivative

10.005 **Antileukemic Activity of LOE227, a Novel N-Aryl Azacoumostan, and its Synergism with the Apoptosis Inducer Venetoclax**. Castro CM[1], Feijó JRN[1], Novas RCV[2], Vieira JBN[1,3], Desidério GA[1,3], Carvalho MT[2], Lima JM[1,3], Bastos RS [1], Paier CK[1], Carneiro LSA[4], Pessoa C[1,3], Buarque CD[2] [1]UFC, Lab. of Experimental Oncology, Drug Research and Development Center, Brazil; [2]PUC-Rio, Dept Chemistry, Brazil; [3]UFC, PPG Pharmacology, Brazil; [4]UFRRJ, Dept Organic Chemistry, Institute of Chemistry, Brazil

Leukemia ranks among the leading causes of cancer-related mortality and comprises distinct subtypes driven by genetic and epigenetic alterations that determine therapeutic approach [F. Bray, CA Cancer J. Clin. v. 74, p. 229, 2024]. Despite advances in targeted chemotherapy, treatment remains challenged by adverse effects and drug resistance [D. Richter, J. Leuk., v. 13, p. 434, 2025]. Identifying new compounds from diverse chemical classes and combining agents with complementary mechanisms of action are critical strategies to overcome these limitations. Azacoumestane molecules represent a promising chemical scaffold for the development of novel anticancer agents. This study evaluated the antiproliferative activity and selectivity of LOE227, an azacoumestane-class compound, against acute myeloid leukemia (AML) cell lines, and investigated its mechanism of action alone and in combination with venetoclax. Cytotoxic activity was initially screened at a single concentration of 50 µM across a panel of cell lines (MOLM-13, HCT-116, MDA- MB-231, SNB-19) using the MTT assay. Compounds with inhibition ≥75% were evaluated to IC_{50} determination (72-hour treatment). Peripheral blood mononuclear cells (PBMCs; Ethics Approval No. 6.253.345) were used to determine the selectivity index (SI) of LSO227. Flow cytometry was performed after 24-hour treatments with LOE227 (4, 8, and 16 µM), alone or combined with venetoclax (4 nM). Cell membrane integrity and cell cycle distribution were assessed by DAPI staining, mitochondrial membrane potential by Rhodamine 123 staining, and apoptosis by Annexin V-FITC staining, using a CytoFLEX LX (Beckman Coulter) flow cytometer. Data are expressed as mean ± SD of at least two independent experiments; statistical analyses were performed using GraphPad Prism ($p < 0.05$). Among the azacoumestane derivatives, LOE227 exhibited the most potent antiproliferative activity against MOLM-13 (AML) cells (IC_{50} = 3.55 µM) and notable selectivity (SI = 6) relative to healthy PBMCs, while all derivatives were more active against AML than solid tumor lines (IC_{50} range: 3.55–34.35 µM). Membrane integrity assays revealed dose- dependent cell death at 8 and 16 µM of LOE227 (18.2% and 38.1%, respectively), with no significant effect on cell cycle distribution. LOE227 disrupted mitochondrial membrane potential at all tested concentrations, and co- treatment with venetoclax (4 nM) significantly enhanced this depolarization ($p < 0.05$). Apoptosis assays demonstrated that LOE227 at 4 and 8 µM induced 17% and 25% apoptotic death, respectively; notably, combining LOE227 (4 µM) with venetoclax (4 nM) increased apoptotic death to 43%, a statistically significant enhancement over either agent alone ($p < 0.001$). LOE227 emerged as a promising lead compound against AML, displaying selective activity towards MOLM-13 cells, mitochondria-mediated apoptotic mechanism, and significant synergism with venetoclax. This work was financed in part by INCTBIO 2, PRONON, MINISTÉRIO DA SAÚDE, FINEP, CNPq, CAPES e FUNCAP.

10.006 **Evaluation of the *in vitro* Antitumor Potential of Flavonoids from a Cytotoxic Extract of Wood Waste from *Andira parviflora* (Ducke) in the Amazon Region**. Mota JF[1], Desiderio GA[1,4], Guimarães CJ[2], Melo JV[1,4], Araújo IM[3], Costa PMS[1], Guimarães AC[3], Paier CRK[1], Pessoa C[1]. [1]UFC, Lab. Experimental Oncology, Brazil; [2]Fiocruz, Institute of Drug Technology (Farmanguinhos), Brazil; [3]UFAM, Brazil; [4]UFC, PPG Pharmacology, Brazil

Introduction: *Andira parviflora* Ducke (Fabaceae), known as "red sucupira," is found primarily in the forests of the Amazon region. Due to its woody nature, the species is widely used by the timber industry. In addition to its economic importance, the genus Andira is characterized by the production of secondary metabolites such as terpenes and flavonoids, which are associated with biological activities. However, there are few studies on the chemical composition of residues from the industrial processing of *A. parviflora*, especially as they relate to cancer. **Objective: '**The aim of this study was to evaluate the cytotoxic potential of phenolic compounds from *A. parviflora* in tumor cell lines. **Methodology:** Cytotoxic potential was assessed using the MTT assay against SNB-19 (astrocytoma), HCT-116 (human colon carcinoma), PC3 (prostate), and HL60 (leukemia) tumor cells; in addition, the non-tumor HaCat cell line (human keratinocytes) was used to assess selectivity. The cells were incubated in 96-well plates in RPMI-1640 or DMEM medium containing 10% FBS and penicillin/streptomycin (Thermo Fisher Scientific Inc, Waltham, MA, USA), maintained at 37 °C with 5% CO_2 and humidification. The cells were treated for 72 h with extracts (LSV) and fractions solubilized in DMSO (Sigma-Aldrich). Briefly, an MTT solution (Sigma-Aldrich) was added to the cell monolayers for 3 h at 37 °C and 5% CO_2. Next, 100% DMSO was added, and the plates were read in a VICTOR® Nivo™ multimode microplate reader (Revvity) at 595 nm. **Results:** Cytotoxic assays revealed that the dichloromethane (LSV02) and ethyl acetate (LSV03) extracts of *A. parviflora* exhibited high inhibition of cell growth against HCT-116, with rates of 93.68% and 84.02%, respectively. Although the LSV02 extract showed strong potency against the HCT-116 and HL60 cell lines, it exhibited low selectivity by also affecting the non-tumor HaCat cells. In contrast, the ethyl acetate extract (LSV03) stood out for its excellent antitumor selectivity, showing no significant cytotoxic effects against non-tumor cells of the HaCat line. It is worth noting that no significant differences were observed in the treatments of SNB-19 and PC3 cells. **Conclusion:** Extracts from *A. parviflora* residue exhibited selective antitumor activity. Further studies could be conducted to elucidate the mechanisms of action of these compounds. **Acknowledgments:** This study was financed in part by INCTBIO2, PRONON, Ministério da Saúde, FINEP, CNPq, CAPES e FUNCAP.

10.007 **Evaluation of BPO-DPPV as a Cytotoxic Agent Against *in vitro*-Induced Chemoresistant Osteosarcoma Cells**. Strauss LC, Pereira THR, Zamariolli LS, Moura TR, Netto AVG, Bincoletto C Unifesp-EPM, Depto Farmacologia, Unesp-Araraquara, Instituto de Química

Introduction: Osteosarcoma (OS) is the most common primary malignant bone tumor. Standard treatment involves surgical resection combined with chemotherapeutic agents such as methotrexate (MTX) and cisplatin (CDDP). However, OS exhibits a high capacity to develop chemoresistance, resulting in elevated mortality rates. One of the main mechanisms of resistance is the overexpression of P-glycoprotein, which actively transports substances from the intracellular to the extracellular compartment, reducing intracellular drug concentration and compromising therapeutic efficacy. Therefore, the development of new compounds capable of overcoming tumor resistance is essential. In this context, palladium-based compounds have shown promising chemotherapeutic potential. **Objectives:** To evaluate the cytotoxic effects the novel palladium–oxime complex (BPO-DPPV) in human osteosarcoma cells (SaOS-2) after *in vitro* induction of chemoresistance. **Methods:** Human osteosarcoma SaOS-2 cells were repeatedly exposed to methotrexate to generate the resistant S-MTX lineage. Cell viability was assessed using the MTT reduction assay after treating SaOS-2 and S-MTX cells with increasing concentrations of methotrexate and BPO-DPPV for 24 hours. Viability was also evaluated in the presence of cyclosporin A, a potent P-glycoprotein inhibitor, to investigate the involvement of this transporter in tumor resistance. P-glycoprotein expression in SaOS-2 cells treated with BPOD-PPV was quantified by immunofluorescence. Cell death modalities induced by the palladium–oxime complex were determined by flow cytometry using simultaneous Annexin V/7-AAD staining. **Results:** MTT assays demonstrated that the viability of the S-MTX lineage treated with methotrexate was higher than that of SaOS-2 cells treated with the same drug, confirming the establishment of resistance. In these resistant cells, exposure to cyclosporin A enhanced the cytotoxic effects of MTX. Additionally, the BPO- DPPV compound exhibited significant and comparable cytotoxicity in both cell lines. Immunofluorescence analysis suggested that P-glycoprotein expression increased at higher concentrations of BPO-DPPV. Flow cytometry revealed that the palladium–oxime complex induced cell death predominantly through apoptosis and late apoptosis. Partial **Conclusions:** The results indicate that the palladium–oxime complex BPO-DPPV exhibits relevant cytotoxic potential in both methotrexate-sensitive and methotrexate-resistant osteosarcoma cells, even in the presence of mechanisms associated with multidrug resistance. Furthermore, the compound was able to induce apoptosis, reinforcing its potential as a candidate for future therapeutic strategies in osteosarcoma treatment. **Financial support:** FAPESP, CNPq, and CAPES.

10.008 **Antileukemic Activity of Synthetic Naphthoquinones in HL-60 Cells: Antiproliferative Effects and Morphological Alterations**. Pinheiro KS[1], Oliveira DA[2], Lima AB[3], Oliveira FL[4], Zelaya EAE[4], Silva EL[4], Moraes LGC[5], Rocha DR[5], Montenegro RC[4]. [1]UFC, Faculty of Pharmacy, Lab Pharmacogenetics, Brazil. [2]UFC, Faculty of, Biotechnology, Lab Pharmacogenetics, Brazil. [3]UFC, PPG in Medical Sciences, Lab Pharmacogenetics, Brazil. [4]UFC, Lab Pharmacogenetics, PPG in Pharmacology, Brazil. [5]UFF, Lab Synthesis of Molecules of Biological Interest, PPG in Chemistry, Brazil.

Introduction: Acute promyelocytic leukemia (APL) is a hematological malignancy characterized by the uncontrolled proliferation of myeloid precursors. Despite significant therapeutic advances, the search for novel compounds with antineoplastic potential remains relevant. In this context, synthetic naphthoquinones have emerged as promising antitumor agents due to their cytotoxic, antiproliferative, and pro-apoptotic activities reported in several cancer models. This study aimed to evaluate the antiproliferative activity and morphological effects induced by the synthetic naphthoquinones NF26-1, NF26-2, and NF26-3 in HL-60 cells. **Methods:** HL-60 cells were cultured in RPMI-1640 medium supplemented with 10% fetal bovine serum (FBS) and 1% antibiotic solution and maintained at 37 °C in a humidified atmosphere containing 5% CO_2. Initially, ten synthetic naphthoquinones were screened at a concentration of 10 µM. The selected compounds (NF26-1, NF26-2, and NF26-3) were subsequently evaluated using concentration-response curves (0.156–10 µM) to determine their half-maximal inhibitory concentrations (IC_{50}). For cell viability assays, 6×10^3 cells/well were seeded into 96-well plates and incubated for 72 h. Doxorubicin was used as a positive control. Cell viability was assessed using the Alamar Blue® assay (0.1 mg/mL), followed by fluorometric analysis (560/590 nm). For morphological evaluation, cells were treated for 72 h, subjected to cytocentrifugation, stained using a panoptic staining method, and analyzed under light microscopy. **Results:** NF26-1, NF26-2, and NF26-3 exhibited potent antiproliferative activity against HL-60 cells, with IC_{50} values of 0.5, 0.7, and 0.6 µM, respectively. Morphological analysis of the negative control group revealed cells with a high nucleus-to-cytoplasm ratio and frequent mitotic figures, consistent with intense proliferative activity. In contrast, treated cells displayed morphological alterations associated with cell death, including apoptotic blebbing, cytoplasmic vacuolization, cellular debris, micronuclei, multinucleated giant cells, and features suggestive of late-stage apoptosis. Furthermore, the presence of micronuclei and multinucleated giant cells indicates the occurrence of genetic damage and mitotic disturbances associated with exposure to the evaluated compounds. **Conclusion:** The synthetic naphthoquinones NF26-1, NF26-2, and NF26-3 demonstrated significant antiproliferative activity against HL-60 cells, with IC_{50} values in the submicromolar range, and induced morphological alterations consistent with cell death. Collectively, these findings suggest that these compounds exert pronounced cytotoxic effects on HL-60 cells, supporting their potential as antileukemic agents. These preliminary results provide a foundation for future studies aimed at confirming apoptosis induction and elucidating the cellular and molecular mechanisms underlying their biological activity.

10.009 **Melittin as a Potential Therapeutic Agent Against Bladder Cancer: Effects on Cell Viability, Migration, and Cell Cycle Regulation**. Brayn GA1; Poiato GEH1; Oliveira AMB1; Porto RM2; Silva GN3; Almeida TC1; Picolo G1. 1 Lab Pain and Signaling, IBu, São Paulo, Brazil; 2 Lab Development and Innovation, IBu, São Paulo, Brazil; 3 Toxicogenetic, Epidemiological and Clinical Study and Research Group, Federal University of Ouro Preto, Ouro Preto, Brazil.

Introduction: Bladder cancer is one of the most incident types of cancer in Brazil. The current treatment for its muscle invasive form is the complete removal of the bladder and surrounding organs accompanied by adjuvant chemotherapy with cisplatin and gemcitabine. Both the surgery and the antineoplastic drugs cause severe and lasting side effects, not only reducing quality of life but also compromising patience adherence. Thus, it is relevant to search for new therapeutic options which are better tolerated. Melittin is bee venom's most abundant peptide and main pharmacological component. In other types of cancer, such as breast cancer, lung cancer, melanoma and hepatocellular carcinoma, melittin has exhibited antitumoral effects. **Objectives:** To study the effects of melittin on T24 bladder cancer cell line and understand its mechanisms of action. **Methods:** Cell viability was measured after 24, 48 and 72 hours of treatment with melittin at concentrations 1.25-10 µg/mL by MTT assay. Effects on cell cycle were investigated by flow cytometry after treatment with melittin at concentrations 3.75 and 5.0 µg/mL for 24 hours. Cell death mechanism was assessed by flow cytometry after treatment with melittin at concentrations 3.75-10 µg/mL for 24 hours. Akt and p-Akt expression after treatment with melittin at 5.0 µg/mL for 24 hours was measured by Western Blotting. **Results:** In all analyzed timeframes, melittin was able to significantly reduce viability at concentrations 5-10 µg/mL. At 5.0 µg/mL, melittin increased the number of cells at the S phase of the cycle and reduced the number at the G0/G1 phase. Melittin decreased the number of viable cells and increased the number of recent apoptotic cells at concentrations 7.5 and 10 µg/mL. No alteration in p-Akt/Akt expression was observed after treatment with melittin. **Conclusions:** Melittin exhibited promising antitumor effects in bladder cancer cells, affecting cellular proliferation and survival through mechanisms associated with cell cycle disruption and induction of apoptosis. Since no changes were observed in the p-Akt/Akt ratio, its effects may involve alternative signaling pathways independent of Akt modulation. Overall, these findings reinforce the therapeutic potential of melittin as a candidate for bladder cancer treatment. **Acknowledgements:** Multi-User Laboratory – Flow Cytometry Facility **Financial support** Information: FAPESP/CETICS (2013/07467-1), PIBIC Program/CNPq, Butantan Institute.

10.010 **A Role for Female Sex Hormone Receptors and Stromal Remodeling in the Differential Incidence of Tongue Base Cancer in Male and Female HPV16-Transgenic Mice**. Rodrigues TAR[1], Neto CPO[1], Medeiros-Fonseca B[2], Andrade FE[3], Oliveira PA[2], Bastos MMSM[4], Medeiros R[5], Gil da Costa RM[1,2,3,4,5]. [1]UFMA, PPG in Adult Health, Brazil. [2]University of Trás-os-Montes and Alto Douro, Centre for the Research and Technology of Agro-Environmental and Biological Sciences, Portugal. [3]UEMA, Dept Pathology, Brazil. [4]University of Porto, Lab for Process Engineering, Environment, Biotechnology and Energy, Portugal. [5]Portuguese Institute of Oncology in Porto Research Centre, Molecular Oncology and Viral Pathology Group, Portugal.

A growing proportion of head and neck squamous cell carcinomas (HNSCC) are associated with infection by high-risk human papillomavirus (HPV). Although HPV-positive HNSCC is significantly more frequent in men, the biological mechanisms underlying this sex disparity remain poorly understood. This study aimed to determine the incidence of tongue base cancer in male and female HPV16-transgenic mice and to investigate the role of female sex hormone receptors and stromal remodeling in susceptibility to HPV-associated carcinogenesis. Tongue samples from 30-week-old HPV16-transgenic male (n=80) and female (n=90) FVB/n mice, together with age-matched wild-type male (n=10) and female (n=10) controls, were evaluated histologically for intraepithelial and invasive lesions. Immunohistochemical analyses were performed to assess the expression of estrogen receptor alpha (ERα), estrogen receptor beta (ERβ), progesterone receptor (PR), and matrix metalloproteinase-2 (MMP2). Stromal collagen remodeling was evaluated using Picrosirius Red staining. Female HPV16-transgenic mice exhibited strong ERα and ERβ expression in both intraepithelial and invasive lesions. This pattern was accompanied by increased MMP2 expression and marked collagen remodeling within the tumor microenvironment. In contrast, male mice showed minimal ERα, ERβ, and MMP2 expression and largely preserved collagen organization. These findings confirm the association between HPV16 expression and tongue base carcinogenesis in both sexes. Moreover, the higher incidence of lesions observed in female mice, compared with male mice, was associated with enhanced expression of estrogen receptors, increased MMP2 activity, and extensive stromal remodeling. These results suggest that female sex hormone signaling may contribute to HPV- induced oral carcinogenesis through modulation of extracellular matrix remodeling and tumor progression.

10.011 **Oxidative Stress-Associated Cytotoxicity of a Selenium Compound in the HeLa Cervical Cancer Cell Line**.

Januario VHS[1], Rodrigues JS[1], Santana PS[1], Silvestre GFG[2], Ferreira RC[2], Sousa NF[3], Athayde-Filho PF[4], Souza HDS[4], Scotti MT[3], Scotti L[3], Amorim GMW[2], Loureiro PBA[2], Goncalves JCR[2], Sobral MV[2] [1]UFPB, Health Sciences Center, ONCOFAR, Undergraduate in Pharmacy, Brazil, [2]UFPB, Health Sciences Center, ONCOFAR, PPG in Bioactives Natural and Synthetic Products, Brazil, [3]UFPB, Health Sciences Center, PPG in Bioactives Natural and Synthetic Products, Brazil, [4]UFPB, PPG in Chemistry, Brazil

Introduction: Despite advances in cervical cancer treatment, important limitations such as toxicity, low selectivity, and tumor resistance reinforce the need for novel therapeutic alternatives. Selenium-based compounds have shown promising antitumor activity in experimental cancer models. In this context, N-(4-methylphenyl)benzoseleno-ethenolactamide (NC31), a novel selenium compound with reported leishmanicidal and antimicrobial activities, has not yet been investigated for its antitumor potential in cervical cancer. Cervical cancer remains one of the leading causes of cancer-related mortality among women worldwide and is strongly associated with persistent infection by high-risk human papillomavirus (HPV), representing an important global public health challenge. **Objective:** This study aimed to evaluate the cytotoxic profile of NC31 and investigate its role in the modulation of oxidative stress and Mitogen-Activated Protein Kinase (MAPKs) pathways in the human cervical câncer HeLa cell line. **Methods:** Cytotoxicity was assessed by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay in HeLa cells. The involvement of oxidative stress in NC31-induced cytotoxicity was investigated by pretreating cells with N-acetylcysteine (NAC, 5 mM) prior to NC31 exposure, followed by cell viability assessment. To investigate MAPK pathway involvement, cells were pretreated with JNK (SP600125), MEK/ERK1/2 (U0126), and p38 MAPK (PD169316) inhibitors before NC31 exposure, followed by cell viability assessment. Data are presented as mean ± SEM and analyzed by one-way ANOVA followed by Tukey's test. **Results:** NC31 exhibited marked cytotoxic activity against HeLa cells with a half maximal inhibitory concentration (IC50) value of 5.03 ± 0.32 μM. The antioxidant NAC significantly prevented NC31-induced cytotoxicity, restoring cell viability to 100.60 ± 2.90% and 88.71 ± 2.28% after treatment with 5 and 10 μM, respectively ($p < 0.05$), suggesting the participation of reactive oxygen species (ROS) in the compound-induced cytotoxic effects. Among the MAPK pathways evaluated, pretreatment with the JNK inhibitor significantly potentiated NC31-induced cytotoxicity, reducing cell viability to 31.63 ± 2.93% ($p < 0.05$). In contrast, pretreatment with MEK/ERK1/2 and p38 MAPK inhibitors did not significantly alter NC31 cytotoxicity. **Conclusion:** NC31 exhibited cytotoxic activity against HeLa cervical cancer cells, with its effects appearing to be associated with oxidative stress. In addition, JNK inhibition potentiated NC31-induced cytotoxicity, suggesting a protective role of this pathway against the compound-induced effects in HeLa cells. Collectively, these findings highlight the antitumor potential of NC31 and support further non-clinical investigations into its mechanism of action in cervical cancer models. **Financial support** CNPq, CAPES and FAPESQ-PB.

10.012 **Prospecting Marine Bacteria Associated with *Zoanthus sociatus* from the Piauí Coastline with Anticancer Potential**. Pena JMP[1], Almeida RC[1], Silva JYG[1], Pessoa ODL, Guimarães LA[3], Florêncio KGD[1], Wilke DV[1] [1]UFC, Drug Research and Development Center, Dept Physiology and Pharmacology, School of Medicine, Ceara, Brazil. [2]UFC, Dept Organic and Inorganic Chemistry, Sciences Center, Ceara, Brazil. [3]UFPI-Senador Helvidio Nunes de Barros, Piaui, Brazil.

Introduction: Cancer is one of the most deadly diseases worldwide. Marine organisms constitute a highly promising source of compounds with anticancer potential. However, obtaining secondary metabolites from marine invertebrates still faces limitations such as low yield, or challenging supply by synthesis due to structural complexity. Then marine bacteria emerge as a sustainable biotechnological alternative to obtain bioactive molecules. Nevertheless, marine bacteria from the coast of Piauí, Brazil, remain largely unexplored regarding their anticancer potential. **Objective:** To investigate the cytotoxicity in cancer cells of organic extracts obtained from bacteria associated with the zoanthid *Zoanthus sociatus* from Piaui coast. **Methods:** Approximately 10 g of *Z. sociatus* were collected manually at Coqueiro Beach, Piauí (SISBIO No. 94324-3), sprayed with 70% alcohol, washed with sterile sea water, and stored at -70°C. Zooids were washed with sea water to release the associated sediment and both were used as samples for bacteria isolation. Sediment was processed by 2 methods, drying (24h) on laminar flow and stamping using sterile polyurethane sponges and dilution in sterile artificial sea water followed by heating (56oC, 15 min), and zooids were processed by grinding and dilution in sterile artificial sea water. These samples were plated in 1- solid rich nutrient media (A1) or 2- sea water only (SWA) supplemented with cycloheximide to inhibit fungi growth and observed until 2 months to recover and isolate bacteria strains. The crude extracts were obtained from solid A1 cultures by ethyl acetate extraction under sonication (35oC, 20 min). Extracts were evaluated for cytotoxic activity in human colorectal cancer cells (HCT-116) and melanome (B16-F10) by the sulforhodamine B (SRB) assay at 50 µg/mL and 72 h incubation. A time zero plate with untreated cells allowed distinguishing between cell death (cytotoxicity) and cell growth inhibition (cytostaticity). Extracts that inhibited >75% of cell growth were considered active. **Results:** The bacteria isolation procedures resulted in 50 isolated strains, of which 58% from *Z. sociatus* specimen and 42% were isolated from associated sediment. To date, 16 bacterial cultures from *Z. sociatus* were successfully extracted and screened against the tumor cells. Among these, 8 extracts (50%), all Gram+, were active in HCT-116 cells. Additionally, 5 extracts exhibited cytotoxic activity - with 2 promoting 100% cell death - whereas 3 extracts showed a cytostatic profile. **Conclusion:** Bacteria associated with the zoanthid *Z. sociatus*, from the Piauí coast constitute a promising source of bioactive substances with anticancer potential. Further studies are ongoing toward the bacteria identification and chemical characterization, and evaluation of the active compounds produced by these marine bacteria.

10.013 **WIN55,212-2 Reduces Cell Migration in a Murine Colorectal Adenocarcinoma Cell Line (CT26. WT) Through Alterations in Oncogenic Pathways**. Bezerra BS[1], França JC[2], Pereira AF[2], Nascimento RR[2], Moura MNS[2], Moraes MEA[3], Wong DVT[2], Brito DMS[4], Zelaya EAE[4], Oliveira LLB[3], Paier CRK[3], Montenegro RC[4], Souza PFN[4], Vale ML[2] [1]UFC, Faculty of Medicine, Lab Inflammation and Cancer Pharmacology, Brazil; [2]UFC, Faculty of Medicine, Lab Inflammation and Cancer Pharmacology, PPG Pharmacology, Brazil; [3]UFC, Faculty of Medicine, Lab Experimental Oncology, PPG Pharmacology, Brazil; [4]UFC, Faculty of Medicine, Lab Pharmacogenetics, PPG Pharmacology, Brazil

Introduction: Colorectal cancer (CRC) is the third most common cancer worldwide, involving multiple mechanisms that drive tumor progression and the development of metastases. In this context, cell migration is a key process in tumor spread. In this setting, the epithelial-mesenchymal transition (EMT) process, loss of adhesion, and the formation of protrusions can lead to cytoskeletal remodeling and increased migratory capacity. Furthermore, oncogenic pathways stimulate EMT. In this process, cannabinoids have shown antitumor potential in various experimental models. Among them, the non- selective cannabinoid agonist WIN55,212-2 (WIN) stands out for its potential antitumor effect; however, its anti-migratory mechanisms in colorectal adenocarcinoma cell lines remain largely unexplored. **Objectives:** Therefore, the aim of this study is to evaluate the effects of WIN55,212-2 on cell migration and to identify changes in proteins and pathways associated with cytoskeletal reorganization in CT26.WT cells. **Methods:** The IC50 values for the control and treated groups were determined at 72 hours. CT26.WT cells were treated with WIN55,212-2 and subjected to a wound healing assay. In addition, shotgun proteomics analysis was performed, along with Gene Ontology (GO) analysis and protein-protein interaction network analysis. As a result, proteins differentially expressed in relation to cytoskeletal organization, cell migration, and cell adhesion were analyzed. Additionally, the AKT/mTOR and NF-κB pathways were analyzed by immunofluorescence. Data were considered statistically significant at a p-value < 0.05. **Results:** The cannabinoid exhibited an IC50 of 6.69 μM after 72 hours of treatment. The wound healing assay showed a 36% reduction in wound closure within 36 hours. Proteomic analysis identified that proteins depleted by WIN55,212-2, such as TPM3, FLNB, TMOD3, the Arp2/3 complex, and radixin, participate in the stabilization of actin filaments, the formation of invasive protrusions, and cellular remodeling. Furthermore, the increase in MBNL1 protein and the reduction in CNBP suggest suppression of the epithelial-mesenchymal transition (EMT) and of mechanisms associated with the expression of pro-oncogenic genes and metalloproteinases. Collectively, there was an inhibition of the PI3K/Akt/mTOR pathway by 34.92% in p-AKT levels and 33.46% in p-mTOR levels, as well as a 76% suppression of NF-κB compared to cells in the control group, suggesting a reduction in cellular mechanisms for tumor migration and progression. **Conclusion:** Thus, WIN55,212-2 modulated proteins associated with cytoskeletal reorganization and the PI3K/Akt/mTOR pathway, reducing events critical for EMT, cell migration, and tumor progression. These findings therefore underscore the importance of WIN55,212-2 in its potential antimetastatic effect in colorectal cancer. **Financial support:** UNIVERSAL/FUNCAP; CNPq; CAPES

10.014 **Effects of a *Fucus vesiculosus* Extract on the Progression of Epithelial Carcinogenesis in HPV16-Transgenic Mice**. Bastos HAC[1], Belfort MFA[1], Santos CED[1],Bezerra HRR[1], Lima LAS[1], Palhano NBM[1], Moreno AVP[1], Medeiros-Fonseca[2], Faustino-Rocha AI[2], Oliveira PA[2], Medeiros R[3], Bastos MMSM[4], Gil da Costa RM[1,2,3,4], Brito HO[1] [1]UFMA, Research Center For Experimental and Clinical Physiology and Pharmacology (NEC), Bioanalyses Lab (LabIO), Brazil; [2]University of Trás-os-Montes and Alto Douro (UTAD) Centre for the Research and Technology of Agroenvironmental and Biological Sciences (CITAB), Portugal; [3]Research Center of IPO Porto, Molecular Oncology and Viral Pathology Group, Portugal; [4]University of Porto, Lab for Process Engineering, Environment, Biotechnology and Energy (LEPABE), Portugal

Human papillomavirus (HPV) is the most prevalent sexually transmitted infection worldwide and is associated with substantial morbidity and mortality related to epithelial neoplasms, particularly cervical cancer. Despite advances in vaccination and screening programs, therapeutic options remain limited and may be associated with adverse effects. Therefore, the search for novel preventive and therapeutic strategies remains necessary. Fucus vesiculosus, a marine alga rich in fucoidans and phlorotannins, has demonstrated antioxidant and antitumor properties in several preclinical studies. This study aimed to evaluate the effects of a Fucus vesiculosus extract on the progression of epithelial lesions in HPV16-transgenic mice. HPV16-transgenic mice expressing the viral early region genes under the control of the keratin-14 (Krt14) promoter received a Fucus vesiculosus extract incorporated into the diet at concentrations of 0.1 g/g, 0.2 g/g, or 0.3 g/g. Histological sections of skin and tongue tissues were evaluated and compared with untreated HPV-positive controls. Lesion frequency and severity were assessed using Fisher's exact and Kruskal–Wallis tests, considering $p<0.05$ as statistically significant. In HPV-positive animals, treatment with Fucus vesiculosus was associated with a lower frequency of skin carcinoma (20% in the 0.1 g/g and 0.2 g/g groups and 0% in the 0.3 g/g group) and oral dysplasia (40% reduction in the 0.3 g/g group) compared with untreated HPV- positive controls. However, these differences did not reach statistical significance ($p=0.444$, Fisher's exact test). Likewise, Kruskal–Wallis analysis revealed no significant differences in lesion progression in the skin ($H=4.73$; $df=3$; $p=0.193$) or tongue ($H=3.04$; $df=3$; $p=0.385$). Nevertheless, mean rank values suggested a tendency toward reduced lesion severity in animals treated with the highest dose of the extract compared with HPV-positive controls, both in skin (6.8 vs. 13.4) and tongue tissues (7.5 vs. 13.5). Fucus vesiculosus extract demonstrated a potential protective effect against HPV-induced epithelial lesions, particularly at the highest tested dose. Although statistical significance was not achieved, the observed reduction in lesion frequency and severity supports further investigation in studies with larger sample sizes.

10.015 **Evaluation of the Resistance-Modulating Effect of the Alkaloids EB-PA and EB-PB in Cisplatin-Resistant Lung Cancer Cells**. Silveira TSN[1], Madrid MFM[2], Moraes-Filho MO[3], Pessoa CÓ[4], Rocha DDR[5] . [1]UFC, Dept Pharmacy, Brazil [2]USP, Faculty of Medicine, Brazil. [3]UFC, PPG in Pharmacology, Brazil. [4]UFC, PPG in Pharmacology, Brazil. [5] UFC, Lab. of Experimental Oncology, Drug Research and Development Center, Brazil

Introduction: Multidrug resistance (MDR) represents one of the major challenges in lung cancer treatment and is frequently associated with the overexpression of ABC transporters, such as MDR1, MRP1, and MRP2, which are responsible for chemotherapeutic drug efflux and reduced therapeutic efficacy. In this context, natural compounds have been investigated as potential modulators of tumor resistance, including alkaloids isolated from Erythroxylum bezerrae. **Objective:** To develop a cisplatin-resistant cell line and evaluate the modulatory potential of the alkaloids EB-PA and EB-PB in chemoresistant lung cancer cells. **Methods:** The resistant A549DDP20 cell line was developed through gradual and continuous exposure to cisplatin. Cytotoxicity, colony formation, and flow cytometry assays were performed to evaluate Rhodamine-123 efflux. **Results:** The A549DDP20 cell line exhibited resistance to cisplatin, with an IC50 value of 171.30 µM, whereas the parental A549 cell line showed an IC50 value of 10.62 µM, corresponding to an approximate 16-fold resistance index. Among the evaluated compounds, EB-PA demonstrated the greatest potential to modulate resistance, increasing intracellular Rhodamine-123 accumulation after 3 and 24 hours of treatment, suggesting functional inhibition of efflux transporters. Furthermore, combined treatments with EB-PA and cisplatin significantly reduced cell viability, cell density, and clonogenic capacity in resistant cells, indicating potentiation of the cytotoxic effect of cisplatin. **Conclusion:** These results demonstrate that the alkaloid EB-PA has potential as a chemosensitizing agent, increasing the response of A549DDP20 cells to cisplatin and highlighting its relevance as a candidate adjuvant therapeutic agent for multidrug-resistant lung tumors. **Acknowledgments:** This study was funded by INCTBIO2, PRONON, the Brazilian Ministry of Health, FINEP, CNPq, CAPES, and FUNCAP.

10.016 **PI3K Gamma and PI3K Delta Expression in Breast Cancer Before and After Neoadjuvant Chemotherapy: Association with Pathological Response**. Paulo CKF[1], Cavalcante DIM[2], Alves BES[1], Sampaio MJS[1], Maia IFVC[1], Wong DVT[1], Lima-Júnior RCP[1] [1]UFC, Dpt of Physiology and Pharmacology, Lab Inflammation and Cancer Pharmacology, Drug Research and Development Center, Brazil; [2]UFC, Dpt Pathology and Forensic Medicine, Brazil.

Introduction: Mutations in the PIK3CA gene are associated with alterations in breast carcinogenesis in about 30 to 40% of cases. This gene is part of the PI3K/AKT/mTOR signaling pathway, a major regulator of cell growth and survival that is often activated in neoplasms. Conversely, the PI3K gamma and PI3K delta isoforms are concentrated in the immune compartment, with higher expression of the Delta isoform in leukocytes than in epithelial cells. Thus, they modulate the immunosuppressive tumor microenvironment (TME) and drug resistance. However, the expression of these isoforms before and after neoadjuvant chemotherapy (NACT) has not yet been explored in breast cancer. **Objectives:** To analyze the differential expression of PI3K gamma and PI3K delta in breast cancer and to correlate the expression pattern with tumor response to NACT. **Methods:** This study included patients diagnosed with hormone receptor-positive (HR+) or triple-negative (TN) invasive carcinomas undergoing NACT with Doxorubicin, Cyclophosphamide, and a Taxane (n=30). The expression of PI3K gamma and delta was evaluated by immunohistochemistry in core biopsies of breast carcinomas and in surgical specimens after NACT. Pathological response to therapy was defined as complete (pCR), partial, or no response, as determined by the evaluation of the surgical specimen. Statistical analysis was performed using the Chi-square or paired Wilcoxon test. GraphPad Prism 9.0 software was used for analysis, and $p < 0.05$ was considered significant. Approval by the Research Ethics Committee: Nº 4.664.756 (ICC) and Nº 4.470.803 (HUWC). **Results:** pCR was observed in only 15.1% of patients, with a predominance in the TN group (n=9). In the pre-NACT samples, tumor cells showed high PI3K gamma expression and low PI3K delta expression. After cytotoxic treatment, the expression of the markers diverged: PI3K gamma decreased (p=0.0039), while PI3K delta increased (p=0.0312), with 15% of cases showing high PI3K delta expression at the end of treatment. **Conclusion:** We observed variations in the expression of PI3K gamma and PI3K delta isoforms. The near-universal expression of PI3Kgamma in pre-treatment tumor cells suggests an intrinsic role in promoting an immunosuppressive TME. On the other hand, the increase in PI3K delta expression in residual tumor cells after NACT was a finding not previously reported in the literature. This may reflect a selection of subclones that, by expressing isoforms of immune cells, exert a more effective interaction with the tumor microenvironment, which might be associated with resistance mechanisms. **Financial support:** CNPq, CAPES, ICC, EBSERH.

10.017 **The Role of Kinin Receptors in a Mouse Model of Chemically-Induced Oral Cancer**. Neculqueo GW[1,2], Farias ABS[2], LG[2], Estrázulas M[1,2], Campos MM[1,2] [1]PUCRS, PPG Medicina e Ciências da Saúde, Brazil. [2]FADIC-PUCRS, Escola de Ciências da Saúde e da Vida, Brazil.

Introduction: Head and neck squamous cell carcinoma (HNSCC) is an aggressive cancer strongly associated with alcohol consumption and tobacco exposure, besides HPV infection (Feng Y. Oncol Rep, 51:79, 2024). Kinin receptors have been identified in various tumor types and are thought to play a key role in cancer progression (Deepak K. Biochim Biophys Acta Rev Cancer, 1877:188807, 2022). **Objectives:** This study examined the effects of B1 (R-954) and B2 (HOE140) receptor antagonists in a murine model of chemically- induced oral carcinogenesis. Furthermore, we assessed the time course of kinin receptor expression throughout carcinogenesis induction. **Methods:** C57BL/6 mice of both sexes were used following approval by the local Animal Ethics Committee (11350). Oral carcinogenesis was induced with 4-nitroquinoline 1-oxide (4-NQO; 50 µg/mL in drinking water) for 16 weeks. From week 20 onward, mice received daily treatments for 7 days as follows: negative control, tumor control (4-NQO), cisplatin (2 mg/kg, i.p.), HOE140 (50 nmol/kg, s.c.), or R-954 (160 nmol/kg, s.c.). Animals were euthanized at week 21 for sample collection. Additionally, the temporal expression of kinin B1 and B2 receptors was evaluated by immunohistochemistry at several time points. Accordingly, mice exposed to 4-NQO were euthanized at weeks 2, 5, 8, 11, 14, 17, and 20. Tongues were collected and fixed in 10% formaldehyde for further analysis. **Results:** All treatments significantly reduced the number of macroscopic lesions compared with the tumor control (4-NQO) ($p < 0.01$); however, only HOE140 significantly reduced the tumor areas ($p = 0.02$). The lesions were classified as dysplasia or carcinoma by histopathological analysis. Odds ratio analysis demonstrated that HOE 140 significantly reduced carcinoma development compared with the tumor control (4-NQO) ($OR = 0.17$, $p = 0.041$), corresponding to 83% reduction. Cisplatin showed a similar trend ($OR = 0.195$), although without statistical significance ($p = 0.062$), whereas R-954 showed no effect ($OR \approx 0.91$, $p = 0.918$). Temporal immunohistochemical analyses revealed distinct expression patterns for kinin receptors during carcinogenesis. B1 receptor expression increased significantly from week 5 onward in 4-NQO–treated animals and remained elevated until the end of the protocol, peaking at 17 weeks. B2 receptor expression increased as early as week 2, steadily rising until week 14, then gradually declining towards week 20. **Conclusion:** These findings provide novel *in vivo* evidence for the involvement of kinin receptors in HNSCC progression and highlight B2 receptor blockade as a potential therapeutic strategy in oral carcinogenesis.

10.018 **KCNQ1OT1 Overexpression Marks a High-Risk Subset of Intermediate-Risk AML with FLT3-ITD Enrichment and Poor Survival**. Oliveira KAF[1,2]; Scandolara TB[1,3]; Sales SLA[1,4]; Maranhão SS[1]; Farias IR[3]; Mota JA[1,4]; Gress LSB[1,4]; Macêdo SMN[1]; Melo VB[5] ; Soares IF[1,6]; Ramos IA[7]; Xavier EEP[1,8]; Pessoa C[1,4]; Bezerra LRPS [3] [1]UFC, Experimental Oncology Lab, Center for Research and Drug Development, Brazil; [2]UFC, Dept Biology, Brazil; [3]UFC, Graduate Program in Translational Medicine, Brazil; [4]UFC, Dept Physiology and Pharmacology, Graduate Program in Pharmacology, Brazil; [5]UFMG, Dept Genetics, Ecology and Evolution, Institute of Biological Sciences, Brazil; [6]UNIFOR, Center for Health Sciences (CCS), Brazil; [7]UFC, Faculty of Medicine, Brazil; [8]UFC, Faculty of Pharmacy, Brazil; [9]UFC, Dept Child and Adolescent Health, Brazil.

Intoduction: Epigenetic alterations are central to acute myeloid leukemia (AML) pathogenesis, influencing transcriptional programs linked to clonal expansion and disease progression. Genomic imprinting regulates genes involved in proliferation, differentiation, and cell survival. The KvDMR locus (11p15.5) controls an imprinted domain encompassing KCNQ1OT1, KCNQ1, CDKN1C, and PHLDA2. Although alterations at this locus have been described across human neoplasms, their clinical relevance in myeloid neoplasms remains poorly understood. **Objectives**: To evaluate KvDMR-regulated gene expression in primary MDS and secondary AML samples, and to extend the investigation to de novo AML using a large public cohort stratified by molecular risk. **Methods:** Primary bone marrow samples from patients with primary MDS (n=70) and secondary AML (n=11) were analyzed by RT-qPCR for KCNQ1OT1, KCNQ1, CDKN1C, and PHLDA2 expression, correlated with clinicopathological variables (CAAE:40698620.5.0000.5054). Given limited associations in primary samples due to sample size, *in silico* analysis was extended to de novo AML using cBioPortal (619 samples, 562 adults). cBioPortal patients were stratified by European LeukemiaNet (ELN) criteria and subdivided by median gene expression. Overall survival (OS), molecular features, and hematological parameters were analyzed per subgroup. **Results:** In primary MDS and secondary AML samples, KvDMR gene expression was largely unassociated with clinicopathological or prognostic parameters ($p>0.05$). in silico analysis of de novo AML revealed that only KCNQ1OT1 demonstrated prognostic impact. In the ELN intermediate-risk group, high KCNQ1OT1 expression associated with shorter OS ($p=0.046$), enrichment for FLT3-ITD ($p<0.01$), higher FLT3-ITD allelic ratio ($p<0.001$), and greater peripheral blood blast percentage ($p<0.001$). In the favorable-risk group, high KCNQ1OT1 also correlated with FLT3-ITD presence and higher bone marrow blast percentage ($p<0.01$). KCNQ1, CDKN1C, and PHLDA2 showed no association with OS. **Conclusion:** While KvDMR gene expression showed limited clinical associations in MDS and secondary AML, high KCNQ1OT1 expression identified a worse-prognosis subset within intermediate-risk de novo AML, enriched for FLT3-ITD and increased leukemic burden. These findings support KCNQ1OT1 as a candidate complementary biomarker for prognostic refinement and warrant investigation in therapeutic strategies combining FLT3 inhibitors and epigenetic modulation. **Financial support**: This work was financed in part by INCTBIO 2, PRONON, MINISTÉRIO DA SAÚDE, FINEP, CNPq, CAPES e FUNCAP.

10.019 **Evaluation of the Therapeutic Potential of Cirsimarina in the Topical Treatment of Urogenital Lesions in Experimental Penile Cancer**. Moreno AVP[1], Santos CED, Bezerra HRR[1,2], Bastos HAC[1,2], Belfort MFA[1,2], Palhano NBM[1,2], Baltazar RS[1,2], Pozes AB[1,2], Borges, ACR [1,2], Borges, MOR [1,2],Rocha CQ[1], Brito HO [1,2 1]UFMA, Research Center for Experimental and Clinical Physiopathology and Pharmacology, Brazil; [2]UFMA, Pharmacology Lab, Brazil; [3]UFMA, Dept Chemistry, Federal University of Maranhão

Penile cancer is a rare neoplasm that can occur in an HPV-dependent or HPV- independent manner, with a high incidence in Maranhão, Brazil. Despite the existence of transgenic models for HPV16, there are still no well-established experimental models for the study of HPV-independent penile cancer. Thus, the present study aimed to morphologically evaluate the penile,lingual, prostatic, and testicular tissues of an experimental model of HPV-independent penile carcinogenesis model induced in Wistar rats treated with carrageenan (CG) and 4-nitroquinoline-1-oxide (4NQO), as well as to investigate the therapeutic effects of cirsimarin (cirsitakaoside),a flavonoid isolated from Scoparia dulcis L. Histopathological analyses were performed qualitatively using haematoxylin-eosin and Picrosirius staining. In the control group, the tissues showed preserved morphology. Animals exposed to CG and 4NQO developed chronic inflammation of the glans and prepuce, epithelial hyperplasia, neovascularization, and difficulty in preputial retraction. Rare condylomas were also observed, while one animal developed well-differentiated penile intraepithelial neoplasia (PeIN) .In the tongue, ulcerative stomatitis was observed, characterized by epithelial disorganization, necrosis, and intense inflammatory infiltrate. In contrast, animals treated with cirsimarin showed attenuation of inflammatory alterations, especially at the higher dose, with partial preservation of tissue architecture and absence of proliferative lesions. Treatment with cirsimarin at a dose of 10 mg/kg promoted partial reduction of penile and oral inflammation, whereas the dose of 20 mg/kg demonstrated a greater anti-inflammatory effect, preservation of epithelial integrity, and reduction of inflammatory infiltrates. Moreover, cirsimarin reduced body weight, adipose tissue mass, and total cholesterol levels, increased thymus and adrenal gland weights, and reduced liver, kidney, and testicular weights. No histopathological alterations were identified in the prostate and testes in any experimental group, demonstrating that the lesions remained restricted to penile tissue. In conclusion, the study successfully established a reproducible experimental model of HPV-independent penile carcinogenesis associated with chronic inflammatory processes. Furthermore, cirsimarin demonstrated promising anti-inflammatory, antiproliferative, and metabolic effects, suggesting therapeutic potential for lesions related to HPV-independent penile cancer.

10.020 *In vitro* Evaluation of the Cytotoxic Potential of the Petroleum Ether Extract from the Stem Bark of *Annona vepretorum* Mart. Santos PBG[1], Abreu-Junior AR[2], Gomes KNC[1], Alexandre HMS[2], Marques KKG[2], Pereira ERM[2], Santana PVS[2], Araújo YKOA[1], Januario VHS[1], Silva ICF[2], Tavares JF[2], Dutra LM[3], Costa EV[4], Sobral MV[2], Gonçalves JCR[2]. [1]UFPB, Health Sciences Center, ONCOFAR, Pharmacy, Brazil, [2]UFPB, Health Sciences Center, ONCOFAR, PPG in Bioactive Natural and Synthetic Products, Brazil, [3]UFPR, Dept Chemistry, Brazil, [4]UFAM, Dept Chemistry, Brazil

Introduction: Cancer is the second leading cause of death worldwide, and current therapies present limitations such as low selectivity, toxicity, adverse effects, and drug resistance. In this context, natural products represent an important source of antitumor compounds. The species *Annona vepretorum* Mart. (Annonaceae) presents cytotoxic activity described in the literature. Thus, this study aimed to evaluate the *in vitro* cytotoxicity of the petroleum ether extract from the stem bark of *Annona vepretorum* Mart. (PEE-Av) against different human tumor cell lines of clinical relevance. **Methods:** PEE-Av was obtained from a specimen of Av collected in Poço Redondo - SE, Brazil (SISGEN: ACAAA36). According to a previous phytochemical characterization showed that the petroleum ether stem bark extract used in this study is rich in ent-kaurane diterpenes, with ent-3β-hydroxy-kaur-16-ene as the major constituent and the previously unreported ent-3β-hydroxy-kaur-16-en-19-al among its constituents (Dutra, LM. Bioorg. Med. Chem. Lett., v. 24, p. 3315, 2014). Cytotoxicity was evaluated through the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay against human colorectal adenocarcinoma (HCT-116, HT-29, and LoVo), breast adenocarcinoma (MCF-7), and melanoma (SK-MEL-28) cells, as well as non-tumorigenic human keratinocytes (HaCaT). Data were expressed as the mean ± SEM and analyzed by one-way ANOVA, followed by Tukey's test ($p < 0.05$). Half-maximal inhibitory concentrations (IC_{50}) were determined via non-linear regression using the Hill equation and the selectivity index (SI) determined by the non-tumor/tumor IC50 ratio. **Results:** An initial cytotoxic screening of PEE-Av was conducted at 25 and 100 µg/mL. After 72 hours, PEE-Av significantly decreased cell viability in all tested lines, exhibiting cell line-specific efficacy. The colorectal adenocarcinoma cell lines presented the greatest cytotoxic effect, with the greatest reduction in cell viability observed in HCT-116 (IC_{50}: 15.49 ± 2.28), followed by HT-29 (IC_{50}: 17.61 ± 2.27) and LoVo (IC_{50}: 46.76 ± 8.59). The cytotoxic effect was significant ($p < 0.05$) from the concentration of 6.25 µg/mL for HCT-116 and HT-29, while in LoVo the significant response was observed from 12.5 µg/mL. In contrast, the non-tumor cell line derived from immortalized keratinocytes, HaCaT, presented lower cytotoxicity (IC50: 75.55 ± 2.50). After 72 h, the SI values for HCT-116, HT-29, and LoVo were 5.0, 4.4, and 1.65, respectively. **Conclusion:** In conclusion, PEE-Av exhibits potent and selective cytotoxicity against colorectal adenocarcinoma cell lines, particularly HCT-116 and HT-29. These findings highlight its potential as a selective antitumor agent and warrant further investigation into its underlying mechanisms. **Financial support:** CAPES, CNPq, and FAPESQ.

10.021 **Evaluation of the Cytotoxic Activity of** *Conyza bonariensis* (L). **Cronquist. in Breast Cancer Cells**. Araújo YKO[1], Abreu-Junior AR[2], Gomes KNC[1], Santos PBG[1], Pereira ERM[1], Alexandre HMS[2], Santana JP[1], Januario VHS[1], Silvestre GFG[1], Castro IO[1], Amorim GMW[2], Tavares JF[2], Sobral MV[2], Gonçalves JCR[2]. [1]UFPB, Health Sciences Center, ONCOFAR, Undergraduate in Pharmacy, Brazil. [2]UFPB, Health Sciences Center, PPG in Bioactive Natural and Synthetic Products, Brazil.

Introduction: Breast cancer is the most frequently diagnosed type of cancer in women and the fifth leading cause of cancer death worldwide. Currently, chemotherapy is one of the main treatment strategies, but it has limitations due to its non-selective cytotoxicity, also affecting healthy cells. In this context, the search for new effective antitumor therapies with low toxicity becomes necessary. Traditional medicine has contributed to the discovery of new drugs derived from medicinal plants. In this context, the species *Conyza bonariensis* (Asteraceae) stands out for its cytotoxic effect against cancer cells. **Objectives:** To investigate the cytotoxic effect of *C. bonariensis* essential oil (CbEO) on an *in vitro* breast cancer cell line. **Methods:** CbEO (SisGen-Brazil: A7B0B64) was obtained and characterized at the Multi-user Laboratory for Analysis and Characterization (LMCA/UFPB). To assess cell viability, the MTT cytotoxicity assay was used on human breast adenocarcinoma cells (MCF-7) and treated with different concentrations of CbEO (5-500 µg/mL) for 48 h. The type of cell death (necrosis/apoptosis) was evaluated by double staining the cells with acridine orange and propidium iodide (AO/PI) after 48 h of treatment, using confocal laser scanning microscopy (Biofoton Lab/UFPB). Data were analyzed by one-way ANOVA and Dunnett or Bonferroni post-tests, and significance considered when $p<0.05$. CI50 values were obtained by non-linear regression using the Hill equation. **Results:** The CbEO reduced cell viability compared to the control group (100 ± 14.7%) to 68.22 ± 20.51% at the lowest concentration tested (5 µg/mL). At concentrations of 50 µg/mL and 500 µg/mL, there was a significant reduction ($p < 0.05$) with a decrease in viability to 44.4 ± 5.80% and 38.5 ± 6.64%, respectively, in addition to 24.3 ± 3.94% for doxorubicin (5 µg/mL), the standard drug used as a positive control. The 48-hour CI50 obtained was 55.7 ± 1.9 µg/mL. The type of cell death was investigated by confocal laser microscopy, revealing that the group treated with the CbEO CI50 had the highest percentage of cells in late apoptosis (58.78 ± 10.28%), followed by early apoptosis (37.70 ± 12.09%) compared to the control group (99.72 ± 0.182%). There was no significant increase in necrotic cells (0.167 ± 0.167). **Conclusion:** The results showed that CbEO promoted a cytotoxic effect on the MCF-7 cell line, reducing cell viability through the induction of cell death by apoptosis. Therefore, the results provide a basis for future studies aimed at evaluating the antitumor mechanism and its potential for pharmaceutical application. **Financial support:** Propesq-UFPB, FAPESQ, CAPES e CNPq.

10.022 *In vitro* Screening of Synthetic Compounds with Cytotoxic Activity Against Human Tumor Cells. Araujo CM[1,2], Oliveira VS[1,2], Souza SF[3], Alves RJ[4], Aquino YS[3], Lavorato SN[3], Soares, MBP[1,2], Meira CS[1,2] [1]Fiocruz-BA, Salvador, [2]SENAI CIMATEC-BA, Salvador, [3]UFOB, Barreiras, [4]UFMG, Belo horizonte.

Introduction: The identification of new compounds with cytotoxic activity against tumor cells remains relevant for anticancer drug discovery. Medicinal chemistry enables the synthesis and screening of structurally diverse molecules derived from bioactive scaffolds. In this study, synthetic chalcones (S1 and S2), aminopyrimidines (S3 and S4), and epichlorohydrin-derived analogues of dehydrozingerone (S6) and ferulic acid (S7) were investigated for their cytotoxic activity. **Objectives:** To screen synthetic compounds for cytotoxic activity against human tumor cell lines and evaluate their effects on a non-tumorigenic human cell line. **Methods:** HepG2, PANC-1, U-87 MG, and non-tumorigenic MRC-5 cells were cultured in DMEM supplemented with 10% fetal bovine serum and 1% penicillin/streptomycin at 37 °C and 5% CO_2. Six synthetic compounds were screened at a single concentration of 50 µM for 72 h. Cell viability was determined using the AlamarBlue assay, and the results were expressed as percentage of inhibition relative to untreated controls. Doxorubicin (1 µM) was used as a positive control. **Results:** Overall, U-87 MG was the most sensitive tumor cell line, with S7 showing the highest activity (53.23% ± 0.8 inhibition), followed by S6 (34.26% ± 1.7). S7 was also the most active compound against PANC-1 (46.52% ± 1.9), while S1 and S6 showed the highest activity against HepG2 (32.52% ± 4.2 and 32.80% ± 3.1, respectively). S1 showed a favorable preliminary selectivity profile, with approximately two- fold higher inhibition of HepG2 than MRC-5 cells (15.47% ± 1.6). S3 also showed preferential activity against U-87 MG (26.80% ± 1.8) compared with MRC-5 (14.50% ± 0.7). Although S7 was the most active compound, its effect on MRC-5 cells (39.0% ± 10.0) indicated a narrower tumor/non-tumor differential. S6 showed similar activity in tumor and MRC-5 cells, suggesting limited selectivity, whereas S4 was the least active compound overall. **Conclusion:** Among the compounds evaluated, S7 showed the highest cytotoxic activity, particularly against U-87 MG and PANC-1 cells, although its effect on MRC-5 cells indicates limited tumor selectivity under the conditions tested. Overall, these findings reinforce the investigated chemical classes as relevant sources of bioactive molecules and support further studies aimed at identifying and optimizing compounds with improved antitumor activity and selectivity. **Financial support:** FAPESB.

10.023 **Evaluation of Cytoplasmic SMAD3 Immunoexpression and Its Association with Clinical Outcomes in Inflammatory Breast Cancer**. Teixeira-Filho JIF[1], Batista RER[1], Alves BES[1], Barrozo AEO[1], Maia IFVC[1], Arruda LM[2], Leitão RFC[3], Cavalcante DIM[4], Rogatto SR[5], Lima-Júnior RCP[1], Wong DVT[1]. [1]UFC, Dpt of Physiology and Pharmacology, Lab Inflammation and Cancer Pharmacology, Drug Research and Development Center, Brazil; [2]Haroldo Juaçaba Hospital, Cancer Institute of Ceará, Brazil; [3]UFC, Dpt of Morphology, Brazil; [4]UFC, Dpt of Pathology and Forensic Medicine, Brazil; [5]Unesp, Botucatu Medical School Hospital, Brazil.

Introduction: Inflammatory Breast Cancer (IBC) is a rare and aggressive clinical presentation of breast cancer associated with rapid progression, early metastasis, and poor clinical outcomes. Mothers Against Decapentaplegic Homolog 3 (SMAD3), a protein that mediates the transforming Growth Factor-beta (TGF-β) signaling pathway, orchestrates an important role in the regulation of cell proliferation, differentiation, epithelial–mesenchymal transition, and apoptosis. Therefore, the role of SMAD3 in IBC remains poorly characterized and requires further investigation. **Objectives:** Evaluate SMAD3 expression in samples by patients with IBC and non-IBC and associated with clinical and pathological parameters. **Methods:** This is a retrospective study. Formalin- fixed paraffin-embedded (FFPE) tumor samples and clinicopathological data (age at diagnosis, family history, presence of hormone receptors and HER2 status, metastasis, and Ki-67, a proliferation cell marker) were prospected from 18 IBC and 16 non-IBC subjects from 2015 to 2020. FFPE tissue samples were subjected to immunochemistry staining of SMAD3 expression. The coloration was quantified using FIJI ImageJ software. Statistical analysis was performed using the t-test and Two-Way ANOVA. $P<0.05$ was accepted. Study approval number: 5.010.710. **Results:** SMAD3 demonstrated cytoplasmic positivity in neoplastic cells. Furthermore, in the primary tumor and at progression stages of IBC disease, including locoregional metastasis and emboli tumor, the SMAD3 expression is not lost, but remains present in neoplastic cells that migrated to these locations, even though these may have undergone clonal differentiation during the clinical course of the disease. The IBC patients added in this study had comparable patterns of overweight/obesity, TNM stage, distant metastasis, and expression levels of ER, PR, HER, and Ki-67 above 20% ($p> 0.05$ vs. non-IBC). In the comparison between the groups, SMAD3 expression in cytoplasmic immunostaining of tumor cells was higher in patients with IBC [$p=0.0026$]. Higher percentage SMAD3 protein expression was associated with molecular subtype luminal in IBC subjects versus luminals non-IBC subjects [$p=0.0385$], when patients were stratified according to the clinicopathological parameters. The sample size was limited due to the difficulty in access to more IBC samples. **Conclusions:** SMAD3 expression may play a significant role in the oncogenesis of IBC; however, it should be interpreted in conjunction with other oncogenic signaling pathways, particularly the TGF-β pathway, to better understand its potential as a biomarker and therapeutic target.
Financial support: PPSUS/FUNCAP-SESA-Decit/MS-CNPq; CAPES.

10.024 **Use of Antidepressants and Potential Drug Interactions in Oncology Patients - A Bibliographic Review**. Moura AVL[1], Silva HCO[1], Medeiros AC[1], Oliveira IS[2], Lima IPG[3], Ferreira MDL[4] [1]FACENE, Graduação Farmácia, João Pessoa, PB, Brazil; [2]Unileya, Pós Farmácia Clínica Oncológica, João Pessoa, PB, Brazil; [3]FACENE, Saúde da Família, João Pessoa, PB, Brazil; [4]FACENE, João Pessoa, PB, Brazil

Introduction: Oncology patients frequently present depressive symptoms due to the psychological impact of cancer diagnosis and chemotherapy. Depression affects more than 300 million people worldwide and is highly prevalent in oncology. Although antidepressants are often necessary, polypharmacy involving antineoplastic agents, supportive medications, and drugs for comorbidities increases the risk of drug-drug interactions. Shared metabolism through the cytochrome P450 system may reduce therapeutic efficacy or increase toxicity. **Objectives:** To analyze the incidence of potential drug-drug interactions in cancer patients using antidepressants and chemotherapeutic agents, based on scientific evidence, and discuss the role of the clinical pharmacist in preventing and managing these interactions. Methods. This descriptive and exploratory literature review with a quantitative-qualitative approach searched the LILACS, SciELO, MEDLINE, and BVS databases using the descriptors antineoplastic agents, drug interactions, antidepressants, and oncology patients. Studies published within the last 10 years were included. The analysis focused on a clinical study conducted at a hospital in southern Brazil involving 50 hospitalized oncology patients undergoing chemotherapy (Kuhn et al., Rev. Bras. Farm. Hosp., v.11, n.2, 2020). **Results:** Of the 50 patients, 42% (n=21) used antidepressants, with a mean of 1.2 drugs per patient. Selective serotonin reuptake inhibitors were the most prescribed class (76%), with escitalopram accounting for 33% of antidepressant users. Overall, 90% (n=45) presented potential drug-drug interactions. Among antidepressant users, 62% (n=13) had contraindicated interactions and all presented major interactions. The main contraindicated combinations were sertraline with dipyrone, increasing bleeding risk, and escitalopram with metoclopramide, increasing the risk of extrapyramidal reactions and neuroleptic malignant syndrome. Therapeutic substitution with acetaminophen, ondansetron, or dimenhydrinate may reduce these risks. **Conclusion:** Concomitant use of antidepressants and antineoplastic agents is common in oncology patients and may result in clinically significant drug-drug interactions. Clinical pharmacists are essential for prescription review, identification of interactions, and recommendation of safer therapeutic alternatives, contributing to patient safety and treatment optimization. **Financial support** Information. None. Acknowledgments. To Faculdade de Enfermagem Nova Esperança (FACENE) for institutional support.

10.025 **Extracellular Matrix Changes Associated with Penile Carcinogenesis: A Comparative Study**. Bezerra HRR[1], Belfort MFA[1], Santos CED[1], Bastos HAC[1], Palhano NBM[1], Cavalcante DCS[1], Baltazar RS[1], Viana Sousa F[1], Moreno AVP[1], Medeiros-Fonseca[2], Faustino-Rocha AI[2], Oliveira PA[2], Medeiros R[3], Bastos MMSM[4], Brito HO[1], Gil da Costa RM[1,2,3,4]. [1]UFMA, Research Center For Experimental and Clinical Physiology and Pharmacology (NEC), Bioanalyses Lab (LabIO), Brazil; [2]University of Trás-os-Montes and Alto Douro, Centre for the Research and Technology of Agroenvironmental and Biological Sciences , Portugal; [3]Research Center of IPO Porto, Molecular Oncology and Viral Pathology Group, Portugal; [4]University of Porto, Lab for Process Engineering, Environment, Biotechnology and Energy, Portugal.

Introduction: Two forms of penile cancer are recognized: one associated with human papillomavirus (HPV) and another HPV-independent. Cancer invasion involves changes in the extracellular matrix; however, the characterization of these alterations in penile cancer remains poorly understood. Studies comparing transgenic animals and human tissues are important to be conducted. **Objectives:** This study aimed to characterize extracellular matrix remodeling during human and murine penile carcinogenesis. **Methodology:** Twenty-seven tumor and adjacent tissue samples were obtained from the Maranhão Tumor and DNA Biobank and stained with hematoxylin-eosin, Masson's trichrome, picrosirius red, and periodic acid-Schiff (PAS). Matched frozen samples were used for DNA extraction, HPV detection by nested PCR, and genotyping. **Results:** Penile tissues from 30-week-old FVB/n mice representing normal tissue (n = 4, wild- type), penile intraepithelial neoplasia (n = 4, HPV16-transgenic), and poorly differentiated squamous cell carcinoma (n = 1, HPV16-transgenic) were stained with picrosirius red. Among human samples, 37.03% (10/27) were HPV-positive, 37.03% (10/27) were HPV-negative, and seven samples could not be analyzed due to poor DNA quality. HPV11 was the most frequently detected genotype, and 29.6% of cases showed multiple HPV infections. PAS staining demonstrated loss of basement membranes in tumor samples without accumulation of extracellular mucins. Masson's trichrome and picrosirius red staining revealed extensive disruption of the collagen network in all tumor samples, with tumor foci surrounded by scant stromal tissue or remnants of Buck's fascia. Under polarized light, picrosirius red staining demonstrated a preferential loss of type III collagen fibers, with only a few remaining type I fibers. In HPV16-transgenic mice, condensed type I and III collagen fibers were observed in the lamina propria underlying intraepithelial lesions, whereas extensive collagen loss was evident in carcinoma tissue. **Conclusion:** These findings indicate that penile cancer is characterized by marked extracellular matrix remodeling that begins during the intraepithelial stage and progresses to collapse of the collagen network, independently of HPV status and without accumulation of extracellular neutral mucins.

10.026 **A Selenium Compound Induces Apoptotic Cell Death in HeLa Cervical Cancer Cells**. Rodrigues JS[1], Loureiro PBA[2], Farias APGM[2], Amorim GMW[2], Pereira ERM[2], Souza HDS[4], Silva ICF[2], Marques KKG[2], Queiroga LM[2], Scotti L[3], Scotti MT[3], Souza NF[3], Athayde Filho PFA[4], Sobral MV[2], Gonçalves JCR[2] [1]UFPB, Health Sciences Center, ONCOFAR, Undergraduate in Pharmacy, Brazil, [2]UFPB, Health Sciences Center, ONCOFAR, PPG in Bioactive Natural and Synthetic Products, Brazil, [3]UFPB, Health Sciences Center, PPG in Bioactives Natural and Synthetic Products, Brazil, [4]UFPB, PPG in Chemistry, Brazil.

Introduction: Cervical cancer (CC) represents a major public health concern and remains among the leading causes of cancer-related deaths in women worldwide, with an increasing incidence in Brazil. Persistent infection by high-risk human papillomavirus (HPV) is the main factor associated with CC development, and vaccination is an important preventive strategy. Despite advances, current therapies still present limitations, highlighting the need for new therapeutic alternatives. The compound N-(4-methylphenyl)benzoseleno- ethylenolactamide (NC31) has shown leishmanicidal and antimicrobial activities, and has also demonstrated selective cytotoxicity toward HeLa, a CC cell line. **Objective:** This study aimed to investigate the type of cell death and mitochondrial membrane potential alterations induced by NC31 in HeLa. **Methods:** The cell death profile was evaluated after 24 hours of treatment with NC31 (2.5, 5, and 10 μM), corresponding to the 50% inhibitory concentration (IC50 value), half, and double this concentration, using the acridine orange/propidium iodide (AO/PI) assay by confocal microscopy. Nuclear alterations associated with cell death were assessed by the Hoechst 34580 assay after treatment with NC31 (5 and 10 μM) for 24 hours using a laser scanning confocal microscope. The association between cell death and mitochondrial membrane potential alterations was investigated by the JC-1 (5,5',6,6'-tetrachloro-1,1',3,3'-tetraethylbenzimidazolylcarbocyanine iodide) assay after treatment with NC31 (5 and 10 μM) for 24 hours. Results were presented as mean ± SEM and statistically analyzed using one-way ANOVA followed by Tukey's multiple comparisons test. **Results:** The AO/PI assay demonstrated a significant increase in early apoptotic cells after treatment with NC31 (2.5 μM: 86.23 ± 3.56%; 5 μM: 78.34 ± 8.77%; 10 μM: 35.62 ± 8.06%; $p<0.05$ for all), while the highest concentration also increased late apoptosis/necrosis (64.38 ± 8.06%; $p<0.05$). The Hoechst assay demonstrated a 1.85 ± 0.07-fold and 2.53 ± 0.06-fold increase in fluorescence intensity after treatment with 5 and 10 μM NC31, respectively ($p < 0.05$). Finally, NC31 reduced the JC-1 aggregate/monomer fluorescence ratio from 2.01 in the control group to 0.27 and 0.22 ($p<0.05$ for both) after treatment with 5 and 10 μM, respectively. **Conclusion:** NC31 induced apoptotic cell death in HeLa, nuclear alterations, and mitochondrial membrane depolarization. The marked reduction in the JC-1 aggregate/monomer fluorescence ratio suggests the involvement of the intrinsic apoptotic pathway in the cytotoxic effects induced by the compound. Furthermore, the previously observed selective cytotoxicity toward HeLa cells reinforces the antitumor potential of NC31 and supports further investigations into its mechanism of action in CC models. **Financial support**: CNPq, CAPES, and FAPESQ-PB.

10.027 **Docetaxel-Loaded Alginate Nanoparticles Increase Selectivity and Apoptotic Cell Death in Triple-Negative Breast Cancer Cells**. Pereira ERM[1], Alexandre HMS[1], Abreu-Junior AR[1], Santos PBG[2], Gomes KNC[2], Araujo YKO[2], Queiroga LM[1], Januario VHS[2], Farias APGM[1], Silva ICF[1], Marques KKG[1], Mendes AN[3], Filgueiras LA[3], Sobral MV[1], Gonçalves JCR[11]UFPB, Lab Oncopharmacology (ONCOFAR), PPG in Natural and Synthetic Bioactive Products, Brazil; [2]UFPB, Lab Oncopharmacology (ONCOFAR), Pharmacy undergraduate student, Brazil; [3]UFPI, Dept Biophysics and Physiology, Lab Innovation in Science and Technology (LACITEC), Brazil

Introduction: Triple-negative breast cancer (TNBC) is associated with high aggressiveness and therapeutic limitations related to the toxicity of conventional chemotherapeutics, including taxanes. In this context, biocompatible polymeric nanosystems have emerged as promising strategies to improve antitumor efficacy and selectivity. The nanoparticles analyzed in this study were previously developed and physicochemically characterized by the Laboratory of Pharmaceutical Innovation and Nanotechnology (LACITEC), Federal University of Piauí (UFPI). **Objectives:** To evaluate the *in vitro* cytotoxic activity and cell death mechanism induced by oxidized sodium alginate nanoparticles containing docetaxel (DTx@Alg) in TNBC cells (MDA-MB-231), compared with free docetaxel (DTx) and empty nanoparticles (ENP). Methods: Cytotoxicity was evaluated by the Trypan Blue exclusion assay in MDA-MB-231 and HEK-293 cells exposed to DTx@Alg, DTx, and ENP at concentrations ranging from 0.001 to 10 µg/mL. Cell death was assessed by acridine orange/propidium iodide double staining and confocal microscopy after 48h of treatment. **Results:** DTx@Alg significantly reduced cell viability in MDA-MB-231 cells while showing lower toxicity in healthy HEK-293 cells. ENP did not exhibit significant cytotoxicity. DTx@Alg showed an IC50 value of 0.0027 µM in MDA- MB-231 cells and 1.1970 µM in HEK-293 cells, resulting in a selectivity index (SI) of 443.3, whereas free DTx presented IC50 values of 0.0155 µM and 0.0350 µM, respectively, with an SI of 2.26. These results indicate that DTx@Alg exhibited approximately 196-fold higher selectivity toward tumor cells compared with free DTx. Cell death analyses demonstrated that DTx@Alg predominantly induced early apoptosis (62.48 ± 4.42%), whereas DTx induced higher levels of late apoptosis/necrosis (47.13 ± 9.76%). Morphological features of apoptosis, including membrane blebbing and apoptotic bodies, were observed following DTx@Alg treatment. **Conclusion:** The DTx@Alg nanosystem demonstrated high *in vitro* antitumor potential against TNBC by increasing docetaxel pharmacological potency and selectivity while predominantly inducing apoptotic cell death.

10.028 **Cytotoxicity of the Selenium Compound NC36 in Human Cervical Cancer Cells**. Lyra GB[1], Silva ICF[1], Amorim GMW[1], Dantas MM[1], Castro IO[1], Farias APGM[1], Pereira ERM[1], Loureiro PBA[1], Sousa NF[2], Souza HDS[3], Athayde-Filho PF[3], Scotti L[2], Scotti MT[2], Gonçalves JCR[1], Sobral MV[1] [1]UFPB, Health Sciences Center, ONCOFAR, PPG in Natural and Synthetic Bioactive Products, Brazil. [2]UFPB, PPG in Natural and Synthetic Bioactive Products, Brazil. [3]UFPB, PPG in Chemistry, Brazil.

Introduction: Cervical cancer is one of the most common malignancies among woman and is strongly associated with persistent human papillomavirus (HPV) infection. Despite advances in vaccination, it remains a major public health concern, especially in developing countries. Limitations of conventional therapies, including tumor resistance and adverse effects, highlight the need for new therapeutic approaches. In this context, selenium compounds have attracted attention due to their selective cytotoxicity and ability to modulate pathways involved in tumor progression. Among them, N-(4-chlorophenyl)benzoselene-ethylenelactamide (NC36) has emerged as a promising compound with previously reported antiparasitic and antibacterial activities. **Objectives:** To evaluate the cytotoxic effects of the selenium compound NC36 in the HeLa human cervical cancer cell line and investigate the roles of oxidative stress and mitogen-activated protein kinases (MAPKs) in its mechanism of action, as well as its cytotoxicity in the HEK-293 human embryonic kidney cell line. **Methods:** The cytotoxicity of NC36 was evaluated using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, and the half-maximal inhibitory concentration (IC50) and selectivity index (SI) were determined. The involvement of reactive oxygen species (ROS) was investigated by pretreatment with N-acetylcysteine (NAC, 5 mM). The roles of ERK, p38, and JNK MAPKs were investigated using selective pharmacological inhibitors. Data were expressed as mean ± standard error of the mean (SEM) and analyzed by one-way analysis of variance (ANOVA), followed by Tukey's post hoc test. **Results:** NC36 showed potente cytotoxic activity in HeLa cells, with an IC50 value of 5.98 ± 0.41 µM, whereas in HEK-293 cells the IC50 value was 82.14 ± 2.46 µM, resulting in a SI of 13.73. Pretreatment with NAC increased cell viability after NC36 exposure, from 45.33% to 98.65% at 5 µM and from 45.06% to 75.21% at 10 µM. However, this effect was compatible with the isolated action of the antioxidant, indicating that the cytotoxic effects of NC36 were not significantly affected by ROS reduction. Regarding MAPKs, ERK and p38 inhibitors did not promote significant changes in NC36 induced cytotoxicity. In contrast, JNK inhibition potentiated the cytotoxic effect of the compound, reducing HeLa cell viability from 50.66 ± 4.41% to 36.86 ± 3.28%. **Conclusion:** NC36 showed selective cytotoxic activity against human cervical cancer cells. The results suggest that oxidative stress is not involved in the cytotoxic mechanism induced by NC36, whereas JNK inhibition potentiated its effects. Further investigations into the interaction between NC36 and the JNK pathway are necessary. These findings reinforce the antitumor potential of NC36. **Financial support:** CNPq, CAPES and FAPESQ-PB.

10.029 Evaluation of the Genotoxic and Tumorigenic Potential of Chromomycin A3 in *Drosophila Melanogaster*. Reis MA, Ribeiro RMS, Araújo DD, Bahia GFM, Castro AJS, Marinho Filho JDB, Araújo AJ LCCDelta-UFDPar, Lab Cultura de Células, Brazil.

Chromomycin A3 (CMA3) is an antitumor antibiotic produced by Streptomyces griseus with high affinity for GC-rich regions of DNA, inhibiting gene transcription and replication. Despite its recognized antineoplastic potential, its clinical use has been limited due to high systemic toxicity, while information on its genotoxic and carcinogenic effects *in vivo* remains scarce. This study investigated the cytotoxic, genotoxic, mutagenic, and tumorigenic potential of CMA3 in *Drosophila melanogaster*. Cytotoxicity was assessed by larval survival assay in third-instar larvae exposed to CMA3 at concentrations of 0.625 and 6.25 µg/mL. Genotoxicity was assessed by the Somatic Mutation and Recombination Test (SMART), developed by Graf et al. (1984), using standard crosses (ST: flr^3 females × mwh males) and high metabolic bioactivation crosses (HB: ORR; flr^3 females × mwh males). Larvae were exposed to CMA3 (0.625 and 6.25 µg/mL) for 48 hours, with doxorubicin (0.125 mg/mL) as a positive control and DMSO as a negative control. 120 wings per group were analyzed under an optical microscope (40×), classifying the spots as small single, large single, and twin. Tumorigenic potential was evaluated by the Epithelial Tumor Clone Detection Test (ETT/wts), through crosses between wts/TM3,Sb^1 females and mwh/mwh males, with analysis of 200 individuals per group under a stereomicroscope. Statistical diagnoses were determined by the multiple decision procedure (Frei & Würgler, 1988) and confirmed by the Mann-Whitney/Wilcoxon U test. In the survival assay, the 0.625 µg/mL dose preserved larval viability analogous to the negative control, while 6.25 µg/mL promoted a marked dose-dependent reduction, an effect attenuated in the HB cross by the higher cytochrome P450 activity. In the SMART assay, isolated CMA3 showed predominantly negative diagnoses for mutagenicity. In the antimutagenic analysis, the CMA3 + DOX combination reduced the frequency of spots in both crosses, with inhibition percentages of 36.7% and 29.31% in ST and 34.5% and 10% in HB, for concentrations of 0.625 and 6.25 µg/mL, respectively. In the ETT assay, CMA3 did not induce significant tumor clone formation at any of the tested concentrations, with a dose-dependent reduction trend observed in tumor frequency at the highest concentration evaluated. Taken together, the results indicate that CMA3 did not exhibit mutagenic or carcinogenic potential under the experimental conditions employed. However, the increased genetic damage in association with doxorubicin suggests caution in contexts of combined exposure. Additionally, the reduction in tumor frequency observed in the ETT is consistent with the previously described antiproliferative profile for the molecule, reinforcing the importance of *in vivo* models in the toxicological evaluation of complex bioactive compounds.

10.030 **Harpalicinone Induces Programmed Cell Death by Mitochondrial Depolarization In HCT-116 Cells**. Ribeiro, RMS[1], Machado, FS[1], Pereira, FIA[1], Oliveira, MP[1], de Sá, RE[1], Araujo, RM[2], Silva, SANM[1], Marinho-Filho, JDB[1], Araújo, AJ[1]. [1]UFDPar, Lab Cultura de Células do Delta, Brazil, [2]UFRN, Instituto de Química, Brazil.

Introduction: Cancer is one of the leading causes of death worldwide. Many natural bioactive molecules have demonstrated therapeutic potential against this disease. Flavonoids are natural compounds with several biological activities, including antitumor effects. **Objetive: **To evaluate the cytotoxicity of Harpalicinone (HBF), a flavanone isolated from Harpalyce brasiliana Benth. **Methods:** The cytotoxicity of HBF was evaluated by the MTT assay in colorectal (HCT-116), pancreatic (PANC-1), breast (MDA-MB-231), lung (NCI-H460), and leukemia (HL-60 and K562and non-tumoral (HaCaT) cell lines. As HCT-116 was the most sensitive cell line, continuous and intermittent exposure protocols with HBF were subsequently performed. Plasma membrane integrity and morphological alterations were evaluated by trypan blue exclusion, panoptic staining, immunofluorescence, and flow cytometry using propidium iodide and rhodamine 123. **Results:** HBF was cytotoxic to NCI-H460 (IC_{50} = 22,0 µg/mL), PANC-1 (14,6 µg/mL) and was more potent against HCT-116 cells (IC_{50} = 9.4 µg/mL at 72 h), while MDA-MB-231, HL-60, K562, and HaCaT cells exhibited IC_{50} values >25 µg/mL. In HCT-116 cells, the IC50 decreased from 16.5 µg/mL at 24 h to 13.6 µg/mL at 48 h. In the intermittent exposure assay, the IC_{50} remained above 25 µg/mL after 24 h but decreased to 10.7 µg/mL after 48 h, indicating a progressive time-dependent cytotoxic effect. The trypan blue assay showed a concentration-dependent reduction in viable cells without a proportional increase in non-viable cells. Morphological analyses revealed cell death-related alterations, including reduced cell density, cell rounding, bleb formation, multinucleation, and nuclear condensation, especially at 19 µg/mL, similarly to doxorubicin-treated cells. Immunofluorescence at 9.5 µg/mL confirmed morphological disorganization, reduced cell density, and the presence of apoptotic bodies. Flow cytometry analysis revealed that HBF did not induce plasma membrane damage but caused an increase in the SubG0/G1 population and mitochondrial depolarization, with increases of up to 3.6-fold compared to the negative control, particularly at the highest concentration. **Conclusion:** HBF exhibited greater cytotoxicity against HCT-116 cells by inducing mitochondrial damage, DNA fragmentation, and programmed cell death, thereby reducing mitotic progression. These findings suggest that HBF is a promising candidate for colorectal carcinoma therapy; however, further studies are required to elucidate its mechanisms of action and evaluate its *in vivo* efficacy and safety. **Financial support:** CAPES; CNPQ; INCT BioNat; INCT Polysaccharides, INCT Nature.

10.031 **Evaluation of the Compound LOE2208 as a potential epigenetic modulator in the Treatment of Acute Myeloid Leukemia** (**AML**). Mota JA[1,2], Sales SLA[1,2], Manso MP[3], Bastos RS[1,2], Gress LSB[1,2], Desiderio GA[1,2], Oliveria KAF[1], Macêdo SMN [1], Vieira-Neto JB[1,2], Scandolara TB[1], Maranhão SS[1,2], Pessoa CÓ[1,2], Furtado CLM[4]. [1]UFC, Lab. of Experimental Oncology, Drug Discovery and Development Center, Brazil; [2]UFC, PPG in Pharmacology. [3]INCa, Research Center, Brazil. [4]UFMG, Dept Genetics, Ecology and Evolution, Institute of Biological Sciences, Brazil.

Introduction: Acute myeloid leukemia (AML) is a heterogeneous hematological neoplasm characterized by genetic and epigenetic alterations associated with disease progression and therapeutic resistance. Despite recent advances, current treatments remain limited by relapse, toxicity and resistance. Epigenetic drugs (epidrugs) have emerged as promising therapeutic strategies, particularly in hematological cancers. Isoflavonoid compounds have gained attention due to their ability to modulate epigenetic mechanisms with selective cytotoxicity. **Objective:** This study aimed to evaluate the cytotoxic activity of LOE2208 and investigate its potential as an epigenetic modulator in AML cells. **Methods:** Cytotoxicity was assessed by MTT assay in KG-1 cells after 24h and 72h, using doxorubicin as a positive control. Human peripheral blood mononuclear cells (PBMCs) (protocol: 4.505.89) were used to determine selectivity. Cell cycle distribution and membrane integrity were analyzed by flow cytometry after 24h and 48h of treatment. Gene expression of G2/M-related genes and DNA methyltransferases (DNMTs) was evaluated by RT-qPCR after 24h and 6h of treatment, respectively. **Results:** LOE2208 exhibited antiproliferative activity in KG-1 cells, with IC50 of 1.5 μM (24h) and 1.0 μM (72h), showing greater cytotoxicity than doxorubicin at 24h (IC50 = 1.8 μM). No significant cytotoxicity was observed in PBMCs, suggesting selectivity. Treatment induced loss of membrane integrity at concentrations ≥3μM (24h) and ≥2μM (48h). A significant accumulation of cells in G2/M phase was observed at both time points ($p<0.0001$). Gene expression analysis showed downregulation of AURKB after 24h at a concentration of 1.5 μM ($p<0.02$) and in DNMT2 expression ($p<0.05$) after 6 hours from a concentration of 1.5 μM. LOE2208 also reduced DNMT1 expression compared to azacitidine ($p<0.05$), although without significant difference relative to untreated control. LOE2208 demonstrates selective antiproliferative activity in AML cells, associated with G2/M cell cycle arrest and modulation of epigenetic regulators. **Conclusion:** These findings support LOE2208 as a potential candidate epidrug, warranting further investigation into its molecular mechanisms and therapeutic applicability. **Financial support:** This research was funded by the following organizations CNPq, CAPES, PRONON (NUP 25000.019172/2021-11), MINISTÉRIO DA SAÚDE, INCTBio2, FINEP and FUNCAP. Keywords: Acute myeloid leukemia; epigenetics; DNMT; cell cycle; isoflavonoids

10.032 **AMTAC-17 Promotes Apoptosis and Modulates Oxidative Status in HCT-116 Colorectal Cancer Cells**. Queiroga LM[1]; Silva DKF[1]; Duarte SS[1]; Dantas MM[1]; Lisboa TMH[1]; Januário VCS[2]; Santana JP[2]; Farias APGM[1]; Ramalho IGS[1]; Ferreira RC[1]; Lyra GB[1], Pinheiro-Segundo MAS[3], Moura RO[4], Gonçalves JCR[1]; Sobral MV[1] [1]UFPB, Health Sciences Center, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]Health Sciences Center, ONCOFAR, Undergraduate in pharmacy, Brazil. [3]UFPE, PPG in Pharmaceutical Sciences, Brazil. [4]UEPB, Dept Pharmacy, Drug Development and Synthesis Lab, Brazil

Introduction: Cancer remains a major global public health challenge, demanding more effective and less toxic therapeutic strategies. In this context, spiro-acridine compounds have emerged as promising antitumor agents due to their ability to interact with DNA and inhibit enzymes involved in cell proliferation, such as topoisomerases. Among the spiro-acridine derivatives, the (E)-5'-oxo-1'-((3,4,5-trimethoxy-benzylidene)amino)-1',5'-dihydro-10H-spiro[acridine-9,2'-pyrrole]-4'-carbonitrile (AMTAC-17) has previously demonstrated cytotoxic activity in different tumor cell lines, particularly against HCT-116 colorectal carcinoma cells, in addition to antitumor effects in an Ehrlich carcinoma model. **Objective:** This study aimed to investigate the mechanisms involved in the cytotoxic effects of AMTAC-17 in HCT-116 cells, focusing on apoptosis induction and oxidative stress modulation. **Methods:** HCT-116 cells were treated with AMTAC-17 at concentrations corresponding to the half maximal inhibitory concentration (IC_{50}) and its double (30 and 60 µM, respectively) for 48 h. Phosphatidylserine externalization was assessed by Annexin V/PI double staining by flow cytometry. Cell morphology and death profile were evaluated by acridine orange/propidium iodide (AO/PI) staining using confocal microscopy, based on membrane integrity and chromatin condensation patterns. Reactive oxygen species (ROS) production was quantified by flow cytometry using the DCFH-DA fluorescent probe. Data are presented as mean ± SEM and analyzed by one-way ANOVA followed by Tukey's test. **Results:** After 48 h of treatment, AMTAC-17 significantly increased phosphatidylserine externalization, as evidenced by higher percentages of Annexin V-positive cells (30 µM: 13.49 ± 0.61%; 60 µM: 14.65 ± 0.68%) and Annexin V/PI-double-positive cells (30 µM: 38.27 ± 0.71%; 60 µM: 40.76 ± 1.65%) compared with controls ($p < 0.05$ for all). Confocal microscopy following acridine orange/propidium iodide (AO/PI) staining revealed morphological features suggestive of apoptosis after AMTAC-17 treatment, including membrane blebbing, chromatin condensation, nuclear fragmentation, and the presence of double-stained cells. Furthermore, AMTAC-17 significantly reduced reactive oxygen species (ROS) levels at both concentrations, as indicated by lower mean fluorescence intensity (MFI) values at 30 µM (7.84 ± 0.08) and 60 µM (8.12 ± 0.14) compared with the control group ($p<0.05$ for both). **Conclusion:** AMTAC-17 induced cellular alterations associated with apoptotic cell death in HCT-116 cells, as suggested by phosphatidylserine externalization and apoptotic morphological features. In addition, the compound significantly reduced ROS levels, indicating modulation of oxidative status. Together with previous evidence of cytotoxic and *in vivo* antitumor activity, these findings reinforce the therapeutic potential of this spiro-acridine derivative and support further non-clinical investigations in colorectal cancer models.

10.033 **Cytotoxicity of an Indium-Based Coordination Complex in Colorectal Cancer Cell Lines: Evidence of Oxidative Stress Involvement**. Silva ICF[1], Lyra GB[1], Souza RRM[1], Dantas MM[1], Rodrigues JS[2], Amorim GMW[1], Silvestre GFG[1], Ferreira RC[1], Santana JP[2], Gomes KNC[2], Carvalho LR[3], Faria WMA[3], Tavares EC[3], Goncalves JCR[1], Sobral MV[1]. [1]UFPB, Health Sciences Center, ONCOFAR, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]UFPB, Health Sciences Center, ONCOFAR, Undergraduate in pharmacy, Brazil. [3]Unifei, Institute of Physics and Chemistry, LaCSin, Brazil.

Introduction: Colorectal cancer (CRC) remains a major global health challenge, and current chemotherapeutic approaches are still limited by systemic toxicity, low selectivity, and tumor resistance. In this context, organometallic compounds have emerged as promising therapeutic alternatives due to their potential antitumor activity. Previous studies have shown that bis(N-4-chlorophenylsulfonyldithiocarbimato)indium(III) tetraphenylphosphonium (InEP), an indium-based organometallic complex, exhibits cytotoxic activity in HCT-116, SK-MEL-28, and MCF-7 cells, particularly against HCT-116 colorectal carcinoma cells, supporting further investigations in colorectal cancer cell lines to better elucidate its effects. **Objectives:** To evaluate the cytotoxic activity of InEP in human colorectal cancer cell lines, investigate its selectivity profile, and assess the involvement of reactive oxygen species (ROS) in its mechanism of action. **Methods:** Cytotoxic activity was evaluated in the colorectal cancer cell lines HCT-116, HT-29, and LoVo, as well as in non-tumoral HaCaT keratinocytes, using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay after 72 hours of treatment, and half maximal inhibitory concentrations (IC_{50}) values were determined. To investigate the involvement of oxidative stress in InEP-induced cytotoxicity, HT-29 cells were pretreated with N-acetylcysteine (NAC) prior to compound exposure, followed by reassessment of cell viability. Data are presented as mean ± standard error of the mean (SEM). **Results:** InEP exhibited marked cytotoxic activity in colorectal cancer cell lines, with greater sensitivity observed in HT-29 cells (IC_{50}: 4.86 ± 0.88 μM), followed by HCT-116 (7.95 ± 0.86 μM) and LoVo cells (84.60 ± 6.3 μM). Lower cytotoxicity was observed in HaCaT keratinocytes (IC_{50}>100 μM). In HT-29 cells, treatment with InEP (5 and 10 μM) for 72 h significantly reduced cell viability (49.02 ± 3.91% and 46.54 ± 2.60%, respectively; $p<0.05$). NAC pretreatment significantly attenuated InEP-induced cytotoxicity, restoring cell viability to 87.77 ± 0.93% and 83.32 ± 2.06% at 5 and 10 μM, respectively ($p<0.05$). **Conclusion:** InEP exhibited cytotoxic activity against colorectal cancer cells, with evidence of selectivity over non-tumoral keratinocytes. Moreover, differences in sensitivity among colorectal cancer cell lines may be associated with the biological particularities of each cellular model, including tumor origin, molecular features such as genetic and epigenetic alterations, and chemoresistance mechanisms. The protective effect of NAC pretreatment suggests the involvement of ROS in the compound-induced cytotoxicity. Collectively, these findings reinforce the therapeutic potential of InEP and support further investigations in colorectal cancer models. **Support**: CNPq and CAPES.

10.034 **Selective Cytotoxicity of Novel Thiazole Derivatives Against PC-3 Prostate Cancer Cells**. Paier CRK[1], Brito TL[4], Pessoa CO[2], Almeida MCM[1], Nepomuceno FWAB[1,3], Queiroz BRA[1], Gomes JPP[2], Desiderio GA[2], Oliveira JF[1,3] [1]UFC Graduate Program in Translational Medicine, , Fortaleza, Ceará, Brazil; [2]UFC, Graduate Program in Pharmaceutical Sciences, Fortaleza, Ceará, Brazil; [3]Unilab, Institute of Health Sciences, Redenção, Ceará, Brazil, [4]NPDM-UFC, Lab of Experimental Oncology, Drug Research and Development Center

Introduction: According to the National Cancer Institute (INCA), approximately 780,000 new cancer cases are estimated to occur annually in Brazil during the 2026–2028 triennium.. Despite therapeutic advances, conventional chemotherapeutic agents still present important limitations, including high toxicity, low tumor selectivity, development of cellular resistance, and elevated costs, which are particularly relevant in the context of the public healthcare system. In this scenario, the search for new compounds with antineoplastic potential is essential. Thiazoles derivatives have attracted attention due to their promising cytotoxic activity across different tumor models, acting through multiple mechanisms such as the activation of the apoptotic caspase cascade, phase-specific cell cycle arrest, and ROS-mediated oxidative stress. **Objectives:** To evaluate the cytotoxic potential of thiazole derivatives (TZ3 - TZ7) against tumor and non-tumor cell lines (human and/or murine). **Methods:** Antiproliferative activity against human tumor and non-tumor cell lines (HCT-116, PC-3, SNB-19, HL-60, NCI-H460, L-929, and MRC-5) was evaluated using the MTT assay after 72 h of incubation with the test-compounds. (0.40 - 50 µM). The cells were cultured in RPMI or DMEN medium, supplemented with 10% fetal bovine serum and 1 % antibiotics, and maintained in an incubator at 37 ºC and an atmosphere containing 5 % CO2. Doxorubicin (Dox) was used as a positive control and the negative control received the same amount of DMSO. Absorbances were obtained using a plate spectrophotometer at 595 nm. The absorbances obtained were used to calculate the IC50 (concentration capable of reducing cell viability to 50%) of the samples by non-linear regression using the GraphPad Prism version 8.0 program. Each sample was tested in triplicate from three independent experiments (n=3/experiment). **Results:** Among the synthesized molecules, TZ-3, TZ-5, TZ-7, and TZ-8 emerged as the most promising derivatives, exhibiting IC50 values below 10 µM in at least one tumor cell line. TZ-5 demonstrated the most expressive activity against PC-3 prostate cancer cells, with an IC50 value of 4.70 ± 0.90 µM, while remaining inactive against non-tumoral MRC-5 and L-929 cells (IC50 > 50 µM). Similarly, TZ-8 displayed selective activity toward PC-3 cells, with an IC50 value of 9.99 ± 3.30 µM and absence of detectable toxicity against the non-tumoral models.. **Conclusion:** Among the tested compounds, TZ3, TZ5, TZ7, and TZ8 stood out by presenting IC50 values below 10 µM in at least one human tumor cell line. In addition, TZ5 and TZ8 exhibited a strong and selective cytotoxic effect against PC-3 cells, supporting further studies involving an expanded panel of prostate cancer cell lines, followed by investigations of cell death patterns and mechanisms of action.

10.035 **VLA-4 Integrin and VEGFR Blockade Regulates B16F10 Melanoma Adhesion, Migration and Proliferation**.
Cavalcante KDM[1], Cavalcante MLS[1], Paixão MS[2], Lima KFN[1], Monte SJH[3], Pereira EM[3], Guimarães PPG[4], Sousa JMC[5], Ferreira PMP[1,6,7], Dittz D[1,5] [1]UFPI, Graduate Program in Pharmacology, Brazil; [2]UFPI, School of Pharmacy, Brazil; [3]UFPI, Immunogenetics and Molecular Biology Lab (LIB), Brazil; [4]UFMG, Dept Biophysics and Physiology, Brazil; [5]UFPI, Dept Biochemistry and Pharmacology, Brazil; [6]UFPI, Experimental Cancerology Lab (LabCancer), Brazil; [7]UFC, Experimental Oncology Lab (LOE), Drug Development Research Center (NPDM), Brazil.

Introduction: Integrins and VEGF receptors cooperatively regulate tumor progression, yet the contribution of α4β1 integrin (VLA-4) to VEGFR-driven phenotypes remains poorly understood. Given the involvement of both pathways in cell survival, migration and metastatic dissemination, this work aimed to investigate whether VLA-4 modulates the cellular response to VEGFR inhibition in murine metastatic melanoma cells. **Methods:** B16F10 melanoma cells were transfected with lipid-polymer hybrid nanoparticles carrying anti-VLA-4 siRNA (100 nM, 48 h). Control and VLA-4-kd cells were subsequently treated with sorafenib (SOR - 3 µg/mL, 24 h) and evaluated for viability, adhesion to L929 and SVEC4-10 cells, L929-derived ECM, migration, invasion, clonogenicity and AKT/ERK1/2 signaling. **Results:** VLA-4 silencing (~50%) potentialized SOR IC50 (7.02 ± 0.90 µg/mL for B16F10 vs 4.79 ± 0.25 µg/mL for B16F10-VLA-4-kd; $p<0.05$). Basal adhesion to L929 fibroblasts was strongly dependent on VLA-4, decreasing 51.6% after silencing. Under VEGFR inhibition, B16F10 adhesion to L929 decreased 40.1% and by 76.5% in VLA-4-kd cells ($p<0.05$), indicating cooperative regulation of tumor–fibroblast interactions. In contrast, VEGFR blockade reduced adhesion to fibroblast-derived ECM in both cell lines ($p<0.05$), although the effect was markedly attenuated following VLA-4 silencing, with reductions of 37.9% and 15.1% in B16F10 and VLA-4-kd cells, respectively. Furthermore, VEGFR inhibition, but not VLA-4 silencing, reduced adhesion and transendothelial migration to SVEC4-10 cells in both B16F10 and VLA-4-kd cells ($p<0.05$), indicating that the response to VEGFR blockade is independent of VLA-4. VLA-4 silencing increased by 59% the time for 50% closure of scratch-wound and reduced by 17.5% transwell invasion of B16F10 cells ($p<0.05$). SOR reduced migration and invasion of B16F10 but not of B16F10-VLA-4-kd cells ($p<0.05$), showing the involvement of VLA-4 in these effects of VEGFR inhibitor. In the clonogenic assay, colony area decreased by 63.3% in VLA-4-kd cells and SOR further reduced near 37% colony area in both B16F10 and B16F10-VLA-4-kd cells. Mechanistically, SOR markedly suppressed AKT activation in B16F10, whereas this response was attenuated after VLA-4 silencing, while ERK1/2 remained unaffected. **Conclusion:** VLA-4 acts as a context-dependent regulator of VEGFR signaling in melanoma. While VLA-4 silencing sensitizes melanoma cells to VEGFR inhibition and potentiates the suppression of tumor–fibroblast interactions and clonogenic growth, it simultaneously attenuates VEGFR-dependent control of adhesion, migration, invasion and AKT phosphorylation. These findings highlight the role of VLA-4 integrin in VEGFR-mediated cellular events in melanoma cells. **Support**: CAPES and CNPq.

10.036 **Antiproliferative and Acute Toxicological Effects of Antidepressanhts Drugs with Repurposing Potential against Cancers**. Fernandes GS[1], Rocha KF[2,3], Souza RP[1,2], Sousa RWR[1], Freitas MM[1], Almeida ML[1], Esteves JC[1], Barbosa SLM[1], Oliveira AP[2], Oliveira ECA[3], Dittiz D[4]; Ferreira PMP[1,51]UFPI, Lab Experimental Cancerology (LabCancer), Dept Biophysics and Physiology; [2]UFPI, Lab Cardiovascular Pharmacology (Lafac), PPG in Pharmacology; [3]Toxicological Genetics Lab (Labgetox), Dept Biochemistry and Pharmacology; [4]UFPI, Lab Antineoplastic Pharmacology (Lafan), Dept Biochemistry and Pharmacology; [5]UFC, Lab Experimental Oncology (Loe), Dept Physiology and Pharmacology, Brazil

Introduction: Drug repurposing has emerged as a promising strategy for cancer therapy by reducing the time, costs, and toxicological risks associated with the development of new anticancer agents. In addition to their established clinical safety profiles, several non-oncological drugs have demonstrated the ability to modulate signaling pathways involved in tumor cell proliferation, survival, and apoptosis. Among them, antidepressants have attracted increasing attention due to their antiproliferative effects in different tumor models. **Objective:** To investigate the *in vitro* antiproliferative and acute toxic effects of clinically used antidepressant drugs. **Methods:** Acute toxicity was first assessed using the Artemia salina bioassay, in which 48-h-hatched larvae (n = 10/concentration) were exposed to concentrations ranging from 1 to 1000 µg/mL for 24 h. For the *in vitro* cytotoxicity assays, tumor (MDA-MB-231, breast; HCT-116, colon; PC-3, prostate; HL-60, leukemia; NCI-H460, lung; SNB-19 and U-87, glioblastoma) and non-tumor (HaCaT, keratinocyte) cell lines were initially exposed to a single concentration (25 µg/mL) of all compounds. Based on the screening results, the most active drugs, amitriptyline (AMI) and fluoxetine (FLU), were further evaluated over a concentration range of 0.19–25 µg/mL using the MTT assay. Subsequently, U-87 cells treated with AMI and FLU were subjected to morphological analysis by light microscopy. **Results:** With the exception of desvenlafaxine, all drugs were classified as highly toxic (LC_{50} < 100 µg/mL) to A. salina larvae. AMI and FLU exhibited LC_{50} values of 5.9 (4.4–8.0) and 9.3 (5.1–17.1) µg/mL, respectively. Both compounds showed low selectivity toward tumor cells. U-87 cells were more sensitive to FLU than to AMI, with IC_{50} values of 11.3 (5.3–25.7) and 13.1 (6.6–28.2) µg/mL (47.1 and 36.5 µM, respectively). Morphological analysis revealed reduced cell density, cytoplasmic vacuolization (more pronounced with FLU), retraction of cellular extensions, nuclear condensation (pyknosis), cytoplasmic shrinkage, and apoptotic bodies. **Conclusion:** Antidepressants exhibited high acute toxicity toward A. salina nauplii, whereas AMI and FLU demonstrated promising cytotoxic activity against tumor cell lines, particularly glioblastoma cells. The morphological alterations observed in U-87 cells are consistent with apoptosis, supporting the potential of tricyclic antidepressants and selective serotonin reuptake inhibitors as candidates for glioblastoma drug repurposing. Further preclinical and clinical studies are required to confirm their safety and therapeutic efficacy. **Financial support:** CAPES and CNPq.

10.037 **Copper(II) Coordination of Schiff Base Ligands Modulates Anticancer Activity in Melophen-Type Complexes**. Silva KKF[1,2], Andrade ASA[2], Araújo DAM[2], Cavalcanti ETDN[3], Lemos SG[3], De Souza-Ferrari J[2,3], Dantas BB[1,2,4] [1]UFCG, Curimataú Cancer Observatory (OCC), Brazil. [2]UFPB, PPG in Biotechnology – Northeast Biotechnology Network (Renorbio), Brazil. [3]UFPB, Dept Chemistry, Brazil. [4]UFCG, PPG in Natural Sciences and Biotechnology, Brazil

Introduction: Platinum(II) metallodrugs have limited use due to tumor resistance and systemic toxicity. Essential metals such as copper have emerged as candidates for low-toxicity metallodrugs, with their biological relevance and distribution in the human body. However, compounds simultaneously targeting tumor microenvironment features, including cell proliferation and angiogenesis, remain underexplored. **Objectives:** To evaluate the anticancer potential of four novel copper(II) complexes (CuAc–Sb1–4), melophen-type Schiff base analogs, their ligands (Sb1–4), and metal precursor (CuAc). **Methods:** Toxicity was assessed at 25–200 μM using (i) Artemia salina nauplii assay and (ii) hemolysis assay in human erythrocytes, approved by the Research Ethics Committee (CAAE: 50349221.3.0000.0154). Anticancer activity was determined by (i) evaluating antiproliferative effect in MDA-MB-231 (human triple-negative breast cancer) and U-373 MG (human glioblastoma) cells, using the MTT assay (25–100 μM), and (ii) investigating antiangiogenic effect using the chorioallantoic membrane (CAM) assay of *Gallus gallus domesticus* embryos (10 μM). Data were expressed as mean ± SEM, and statistical comparisons were performed using one- or two-way ANOVA followed by Tukey's post hoc test, with $p<0.05$ indicating significance. **Results:** CuAc reduced Artemia salina nauplii viability at 200 μM compared with 0.9% NaCl ($p<0.05$), with LC_{50} of 172.4 ± 1.07 μM, whereas the ligands maintained high viability ($p>0.05$) with LC_{50} >200 μM. Copper(II) complexes reduced nauplii viability ($p<0.05$), although most exhibited LC_{50} >100 μM, except CuAc–Sb2, with LC_{50} of 34.86 ± 1.39 μM. Consistently, CuAc and CuAc–Sb2 induced high hemolysis at 200 μM, with 10.17 ± 2.7% and 14.29 ± 1.7% ($p<0.05$), respectively, while the remaining compounds showed low hemolytic activity, comparable to 0.9% NaCl, with 1.3 ± 0.1% ($p>0.05$). Antiproliferative effect varied among compounds, with CuAc showing IC_{50} >100 μM, whereas among the ligands only Sb3 and Sb4 were active, with IC_{50} 63.33 ± 1.42 μM and 21.55 ± 1.35 μM against glioblastoma, respectively. Copper(II) complexes showed greater antiproliferative potential, notably CuAc–Sb1, CuAc–Sb3, and CuAc–Sb4, with IC_{50} 13.43 ± 1.81 μM, 19.05 ± 1.17 μM, and 11.64 ± 1.03 μM for glioblastoma, and 59.74 ± 1.18 μM, 26.82 ± 1.28 μM, and 21.06 ± 1.04 μM for triple-negative breast cancer, respectively, while CuAc–Sb2 showed activity restricted to glioblastoma, with IC_{50} 52.43 ± 1.08 μM. Regarding the antiangiogenic effect, ligands reduced vessel size after 6h, with a reduction in the number of junctions after 24h for Sb1, Sb3, and Sb4 compared to 0h ($p<0.05$), whereas CuAc and copper(II) complexes reduced all analyzed vessel parameters at 6h, with more pronounced effects at 24h ($p<0.05$). **Conclusion:** Coordination of Schiff base ligands with CuAc enhances anticancer activity in melophen-type complexes, yielding bioactive species at subtoxic concentrations. **Financial support**: CAPES, FAPESQ, CNPq.

10.038 **Decyl Butyrate-Loaded Cubosomes: A Nose-to-Brain Approach Against Glioblastoma in a Preclinical Model**. Pimentel RS[1,7], Souza LCS[1,7], Ribeiro IRS[2], Silva FFF[3], Santos ARC[4,7], Eberhardt MJ[5], Spingolon G[5], Castro NET[5], Silveira ER[6], Santos DYAC[6], Rocha HVA[3], Martins MA[1,7], Frozza RL[4,7], Poletto F[5], Bernardi A[1,7]. [1]Fiocruz, Lab. of Inflammation, Brazil. [2]CNPEM, Brazilian Synchrotron Light Lab., Brazil. [3]Fiocruz, Lab. of Micro and Nanotechnology, Brazil. [4]Fiocruz, Lab. on Thymus Research, Brazil. [5]UFRGS, PPG Química, Brazil. [6]USP, Lab. of Phytochemistry, Brazil. [7]Fiocruz, PPG Biologia Celular e Molecular, Brazil.

Introduction: Glioblastomas (GBMs) are the most aggressive primary brain tumors, with poor prognosis and high recurrence rates despite available therapies. Drug delivery to the central nervous system remains challenging due to the blood–brain barrier. Cubosomes (Cub), lipid-based nanoparticles with high loading capacity, mucoadhesive properties, and structural stability, have emerged as promising platforms for intranasal nose-to-brain delivery. **Objectives:** To develop and characterize decyl butyrate-loaded Cub as a potential non-invasive strategy for GBM treatment. **Methods:** Cub formulations were prepared using phytantriol and Pluronic® F-127 with decyl butyrate, 1-decanol, or without additives. Physicochemical and structural characterization was performed by dynamic light scattering (DLS), small-angle X-ray scattering (SAXS), cryogenic transmission electron microscopy (Cryo-TEM), and gas chromatography–mass spectrometry (GC-MS). Nose-to-brain delivery was evaluated in healthy C57BL/6 mice using fluorescent Rhodamine B-labeled Cub. Cytotoxicity was assessed in C6, GL261, and U138-MG glioma cell lines (MTT assay), while toxicity was evaluated in organotypic hippocampal slices from healthy rats using LDH release and TUNEL staining. For *in vivo* toxicity studies, mice were treated for 14 days, followed by histological evaluation of major organs and blood biochemical analyses. For the *in vivo* GBM model, GL261 cells were implanted into C57BL/6 mice followed by treatment with different formulations for 10 days. Tumor progression and histopathological features were evaluated. Data is presented as mean ± SD from independent experiments, with statistical significance set at $p \leq 0.05$. **Results:** Cub showed nanoscale diameters (154–273 nm), low polydispersity (0.1–0.2), near-neutral zeta potentials, and pH values between 4.6 and 6.6. SAXS and Cryo-TEM confirmed a Pn3m cubic phase, while GC-MS demonstrated high incorporation efficiency (≥99%). Intranasal administration of Rhodamine B-labelled Cub produced detectable brain fluorescence, confirming effective nose-to-brain delivery. Decyl butyrate-loaded Cub reduced GBM cell viability in a concentration-dependent manner, with IC_{50} values of 48.0 µM (C6), 102.4 µM (GL261), and 120.2 µM (U138-MG) ($p<0.0001$), whereas blank Cub and free decyl butyrate showed no significant effects. No toxicity was observed in healthy tissues and biochemical analyses. Treatment also reduced histopathological features associated with grade IV GBM malignancy. **Conclusion:** Decyl butyrate-loaded cubosomes present a promising, non-invasive nanocarrier platform for glioblastoma therapy. They combine efficient nose-to-brain delivery and selective anti-glioma activity with a highly favorable safety profile in healthy tissues, effectively reducing tumor malignancy *in vivo*.

10.039 **Investigation of a Low-Anticoagulant Heparin with the Potential to Inhibit Cancer Dissemination by Blocking Tumor Cell–Endothelium Interactions**. Roberto-Fernandes C, Motta JM, Lima AGF, Morandi V, Mourão PAS, Pereira MS. UFRJ, HUCFF, Brazil; UERJ, Lab. of Endothelial Cell Biology and Angiogenesis, Brazil

Introduction: Metastasis is the leading cause of death in cancer patients. During metastatic dissemination, circulating tumor cells should interact with endothelial cells via VCAM-1 to extravasate the vessel. It was shown that porcine heparin (unfractionated, named HPI), a glycosaminoglycan composed by repetitive disaccharides of uronic acid and glucosamine, may interfere both with P-selectin and VCAM-1 binding. Recently, our group purified by ion exchange chromatography a fraction from bovine heparin that displays low anticoagulant potential, named LABH (~15% porcine UFH). The advantage of LABH is its reduced risk of bleeding side effects. Our aim was to investigate the LABH potential as an antimetastatic agent *in vivo* and evaluate *in vitro* its ability to interfere with tumor cell-endothelium interactions. **Methods:** For this, we challenged 8-12 weeks C57Bl/6 mice with 4 mg/kg of porcine UFH or LABH followed by intravenous injection of B16F10 cells (murine melanoma) (CEUA protocol number: 027/22), pretreated or not with VLA4 (integrin α4β1 - a VCAM-1 ligand) mAb. After 21 days, lungs were collected and metastatic foci were counted. *In vitro*, primary endothelial cells (HUVECs, isolated from umbilical cords provided by Carmela Dutra Maternity Hospital) were incubated for 2 hours with MV3 cells (human melanoma, provided by BCRJ) in the presence of the heparins. Additionally, we performed an experiment with immobilized VCAM-1 and added MV3 cells. Finally, MV3 cells were also evaluated in a scratch assay to cell migration and an invasion assay to geltrex (basal lamina) with transwell. **Results:** The number of metastatic foci was strongly reduced when animals were treated with porcine UFH or LABH (~70% inhibition). Similar reduction was observed in mice pretreated with VCAM-1 mAb (~60% inhibition). With regard to the molecular mechanism, both heparins were efficient in blocking MV3-endothelial cell contact, beyond suppressing cell adhesion to VCAM-1. About the final approach, although neither heparin altered the wound closure, LABH reduced the MV3 invasion, whereas HPI increased at the same concentration (100 µg/mL). **Conclusion:** In summary, despite presenting negligible anticoagulant activity, LABH maintained the antimetastatic potential previously described for the porcine standard heparin and demonstrated an interesting multitarget effect to suppress metastasis without bleeding risk.

10.040 **Selective Antiproliferative Activity of** *Ampelozizyphus amazonicus* **Infusion in HeLa Cells**. Chelotti ME[1], Turra BO[2], Bonotto NCA[1], Silva ES[2], Escher ALK[2], Miranda J[2], Cruz IBM[3], Barbisan F[1] [1]UFSM, Biogenomics Lab, PPG in Pharmacology, Brazil; [2]UFSM, Biogenomics Lab, Brazil, [3]Funati, Open University Foundation for the Third Age, Manaus, Brazil.

Introduction: Cervical cancer remains one of the leading causes of cancer- related mortality among women worldwide. Limitations associated with conventional chemotherapy, such as toxicity and tumor resistance, reinforce the need for new therapeutic strategies. In this context, natural products have attracted attention due to the presence of bioactive metabolites with potential antineoplastic activity. *Ampelozizyphus amazonicus* (Saracura-mirá, SM), an Amazonian species traditionally used by Indigenous peoples for the treatment of hormone-related cancers, contains compounds with relevant biological properties. **Objective:** To evaluate the effects of SM bark infusion on healthy HFF-1 cells and HeLa cervical cancer cells, as well as to investigate the adjuvant potential of the association between SM and the reference chemotherapeutic agent Paclitaxel. **Methods:** The infusion was prepared using 1.5575 g of plant bark in 250 mL of water at 80 °C for 15 minutes. Initially, HFF-1 and HeLa cells were exposed to different concentrations of the infusion (0, 1, 10, 50, 100, and 500 µL/mL) for cell cycle analysis. Based on the results, the concentration of 100 µL/mL was selected for combination assays with paclitaxel (10 nM) in HeLa cells. Cell viability assays using the neutral red uptake method and cell growth curve analyses were performed. Data were analyzed by one- or two-way ANOVA followed by Tukey's post hoc test, considering significance at $p < 0.05$. **Results:** In HFF-1 cells, SM infusion maintained cell viability comparable to the control group and preserved the cell population in proliferative phases of the cell cycle. In contrast, HeLa cells showed reduced cell proliferation, particularly at the concentration of 100 µL/mL, indicating an antiproliferative effect. The combination of SM and paclitaxel promoted a significant reduction in cell viability compared with treatment with paclitaxel alone. In the cell growth curve analysis, decreased proliferative rates were observed on days 1 and 3 of exposure. **Conclusion:** The results demonstrate that SM infusion exhibits antiproliferative activity in HeLa cells associated with low cytotoxicity in HFF-1 cells. Furthermore, the combination with paclitaxel enhanced the reduction in cell viability, suggesting a possible adjuvant effect and selectivity toward tumor cells. Additional studies are needed to elucidate the mechanisms involved and confirm its therapeutic potential.

10.041 **The Compartmentalized Expression Profile of T-Box Transcription Factor 15 in Inflammatory Breast Cancer: Differential Profiles and Association with Clinicopathological Features**. Alves BES[1], Barrozo AEO[1], Teixeira-Filho JIF[1], Maia IFVC[1], Batista RER[1], Coimbra RLS[1], Cajado AG[1], Arruda LM[2], Cavalcante DIM[3], Lima V[4], Diaz LAC[5], Alves APNN[5], Lima-Júnior RCP[1], Rogatto SR[6], Wong DVT[1]. [1]UFC, Dpt of Physiology and Pharmacology, Lab Inflammation and Cancer Pharmacology, Drug Research and Development Center, Brazil; [2]Haroldo Juaçaba Hospital, Cancer Institute of Ceara, Brazil; [3]UFC, Dpt of Pathology and Forensic Medicine, Brazil; [4]UFC, Dpt of Physiology and Pharmacology, Osteoimmunopharmacology Lab, Drug Research and Development Center, Brazil; [5]UFC, Dpt of Dental Clinic, Stomatology and Oral Pathology Sector, Faculty of Pharmacy, Dentistry and Nursing, Brazil; [6]Unesp, Botucatu Medical School Hospital, Brazil.

Introduction: Inflammatory Breast Cancer (IBC) is a rare clinical breast cancer presentation with rapid progression, early metastasis, and profound therapeutic resistance. The T-Box Transcription Factor 15 (TBX15) has been studied and associated with different types of cancer, such as colorectal, hepatocellular, and pancreatic carcinoma, stimulating unfavorable prognosis malignant neoplastic cells. Therefore, the role of TBX15 in IBC remains unclear. This study evaluated the differential expression of TBX15 in subjects with IBC versus non-IBC and its association with the clinicopathological parameters. **Methods:** This is a retrospective study. Formalin-fixed paraffin-embedded (FFPE) tumor samples and clinicopathological data (age at diagnosis, BMI, family history, presence of hormone receptors and HER2 status, metastasis, and Ki-67, a proliferation cell marker) were collected from 16 IBC and 16 non-IBC subjects from 2017 to 2022. TBX15 immunochemistry expression was evaluated in the primary tumor, peritumoral tissue, locoregional metastasis, and tumor emboli. The coloration was quantified using FIJI ImageJ software and scored by pathologists. Statistical analysis was performed using the t-test and Two-Way ANOVA. $P<0.05$ was accepted. CEP approval number: 5.010.710. **Results:** TBX15 demonstrated strong cytoplasmic and nuclear positivity in neoplastic cells and normal cells. Moreover, in the primary tumor and at progression stages along the clinical course of IBC disease, including locoregional metastasis, emboli tumor, and peritumoral tissue, the TBX15 expression remains strong, especially in locoregional metastasis, as demonstrated by immunostaining [p=0.0498]. The IBC patients showed comparable patterns of overweight/obesity, TNM stage, distant metastasis, and ER, PR, HER, and Ki-67 expression levels above 20% ($p>0.05$ *vs*. non-IBC). Regarding TBX15 expression in tumor cells, strong cytoplasmic and nuclear immunostaining was higher in IBC patients [p=0.0190; p=0.0411, respectively]. When patients were stratified according to clinicopathological parameters, a trend toward a higher percentage of TBX15 protein expression was observed in positive lymph node involvement samples (298,3±160,3) compared with negative lymph node involvement samples (87.1±0.0) in IBC subjects [p=0.0704]. IBC patients with a family history of cancer had more cytoplasmic TBX15 expression versus non-IBC patients [p=0.0053]. The sample size was limited due to the rarity of the disease. **Conclusions**: In this study, TBX15 showed differential cytoplasmic expression in Inflammatory Breast Cancer. The presence of TBX15 at different stages of IBC progression can indicate a role unknown yet in the poor prognosis associated with this aggressive disease. Furthermore, the TBX15 protein was more frequent in the IBC group than in the non-IBC group. **Financial support**: FUNCAP; Decit/MS/CNPq and CAPES.

10.043 **Toxicogenetic Characterization of the Synthetic Hydroxylated Chalcone CH-A3**. Bahia GFM[1], Castro AJS[1], dos Reis MA[1], Pérez CN[2], Valeze AB[3], Ribeiro RMS[1], Souza JMT[1], Marinho-Filho JDB[1], Araújo AJ[1] [1]UFDPar, Lab Cultura Celular do Delta, Brazil, [2]UFG, Instituto de Química, Brazil, [3]IFMT, campus Cuiabá, Brazil

Introduction: Chalcones are a class of compounds widely investigated due to their diverse pharmacological properties, including anti-inflammatory, antioxidant, and antitumor activities. Interest in these molecules mainly arises from their structural versatility, which allows modulation of their biological activities and therapeutic potential. Previous studies conducted by our research group demonstrated that the synthetic hydroxylated chalcone CH-A3 exhibits selective cytotoxicity against tumor cell lines, particularly oral squamous cell carcinoma cells (SCC-4), while showing reduced effects on non-tumorigenic cells (MCF-10A).**Objectives:** The present study aimed to evaluate the mutagenic, antimutagenic, carcinogenic, and anticarcinogenic effects of CH-A3 using the experimental model of *Drosophila melanogaster* through the Somatic Mutation and Recombination Test (SMART) and the Epithelial Tumor Clone Detection Test (ETT). **Methods:** Mutant strains carrying the genetic markers multiple wing hairs (mwh), flare (flr^3), and warts (wts) were employed. In the SMART assay, standard (ST) and high bioactivation (HB) crosses were performed, the latter characterized by increased cytochrome P450 enzyme expression, simulating mammalian metabolism. Larvae were treated with CH-A3 at concentrations of 8, 20, and 40 µg/mL, either alone or in combination with doxorubicin (DXR). In the ETT assay, crosses carrying the multiple wing hairs (mwh) and warts (wts/TM3, Sb^1) markers were used. **Results:** The results demonstrated that the mutagenicity of CH-A3 is dependent on the metabolic context. The concentration of 8 µg/mL showed a mutagenic effect in the ST cross, but not in the HB cross, suggesting possible cytochrome P450-mediated metabolic detoxification. Furthermore, CH-A3 did not exhibit antimutagenic activity against DXR in the SMART assay, showing a co-mutagenic effect in the ST cross. In the ETT assay, CH-A3 did not induce carcinogenicity and demonstrated significant anticarcinogenic activity by markedly reducing the frequency of DXR-induced tumors, with the highest efficacy observed at 40 µg/mL. **Conclusion:** In conclusion, CH-A3 demonstrated genetic safety in metabolically competent systems and showed promising potential as a chemopreventive agent or therapeutic adjuvant capable of modulating chemotherapy-induced carcinogenesis. **Financial support:** CAPES; CNPQ; INCT BioNat; INCT Polysaccharides and INCT Nature.

10.044 **Cytotoxic and Pro-Apoptotic Effects of *Annona vepretorum* Extract on Human Colorectal Adenocarcinoma Cells**. Abreu-Junior AR[1], Santos PBG[2], Gomes KNC[2], Araújo YKO[2], Pereira ERM[1], Alexandre, HMS[1], Queiroga LM[1], Farias APGM[1,2], Silva ICF[1], Amorim GMW[1], Dutra LM[3], Costa EV[4], Tavares JF[1,2], Sobral MV[1,2], Gonçalves JCR[1,2]. [1]UFPB, PG Program in Bioactive Natural and Synthetic Products, Brazil; [2]UFPB, Dept Pharmaceutical Sciences, Brazil; [3]UFPR, Dept Chemistry, Brazil; [4]UFAM, Dept Chemistry, Brazil.

Introduction: Despite therapeutic advances, chemotherapy for colorectal cancer (CRC), the third most frequently diagnosed malignancy worldwide and in Brazil, still presents limitations due to lack of selectivity, systemic toxicity, adverse effects, and tumor resistance. The search for more selective and less toxic antitumor agents has driven the investigation of bioactive natural substances. In this context, the native species from northeastern Brazil, *Annona vepretorum* Mart. (Annonaceae), has shown *in vitro* cytotoxic activity reported in the literature, although its mechanism of action remains poorly elucidated. **Objectives:** This study aimed to evaluate the cytotoxic potential of the petroleum ether extract from the stem bark of *A. vepretorum* (PEE-Av) in CRC cells and to investigate its mechanism of cell death. **Methods:** Cytotoxicity of the extract (3.12–200 µg/mL) or the standard drug doxorubicin (DXR) (0.078–10 µM) was evaluated by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) cell viability assay in colorectal adenocarcinoma cells (HCT 116) and healthy keratinocytes (HaCaT). The type of cell death (apoptosis/necrosis) was analyzed by acridine orange and propidium iodide staining, evaluated by confocal microscopy. Data were expressed as mean ± SEM and analyzed by one-way ANOVA followed by Tukey's test ($p < 0.05$). IC_{50} values were determined by non-linear regression using the Hill equation, and the selectivity index (SI) was calculated as the ratio between HaCaT and HCT 116 IC_{50} values. **Results:** After 48 h of treatment, PEE-Av significantly reduced ($p < 0.05$) the viability of HCT 116 cells from 6.25 µg/mL onward, and of HaCaT cells from 60 µg/mL onward, yielding IC50 values of 14.66 ± 3.49 µg/mL (HCT 116) and 85.62 ± 2.42 µg/mL (HaCaT). DXR showed a significant effect from 0.31 µM onward in both cell lines, with IC50 values of 4.30 ± 0.99 µM (HCT 116) and 0.64 ± 0.98 µM (HaCaT). The selectivity index (SI) of the extract in HCT 116 cells was 5.84, higher than that of DXR (0.14). Confocal microscopy showed that, after 48 h of incubation with the IC50 concentration (14 µg/mL), half IC50 (7 µg/mL), or DXR (2.5 µM), CRC cells exhibited apoptotic morphological alterations. The number of cells in early apoptosis increased significantly ($p < 0.05$) from 1.95 ± 0.5% in the control group to 72.33 ± 3.45% and 27.39 ± 4.46% at 7 and 14 µg/mL, respectively, whereas late apoptosis increased from 0.00 ± 0.00% (control) to 26.41 ± 3.51% and 71.44 ± 4.49%, respectively. PEE-Av did not significantly increase necrosis, unlike DXR. **Conclusion:** PEE-Av demonstrated selective cytotoxic activity in HCT 116 cells through the induction of apoptotic cell death and low promotion of necrosis. Therefore, *Annona vepretorum* stands out as a potential source of bioactive compounds for the development of new therapies against CRC. **Financial support:** PROPESQ-UFPB, FAPESQ, CAPES, and CNPq.

10.045 **The Thiosemicarbazone Derivative (PR-14) Promoted Alterations in the Cell Cycle and Induced Apoptosis in Lung Cancer Cells**. Carvalho VM[1], Nascimento ACM[1], Costa VCM[1], Silva TD[1], Barbosa FHS[1], Mendonça MJLV[1], Silva JOR[1], Silva BO[1], Souza GA[1], Gomes JPA[1], Soares JR[1], Lima MCA[2], Pitta MGR[1], Rego MBM[1], Pereira MC[1] [1]UFPE, Center for Research in Therapeutic Innovation - Suely Galdino (NUPIT-SG), Graduate Program in Therapeutic Innovation (PPGIT), Brazil. [2]UFPE, Dept Antibiotics, Graduate Program in Therapeutic Innovation (PPGIT), Brazil.

Introduction: Lung cancer is the leading cause of cancer-related death, with its severity attributed to late diagnosis, recurrence, and resistance to available therapies. Although cisplatin is widely used in chemotherapy, its adverse effects drive the search for new therapeutic alternatives. In this context, thiosemicarbazones (TSCs) represent a promising class of molecules, as they exhibit antineoplastic potential by inhibiting tumor proliferation and inducing cell death through the generation of reactive oxygen species (ROS). **Objectives:** To evaluate the *in vitro* antineoplastic activity of the TSC derivative named PR-14 in non-small cell lung carcinoma (NSCLC) cell lines, A549 and H1299. **Methods:** Cytotoxicity was evaluated using the MTT assay. Cell cycle analysis, induction of apoptosis and necrosis, as well as ROS generation, were assessed by flow cytometry using propidium iodide (PI), Annexin V-APC/PI, and dihydroethidium (DHE) staining, respectively. Flow cytometry data were analyzed using FlowJo™ software (v10.8.1). Statistical analysis was performed using GraphPad Prism® (v9.3.0). For normally distributed data, Student's t-test and one-way ANOVA were applied. For non-parametric data, the Kruskal–Wallis test was used. The level of significance adopted was $p < 0.05$. **Results:** PR-14 showed significant cytotoxicity in both cell lines, with an inhibitory concentration (IC50) ± standard deviation of 22 µM ± 4.5 in the A549 cell line and 12.4 µM ± 0.9 in the H1299 cell line. In cell cycle analysis, the derivative significantly increased the percentage of cells in the G2/M phase ($p < 0.05$) in the A549 cell line after 24 and 48 h of treatment, compared to the 0.1% DMSO control. In the H1299 cell line, there was an accumulation of cells in the S phase over the same exposure periods ($p < 0.05$). In addition, the compound induced apoptosis and necrosis in the A549 cell line after 24, 48, and 72 h of treatment ($p < 0.05$). In the H1299 cell line, PR-14 also induced apoptosis at all evaluated time points ($p < 0.01$), while necrosis was detected only after 72 h of exposure ($p < 0.05$). Furthermore, the derivative significantly increased ROS levels in both cell lines after 24, 48, and 72 h of exposure ($p < 0.01$). **Conclusion:** The evaluated compound exhibited cytotoxicity in NSCLC cell lines, associated with cell cycle arrest, induction of apoptosis and necrosis, and increased ROS production. However, further studies are required to elucidate its mechanisms of action to consolidate its potential as a drug candidate for the treatment of NSCLC.

10.046 **A New Indium(III) Sulfonyldithiocarbimate Complex Exhibits *in vitro* Anticancer Activity Against Colorectal Cancer Cells**. Souza RRM[1], Marques KKG[1], Dantas MM[1], Silvestre GFG[1], Rodrigues JS[2], Santos PBG[2], Santana JP[2], Lyra GB[1], Gomes KNC[2], Carvalho LR[3], Faria WMA[3], Tavares EC[3], Gonçalves JCR[1], Ferreira RC[1], Sobral MV[1] [1]UFPB, Health Sciences Center, ONCOFAR, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]UFPB, Health Sciences Center, ONCOFAR, Undergraduate in pharmacy, Brazil. [3]UNIFEI, Institute of Physics and Chemistry, LaCSin, Brazil.

Introduction: Colorectal cancer (CRC) is among the most prevalent and lethal cancers worldwide, while current therapies remain limited by toxicity and chemoresistance. In this context, metal-based compounds, particularly indium(III) complexes, have emerged as promising antitumor candidates. Recently, six novel indium(III) complexes were evaluated for cytotoxicity in tumor cell lines, with HCT-116 colorectal carcinoma cells showing the highest sensitivity. Among them, bis(N-methylsulfonyldithiocarbimato)indium(III) tetraphenylphosphonium (InFP) exhibited the greatest cytotoxic activity, supporting further investigation in CRC cells. **Objectives:** To evaluate the cytotoxic activity of InFP in colorectal cancer cell lines and investigate apoptosis-associated morphological alterations and mitochondrial membrane potential changes involved in its antitumor effects. **Methods:** Cytotoxic activity of InFP was evaluated in the colorectal cancer cell lines HCT-116, HT-29, and LoVo, as well as in non-tumoral embryonic kidney HEK-293 cells, using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay after 72 h of treatment. Apoptosis-associated morphological alterations were investigated by confocal laser fluorescence microscopy using acridine orange/propidium iodide (AO/PI) and Hoechst 34580 staining. JC-1 staining was used to evaluate mitochondrial membrane potential (ΔΨm). Data are expressed as mean ± SEM of three independent experiments and analyzed by one-way ANOVA followed by Tukey's test ($p < 0.05$). **Results:** InFP showed potent cytotoxicity in colorectal cancer cells, with greater sensitivity in HCT-116 (IC50: 2.87 ± 0.14 μM) and HT-29 cells (3.86 ± 0.35 μM), whereas LoVo and non-tumoral HEK-293 cells showed lower sensitivity (49.9 ± 8.0 μM and 107.7 ± 2.1 μM, respectively). Notably, InFP exhibited high selectivity index toward HCT-116 (SI: 37.53) and HT-29 cells (SI: 27.83). Based on cytotoxicity findings, HCT-116 cells were selected for further investigation of cell death mechanisms. AO/PI staining evidenced chromatin condensation and fragmentation, membrane blebs, and apoptotic bodies after 48 h of treatment with InFP. Quantification showed a significant increase in early apoptotic cells at 1.5 μM (71.62 ± 3.76%), whereas 3 and 6 μM significantly increased late apoptosis (76.57 ± 1.15% and 84.29 ± 1.03%, respectively) ($p<0.05$ for all). Hoechst 34580 staining reinforced these findings, increasing fluorescence intensity by 2.22- and 2.73-fold at 1.5 and 3 μM of InFP, respectively ($p<0.05$). Finally, JC-1 staining revealed a marked reduction in the aggregate/monomer fluorescence ratio at 3 μM (0.124), compared with control (1.47). **Conclusion:** InFP exhibited selective cytotoxicity toward colorectal cancer cells. Its cytotoxicity effects were associated with apoptosis induction and mitochondrial membrane depolarization, supporting the involvement of the intrinsic apoptotic pathway.

10.047 **Apoptosis Induction by the Angucycline Saquayamycin B1 in Melanoma Cells: Involvement of Oxidative Stress and MAPK Signaling**. Silvestre GFG[1], Souza RRM[1], Marques KKG[1], Dantas MM[1], Duarte SS[1], Castro IO[1], Ramalho IGS[1], Queiroga LM[2], Araújo YKO[2], Cibulski S[3], Nascimento IJS[4], Moura RO[4], Tavares JF[5], Gonçalves JCR[1], Sobral MV[1]. [1]UFPB, ONCOFAR, PPG of Bioactive Natural and Synthetic Products, Brazil. [2]UFPB, ONCOFAR, Undergraduate in Pharmacy, Brazil. [3]UFRN, FACISA, Faculty of Health Sciences, Brazil. [4]UEPB, LDSF, PPG of Pharmaceutical Sciences, Brazil. [5]UFPB, LMCA, PPG of Bioactive Natural and Synthetic Products, Brazil.

Introduction: Melanoma is a highly aggressive skin cancer characterized by rapid progression, metastatic potential, and resistance to conventional therapies. Streptomyces, a rich source of bioactive metabolites, has yielded several compounds with cytotoxic activity. Saquayamycin B1 (SQ-B1), an angucycline isolated from Streptomyces sp. I072, has recently shown potent activity against resistant melanoma cell lines through disruption of redox homeostasis. However, its effects on apoptosis and the molecular mechanisms underlying its cytotoxicity remain unclear. **Objective:** To investigate the effects of SQ-B1 on apoptosis, intracellular oxidative stress, and of mitogen-activated protein kinase (MAPK) signaling pathways in SK-MEL-28 human melanoma cells. **Methods:** Apoptosis was assessed after 48 h of treatment with SQ-B1 (0.5, 1, and 2 µM) by flow cytometry using Annexin V-FITC/propidium iodide (PI) staining. Reactive oxygen species (ROS) production was measured using 2′,7′-dichlorodihydrofluorescein diacetate (DCFH-DA) in a kinetic analysis (5–90 min). Cell viability in the presence of N-acetylcysteine (NAC, 5 mM) or MAPK inhibitors targeting extracellular signal-regulated kinase (ERK1/2; U0126), c-Jun N-terminal kinase (JNK; SP600125), and p38 mitogen-activated protein kinase (p38 MAPK; PD169316) was determined by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay after 72 h. MAPK modulation was analyzed by flow cytometry after 48 h of treatment, and molecular docking was performed to characterize SQ-B1 interactions with p38 and ERK1/2. Data are presented as mean ± SEM and analyzed by one-way ANOVA followed by Tukey's test ($p < 0.05$). **Results:** SQ-B1 significantly increased early apoptosis after 48 h, reaching 13.18% (0.5 µM), 33.00% (1 µM), and 57.92% (2 µM), compared with 1.12% in control cells ($p < 0.05$). Kinetic analysis demonstrated rapid oxidative stress induction, with ROS levels peaking at 20 min (1 µM: 6.90-fold; 2 µM: 11.29-fold; $p < 0.05$). NAC pretreatment prevented SQ-B1-induced cytotoxicity, maintaining cell viability at levels comparable to controls. Flow cytometry revealed marked MAPK modulation, with significant increases in JNK (1 µM: 1.40%; 2 µM: 7.07% vs. 0.27%), p38 MAPK (1 µM: 32.94%; 2 µM: 98.87% vs. 0.53%), and ERK1/2 labeling (1 µM: 37.17%; 2 µM: 96.76% vs. 0.10%; $p < 0.05$ for all). However, pretreatment with individual MAPK inhibitors did not prevent SQ-B1 cytotoxicity. Molecular docking indicated stronger and more stable binding of SQ-B1 to p38 than to ERK1 or ERK2, with fit scores of 53.74, 44.73, and 32.59, respectively. **Conclusion:** SQ-B1 induced apoptosis in SK-MEL-28 cells through a mechanism dependent on oxidative stress and associated with modulation of p38 MAPK and ERK1/2 signaling, reinforcing its potential as a candidate antitumor agent against melanoma.

10.048 **Extracellular Vesicle-Mediated Modulation of the Melanoma-Macrophage Axis: A New Pharmacological Approach Using Low-Anticoagulant Heparin**. Pacheco-Silva NV[1], Cahu TB[1,2], Thaumaturgo MAS[2], Santos RCM[2], Bagri KM[3], Mermelstein C[3], Rizzo J[4], Castelo-Branco MTL[1], Todeschini AR[2], Pereira MS[1]. [1]UFRJ, HUCCFF, Brazil, [2]UFRJ, Lab Gliocobiologia Estrutural e Funcional, Brazil, [3]UFRJ, Lab Diferenciação Muscular, Instituto de Ciências Biomédicas, Brazil, [4]UFRJ, Lab Físico-Química Biológica Aída Hassón Voloch, Brazil.

Introduction: Heparan sulfate (HS) proteoglycans play an important role in extracellular vesicle (EV) mediated intercellular communication, participating in processes such as vesicular biogenesis, release, and uptake. In the tumor microenvironment, these vesicles contribute to the establishment of a pro-tumor inflammatory state through the transfer of biomolecules between tumor cells and immune cells. Low-anticoagulant bovine heparin (LABH) exhibits structural similarity to HS, making it a molecule of interest for investigating the modulation of EV-mediated cellular communication. **Objective:** To evaluate the effects of LABH on the release, properties, and biological activity of EVs derived from B16F10 cells and RAW 264.7 macrophages, as well as its impact on the communication between tumor and inflammatory cells. **Methodology:** EVs were obtained from B16F10 and RAW 264.7 cell cultures incubated in the presence or absence of LABH. The EVs were characterized by transmission electron microscopy (TEM), flow cytometry, NanoSight (nanoparticle tracking analysis), and protein quantification using the BCA assay. For functional evaluation, RAW 264.7 macrophages were stimulated with LPS and incubated with EVs derived from B16F10 cells cultured in the presence or absence of LABH. Nitric oxide (NO) production was determined using the Griess assay, and cell viability was assessed by MTT assay. Cytokine profile analysis is currently underway. Cell migration assays were also performed. Cytoskeletal reorganization was evaluated by F-actin and DAPI staining. **Results:** Incubation of B16F10 and RAW 264.7 cells with LABH modulted the properties of released EVs, including changes in the vesicular size profile. A reduction in the protein content of B16F10-derived EVs and an increase in RAW 264.7-derived EVs were observed following LABH-associated conditions. In LPS-stimulated RAW 264.7 macrophages, B16F10-derived EVs modulated NO production, showing a trend toward reduction level under LABH. Cell viability assays demonstrated the absence of significant cytotoxicity. Direct exposure to LABH promoted actin cytoskeletal reorganization, with increased cell spreading and formation of cytoplasmic protrusions. Furthermore, EVs derived from LABH-treated cells promoted increased migration of RAW 264.7 cells. **Conclusion:** The results demonstrate that LABH modulates the structural and functional properties of EVs derived from tumor and inflammatory cells, impacting processes associated with intercellular communication in the tumor microenvironment. The observed changes in NO production, cell migration, and cytoskeletal reorganization suggest that LABH interferes with mechanisms related to EV biology without inducing significant cytotoxicity. Due to its structural similarity to HS and its low anticoagulant activity, LABH emerges as a promising molecule for investigating the modulation of EV-mediated tumor related communication.This work received financial support from CNPq and FAPERJ.

10.049 **Systems Biology Identifies a Chaperone-Mediated Network Associated with Doxorubicin Response and Poor Survival in Triple-Negative Breast Cancer**. Silva JYG[1], Azevedo GM[2], Dalmolin RJS[2], Wilke DV[1] [1]UFC, PPG Pharmacology, Brazil [2]UFRN, Bioinformatics Multidisciplinary Environment - BioME, IMD, Natal, Brazil

Introduction: Triple-negative breast cancer (TNBC) is the most aggressive breast cancer subtype, characterized by poor prognosis, high recurrence rates, and elevated mortality. Understanding the molecular determinants of chemotherapy response is critical for improving patient outcomes. Doxorubicin chemotherapy triggers complex transcriptomic responses in breast cancer cells, and chaperones mediate drug sensitivity and resistance. *In vitro* models capture limited human disease complexity, however integrating experimental findings with clinical datasets aids validation of the prognostic value of these stress-response proteins. Objectives To characterize the transcriptional response of triple-negative breast cancer (MDA-MB-231) cells to doxorubicin and evaluate whether candidate chaperone hub genes predict overall survival in patient cohorts. Methods RNA-seq data from 12 MDA-MB-231 mouse xenografts (BioProject PRJNA607780) were analyzed by unifying treated samples ("Doxorubicin") against vehicle ("Control"). The Workflow included host decontamination (STAR), quantification (Kallisto, GRCh38), and gene aggregation (tximport). After filtering (<10 reads), counts were VST-transformed for PCA. Differential expression was modeled in DESeq2 using Negative Binomial GLMs (p-value and padj < 0.01).Functional enrichment analysis for GO Biological Processes and KEGG pathways was performed using Over-Representation Analysis (ORA) via clusterProfiler. A PPI network was built via STRING using the combined score from co-expression, experimental, and curated-database channels (score ≥ 0.7), and upstream transcription factor activity was inferred with DoRothEA/VIPER. Additionally, WGCNA was performed to identify highly connected co-expression hub genes. Hub genes were selected by module membership (kME) and intersected with a curated chaperone list from GeneCards. The six top-ranked chaperone hubs were subsequently evaluated in 1,072 TCGA-BRCA cases using overall survival analysis. Results DESeq2 isolated 1,655 significant DEGs (830 upregulated, 825 downregulated), highlighting RAB11FIP1, CDA, and CPT1C. ORA exposed 198 terms activated in upregulated genes (cytoskeleton, chemotaxis, IL-17/AGE-RAGE) and 4 in downregulated genes. VIPER inferred shifts across 169 TFs, showing activation of JUN, CEBPB, and NFKB1, and repression of SIX5, IRF3, and E2F4. Clinical data investigation showed that high expression of 4 chaperones correlates with worse overall survival: C1GALT1C1 (p=0.00074), FBXO46 (p=0.017), CTSF (p=0.031), and CLGN (p=0.035). SCG5 (p=0.21) and APP (p=0.29) also were highly expressed, however, without correlation with overall survival. **Conclusion:** Our analysis bridges *in vitro* chemo-stress signatures with TNBC clinical data. Elevated expression of C1GALT1C1, FBXO46, CTSF, and CLGN correlates with lower patient survival, suggesting these chaperones confer tolerance to unfolded protein response and stand as prognostic markers and therapeutic targeting candidates.

10.050 **Selective Cytotoxicity of the Selenium Compound NC41 in HeLa Cervical Cancer Cells: Evidence of Intrinsic Apoptosis**. Amorim GMW[1], Lyra GB[1], Loureiro PBA[1], Dantas MM[1], Marques KKG[1], Castro IO[1], Abreu-Junior AR[1], Silva ICF[1], Sousa NF[3], Souza HD[2], Athayde-Filho PF[2], Scotti MT[3], Scotti L[3], Gonçalves JCR[1], Sobral MV[1] [1]UFPB, Lab. of Oncopharmacology, PPG in Natural and Synthetic Bioactive Products, Brazil. [2]UFPB, PPG in Chemistry, Brazil. [3]UFPB, PPG in Natural and Synthetic Bioactive Products, Brazil.

Introduction: Cervical cancer remains a major public health challenge and one of the leading causes of cancer-related mortality among women worldwide. Treatment-associated toxicity and tumor resistance continue to compromise therapeutic outcomes, reinforcing the need for more effective antitumor strategies. Selenium-containing compounds have emerged as promising candidates due to cytotoxic, pro-apoptotic, and redox-modulating properties in tumor cells. N-(4-nitrophenyl)benzoseleno-ethylenolactamide (NC41), a synthetic selenium compound, has shown biological properties such as leishmanicidal and antimicrobial activities; however, its antitumor potential remains poorly explored. **Objectives:** To evaluate the *in vitro* antitumor activity of NC41, determine its cytotoxic and selectivity profiles, and investigate apoptosis- associated cellular alterations in the HeLa human cervical cancer cell line. **Methods:** Cytotoxic activity was evaluated in human tumor cell lines (SK-MEL-28, HeLa, HCT-116, MCF-7, and MDA-MB-231) and non-tumoral HEK-293 cells using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay after 72 h of treatment. Half maximal inhibitory concentration (IC_{50}) values were determined, and the selectivity index (SI) was calculated. Morphological and apoptosis-associated alterations induced by NC41 in HeLa cervical cancer cell line were assessed after 24 h of treatment by confocal microscopy using acridine orange/propidium iodide (AO/PI), Hoechst 34580, and 5,5',6,6'-tetrachloro-1,1',3,3'-tetraethylbenzimidazolylcarbocyanine chloride (JC-1) staining. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test, and data are presented as mean ± SEM. **Results:** NC41 exhibited cytotoxic activity in all tumor cell lines, with greater sensitivity observed in HeLa cells (IC50: 5.03 ± 0.45 µM) and lower cytotoxicity in HEK-293 cells (IC50: 93.00 ± 16.13 µM), resulting in a selectivity index of 18.49. AO/PI staining revealed a significant increase in early apoptotic cells after treatment with 2.5, 5, and 10 µM of NC41 (83.76 ± 4.23%, 81.72 ± 1.21%, and 84.25 ± 2.07%, respectively; $p < 0.0001$). Hoechst 34580 staining demonstrated increased fluorescence intensity at 5 and 10 µM, corresponding to 2.40 ± 0.07-fold and 2.54 ± 0.05-fold relative to the control group, respectively ($p < 0.0001$), along with chromatin condensation and nuclear fragmentation. Additionally, JC-1 staining significantly reduced the aggregate/monomer fluorescence ratio at 5 µM (0.24 ± 0.02) and 10 µM (0.20 ± 0.01) ($p < 0.0001$). **Conclusion:** NC41 exhibited potent and selective cytotoxicity against HeLa cervical cancer cells, inducing apoptosis-associated alterations, including nuclear damage and mitochondrial membrane depolarization, suggesting intrinsic apoptosis. These findings highlight the antitumor potential of NC41 for cervical cancer treatment. **Financial support**: CAPES, CNPQ and FAPESQ.

10.051 **Oviedomycin Triggers Cytotoxicity in Human Colorectal Carcinoma Cells via Oxidative Stress and Mitochondrial Apoptosis**. Dantas MM[1], Alexandre HMS[1], Castro IO[1], Silvestre GFG[1], Souza RRM[1], Marques KKG[1], Lyra GB[1], Abreu-Júnior AR[1], Ramalho, IGS[1], Duarte SS[1], Oliveira GD[2], Tavares JF[2], Cibulski SP[3], Gonçalves JCR[1], Sobral MV[1] [1]UFPB, Health Sciences Center, ONCOFAR, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]UFPB, Multiuser Lab for Characterization and Analysis, PPG in Bioactive Natural and Synthetic Products, Brazil. [3]UFRN, Faculty of Health Sciences of Trairi (FACISA), Brazil

Introduction: The search for new therapeutic agents against colorectal cancer remains essential due to the limitations and resistance associated with conventional treatments. In this contexto, natural products isolated from *Streptomyces* species are promising sources of antineoplastic compounds. Oviedomycin, an angucycline-derived phenolic compound isolated from *Streptomyces* sp. UEPB11A from the Caatinga biome, has been mainly investigated in biosynthetic studies, with limited evidence of cytotoxic activity. **Objective:** To evaluate the cytotoxic activity of Oviedomycin in HCT-116 colorectal carcinoma cells and investigate the involvement of oxidative stress, apoptosis, and mitochondrial membrane alterations in its mechanism of action. **Methods:** Cytotoxic activity was assessed in HCT-116 cells and non-tumoral HaCaT keratinocytes using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay after 72 h of treatment, determining half maximal inhibitory concentration (IC_{50}) values and selectivity index. Antiproliferative activity was evaluated by clonogenic assay after 48 h exposure to Oviedomycin (3.75 and 7.5 µM). Oxidative stress involvement was investigated by pretreating HCT-116 cells with N-acetylcysteine (NAC, 5 mM) before compound exposure, followed by reassessment of cell viability. Apoptosis was analyzed by Annexin V-FITC/propidium iodide (PI) staining and flow cytometry, while mitochondrial membrane potential was assessed by JC-1 staining and confocal microscopy. Data are presented as mean ± SEM and analyzed by ANOVA followed by Tukey's post hoc test ($p<0.05$). **Results:** Oviedomycin showed cytotoxic activity against HCT-116 cells (IC_{50}: 16.05 ± 2.52 µM), whereas lower cytotoxicity was observed in HaCaT cells (IC_{50} >100 µM), resulting in a selectivity index of 6.23. In the clonogenic assay, 7.5 µM significantly reduced colony formation by approximately 20% versus control ($p<0.05$). NAC pretreatment attenuated Oviedomycin-induced cytotoxicity, increasing cell viability from 63.94 ± 1.47% to 85.32 ± 3.08% at 15 µM and from 41.32 ± 1.91% to 66.40 ± 1.03% at 30 µM ($p<0.05$). Annexin V/PI staining showed increased total apoptotic cells at 15 µM (17.05 ± 1.04%) and 30 µM (40.93 ± 1.96%). Moreover, JC-1 staining significantly reduced ($p<0.05$) the aggregate/monomer fluorescence ratio at 15 µM (0.31 ± 0.01) and 30 µM (0.35 ± 0.02) versus untreated cells (4.20 ± 0.20). **Conclusion:** Oviedomycin exhibited promising antitumor activity in HCT-116 cells, characterized by selective cytotoxicity, reduced clonogenic potential, and apoptosis induction, possibly via the mitochondrial pathway. The protective effect of NAC supports the involvement of oxidative stress in compound-induced cytotoxicity. These findings highlight the therapeutic potential of Oviedomycin and support further investigation of its mechanism of action and potential application as a therapeutic candidate against colorectal cancer. **Financial support:** CAPES. CNPq e FAPESQ-PB.

10.052 **Organoselenium Compounds and Sulfur Analogues Exhibit Cytotoxicity in Human Glioma Tumor Cell Lines**. Ramalho IGS[1], Souza RRM[1], Marques KKG[1], Januário VHS[2], Rodrigues JS[2], Queiroga LM[1], Farias APGM[1], Firmino-Silva IC[1], Lyra GB[1], Mendonça-Júnior FJB[1], Sobral MV[1], Ferreira RC[1], Gonçalves JCR[1]. [1]UFPB, Health Sciences Center, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]UFPB, Health Sciences Center, ONCOFAR, Undergraduate in pharmacy, Brazil

Introduction: Gliomas are the most common primary tumors of the central nervous system and are associated with poor prognosis, particularly in high-grade tumors. Despite advances in current therapeutic approaches, treatment remains limited by tumor heterogeneity, invasive capacity, and resistance to conventional therapies. Therefore, the identification of novel compounds with antitumor activity remains an important strategy in the search for more effective treatments. Organoselenium compounds have attracted considerable interest due to their diverse biological activities, including cytotoxic effects against several cancer types. Similarly, sulfur-containing compounds exhibit antitumor potential and may interfere with processes related to cell proliferation and survival. However, the activity of organoselenium compounds and their sulfur analogues in glioma models remains largely unexplored. **Objective:** Evaluate the cytotoxic activity of organoselenium compounds and sulfur analogues in human glioma cell lines. **Methods:** The *in vitro* antitumor activity of organoselenium compounds and sulfur analogues (20 μM) was assessed in human glioma cell lines (U87-MG, U251-MG, and T98G) using the MTT reduction assay following 72 h of treatment. **Results**: In U87-MG cells, only compound 8CNSel03 significantly reduced cell viability (cell viability: 61.89 ± 0.04%). U251-MG cells were the most sensitive to treatment, exhibiting significant reductions in viability following exposure to compounds 6AMD2 (cell viability: 62.7 ± 0.02%), 8CNSel03 (cell viability: 67.24 ± 0.01%), 6AMD7 (cell viability: 58.02 ± 0.01%), 6CN09 (cell viability: 56.23 ± 0.0%), 6CNSel08 (cell viability: 68.13 ± 0.01%), and 6CN21 (cell viability: 50.38 ± 0.01%). In T98G cells, significant decreases in viability were observed after treatment with 6CNSel11 (cell viability: 68.44 ± 0.02%) and 8CNSel03 (cell viability: 38.27 ± 0.01%). Notably, 8CNSel03 was the only compound capable of significantly reducing cell viability in all three glioma cell lines, demonstrating the most consistent cytotoxic profile among the compounds evaluated. **Conclusion:** The compound exhibited distinct cytotoxic profiles across the glioma cell lines evaluated. Among the tested molecules, 8CNSel03 showed the most promising activity, significantly reducing cell viability in all cell lines evaluated. These results support the selection of compound 8CNSel03 for further investigation and elucidation of its *in vitro* antitumor effects in glioma cell lines.

10.053 **Increased Resistin Expression Predicts Poor Neoadjuvant Chemotherapy Response in Breast Cancer Patients**. Freitas GL[1], Cajado AG[1], Quispe CC[1], Capistrano-Junior VL[2], Caetano ML[1], Saraiva LC[1], Sauda MR[3], Rocha-Filho DR[4], Arruda LM5, Rogatto SR[2], Lima-Junior RCP[1], Wong DVT[1] [1]UFC, Lab Inflammation and Cancer Pharmacology, Brazil. [2]Health Institute, Fortaleza, Brazil. [3]Unesp-Botucatu, Brazil. [4]UFC-Walter Cantídio University Hospital, 5Haroldo Juaçaba Hospital, Cancer Institute of Ceará, Brazil.

Introduction: Obesity may modify the response to antineoplastic therapy through adipose tissue dysfunction, chronic inflammation, and altered adipocytokine secretion. **Aim:** To evaluate adipokine levels in breast cancer (BC) treated with doxorubicin/cyclophosphamide/taxol neoadjuvant chemotherapy (AC-T), investigating associations with treatment response, and metabolic-inflammatory phenotypes. **Methods:** This prospective study included 81 BC patients undergoing AC-T. Clinicopathological, anthropometric, and peripheral blood data were collected before and after treatment. The Proteome Profiler Human Adipokine Array Kit was analyzed by densitometry using ImageJ. Samples were stratified according to treatment response and obesity into responders without obesity (R Ob-) and with obesity (R Ob+), non-responders without obesity (NR Ob-) and with obesity (NR Ob+). Leptin, Resistin, and IL-22 were measured by ELISA. Statistical analyses were performed using GraphPad Prism, SPSS, and Python, adopting $p<0.05$. Longitudinal variations in BMI, waist circumference, IL-22, leptin, and resistin were calculated in Python; data were standardized by Z-score and analyzed by clustering. **Results:** There was a predominance of no special type carcinoma (91.9%), histological grade II tumors (64.2%), Ki-67>14% (76.5%), and Triple-Negative (TN) (28.4%) and non-TN (71.6%) molecular subtypes. 51.6% were postmenopausal and initiated treatment with metabolic alterations and impaired muscle strength (BMI 28.8±4.9kg/m^2, waist circumference 92.7±11.2cm, handgrip strength 19.7kg). At treatment completion, worsening of physical status was observed (BMI 29±5kg/m^2, WC 92.9±11.8cm, handgrip strength 19kg). Pretreatment proteomic signatures demonstrated higher expression levels in NR compared with R. Resistin (IntDen: NR=0.78, R=0.28) was associated with this profile, whereas leptin (IntDen: NR=0.92, R=0.92) did not differ between groups. In obesity, lack of response increased resistin expression (Ob-=+137%, Ob+=+224%), while leptin showed an antagonistic profile (Ob-=+10%, Ob+=-9%). Bioinformatic analysis confirmed longitudinal variation in resistin (=44), with higher levels in lower degrees of clinical response, suggesting treatment-associated inflammatory modulation. Paired ELISA analysis confirmed these findings ($p=0.02$). Clustering analyses identified two metabolic-inflammatory phenotypes: metabolic resilience and greater inflammatory/anthropometric impact. The first phenotype showed better treatment response. PCA demonstrated that 59.1% of patient variance could be explained by BMI, waist circumference, IL-22, resistin, and leptin. **Conclusion:** Patients undergoing AC-T chemotherapy exhibit adipocytokine profiles associated with obesity and therapeutic response, highlighting resistin as a candidate biomarker related to non-response and inflammatory modulation. Ethics approval: Nº 4470803. **Financial support:** CNPq, CAPES, FUNCAP. Keywords: Breast Cancer; Obesity; Neoadjuvant Chemotherapy.

10.054 *In vitro* Evaluation of the Cytotoxic Potential of the Hydroalcoholic Extract and Alkaloid Fraction from the Aerial Parts of *Solanum jabrense* Agra & M. Nee. Alexandre HMS[1], Dantas MM[1], Pereira ERM[1], Castro IO[1], Santos PBG[1], Ramalho IGS[1], Santana PVS[1], Gomes KNC[1], Abreu-Junior AR[1], Araújo YKO[1], Silva AL[1], Tavares JF[1], Agra MF[2], Sobral MV[1], Gonçalves JCR[1] [1]UFPB, Dept Pharmaceutical Sciences, [2]UFPB, Biotechnology Center, João Pessoa, Brazil

Cancer is characterized by genetic alterations that lead to cellular malignancy and represents the second leading cause of mortality worldwide. Among the different cancer types, breast cancer stands out as the most prevalent, accounting for 11.7% of new diagnoses annually. *Solanum jabrense*, a Solanaceae species endemic to Brazil, is rich in alkaloids with potential antitumor activity. This study aimed to evaluate the *in vitro* cytotoxic activity of extracts derived from *Solanum jabrense*, including the hydroalcoholic extract (ESJ) and its alkaloid fraction (FSJ). The cytotoxic potential of ESJ was initially evaluated against tumor cell lines of breast adenocarcinoma (MCF-7 and MDA-MB-231), prostate carcinoma (PC-3), and melanoma (SK-MEL-28), as well as the non-tumoral cell line derived from human embryonic kidney cells (HEK-293). Results were expressed as mean ± standard error of the mean (SEM), and data were analyzed using one-way ANOVA followed by Dunnett's test ($p < 0.05$). ESJ showed greater cytotoxicity against the breast adenocarcinoma cell lines MCF-7 (10.90% ± 0.21) and MDA-MB-231 (13.40% ± 0.15) compared to the control group. Subsequently, the most sensitive cell lines were evaluated at different incubation periods (24 h, 48 h, and 72 h) using the MTT assay, with IC50 values determined and the selectivity index calculated between tumor and non-tumor cell lines. MCF-7 showed greater selectivity to ESJ after 48 h of treatment (IC50: 27.72 ± 0.02 µg/mL; SI: 2.83) compared to HEK-293 (IC50: 78.56 ± 0.08 µg/mL). Therefore, the MCF-7 cell line and the 48 h treatment period were selected to investigate the cytotoxic effect of the alkaloid fraction (FSJ). After 48 h, FSJ demonstrated high selectivity toward MCF-7 (IC50: 35.50 ± 0.10 µg/mL; SI: 15) compared to the non-tumoral HEK-293 cell line (IC50: 527.54 ± 0.30 µg/mL). The results demonstrate that extracts derived from *Solanum jabrense*, especially its alkaloid fraction, exhibit promising cytotoxic activity against the MCF-7 breast adenocarcinoma cell line, reinforcing its potential as a source of antitumor agents. Financial support: CNPq. CAPES. FAPESQ

10.055 **Low-Anticoagulant Bovine Heparin and Its Low Molecular Weight Derivative as Antimetastatic Agents**. Micheli KVA, Motta JM, Oliveira SNM, Hermsdorff-Brandt M, Peres ACL, Mourão PAS, Pereira MS IBqM-UFRJ, Rio de Janeiro, RJ, Brazil

Introduction: Metastasis is responsible for most cancer-related deaths and depends on complex interactions between tumor cells, platelets, and adhesion molecules such as P-selectin. Heparins are widely used anticoagulants and have demonstrated antimetastatic properties, mainly through inhibition of platelet- tumor cell interactions. However, the hemorrhagic risk associated with conventional heparins limits their use as antimetastatic agents. **Objectives:** This study aimed to evaluate the antimetastatic potential of a low- anticoagulant bovine heparin (LABH) and its low molecular weight derivative (LABH-LMWH), as well as to investigate their safety profile and mechanisms involved in metastasis inhibition. **Methods:** Experimental metastasis assays were performed using murine melanoma (B16F10) and colorectal carcinoma (MC38) cells in wild-type and P-selectin knockout C57BL/6 mice. Platelet-tumor cell interactions were analyzed by static adhesion assays and confocal microscopy. Tumor cell-induced thrombocytopenia was evaluated *in vivo*. Anticoagulant activity and hemorrhagic risk were assessed by aPTT, anti-Xa/anti-IIa assays, plasma recalcification, and bleeding tendency assays. Animals were treated with LABH or LABH-LMWH by i.v or s.c. injection. **Results:** LABH and LABH-LMWH showed markedly reduced anticoagulant activity and minimal hemorrhagic effects compared with conventional heparins. *In vivo*, both LABH and LABH-LMWH significantly reduced platelet-tumor cell interactions and pulmonary metastatic foci in melanoma and colorectal murine cancer models, showing that LABH-LMWH also preserved antimetastatic efficacy after subcutaneous administration. Additionally, they also reduced lung weight in metastatic animals. In P-selectin knockout mice, the number of metastatic foci was lower than in control animals, demonstrating the importance of P-selectin; however, heparins were still able to diminish metastatic foci, suggesting that other mechanisms should also be involved. And prior administration of heparins failed to prevent tumor cell-induced thrombocytopenia in knockout animals, unlike what is observed in wild type animals reinforcing the importance of P-selectin during the early stages of metastasis. Interestingly, **Conclusion:** LABH and LABH-LMWH demonstrated significant antimetastatic activity despite their low anticoagulant activity, acting through inhibition of multiple adhesion pathways. LABH-LMWH combines antimetastatic efficacy with an improved safety profile, and a better form of administration for patients, representing a promising candidate for adjuvant cancer therapy.

10.056 **APT20TTMG Suppresses Tumor Cell Growth and Induces Apoptosis Across Multiple Human Cancer Cell Lines**. Oliveira VS[1,2], Lobo EB[1,2], Silva DKC1, Nogueira ML1, Soares ES3, Sinatti VVC3, Silva JC3, Bottos RM3, Leal CBQS3, Meira CS[1,2]. [1]Fiocruz-BA, Salvador, [2]SENAI CIMATEC-BA, Salvador, [3]Aptah Bio Inc., San Carlos, CA, USA.

Introduction: Cancer remains a major global health challenge, accounting for substantial morbidity and mortality worldwide. The limited selectivity, systemic toxicity, and treatment resistance associated with conventional therapies highlight the need for novel therapeutic approaches. Dysregulation of RNA processing pathways contributes to tumor progression and survival, making U1-snRNP-associated mechanisms attractive therapeutic targets. APT20TTMG is an oligonucleotide designed to interact with the U1-snRNP complex and modulate pre-mRNA processing, with potential antitumor activity. **Objectives:** To evaluate the effects of APT20TTMG on metabolic activity, cell proliferation, and apoptosis induction in human tumor cell lines. **Methods:** The study included the human cancer cell lines A375 (melanoma), HCT-116 (colorectal carcinoma), SK-N-SH (neuroblastoma), and U-2 OS (osteosarcoma), as well as the non-tumorigenic MRC-5 human fetal lung fibroblast cell line. Metabolic activity and cell proliferation were assessed by MTT and sulforhodamine B (SRB) assays after 96 and 144 h of exposure to APT20TTMG (0.01–30 μM). Doxorubicin was used as a positive control for A375, HCT-116, U-2 OS, and MRC-5 cells, whereas temozolomide was used for SK-N-SH cells. Apoptosis was evaluated after 96 h by Annexin V-FITC/PI staining and flow cytometry following treatment with APT20TTMG (2.5, 5, and 10 μM). Statistical significance was defined as $p \leq 0.05$. **Results:** APT20TTMG reduced metabolic activity and, more markedly, inhibited cell proliferation in all tumor cell lines evaluated, indicating a predominantly cytostatic effect. Among the tumor cell lines evaluated, HCT-116 was the most sensitive model, exhibiting a 61.7% reduction in metabolic activity and a 93.1% reduction in cell biomass after 144 h of treatment with 30 μM APT20TTMG. In contrast, the non-tumorigenic MRC-5 cell line was substantially less affected by treatment, suggesting preferential activity toward malignant cells. Flow cytometric analysis demonstrated that APT20TTMG induced apoptosis across all cancer cell lines evaluated. HCT-116 cells displayed the strongest response, with approximately 30% of cells undergoing late apoptosis following treatment with 10 μM APT20TTMG. The remaining cancer cell lines also exhibited increased Annexin V positivity, further supporting apoptosis induction. Collectively, these findings indicate that APT20TTMG limits tumor cell expansion through a combination of growth inhibition and apoptosis induction. **Conclusion:** APT20TTMG exhibited a predominantly cytostatic profile, markedly suppressing tumor cell growth while also reducing metabolic activity and inducing apoptosis across multiple human cancer cell lines, with reduced effects on non-tumorigenic cells. These findings support the further development of U1 -snRNP-targeting oligonucleotides as a promising therapeutic strategy for solid tumors.

10.057 **Antileukemic Activity of the Isoflavonoid LOE2208: Cell Cycle Arrest and Apoptosis Induction in Acute Myeloid Leukemia Cell Lines**. Sales SLA[1,2], Maranhão SS[1,2], Vieira-Neto JB[1,2]; Caleffi GS[3], Bastos RSB[1,2], Mota JA[1,2], Macêdo SMN[1,4], Oliveira KAF[1,5], Gress LSB[1,2], Desiderio GA[1,2], Santos ACF[1,6], Sasahara GL[7], Pinheiro RF[7,8], Furtado CLM[9], Pessoa C0[1,2] [1]UFC, Experimental Oncology Lab, Center for Research and Drug Development, Brazil. [2]UFC, Dept Physiology and Pharmacology, Graduate Program in Pharmacology, Brazil. [3]UFRJ, Lab Bioorganic Chemistry (LQB), Walter Mors Institute of Natural Products Research, Brazil. [4]UFC, Dept Biochemistry and Molecular Biology, Brazil. [5]UFC, Dept Biology, Brazil. [6]Uninassau, Dept Pharmacy, Brazil. [7]UFC, Cancer Cytogenomics Lab, Brazil. [8] UFC, Graduate Program in Medical Sciences, Brazil. [9]UFMG, Dept Genetics, Ecology and Evolution, Institute of Biological Sciences, Brazil.

Introduction: Acute myeloid leukemia (AML) is an aggressive hematological malignancy characterized by high molecular heterogeneity and poor clinical outcomes. Despite recent therapeutic advances, treatment resistance and disease relapse remain major clinical challenges, underscoring the need for compounds with distinct mechanisms of action. LOE2208, an isoflavonoid investigated by our group for nearly two decades, has previously demonstrated antitumor activity in various experimental models, including leukemia. However, its specific effects and underlying mechanisms in AML models remain incompletely characterized. **Objective:** To evaluate the antileukemic activity of LOE2208 and characterized the cellular mechanisms underlying its effects in a panel of AML cell lines. **Methods:** Cytotoxic activity was assessed in five AML cell lines (HL-60, MOLM-13, OCI-AML-3, MV4-11, and KG-1) using MTT and ATP-lite assays after 72 h of treatment. Additionally, morphological analyses (hematoxylin and eosin staining), membrane integrity assays, cell cycle distribution, and apoptosis evaluations by flow cytometry, caspase-3/7 activity assays by bioluminescence, and exploratory gene expression analyses of cell cycle regulators by RT-qPCR were performed. **Results:** The compound LOE2208 reduced cell viability and ATP levels in a concentration-dependent manner in all evaluated cell lines. KG-1 and HL-60 cells were the most sensitive to treatment (IC50 ≈ 0.5 and 0.9 µM, respectively), whereas OCI-AML-3 and MV4-11 exhibited greater resistance (IC50 > 1.5 µM). Based on their distinct sensitivity profiles, MOLM-13 and OCI-AML-3 cells were selected for further characterization. After 24 h of treatment, LOE2208 reduced cell density, induced chromatin condensation, and increased cellular debris. Consistent with these findings, treatment significantly increased the PI-positive population, reaching approximately 40–45% in MOLM-13 and 10–30% in OCI-AML-3 cells ($p < 0.05$). Cell cycle analysis revealed a concentration-dependent accumulation of cells in the G2/M phase ($p < 0.05$), indicating disruption of cell cycle progression. This effect was accompanied by induction of apoptosis and a significant increase in caspase-3/7 activity ($p < 0.05$). Furthermore, gene expression analyses revealed modulation of mitotic regulators, including AURKB and MAD2L1, corroborating the observed effects on cell cycle progression. **Conclusion:** Taken together, these findings demonstrate that LOE2208 exhibits antileukemic activity associated with cell-cycle arrest and induction of apoptosis. Considering its activity across distinct AML models and its ability to modulate essential processes involved in tumor cell proliferation and survival, LOE2208 represents a promising compound for further investigation in AML.

10.058 **Antiproliferative Activity and Toxicological Profile of the Hexanic Fraction of *Tocoyena hispidula* Standl. Stems on Eukaryotic Models**. Souza RP[1], Rocha KF[1], Cruz RLC[2], Sousa RCL[3], Esteves JC[4], Sousa EA[5], Freitas MM[3], Sousa RWR[3], Oliveira ECA[2], Ferreira PMP[3],6, Chaves MH[5], Oliveira AP[1] [1]UFPI, Lab Cardiovascular Pharmacology (Lafac), Dept Biophysics and Physiology, PPG Pharmacology; [2]UFPI, Lab Toxicological Genetics (Getox), Dept Biochemistry and Pharmacology; [3]UFPI, Lab Experimental Cancerology (LabCancer), Dept Biophysics and Physiology; [4]UFPI, Lab for Research in Toxicological Genetics (Lapgenic); [5]UFPI, Lab Natural Products, Dept Chemistry; 6UFC, Lab Experimental Oncology (Loe), Dept Physiology and Pharmacology, Brazil.

Introduction: *Tocoyena hispidula* Standl. (Rubiaceae) is a native medicinal species from the Brazilian Cerrado traditionally used to treat gastrointestinal and inflammatory disorders. Phytochemical studies have reported the presence of iridoids, coumarins, triterpenes, and steroids. However, data regarding its toxicological safety remains insufficient. Herein, it was evaluated the antiproliferative and toxicogenetic activities of a hexane fraction obtained from ethanolic extracts of *T. hispidula* stems (FhTH). **Methods:** The hexane fraction was obtained by liquid-liquid partitioning of the ethanolic stem extract (SisGen #AAB530D). Firstly, 24h-exposure was assessed using the Artemia salina bioassay and 48 h-hatched larvae (n=10/concentration). Cytotoxicity was determined by the MTT assay after 72 h of exposure on human astrocytoma (SNB-19), murine melanoma (B-16/F-10), and murine mammary carcinoma (4-T1) cell lines. Next, toxic, cytotoxic, and mutagenic/clastogenic effects were also evaluated by the *Allium cepa* assay through analyses of germination index (GI), mitotic index (MI), cell cycle dynamics, and chromosomal alterations. Data were analyzed by one-way ANOVA followed by Tukey ($p < 0.05$), and IC50 values were calculated by nonlinear regression. **Results:** A significant reduction of nauplii survival was observed at 50 and 100 µg/mL only ($p < 0.05$). FhTH showed differential cytotoxic on the cell lines. SNB-19 cells were the most sensitive [IC50 of 0.96 (0.40-4.69) µg/mL], followed by B-16/F-10 cells [IC50 value of 2.08 (1.53-2.89) µg/mL], and 4-T1 cells [IC50 of 86.97 (41.50-281.80) µg/mL]. FhTH reduced GI of *A. cepa* meristematic cells at 100 µg/mL (48.0 ± 4.5%) when compared to the negative control (95.3 ± 1.5%) and revealed marked antiproliferative activity, with MI decreasing at all concentrations (14.6 ± 2.8, 15.1 ± 4.5, and 11.9 ± 4.1 for 25, 50, and 100 µg/mL, respectively) compared with the negative control (24.1 ± 6.8 %). An increase in interphase cells suggested cell cycle arrest. Genotoxicity/mutagenicity analysis demonstrated a concentration-dependent increase in chromosomal aberrations and induction of chromosomal bridges at all concentrations. At 100 µg/mL, increased frequencies of micronuclei and nuclear buds indicated genomic instability ($p < 0.05$). **Conclusion:** FhTH exhibited antiproliferative action on human, murine and vegetal cells, with antimitotic and cell cycle arrest activity, probable associated to chromosomal damages. These findings contribute to the toxicological characterization of *T. hispidula* and support further studies to identify bioactive compounds and establish safe pharmacological limits.

10.059 **miRNA-181a-5p as a Potential Regulator of the Etoposide Response in Lung Cancer Cells**. Pegado CBS[1,2], Gomes JPA[1,2], Silva BO[1,2], Pereira MC[1,2,3] [1]UFPE, PPG Therapeutic Innovation, Brazil, [2]UFPE, Suely Galdino Center for Research in Therapeutic Innovation, Brazil, [3]UFPE, Dept Physiology and Pharmacology, Brazil

Introduction: Lung cancer is among the neoplasms with the greatest impact on global public health, presenting high mortality rates and significant therapeutic challenges. Although recent advances, such as immunotherapy, have broadened treatment possibilities, access to these approaches remains limited, especially in the Brazilian public health system, where conventional chemotherapy regimens continue to be widely used. In this context, tumor heterogeneity and variability in response to chemotherapy represent significant obstacles to therapeutic efficacy. MicroRNAs (miRNAs), in turn, have been described as important regulators of gene expression, acting in processes related to cell proliferation, apoptosis, and therapeutic response. **Objective:** Considering the regulatory role of miRNAs in tumor therapeutic response, this study investigated the modulation of miR-181a-5p in lung cancer cells treated with etoposide, aiming to understand its possible association with cellular mechanisms induced by the chemotherapeutic agent. **Methods:** Lung adenocarcinoma cell lines H1299 and A549 were cultured and treated with etoposide at IC50 concentrations of 3.18 μM and 15.14 μM, respectively. After 8 and 24 hours of exposure, total RNA extraction, cDNA synthesis, and analysis of relative miR-181a-5p expression were performed by RT-qPCR. Transfection assays using the miRNA inhibitor were performed to determine the optimal transfection time. After standardization, cells were transfected and treated with the IC25 concentration for each cell line, followed by cell viability evaluation using the MTT assay. **Results:** Etoposide treatment promoted increased miR-181a-5p expression in both cell lines. In A549 cells, 4.54- and 8.24-fold increases were observed after 8 and 24 hours of treatment, respectively ($p < 0.01$). In H1299 cells, etoposide induced high miR-181a-5p expression as early as 8 hours, with 63.81- and 64.94-fold increases after 8 and 24 hours, respectively ($p < 0.0001$). Furthermore, transfection with the miR-181a-5p inhibitor promoted a 42.25% increase in cell viability compared to untreated cells. Etoposide treatment reduced cell viability by 22.83%; however, co-treatment with the inhibitor restored viability to levels comparable to the untreated control. These findings suggest that inhibition of miR-181a-5p may promote cell proliferation and reduce sensitivity to etoposide, indicating a possible tumor suppressor role for this miRNA. Conclusion: The differential expression of miR-181a-5p suggests its possible involvement in the modulation of the cellular response to etoposide, highlighting its potential as a biomarker of tumor chemosensitivity. These findings expand the understanding of the molecular mechanisms associated with the chemotherapeutic response in lung cancer and reinforce the relevance of microRNAs as potential therapeutic targets in molecular oncology.

10.060 **Apoptotic and Oxidative Stress-Related Effects of the Organotellurane RF07 in MCF-7 Breast Cancer Cells**.
Castro IO[1], Marques KKG[1], Dantas MM[1], Souza RRM[1], Duarte SS[1], Alexandre HMS[1], Ramalho IGS[1], Ferreira[1], RC, Januário VHS[2], Rodrigues JS[2], Santana JP[2], Sousa JMC[3], Cunha RLOR[4], Gonçalves JCR[1], Sobral MV[1] [1]UFPB, ONCOFAR, PPG in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil; [2]UFPB, ONCOFAR, Undergraduate in pharmacy, Health Sciences Center, Brazil; [3]UFPI, LAPGENIC, PostgraduateProgram in Pharmaceutical Sciences, Brazil; [4]UFABC, Center Natural and Human Sciences, Brazil.

Introduction: Breast cancer remains a public health challenge, and the limitations of conventional chemotherapy, including systemic toxicity and tumor resistance, reinforce the need for novel therapeutic strategies. Organotelluranes, a subclass of organotellurium compounds characterized by tellurium–carbon covalent bonds, have attracted attention due to their biological activities, including antitumor effects. In this context, RF07 [4-{2-chloro-3-[chloromethylidene]-1-oxa-2-(λ^4)-telluraspiro[3.5]non-2-yl}phenyl methyl ether] has demonstrated cytotoxic activity against breast cancer cell lines, including MDA-MB-231 and MCF-7. However, its mechanisms of action remain poorly understood, supporting investigation of its antitumor effects. **Objective:** This study aimed to evaluate the cytotoxic activity of RF07 in MCF-7 breast cancer and MCF-10A non-tumoral breast epithelial cells, investigate its selectivity profile, cell death mechanisms, and effects on oxidative stress. **Methods:** Cytotoxic activity of RF07 was evaluated using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay after 72 h treatment. The involvement of oxidative stress was investigated by pretreating MCF-7 cells with N-acetylcysteine (NAC) prior to RF07 exposure, followed by reassessment of cell viability. Apoptosis induction was analyzed by Annexin V-FITC/propidium iodide (PI) staining and flow cytometry. In addition, nuclear alterations and mitochondrial membrane potential changes associated with cell death were assessed by Hoechst 34580 and JC-1 staining, respectively, using confocal microscopy. Data are presented as mean ± SEM and analyzed by one-way ANOVA followed by Tukey's post hoc test. **Results:** RF07 exhibited cytotoxic activity in MCF-7 cells, with a half maximal inhibitory concentration (IC50) of 3.3 ± 0.08 μM, whereas lower cytotoxicity was observed in MCF-10A cells (IC50: 21.16 ± 0.9 μM), resulting in a selectivity index of 6.41. RF07 significantly ($p<0.05$ for all) increased apoptotic cell death in MCF-7 cells, with higher levels of early and late apoptosis at 3 μM (58 ± 5.5% and 10.64 ± 0.93%, respectively) and late apoptosis/necrosis at 6 μM (94.33 ± 1.92%). Hoechst 34580 staining revealed increased fluorescence intensity in treated cells (1.66 ± 0.11; $p<0.05$) compared to the control (1.0 ± 0.06). JC-1 staining showed increased green/red fluorescence ratios at 3 μM (1.29 ± 0.08) and 6 μM (1.35 ± 0.14) relative to control (0.18 ± 0.01%). NAC pretreatment significantly attenuated RF07-induced cytotoxicity, restoring cell viability to 123.1 ± 5.1% and 99.4 ± 9.7% at 3 and 6 μM, respectively. **Conclusion:** RF07 exhibited selective cytotoxicity toward MCF-7 breast cancer cells. Its antitumor effects appear to be associated with oxidative stress modulation, apoptosis induction, and mitochondrial membrane alterations, suggesting the involvement of the intrinsic apoptotic pathway. **Funding:** CAPES, CNPq and FAPESQ-PB.

10.061 **Oral Cashew Gum** *Anacardium occidentale* **L. Reduces Tumor Growth in a Syngeneic Murine B16-F10 Melanoma Model**. Machado, FS[1]; Alves, GOM[1]; Ribeiro, RMS[1]; Araújo, DD[1]; Aguiar, RPS[1]; Cajado, AG[2]; Lima Junior, RCP[2]; Ribeiro, IS[3],[4]; Paula, RCM[3]; Araujo, AJ[1]; Marinho Filho, JDB[1] [1]UFDPar, Lab Cultura Celular do Delta, Brazil, [2]UFC, Lab Farmacologia da Inflamação do Câncer, Brazil, [3]UFC, Lab Polímeros, Brazil, [4]IFPI, Brazil

Introduction: Melanoma is characterized by high invasive and metastatic potential, and the need for additional therapeutic options has driven the investigation of natural compounds with antitumor activity. Among them, cashew gum (CG) from *Anacardium occidentale*, a polysaccharide widely explored for biomedical applications, has shown biological properties that support its evaluation against tumor progression. **Objectives:** To evaluate the effects of oral CG administration on tumor growth in a syngeneic murine B16-F10 melanoma model, as well as its hematological, biochemical, and molecular impacts. **Methodology:** CG was isolated and characterized by Fourier-transform infrared spectroscopy (FTIR), nuclear magnetic resonance (NMR), size-exclusion chromatography (SEC), and potentiometric titration to determine acidic group content. Cytotoxicity was assessed *in vitro* using B16-F10 cells. For in vivo studies, C57BL/6 mice inoculated with B16-F10 cells received oral CG at 100 or 200 mg/kg/day for 14 days (CG100 and CG200). PBS and cyclophosphamide served as negative and positive controls, respectively. Body weight variation, tumor and organ masses, hematological and biochemical parameters, gene expression by qRT-PCR, and Ki-67 and F4/80 immunolabeling were evaluated. **Results:** Structural analyses confirmed the identity of CG, with a molecular weight of 6.46×10^3 g/mol and acidic group content of 3.7 ± 0.2%. CG showed no cytotoxicity against B16-F10 cells (IC_{50} > 1000 µg/mL). *In vivo*, CG200 reduced tumor mass by 42.1%, whereas cyclophosphamide reduced it by 50.8% compared with PBS. No changes were observed in body weight progression or organ masses. Cyclophosphamide increased neutrophils, reduced lymphocytes, and decreased total leukocyte counts, whereas CG caused no hematological alterations. The remaining hematological parameters were unchanged. Biochemical analysis showed reduced serum urea levels only in the CG200 group. Expression of Il1b, Il4, Il6, Tgfb1, Tlr2, Tlr4, Tlr9, Il12, Il18, Il33, Ifng, MMP-9, MMP-12, and Vegf was unaltered. Immunofluorescence revealed reduced Ki-67 labeling in treated groups and increased F4/80 labeling, especially in CG200. **Conclusion:** Oral CG reduced tumor growth in the syngeneic murine B16-F10 melanoma model without evidence of systemic toxicity, as indicated by unchanged body weight, organ masses, and hematological and biochemical parameters. Increased F4/80 labeling suggests the involvement of monocyte /macrophage-lineage cells in the antitumor response, supporting further investigation of CG as a potential adjuvant therapy for melanoma.

10.062 **Cannabidiol Enhances 5-Fluorouracil Efficacy in Colorectal Cancer: Insights into the Molecular Mechanisms Involved**. Iughetti MF, Pereira THR, Zamarioli LS, Smaili SS, Pereira GJS, Bincoletto C Unifesp-EPM, Dept Pharmacology, Graduate Program in Pharmacology, Brazil

Introduction: Colorectal cancer (CRC) is the third most commonly diagnosed cancer worldwide and is associated with high mortality rates. This high lethality is linked to a scarcity of effective pharmacological treatments. Among the therapeutic strategies investigated to improve treatment outcomes for this disease, cannabinoids derived from *Cannabis sativa* have demonstrated promising antitumor effects in experimental models. **Objective:** The present study aimed to evaluate the therapeutic potential of cannabidiol (CBD) in CRC cell lines, as well as to investigate its ability to modulate cellular responses to the chemotherapeutic agent 5-fluorouracil (5-FU). Material and **Methods:** The HT-29 and SW480 cell lines, derived from primary colorectal tumors, were treated with CBD, and cell viability was assessed by reducing the MTT salt to formazan crystals. The effects of 5-FU, both alone and in combination with CBD, were also evaluated using the same methodology. Cell death pathways: ferroptosis, necroptosis, and apoptosis, were investigated using specific inhibitors for each pathway prior to CBD exposure. Analyses were performed by flow cytometry with double staining using Annexin-V-FITC and 7-AAD. Furthermore, the expression of cleaved caspase-3 and MLKL proteins was examined after treatment with CBD and 5-FU, alone and in combination. Cell proliferative capacity was assessed using a clonogenic assay after seven days of treatment. The expression of cannabinoid receptors CB1 and CB2, as well as transient receptor potential vanilloid 1 (TRPV1), was characterized by immunofluorescence and Western blotting. Their involvement in the cytotoxic effects induced by CBD was evaluated through pretreatment with selective agonists and antagonists, followed by MTT assays. Changes in receptor expression after treatment with CBD and 5-FU were also analyzed. Additionally, the expression of P-glycoprotein (P-gp), a key mediator of drug resistance, was evaluated under the same conditions. **Results:** The results demonstrated that CBD exerts cytotoxic effects on both CRC cell lines (HT-29 and SW480), inducing multiple cell death pathways and increasing the cytotoxicity of 5-FU. Treatment with 5-FU, alone or in combination with CBD, increased the expression of cleaved caspase-3. Regarding the receptors evaluated, it was observed that the effects of CBD are mainly mediated by its interaction with CB2 receptors in the evaluated cell lines. In addition, treatment with 5-FU increased the expression of CB1, CB2, TRPV1, and P-gp, suggesting an adaptive response to cellular stress. These alterations were not observed with CBD alone, indicating that CBD does not activate the same resistance mechanisms. **Conclusion:** Taken together, these findings provide a solid foundation for future investigations into the molecular mechanisms underlying CBD activity and support its potential application as a therapeutic strategy in colorectal cancer, either as monotherapy or in combination with 5-FU to enhance treatment efficacy. **Financial support:** CAPES, FAPESP and CNPq.

10.063 **Targeting the Premetastatic Lung Niche with Heparin in a Colon Adenocarcinoma Murine Model**. Motta JM, Oliveira MR, Hermsdorff-Brandt M, Peres ACL, Pereira MS, Mourão PAS IBqM-UFRJ

Introduction: Colorectal cancer (CRC) is currently the third most prevalent cancer worldwide. Increasing evidence indicates that successful metastatic colonization depends on the prior establishment of a favorable microenvironment in distant organs, known as the premetastatic niche. This process involves extracellular matrix (ECM) remodeling and recruitment of immune myeloid cells, among other alterations. In this study, we aimed to better characterize lung premetastatic niche formation using a murine CRC model and to investigate whether a low-anticoagulant heparin derivative (LABH), previously shown to display antimetastatic activity, could interfere with this process. **Methods:** C57BL/6 mice were subcutaneously inoculated with 5x105 MC38 cells to induce primary tumor development. After 14 days, selected groups received an intravenous injection of MC38 cells (3x105) to induce experimental lung metastasis. Animals were monitored for 28 days and divided into five groups: (1) control; (2) primary tumor only; (3) initial metastasis only (2 weeks); (4) advanced metastasis only (4 weeks); and (5) primary tumor plus 2-week metastasis. In a second set of experiments, two additional groups were included: mice bearing only the primary tumor and treated daily with LABH (8 mg/kg) by intraperitoneal injection, and mice bearing both primary and metastatic tumors treated daily with LABH. Lung histology and collagen deposition were evaluated after 28 days. **Results:** H&E; staining revealed marked lung tissue remodeling, including alveolar architecture disruption, altered cell density, and collagen modifications, particularly in the advanced metastasis and primary tumor plus metastasis groups. Quantitative analysis showed significant increase in alveolar thickening and collapse in primary tumor plus metastasis group compared to control (~40% increase). Picrosirius red staining and immunostaining for collagen types I and IV demonstrated increased collagen I deposition (3.7 a.u. in controls *vs* 8.3 a.u. in primary tumor plus metastasis group) and an altered distribution of collagen IV, despite no significant change in its overall abundance in tumor-bearing groups. Importantly, LABH-treated animals showed improved preservation of lung architecture and reduced pulmonary edema (~30% reduction), suggesting a protective effect against tumor-induced tissue remodeling. **Conclusion:** Our findings demonstrate that the primary tumor alone is sufficient to promote significant alterations in lung architecture, consistent with premetastatic niche formation characterized by collagen I accumulation. Furthermore, LABH treatment attenuated lung structural alterations in tumor-bearing mice, reinforcing its potential as an antimetastatic agent.

10.064 **Target-Based Discovery of an NQO1 Inhibitor with Pro-Apoptotic Effects in Lung Cancer Cells**. Costa PMS, Pereira JVM, Brito TL, Paier CRK, Pessoa C UFC, Lab. of Experimental Oncology, Drug Research and Development Center, Brazil; PPG Pharmacology, Brazil, Northeast Biotechnology Network Program (Renorbio), Brazil

Introduction: NAD(P)H:quinone oxidoreductase 1 (NQO1) is a cytoprotective flavoprotein involved in quinone detoxification and maintenance of cellular redox balance. NQO1 is overexpressed in several malignancies, including lung cancer, where it promotes tumor cell survival, metabolic adaptation, and resistance to oxidative stress, making it an attractive target for anticancer drug development. **Objective:** To investigate the interaction between NQO1 and the novel synthetic inhibitor LOE1001 and evaluate its antiproliferative activity in A549 lung cancer cells. **Methods:** Recombinant human NQO1 was evaluated using endpoint MTT reduction and kinetic NADH consumption assays. LOE1001 (200 nM) was compared with dicoumarol (DIC, 200 nM), used as the positive control. Endpoint enzymatic activity was measured after 10 min, while NADH consumption was monitored for 1 h. Protein- ligand interactions were characterized by thermal shift assay (100 μM ligand), surface plasmon resonance (SPR), and far-UV circular dichroism (CD; 5 μM NQO1 and 10 μM LOE1001). Cytotoxicity was determined by MTT assay after 72 h of treatment (0–250 μM), using doxorubicin as the positive control. Cell cycle distribution, intracellular reactive oxygen species (ROS), and apoptosis were evaluated by flow cytometry. **Results:** LOE1001 inhibited NQO1 enzymatic activity by 96.96% at 200 nM, comparable to dicoumarol (95.79% inhibition), and markedly reduced NADH consumption. Thermal shift analysis revealed an increase of approximately 5°C in NQO1 melting temperature, while SPR demonstrated direct binding with a dissociation constant (Kd) of 9.2 μM. CD analysis showed changes in protein secondary structure upon ligand binding. In A549 cells, LOE1001 exhibited potent antiproliferative activity (IC_{50} < 50 μM), induced G1/S cell cycle arrest, increased intracellular ROS production, and promoted apoptotic cell death. **Conclusion:** LOE1001 is a potent NQO1 inhibitor that directly binds to the enzyme without altering its secondary structure. Pharmacological inhibition of NQO1 disrupts redox homeostasis, leading to oxidative stress, cell cycle arrest, and apoptosis, supporting LOE1001 as a promising lead compound for the development of novel therapies against lung cancer.

10.065 **Serigueleiro Gum Reduces Colorectal Tumor Growth Through Immunomodulatory Mechanisms**. Araújo DD[1], Alves GOM[1], Fortes MM[1], Machado FS[1], Araújo GS[1], Cajado AG[2], Lima Júnior RCP[2], Lopes ALF[3], Medeiros JVR[3], Souza LP[4], Silva FBF[4], Ribeiro FOS[5], Silva DA[5], Araújo AJ[1], Marinho-Filho JDB[1] [1]UFDPar, LCCDelta, Brazil, [2]UFC, LAFICA, Brazil, [3]UFDPar, LIGAT, Brazil, [4]UFDPar, LAPHIS, Brazil, [5]UFDPar, BIOTEC, Brazil

Introduction: Cancer remains one of the leading causes of mortality worldwide, emphasizing the need for novel and effective therapeutic strategies. Natural polysaccharides, such as arabinogalactans, exhibit antitumor and immunomodulatory activities with low systemic toxicity. Serigueleiro gum (SG), an arabinogalactan extracted from *Spondias purpurea* L., has demonstrated *in vivo* antitumor effects associated with modulation of the immune system and tumor microenvironment. **Objectives:** This study aimed to investigate the antitumor potential of SG and elucidate its mechanisms of action through comprehensive *in vitro* analyses using a panel of cancer cell lines and *in vivo* evaluation in a murine colorectal cancer model. **Methods:** *In vitro* cytotoxicity was assessed using the MTT assay in tumor cell lines (HCT-116, SW480, CT26.WT, B16-F10, MCF-7, MDA-MB-231, 4T1, SNB-19, and PC-3) treated with SG (1000 µg/mL) for 72 h. The *in vivo* antitumor effect was evaluated in BALB/c female mice inoculated with CT26.WT murine colorectal cancer cells and treated intraperitoneally with SG at doses of 50 or 100 mg/kg/day for 18 consecutive days (CEUA/UFDPar protocol no. 009/2023). Tumor inhibition was determined by daily tumor volume measurements and final tumor weight. Hematological, biochemical (ALT, AST, urea, and creatinine), and histopathological analyses of organs and tumors were also performed. Cytokine gene expression (*Il1b*, *Il4*, *Il6*, *Tgfb1*, *Tlr4*, *Il18*, *Il12*, *Il33*, and *Ifng*) in tumor tissue was quantified by quantitative real-time polymerase chain reaction (qRT-PCR). Data were analyzed using ANOVA followed by Dunnett's or Tukey's post hoc tests ($p < 0.05$). **Results:** SG exhibited limited *in vitro* cytotoxicity, with inhibition rates below 50% in all tested tumor cell lines. *In vivo*, SG treatment resulted in tumor growth inhibition rates of 32.04% and 1.31% at doses of 50 and 100 mg/kg/day, respectively, compared with the negative control group with statistical significance observed at the 50 mg/kg/day dose. Mice treated with 50 mg/kg/day showed a significant increase in total leukocyte count, without changes in body weight or signs of severe toxicity, displaying only transient hepatic alterations and mild sinusoidal dilation. qRT-PCR analysis revealed significant upregulation of Il1b, Tlr4, and Ifng expression in the tumor microenvironment following treatment with 50 mg/kg/day, suggesting macrophage activation and induction of pro-inflammatory cytokine signaling. **Conclusion:** SG exerts a significant *in vivo* antitumor effect by reducing colorectal tumor growth. This therapeutic activity appears to be primarily mediated by immunomodulatory mechanisms capable of inducing systemic immune activation and enhanced expression of pro-inflammatory cytokines within the tumor microenvironment, highlighting SG as a promising immunostimulatory therapeutic candidate for cancer treatment. **Financial support:** CAPES; CNPQ; FAPEPI; INCT BioNat; INCT Polysaccharides and INCT Nature. Human or Animal Research Ethical Committee Number: This study was approved by the Ethics Committee of the Federal University of Delta do Parnaíba (UFDPar) under protocol number 009/2023

10.066 **A Phenylpropanoid from** *Croton Velutinus* **Modulates Redox Status and MAPK Signaling in MCF-7 Breast Cancer Cells**. Ferreira RC[1], Abrantes RA[1], Duarte SS[1], Sousa VM[1], Souza RRM[1], Queiroga LM[1], Silvestre GFG[1], Castro IO[1], Araújo YKO[2], Abreu LS[3], Velozo ES[4], Goncalves JCR[1], Silva MS[1], Tavares JF[1], Sobral MV[1] [1]UFPB, Health Sciences Center, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]Health Sciences Center, ONCOFAR, Undergraduate in pharmacy, Brazil. [3]UFF, Dept Organic Chemistry, Brazil. [4]UFBA, School of Pharmacy, Research Lab in Materia Medica, Brazil

Introduction: Plant-derived natural products are important sources of bioactive compounds for cancer therapy. Among these, phenylpropanoids have attracted attention due to their broad pharmacological potential. (E)-4-(1-epoxy-7,8-propenyl)phenyl benzoate (CV2), a phenylpropanoid isolated from Croton velutinus (Euphorbiaceae), has shown anti-inflammatory, trypanocidal, and cytotoxic activities, particularly in MCF-7 breast adenocarcinoma cells, although its mechanisms of action remain unclear. **Objective:** To investigate the effects of CV2 on cellular redox status and mitogen-activated protein kinase (MAPK) signaling, including extracellular signal-regulated kinase (ERK), c-Jun N-terminal kinase (JNK), and p38 MAPK, and their involvement in CV2-induced cytotoxicity in MCF-7 cells. Methods: Reactive Oxygen Species (ROS) production was assessed by flow cytometry using 2′,7′-dichlorodihydrofluorescein diacetate (DCFH-DA) after 30 min and 3 h of treatment with CV2 at the half maximal inhibitory concentration IC_{50} and $2\times IC_{50}$ (5 and 10 μM). MAPK modulation was evaluated after 48 h of treatment with CV2 (5 and 10 μM) by flow cytometry using antibodies against p-ERK, p-JNK, and p-p38 MAPK. In addition, cytotoxicity was evaluated after 72 h using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay in the presence or absence of N-acetylcysteine (NAC, 5 mM) or pharmacological inhibitors of ERK (U0126, 5 μM), JNK (SP600125, 5 μM), and p38 MAPK (PD169316, 5 μM). Data were expressed as mean ± SEM and analyzed by one- way ANOVA followed by Tukey's test ($p<0.05$). **Results:** In the DCFH-DA assay, CV2 significantly increased the percentage of fluorescent cells after 30 min (10 μM: 23.78 ± 1.42%) and 3 h of treatment (5 μM: 65.83 ± 0.94%; 10 μM: 64.84 ± 2.78%; $p < 0.05$ for all). In the absence of NAC, CV2 significantly reduced cell viability (5 μM: 27.09 ± 1.02%; 10 μM: 13.90 ± 1.00%; $p < 0.05$ for both), whereas NAC pretreatment attenuated its cytotoxicity (5 μM: 52.47 ± 0.22%; 10 μM: 66.03 ± 0.17%; $p < 0.05$ for both). CV2 also significantly increased the percentage of cells labeled with anti-p-ERK1/2 (5 μM: 22.10 ± 1.22%; 10 μM: 34.10 ± 2.32%), anti-p-JNK1/2 (5 μM: 98.17 ± 0.46%; 10 μM: 98.00 ± 0.28%), and anti-p-p38 MAPK antibodies (5 μM: 93.43 ± 0.32%; 10 μM: 93.88 ± 1.42%) compared with controls ($p < 0.05$ for all). In addition, pretreatment with JNK (5 μM: 92.81 ± 2.80%; 10 μM: 91.30 ± 2.45%) or p38 MAPK inhibitors (5 μM: 71.50 ± 1.37%; 10 μM: 74.91 ± 1.88%) significantly attenuated CV2-induced cytotoxicity ($p < 0.05$ for all). **Conclusion:** CV2 modulated redox status and MAPK signaling in MCF-7 cells, increasing reactive oxygen species production and ERK, JNK, and p38 MAPK activation. The protective effects of NAC and JNK/p38 inhibitors support the involvement of oxidative stress and MAPK pathways in CV2-induced cytotoxicity, reinforcing its antitumor potential in breast cancer. **Financial support:** CAPES, CNPq and FAPESQ.

10.067 **LOE2208 Induces G2/M Cell Cycle Arrest and Apoptosis in Non-Small Cell Lung Cancer Cells**. Brito TL[1,2], Vieira-Neto JB[1,2], Pereira JVM[1,2], Feijó-Neto JR[1], Pessoa C[1,2,3]. [1]UFC, Lab. of Experimental Oncology, Drug Research and Development Center, Brazil; [2]UFC, PPG Pharmacology, Brazil; [3]UFC, Northeast Biotechnology Network Program (Renorbio), Brazil.

Introduction: Lung cancer remains the leading cause of cancer-related mortality worldwide, with 5-year survival rates below 20%. Isoflavonoid- derived compounds have emerged as promising sources of novel anticancer agents due to their ability to modulate cell cycle progression, mitotic regulation, and apoptotic signaling. However, the therapeutic application of these compounds is often limited by poor solubility, low bioavailability, and insufficient target selectivity. Structurally optimized synthetic analogues may improve these pharmacological properties and antitumor activity. **Objectives:** To evaluate the antiproliferative activity of the synthetic isoflavonoid LOE2208 and its effects on cell cycle progression and cell death in non-small cell lung cancer models. **Methods:** Antiproliferative activity was evaluated by MTT assay after 24 and 72 h of treatment with LOE2208 (0.39–50 μM) in four non-small cell lung cancer (NSCLC) cell lines (A549, HCC827, NCI-H1975, and NCI-H460) and one normal lung fibroblast cell line (MRC-5). LOE2208 was synthesized by our group. Cisplatin (20 μM) and Paclitaxel (0.25 μM), from Sigma-Aldrich, were used as positive controls. Morphological alterations, cell viability, and cell cycle distribution were assessed in NCI-H460 and HCC827 cells by flow cytometry (DAPI staining) after 24 h of treatment with LOE2208 (2.5, 5, 10, and 20 μM). Apoptosis induction was analyzed in NCI-H460 cells by flow cytometry using Annexin V/DAPI staining after 24 h. **Results:** LOE2208 reduced cell viability in a time- and concentration-dependent manner across all NSCLC lines, with limited cytotoxicity against MRC-5 cells (IC50 > 50 μM at both times). At 24 h, IC50 exceeded 50 μM in all tumor lines; at 72 h, the lowest IC50 values were in NCI-H1975 (1.71 ± 0.99 μM) and NCI-H460 (4.54 ± 1.06 μM), followed by A549 (5.89 ± 1.85 μM) and HCC827 (20.25 ± 2.05 μM). At the highest concentration tested (50 μM, 72 h), LOE2208 reduced viability by approximately 61–66% across all four NSCLC lines relative to control. Treatment induced morphological changes consistent with cytotoxicity and increased non-viable cells. Flow cytometry revealed concentration-dependent G2/M accumulation in NCI-H460 and HCC827 cells, reaching over 75% at higher concentrations. In NCI-H460 cells, Annexin V/DAPI staining showed a significant increase in early apoptotic cells, with minimal necrosis. **Conclusion:** LOE2208 exhibited selective antitumor activity against NSCLC models, inducing G2/M arrest and early apoptosis, supporting further investigation of its mechanism of action and potential as an antimitotic agent for lung cancer treatment. Financial Support: INCTBIO2, PRONON, Brazilian Ministry of Health, FINEP, CNPq, CAPES, and FUNCAP.

10.068 **Antitumoral Effects of Melittin on Tridimensional Models of Bladder Cancer**. Gonçalves CFL, Almeida TC, Picolo G. IBu, Pain and Signaling Lab, Brazil.

Introduction: Bladder cancer (BCa) is the most common urinary tract malignancy worldwide. Despite recent approvals of novel therapies for patients facing standard treatment failure or radical cystectomy, prognosis remains limited, driving the search for more effective compounds. Melittin (MEL), the primary amphipathic peptide found in *Apis mellifera* (honeybee) venom, has demonstrated significant antitumoral efficacy in conventional two-dimensional (2D) *in vitro* models. However, since conventional 2D monolayers fail to accurately recapitulate *in vivo* tumor biology, three-dimensional (3D) models offer a more biomimetic platform to bridge this translational gap. **Aim:** This study aimed to investigate the cytotoxic effects of MEL on 3D bladder cancer spheroids. **Methods:** Melittin, isolated from the crude venom by high-performance liquid chromatography (HPLC), is supplied by the company Brapi-Exp, Guarapari, ES, Brazil. T24 and UM-UC-3 derived spheroids were established using agarose-coated plates. Following formation, spheroids were treated with MEL 0 (control), 5 and 10 µg/ml for up to 48 hours, those concentrations were based on our team 2D previous study. Viability was evaluated by the resazurin reduction assay, while size and morphology were estimated using 2D bright-field microscopy images analyzed via ImageJ software. **Results:** After 24-hour treatment, MEL at 5 and 10 µg/ml significantly decreased the viability of both T24 (32 and 45%, $p< 0.01$) and UM-UC-3 spheroids (27 and 60%, $p< 0.01$), compared to the respective controls (no MEL). Spheroid volume and morphology were also markedly altered; treated T24 spheroids exhibited lower volume and a hyper-compacted phenotype at 10 µg/ml for 24h. Reduction of 31,1% and 38,9% compared to time zero and to the control group at 24h, $p<0.0001$. Notably, UM-UC-3 spheroids demonstrated higher sensitivity to the peptide, displaying impaired size and increased compactness after 24h at 5 µg/ml. Reduction of 18% and 65%, at 5 and 10 µg/ml compared to control group at 24h time, $p< 0.01$. **Conclusion:** Our findings demonstrate that MEL exerts potent cytotoxicity and drives architectural remodeling in bladder cancer 3D models. Furthermore, the observed effects are maintained across distinct genetic backgrounds, highlighting the potential of this peptide as a promising candidate for targeted urothelial carcinoma therapies in complex tumor microenvironment. **Financial support:** Butantan Foundation, CNPq and Fapesp.

10.069 **Effects of classical antidepressants in a novel protocol of sarcoma-related depressive-like behavior**. Sousa RWR[1], Santos IL[1], Rodrigues DCN[1], Conceição MLP[1], Freitas MM[1], Nascimento MLLB[2], Almeida ML[1], Sousa RCL[1], Souza RP[3], Batista CL[1], Pereira IC[4], Torres-Leal FL[4], Lopes LS[5], Ferreira PMP[1,6] [1]UFPI, Lab Experimental Cancerology (LabCancer), Dept Biophysics and Physiology; [2]UFPI, Lab Toxicological Genetics Research (Lapgenic), Dept Biochemistry and Pharmacology; [3]UFPI, Lab Cardiovascular Pharmacology (Lafac), Dept Biophysics and Physiology; [4]UFPI, Metabolic Diseases, Exercise and Nutrition Research Group (Domen), Dept Biophysics and Physiology; [5]UFPI, Lab for Research in Experimental Neurochemistry (Lapnex), Dept Biophysics and Physiology, [6]UFC, Lab Experimental Oncology (Loe), Dept Physiology and Pharmacology, Brazil

Introduction: The biological impact of cancer is not limited to physical symptoms, since it also exerts negative neuropsychiatric impacts on the quality of life. Therefore, this study developed and validated a new sarcoma-associated depression protocol and investigated the effects of amitriptyline (AMI) and fluoxetine (FLU) on cancer-related depressive-like behavior. Methods For the depressive-like behavior model, tumor-bearing Swiss (*Mus musculus*; CEUA UFPI #712/2022) transplanted with Sarcoma 180 (S-180) cells (6 x 106 cells) were evaluated 12 days after tumor inoculation. Firstly, exploratory and anxiety responses were assessed using the open field (OFT), elevated plus maze (EPM), and light-dark box tests. Depressive-like behavior was evaluated by the tail suspension (TST), forced swimming (FST), and sucrose preference (SPT) tests. Secondly, S-180-bearing mice received AMI and FLU 20 mg/kg (oral by gavage, 10 days), followed by behavioral evaluations (OFT, TST, and SPT). Oxidative (malondialdehyde, MDA) and nitrosative (nitrite levels, Griess' reaction) markers were measured in the hippocampus and prefrontal cortex. In the third protocol, co-treatment action of AMI or FLU (10 mg/kg, oral) plus 5-FU (10 mg/kg, intraperitoneal; Sigma-Aldrich®) was evaluated in mice as described above. Student's t-test was used for comparisons between two groups. For additional comparisons, one-way ANOVA was followed by Tukey. Results S-180-bearing mice exhibited increased immobility time (135.9 ± 14.8 vs. 62.3 ± 14.5 s) and reduced sucrose preference (91.1 ± 0.1 vs. 95.1 ± 0.1%) when compared to healthy animals. AMI and FLU 20 mg/kg reduced immobility time (40.3 ± 13.8 s and 35.7 ± 14.5 s) and increased sucrose preference (97.4 ± 1.1% and 96.9 ± 1.0%, respectively) in comparison with the negative control group (107.7 ± 9.3 s and 57.3 ± 3.9%). S-180-bearing animals displayed higher MDA levels in prefrontal cortex and hippocampus samples (1000 ± 30.4 and 519.2 ± 25.1 vs. 574.1 ± 111.9 and 369.9 ± 50.9 nmol/g tissue, respectively). Reduction in cortical MDA levels was observed following AMI treatment (539.9 ± 92.8 nmol/g tissue). AMI- and FLU-treated animals exhibited lower hippocampal nitrite concentrations (18.4 ± 7.9 and 26.2 ± 6.0 µM, respectively) compared with untreated tumor-bearing mice (69.3 ± 12.3 µM). Antidepressants + 5-FU reduced immobility time (AMI + 5-FU: 54.3 ± 4.9 s; FLU + 5-FU: 47.8 ± 12.2 s; negative control group: 108.6 ± 7.6 s) and co-treatment increased sucrose preference (AMI + 5-FU: 81.5 ± 1.7%; FLU + 5-FU: 73.0 ± 3.4%; vehicle group: 34.6 ± 8.6%). **Conclusion:** It was showed, for the first time, typical findings of depression in S-180-allograft mice and AMI and FLU, alone or combined with 5-FU, attenuated behavioral and central biochemical alterations, emphasizing the potential of non-clinical protocols to discover new pharmacological tools against cancer-related diseases.

10.070 **Phenotypic Changes of Immunogenic Cell Death Induced by Marine Natural Product Chromomycin A5 in BRAF-Mutant Melanoma**. Florêncio KGD[1], Soeiro JEM[1], Brito TL[1], Teixeira PR[3], Lotufo LVC[3], Pinto FCL[2], Pessoa ODL[2], Wilke DV[1] [1]UFC, Drug Research and Development Center, Dept Physiology and Pharmacology, School of Medicine, Brazil. [2]UFC, Dept Organic and Inorganic Chemistry, Sciences Center, Ceara, Brazil. [3]ICB-USP, Dept Pharmacology, Sao Paulo, Brazil.

Introduction: Immunogenic cell death (ICD) is a regulated form of cell death capable of eliminating tumor cells while promoting adaptive immune responses. This process is characterized by autophagy, endoplasmic reticulum stress, apoptosis, and the emission of danger-associated molecular patterns, including calreticulin (CRT) exposure and extracellular release of HMGB1 and ATP. Chromomycin A5 (CA5), a marine natural product isolated from *Streptomyces* sp. BRA-384, has previously been shown to induce ICD in murine melanoma models. Evaluating its effects on human melanoma models is necessary to assess its translational potential. **Objective:** To evaluate the immunogenic cell death-inducing potential of CA5 in the human melanoma cell line SK-MEL-28 harboring the BRAF V600E mutation. **Methods:** CA5 was isolated, extracted, and purified from *Streptomyces* sp. BRA-384. Cytotoxicity was assessed by the sulforhodamine B (SRB) assay. Flow cytometry analyzed morphological parameters, plasma membrane integrity, cell surface CRT exposure, and HMGB1 release. Gene expression of apoptosis, endoplasmic reticulum stress, and autophagy pathways was evaluated by qPCR 6 and 24 hours after CA5 treatment. **Results:** CA5 exhibited concentration-dependent cytotoxic and cytostatic activity, with a total growth inhibition (TGI) concentration of approximately 4 nM. Flow cytometry revealed increased cell granularity, reduced cell volume, and loss of membrane integrity, features compatible with cell stress and death. Gene expression analyses demonstrated modulation of nine genes associated with apoptosis, endoplasmic reticulum stress, and autophagy pathways. Furthermore, CRT exposure was detected on the cell surface, whereas HMGB1 release was not observed at the evaluated time point. **Conclusion:** CA5 induces *in vitro* features consistent with ICD in human melanoma cells, partially reproducing previous murine findings. These results reinforce the translational potential of CA5 as a promising therapeutic prototype for cancer immunotherapy in aggressive melanomas. **Financial support:** This work was supported by CNPq (grant No. 408549/2024-6), FAPESP (grant No. 2025/27006-6), CAPES (Finance Code 001), and PIBIC-UFC.

10.071 **Selective Cytotoxicity and Apoptosis Induced by a *Croton velutinus* Phenylpropanoid in MCF-7 Breast Cancer Cells**. Farias APGM[1], Abrantes RA[1], Ferreira RC[1], Sousa VM[1], Amorim GMW[1], Silvestre GFG[1], Santana JP[1], Santos PBG[1], Rodrigues JS[1], Abreu LS[2], Velozo ES[3], Silva MS[4], Tavares JF[4], Gonçalves JCR[1], Sobral MV[1]. [1] UFPB, Health Sciences Center, ONCOFAR, PPG in Bioactive Natural and Synthetic Products, Brazil. [2]UFF, Dept Organic Chemistry, Brazil. [3]UFBA, School of Pharmacy, Research Lab in Materia Medica, Brazil. [4]UFPB, Multiuser Lab for Characterization and Analysis, PPG in Bioactive Natural and Synthetic Products, Brazil.

Introduction: Despite advances in cancer management, breast cancer continues to represent a major clinical burden due to its high incidence and mortality. The occurrence of treatment-related toxicity and therapeutic resistance has encouraged the search for safer and more effective compounds. In this regard, naturally derived molecules have emerged as valuable sources of bioactive agents with potential anticancer applications. Croton velutinus (Euphorbiaceae) has emerged as a source of bioactive secondary metabolites with relevant pharmacological properties. Among them, the phenylpropanoid (E)-4-(1-epoxy-7,8-propenyl)phenyl benzoate (CV2) has shown anti-inflammatory and trypanocidal activities, in addition to marked cytotoxicity in human tumor cell lines, particularly breast cancer cells. **Objectives:** To evaluate the cytotoxic activity of CV2 in the MCF-7 human breast adenocarcinoma and non- tumoral MCF-10A breast epithelial cell lines, as well as its effects on cell cycle progression and apoptosis in MCF-7 cells. **Methods:** Cytotoxic activity was evaluated in the MCF-7 and MCF-10A cell lines using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay after 72 h of treatment, with determination of half maximal inhibitory concentration (IC_{50}) values and selectivity index (SI). The effects of CV2 on cell cycle progression and apoptosis in MCF-7 cells were assessed by flow cytometry after 48 h of treatment with CV2, following propidium iodide or Annexin V-FITC/propidium iodide (PI) staining, respectively. Data are presented as mean ± standard error of the mean (SEM) and were analyzed using one-way ANOVA followed by Tukey's post hoc test ($p < 0.05$). **Results:** CV2 exhibited greater cytotoxicity in MCF-7 cells (IC_{50}: 4.63 ± 0.16 μM) than in non-tumoral MCF-10A cells (IC_{50}: 44.09 ± 1.00 μM), resulting in a selectivity index of 9.69. In MCF-7 cells, a significant increase in the percentage of cells in the sub-G1 population was observed after treatment with CV2 at 5 μM (31.77 ± 4.93%) and 10 μM (11.29 ± 0.12%), $p<0.05$ for both, relative to control (3.50 ± 0.10%). Additionally, CV2 treatment significantly increased the percentage of Annexin V-FITC-positive cells at 5 μM (27.78 ± 2.17%) and 10 μM (28.67 ± 1.19%), together with Annexin V-FITC/PI-double-positive cells (5 μM: 22.38 ± 1.32%; 10 μM: 15.83 ± 1.72%), $p<0.05$ for all, relative to control values (0.57 ± 0.10% and 3.56 ± 0.69%, respectively). **Conclusion:** CV2 exhibited promising selective cytotoxicity in MCF-7 human breast adenocarcinoma cells. The increased sub-G1 population indicated DNA fragmentation and suggested apoptosis, further supported by Annexin V/PI staining. Collectively, these findings reinforce the antitumor potential of CV2 and support its further investigation as a candidate for breast cancer therapy. **Financial support:** CAPES, CNPq e FAPESQ- PB.

10.072 **APT20TTMG Exhibits Antiglioblastoma Activity by Inducing Intrinsic Apoptosis and Restoring Dysregulated Splicing-Related Gene Expression in U-87 MG Cells**. Silva DKC[1,2], Oliveira VS[2,3], Lobo EB[2,3], Nogueira ML[2], Soares ES[4], Sinatti VVC[4], Silva JC[4], Bottos RM[4], Leal CBQS[4], Meira CS[1,2,3] [1]UNEB-BA, Salvador, [2]SENAI CIMATEC-BA, Salvador, [3]Fiocruz-BA, Salvador, [4]Aptah Bio Inc., San Carlos, CA, USA.

Introduction: Glioblastoma (GBM) is the most prevalent and aggressive primary brain tumor in adults. The current standard treatment involves maximal surgical resection followed by radiotherapy and chemotherapy, particularly temozolomide (TMZ). However, GBM remains associated with poor outcomes, with a median survival of approximately 14 months and significant impairment of quality of life. Therefore, new therapeutic strategies are urgently needed. Aberrant RNA splicing has emerged as a critical mechanism supporting tumor progression and survival, making U1 snRNP-associated splicing pathways potential therapeutic targets. APT20TTMG is a synthetic single-stranded cDNA oligonucleotide designed to bind U1 snRNPs, aiming to induce cytotoxic effects. **Objectives:** To investigate the cytotoxic and antiproliferative effects of APT20TTMG and characterize its cellular and molecular effects in U-87 MG glioblastoma cells. **Methods:** The cytotoxic effect of APT20TTMG was evaluated using the MTT assay at 0.3, 3, and 30 µM after 96 and 144 h of treatment. Cell proliferation was assessed by the sulforhodamine B (SRB) assay under the same conditions. Cell death patterns were analyzed by flow cytometry using Annexin V-FITC/PI staining at 2.5, 5, and 10 µM. The expression of apoptosis- and splicing-related genes was evaluated by RT-qPCR after 144 h of treatment with 3 µM APT20TTMG. **Results:** After 96 h of treatment, APT20TTMG reduced U-87 MG cell viability by approximately 4%, 20%, and 32% at concentrations of 0.3, 3, and 30 µM, respectively. The antiproliferative effect was more pronounced, reaching approximately 20%, 42%, and 66% at the same concentrations. After 144 h, a similar pattern was observed, with cytotoxicity of approximately 5%, 16%, and 25%, and antiproliferative effects of 32%, 58%, and 61% at 0.3, 3, and 30 µM, respectively. These findings indicate that APT20TTMG exhibits a stronger antiproliferative than cytotoxic effect, suggesting a predominantly cytostatic profile. APT20TTMG induced apoptosis after 96 h, increasing Annexin V-positive cells by approximately three-fold at the highest concentration tested (10 µM). After 144 h, APT20TTMG modulated 13 out of 14 apoptosis-related genes analyzed, increasing the expression of APAF1, CASP3, CASP6, CASP7, CASP9, CYCS, and TP53, while reducing anti-apoptotic genes such as BCL2 and BCL2L1. Consistent with its proposed mechanism of action involving U1 snRNP modulation, APT20TTMG downregulated all 15 evaluated genes associated with this pathway, including SNRNP70, SNRPA, SNRPB, SNRPC, SNRPD2, SNRPD3, SNRPF, SNRPG, SNRNP200, PRPF8, SRSF3, HNRNPA1, and HNRNPA2. **Conclusion:** APT20TTMG exhibited cytostatic activity, induced intrinsic apoptosis, and modulated apoptosis- and splicing-related gene expression, highlighting its potential as a therapeutic strategy for GBM. **Acknowledgments:**: CAPES and FINEP

10.073 **B4OCH3 Reduces Colorectal Cancer Cell Viability and Inhibits Tube Formation in HUVECs**. Oliveira MP, Ribeiro RMS, Rodrigues SS, de Sá RE, de Castro LTS, Machado FS, Pérez CN, Valeze AB, Farsky SHP, Scharf PRS, Marinho-Filho JDB, Araújo AJ UFDPar, Lab Cultura Celular do Delta, Brazil, UFG, Instituto de Química, Brazil, IFMT-Cuiabá, Brazil, USP, Lab Inflamação e Imunotoxicologia, Brazil.

Introduction: Colorectal cancer (CRC) is one of the leading causes of cancer-related mortality worldwide and remains a major clinical challenge due to high recurrence rates and the adverse effects associated with conventional therapies. Chalcones and their derivatives have attracted considerable attention because of their anti-inflammatory, antiproliferative, cell cycle-arresting, and antiangiogenic properties. In this context, the synthesis of bis-chalcones has emerged as a promising strategy to enhance these biological activities and expand their mechanisms of action. **Objectives:** To investigate the antitumor effects of the symmetric bis-chalcone B4OCH3 in CRC cells and its antiangiogenic activity in HUVECs by evaluating viability, proliferation, clonogenicity, morphology, subcellular organization, and tube formation. **Methods:** HCT-116 cells were treated with B4OCH3 (0.66-84.9 µM) for 24, 48, and 72 h. Metabolic viability was evaluated by MTT assay under continuous and intermittent exposure conditions. Membrane integrity and clonogenic potential were assessed using trypan blue exclusion and clonogenic assays, respectively. Morphological changes were analyzed by panoptic staining and immunofluorescence (IF) targeting the nucleus, endoplasmic reticulum, actin cytoskeleton, and mitochondria. Antiangiogenic activity was investigated through tube formation assay in HUVECs. **Results:** B4OCH3 reduced metabolic viability in a time- and concentration-dependent manner, with IC50 values ranging from 15.1 µM (24 h) to 11.5 µM (72 h) under continuous exposure, and from 32.3 µM (3 h) to 11.9 µM (48 h) under intermittent exposure. Trypan blue exclusion demonstrated a reduction in viable cell number without a proportional increase in non-viable cells. Morphological evaluation revealed dose-dependent morphological alterations, including reduced cell density, cytoplasmic retraction and nuclear condensation, and the presence of apoptotic bodies. IF analyses demonstrated nuclear condensation, endoplasmic reticulum stress, actin cytoskeleton disorganization, and perinuclear mitochondrial redistribution. Clonogenic assay showed marked reductions in colony formation to 68%, 38%, and near-complete inhibition at 7.5, 15, and 30 µM, respectively. In HUVECs, B4OCH $_3$ inhibited tube formation in a concentration-dependent manner, leading to collapse of the capillary-like network at 30 µM without significant cytotoxicity (cell viability ~95%), indicating a selective antiangiogenic effect. **Conclusion:** B4OCH3 reduced viability, proliferation, and clonogenic capacity of HCT-116 cells in a time- and concentration-dependent manner, while inducing morphological alterations consistent with programmed cell death. In addition, the compound exhibited selective antiangiogenic activity in HUVECs, supporting a dual-action profile with promising therapeutic potential against colorectal cancer. **Financial support:** CAPES; CNPQ; INCT BioNat; INCT Polysaccharides and INCT Nature and FAPESP.

10.074 **PD-L1 Gene Editing Modulates Proliferation and Response to Compounds in a Cellular Model of prostate cancer**. Pessoa CÓ[1], Manso MP[2], Correia EM[2], Scandolara TB[1], Pinheiro DP[3], Mota JA[1], Sales SLA[1], Maranhão SS[1], Vieira Neto JB[1], Gress LSB[1], Pereira JVM [1], Furtado GP[3], Bonamino MH[2], Furtado CLM[4] [1]NPDM-UFC, Drug Research and Development Center, Fortaleza, Ceara, Brazil; [2]INCa, Research Center, Rio de Janeiro, Rio de Janeiro, Brazil; [3]Fiocruz-CE, Fortaleza, Ceara, Brazil; [4]UFMG, Belo Horizonte, Minas Gerais, Brazil

Immunotherapy based on immune checkpoint inhibitors, such as those acting on the PD-1/PD-L1 axis, has been widely used in various types of tumors. Overexpression of PD-L1 (programmed death-ligand 1) in cancer cells inhibits the activation and proliferation of T lymphocytes by interacting with the PD-1 (programmed cell death protein 1) receptor, favoring immune evasion. In metastatic castration-resistant prostate cancer (mCRPC), anti-PD-L1 monotherapy has limited efficacy, although combinations with other agents show benefits in advanced tumors and/or those with a high mutational burden. Despite the clinical impact in other tumors, the compensatory mechanisms related to the action of PD-L1 in prostate cancer have been little explored, as have the mechanisms of resistance and tumor survival. In this study, PD-L1 gene editing in mCRPC cells (DU-145) was performed using the CRISPR/Cas9 technique, with the use of *in silico* validated sgRNA. The edited cells (PD-L1$^-$) were evaluated by flow cytometry and separated by sorting. PD-L1 editing was confirmed by Sanger sequencing and quantitative PCR. The effects of editing were analyzed based on the cell proliferation, the MTT assay to analyze the response to chemotherapeutic agents (doxorubicin, paclitaxel, cabazitaxel, and docetaxel) and the experimental compound +(-)PTC, followed by the cell cycle assay with these compounds. In sequencing, thymine addition was observed at position 274, and the relative expression of PD-L1 in the edited lineage was reduced by ~50% ($p<0.005$) compared to the unedited lineage (2.5). The PD-L1$^-$ lineage showed slower duplication (62h30min) compared to PD-L1+ (33h27min). MTT assay data showed different IC50 values between the PD-L1+ and PD-L1$^-$ lines, respectively: i) doxorubicin: 403.5 nM and 173.8 nM; ii) paclitaxel: 28.56 nM and 8.32 nM; iii) docetaxel: 4,57 nM and 7,97 nM; iv) cabazitaxel: 9.93 nM and 18 nM; and (v) +(-)PTC: 13.54 µM and 23.36 µM. The EC50 values of the compounds doxorubicin, paclitaxel, and +(-)PTC were statistically significant, with $p < 0.05$. The controls for each cell line and the treatment groups showed statistical significance, demonstrating that the taxanes and the doxorubicin caused a G2/M arrest. Comparing to each other, only cells treated with doxorubicin showed a statistically significant difference in the G1 phase among the cell lines, leading to a greater reduction in the percentage of cells in G1 in the PD-L1- cell line compared to the PD-L1+ cell line These results showed that PD-L1 gene editing was effective, promoting reduced proliferation, altered protein profile, and modulation of drug response, suggesting the need to investigate the mechanisms of tumor resistance related to this checkpoint.

10. DOHaD and Developmental Biology

10.002FR **Maternal Protein Restriction Shapes Hepatic Metabolic Trajectories During Aging in a Sex-Specific Manner**. Vitali PM, Ribeiro IT, Maciel FA, Barata LA, Lemos LS, Fioretto MN, Justulin LA IBB-Unesp-Botucatu, Cellular and Molecular Biology Dept

Introduction: Epidemiological and experimental evidence demonstrates that exposure to stressors during pregnancy and lactation can impair the organ- specific physiology of the offspring, increasing susceptibility to the development of non-communicable diseases. This scenario is encompassed by the Developmental Origins of Health and Disease (DOHaD) concept and is further supported by Maternal Protein Restriction (MPR), a condition associated with deleterious alterations in hepatic metabolism that may differ according to sex. **Objectives:** We evaluated and compared the metabolic profiles of aged male and female rats exposed to MPR, with special emphasis on sex-specific effects on energy metabolism. **Methods:** Sprague Dawley rats were separated into two groups: Rats born from mothers fed a normoprotein diet (CTR, 17% protein) or a hypoprotein diet (GLLP, 6% protein) during gestation and lactation. After weaning, the rats were fed a normoprotein diet until postnatal day (PND)540, when they were euthanized and the livers collected for morphological, metabolic (n=8) and molecular analysis (n=6). The Shapiro-Wilk test was used for normality, with subsequent Student's t-test or Mann-Whitney test, considering significance when $p<0.05$. **Results:** Morphological analyses revealed a significant increase in perilobular inflammatory foci in GLLP male offspring ($p<0.0001$), whereas no such alteration was observed in females, suggesting greater hepatic cellular stress in males. Collagen deposition and reticular fiber organization were not affected in either sex. Serum levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine, urea, glucose, and total cholesterol showed no significant differences between groups. RT-qPCR analyses demonstrated reduced expression of citrate synthase (Cs; $p=0.0202$) and pyruvate dehydrogenase (Pdha; $p=0.0317$) genes in GLLP males, while female offspring remained unaffected, indicating a sex-specific impairment of hepatic energy metabolism and tricarboxylic acid cycle regulation. Expression levels of peroxisome proliferator-activated receptor alpha (Pparα) and gamma (Pparγ) were unchanged in both sexes. **Conclusion:** Taken together, these findings demonstrate that maternal protein restriction exerts sex-specific long-term effects on hepatic physiology during aging. Male offspring exhibited greater susceptibility to hepatic alterations, characterized by increased cellular stress and disruptions in glucose-related energy metabolism, whereas female offspring appeared comparatively protected. These results highlight the importance of MPR as a developmental programming factor influencing liver health and metabolic resilience later in life, with potential implications for healthy aging and longevity. **Financial support** FAPESP Process nº 2023/13012-9.

10.003FR **Perinatal Metabolic Programming: Impact of Maternal Protein Restriction on the Rat Hypothalamic Proteome Across the Lifespan**. Basso CBP, Fioretto MN, Barata LA, Lemos LS, Ribeiro IT, Maciel FA, Justulin LA IBB-Unesp-Botucatu, Cellular and Molecular Biology Dept, Brazil

Introduction: The DOHaD (Developmental Origins of Health and Disease) concept posits that adverse conditions during vulnerable periods of development, such as pregnancy and lactation, have lasting effects throughout life. Maternal protein restriction (MPR) during pregnancy and lactation is a well-established model of perinatal insult that affects neurodevelopment, including the hypothalamus, a region fundamental to energy balance, metabolic homeostasis, and neuroendocrine control. **Objectives:** We established and compared the hypothalamic proteomic profiles of males and females to identify potential biomarkers, molecular pathways affected by MPR. **Methods:** Sprague Dawley rats from mothers fed a normoprotein (CTR, 17%) or low-protein (GLLP, 6%) diet during gestation/lactation were euthanized at postnatal day (PND)21. Hypothalamic samples were analyzed via nanoUPLC-MS/MS (MSE), and data were processed in PLGS/UniProt to identify differentially expressed proteins (DEPs) between groups and sexes (thresholds: $p < 0.05$ for downregulation; $p > 0.95$ for upregulation). Functional analysis and pathway enrichment of DEPs were performed *in silico* using KOBAS 3.0 and Enrichr. **Results:** The results demonstrated significant basal sexual dimorphism in the hypothalamus when comparing male and female CTR groups, exhibiting distinct expressions in the cell cycle, cytoskeletal architecture, and neuromodulatory pathways such as dopaminergic phosphatases and opioids. Males and females GLLP groups developed divergent proteomic adaptations. While males showed structural alterations associated with the immune system, females showed an adaptive profile related to neuroplasticity, possibly modulated by protective hormonal effects. Males presented upregulated synaptic pathways related to the vesicular cycle, oxytocin signaling, and long-term depression, in contrast to downregulated pathways associated with metabolic processes of membrane trafficking and GTPase activity, indicating potential energy impairment, mitochondrial dysfunction, and greater immunological vulnerability. On the other hand, females showed upregulation of developmental pathways, cytoskeletal remodeling such as Rho GTPases, the innate immune system, and proteostasis, demonstrating a profile of structural resilience and neuroplasticity. However, they presented downregulation of Golgi-endoplasmic reticulum trafficking pathways, signaling possible endoplasmic reticulum stress and potential resistance to leptin and insulin, as well as calcium channel and adenylate cyclase pathways, suggesting lower responsiveness to neuroendocrine stimuli related to metabolism and reproduction. **Conclusion:** In conclusion, perinatal malnutrition programs the hypothalamus in a sex-dependent manner early in life, highlighting the need for sex-specific approaches in metabolic programming research.

10.005FR **Maternal Protein Restriction Reprograms the Pituitary Gland in a Sex-Specific Manner from Early Life to Old Age**. Cordeiro GM, Fioretto MN, Barata LA, Lemos LS, Maciel FA, Ribeiro IT, Justulin LA IBB-Unesp- Botucatu, Cellular and Molecular Biology Dept, Brazil

Introduction: Global food insecurity affects more than 820 million people, and protein deficiency remains common among pregnant women in developing countries. According to the Developmental Origins of Health and Disease (DOHaD) concept, maternal undernutrition during critical developmental windows can permanently program offspring physiology, increasing susceptibility to chronic non-communicable diseases (NCDs). This study investigated the effects of maternal protein restriction (MPR) on pituitary morphology, endocrine function, and metabolism in male and female offspring during early life and aging. **Methods:** Sprague-Dawley rats received either a normoprotein (17%, CTR) or low- protein (6%, GLLP) diet throughout gestation and lactation. Offspring were evaluated at postnatal day (PND) 21 and PND540. Histological, molecular, hormonal, and metabolic analyses were performed using standard statistical approaches ($p<0.05$). **Results:** No morphological changes were observed in early life in either sex, during aging, both sexes of GLLP rats showed alterations in chromophil and chromophobe cells ($p=0.0020$M; $p=0.0003$F), and males rats in the total collagen area ($p=0.044$). In gene expression analyses, GLLP males showed an increase in the expression of Pparα ($p=0.0075$) and Prl ($p=0.0002$) early in life, without significant changes in Igf2 and NeuroD4 levels. However, during aging, the expression of all genes evaluated did not differ from the control group, suggesting a gene adaptation throughout life. In contrast, females showed the opposite pattern: while no changes in gene expression were observed early in life, aging showed a reduction in the expression of Pparα ($p=0.0268$), Prl ($p=0.0086$), NeuroD4 ($p=0.0449$), and Igf2 ($p=0.0449$). Observing hormonal parameters by ELISA in male rats, early in life, we found a decrease in T3 ($p=0.002$) and T4 ($p=0.0036$), demonstrating a thrifty phenotype generated by RPM. Meanwhile, in aging, males showed an increase in T4 ($p=0.0166$), aldosterone ($p=0.0005$), and corticosterone ($p=0.0060$). Biochemical tests were performed to evaluate markers of kidney injury, insulin resistance, and cellular stress in aging. In males, we observed increased glucose ($p=0.0205$) and creatinine ($p=0.0256$), while females showed stable parameters. **Conclusions:** MPR induces long-term, sex-specific effects on pituitary biology and systemic metabolism. Males exhibit an early thrifty phenotype followed by endocrine and metabolic disturbances during aging, whereas females develop age-related molecular impairments suggestive of pituitary dysfunction and reproductive senescence. These findings reinforce the importance of maternal nutrition in shaping lifelong endocrine health and support public health strategies aimed at reducing food insecurity during pregnancy. Funding: FAPESP (2024/04347-0).

10.006FR **Effects of Maternal Resistance Training on Growth and Working Memory in Offspring Prenatally Exposed to Valproic Acid**. Barros MRM[1], Silva RAA[1], Nelo SRB[1], Oliveira MCMC[1], Martins MVA[1], Lima RS[2], Silva MLB[2], Pereira TKM[1], Antonio-Santos J[2], Da Silva Aragão R[2] [1]UFPE, PPG Nutrition, Brazil; [2]UFPE, Physical Education

Introduction: Prenatal valproic acid (VPA) exposure disrupts neurodevelopment, altering growth and cognition. Maternal exercise may modulate these developmental outcomes. **Objective:** To evaluate the effects of maternal resistance training during pregnancy on physical growth, somatic development, and working memory in VPA-exposed offspring. **Methods:** Pregnant Wistar rats were divided into four groups: control-untrained (CT-U), control-trained (CT-T), VPA-untrained (VPA-U), and VPA-trained (VPA-T). On gestational day 12.5, dams received VPA (600 mg/kg i.p.) or saline. Training consisted of ladder climbing (5 days/week; 50% max load in week 1, 80% in weeks 2-3). Offspring weight, head measurements, and T-maze working memory (PND 28-31) were evaluated. **Results:** At birth, CT-T males had a greater laterolateral head axis than CT-U (12.15 ± 0.55 vs. 10.83 ± 0.63 mm, p=0.04). On PND 21, VPA-U males weighed less than CT-U (48.29 ± 0.11 vs. 51.50 ± 0.16 g, p<0.0001). However, on PND 42, VPA-T males weighed more than VPA-U (188.56 ± 5.29 vs. 162.95 ± 1.60g, p=0.02). In females, VPA-T showed lower weight on PND 35 than CT-T (120.66 ± 2.69 vs. 133.01 ± 2.13g, p=0.03). Working memory was impaired in VPA-U males compared to CT-U (2.83 ± 0.60 vs. 5.25 ± 0.47 alternations, p=0.03). **Conclusion:** Maternal resistance training affected offspring growth sex-dependently: it enhanced male adolescent weight despite prenatal VPA exposure, but transiently reduced female weight. Additionally, prenatal VPA impaired male working memory. These findings suggest maternal resistance training modulates developmental trajectories after prenatal neurodevelopmental insults in a sex-specific manner.

10.007FR **Influence of Gestational Exposure to Valproic Acid on Growth, Physical Characteristics, and Motor Development in Rats**. Nelo SRB[1]; Silva RAA[1], Barros MRM[1], Oliveira MCMC[1], Martins MVA[1], Lima RS[2], Silva MLB[2], Pereira TKM[1], Antonio-Santos J[2], Da Silva Aragão R[2]. [1] UFPE, PPG Nutrition, Brazil; [2]UFPE, Physical Education, Brazil;

Introduction: Prenatal exposure to valproic acid (VPA) may alter neurodevelopmental processes, potentially affecting physical growth, somatic maturation, and early motor development. Evaluating these outcomes may improve our understanding of developmental trajectories following early insults and help identify early markers of neurodevelopmental disorders. **Objective:** To evaluate growth, physical development, and motor developmental parameters in the offspring of dams exposed to VPA during pregnancy. **Methods:** Pregnant Wistar rats received an intraperitoneal injection of valproic acid (600 mg/kg), dissolved in 0.9% saline, on gestational day 12.5. Control dams received an equivalent volume of saline solution. After birth, litters were standardized, and offspring were assessed for somatic growth, physical characteristics, and developmental milestones. Evaluated parameters included body weight, body length, tail length, head dimensions, eye opening, ear unfolding, and performance in the open surface posture test. **Results:** Male offspring exposed to VPA exhibited lower body weight on postnatal days 14 and 21 compared with controls (PND14: VPA = 29.98 ± 1.04 g vs. CT = 32.66 ± 0.70 g; PND21: VPA = 48.29 ± 0.11 g vs. CT = 51.50 ± 0.16 g). No significant differences were observed between groups regarding body length, tail length, anteroposterior or laterolateral head dimensions, or in female offspring. Male VPA-exposed offspring showed earlier eye opening (postnatal day 14) compared with controls (postnatal day 15), whereas no differences were observed in females. Ear unfolding was not affected by prenatal VPA exposure. In the open surface posture test, female offspring exposed to VPA exhibited a longer latency to move across the surface than controls (VPA 20.7 ± 5.37 s vs. CT 9.0 ± 0.0 s). **Conclusion:** Prenatal exposure to VPA affected growth and developmental parameters in offspring, particularly in males, as evidenced by reduced body weight and earlier eye opening. Additionally, motor performance was impaired in female offspring. These findings suggest that gestational VPA exposure influences early developmental trajectories and further support the validity of this model for investigating mechanisms underlying neurodevelopmental disorders.

10.008FR **Maternal Protein Restriction Compromises Structural, Electrophysiological, and Molecular Cardiac Parameters in Female Rat Offspring During Early Life**. Lemos LS, Gomes LC, Fioretto MN, Barata LA, Ribeiro IT, Maciel FA, Justulin LA IBB-Unesp-Botucatu, Cellular and Molecular Biology Dept

Introduction: Maternal malnutrition is a major risk factor for adverse health outcomes in offspring, including cardiovascular disorders. According to the Developmental Origins of Health and Disease (DOHaD) concept, adverse conditions during critical developmental windows can induce long-lasting physiological adaptations that increase disease susceptibility later in life. Among the experimental models used to investigate these mechanisms, maternal protein restriction (MPR) has been associated with metabolic, cardiovascular, and hypertensive phenotypes in offspring, some of which emerge early in life. **Objectives:** Therefore, this study evaluated the effects of MPR on the cardiovascular morphophysiology of female offspring at postnatal day 21 (PND21). **Methods:** Pregnant rats were allocated to either a Control group (CTR), receiving a normoprotein diet (17% protein), or a Gestational and Lactational Low-Protein group (GLLP), receiving a low-protein diet (6% protein) throughout gestation and lactation. At PND21, female offspring underwent electrocardiographic assessment and were subsequently euthanized for morphological, molecular, and oxidative stress analyses (n=5 per group). The Shapiro-Wilk normality test was used, followed by Student's t-test for parametric data or the Mann-Whitney test for nonparametric data, with $p<0.05$ considered statistically significant. **Results:** Female offspring from the GLLP group exhibited reduced body weight and body length, whereas absolute heart weight was preserved, resulting in increased relative heart weight and suggesting disproportionate somatic growth. Electrocardiographic analysis revealed a shortened P–R interval and decreased heart rate, indicating early alterations in cardiac electrical activity. Morphologically, cardiomyocyte architecture was preserved; however, reduced nuclear width and increased collagen and elastin deposition were observed, in association with reduced pro-MMP-2 activity, indicating early extracellular matrix remodeling but without significant changes in reticular fibers. At the molecular level, GLLP offspring exhibited reduced PRDX3 expression, accompanied by decreased catalase (CAT) activity, reduced glutathione (GSH) levels, and lower lipid peroxidation (TBARS), suggesting alterations in redox regulation and antioxidant homeostasis during early cardiac development. **Conclusion:** Collectively, these findings demonstrate that MPR induces early structural, molecular, oxidative, and electrophysiological alterations in the hearts of female offspring. These adaptations may represent early programming events that increase susceptibility to cardiovascular dysfunction later in life, reinforcing the importance of maternal nutrition in shaping cardiovascular health across generations.

10.009FR **Offspring Voluntary Physical Activity on Skeletal Muscle Weight in a Maternal Obesogenic**. Lopes IGT[1], Silva PHS[1], Vasconcelos BHA[2]; Silva AA[2]; Silva BA, Bandeira VCA[1]; Melo SM[2], Rocha EP[2], Casi EJ[1] [1]UFPE-Vitória Academic Center, Vitória de Santo Antão – PE, Brazil. [2]UFPE, Center of Health Sciences, Nutrition Dept, Recife – PE, Brazil.

Over the past decades, ultra-processed food consumption in Brazil has risen substantially, now approaching one-third of the calories consumed by the population, according to national dietary surveys. This dietary shift has been linked to a broad range of adverse health outcomes and provides important context for experimental models investigating how maternal nutrition shapes offspring metabolism. Fetal metabolic programming investigates how stimuli during critical developmental periods (gestation and lactation) can cause lasting structural and functional alterations in offspring, often manifesting only in adulthood. Maternal exposure to obesogenic diets is central to this field, since nutritional composition during these windows can directly influence metabolically active tissues such as skeletal muscle. Importantly, the obesogenic diet used here does not represent established maternal obesity, but rather a high-fat dietary pattern. Dams received either a Maternal Control Diet (DCMat), based solely on the standard AIN-93G formulation (18% fat), or a Maternal Obesogenic Diet (DOMat, 39% fat) additionally supplemented with condensed milk, offered exclusively to the DOMat group. Condensed milk, an ultra-processed product rich in saturated fat and simple carbohydrates, is linked in the literature to insulin resistance, altered body composition, and impaired muscle development in offspring. Voluntary physical activity has been studied as environmental enrichment that can modulate skeletal muscle hypertrophy and potentially protect against adverse metabolic programming. This study evaluated whether the maternal obesogenic diet, combined with different offspring activity levels (lightly active or active), affects wet and dry muscle weight across muscle groups. After weaning, all offspring received standard chow, isolating maternal programming from direct postnatal diet effects. From day 30, animals had voluntary running-wheel access. On day 40, wheels of the lightly active animals were locked, classifying them as less active, while active animals kept their wheels rolling normally. Four groups were formed: DO+ (active, obesogenic), DO- (lightly active, obesogenic), DC+ (active, control), and DC- (lightly active, control). Soleus, EDL, tibialis anterior, and gastrocnemius muscles were weighed wet, then oven-dried (60°C, 72h) for dry weight. No significant differences in wet or dry weight were found for any muscle across groups, regardless of maternal diet or activity level. This converges with other findings from the same study, where neither low activity nor the obesogenic diet produced the expected metabolic impairments, suggesting that even minimal voluntary activity may attenuate programming effects. **Keywords:** Maternal obesogenic diet. Muscle Hypertrophy. Voluntary exercise. Developmental plasticity. Wistar rats.CEUA No. 116/2024.

10.010FR **Effects of Moderate-Continuous Training on Cardiac Mitochondrial Bioenergetics and Redox Status in Rats Subjected to Early-Life Overnutrition**. Silva JTA, Fernandes MSS, Correia-Filho RC, Melo TSM, Fernandes MP, Lagranha CJ UFPE, Graduate Program in Nutrition, Physical Activity, and Phenotypic Plasticity, Brazil; UEFS, Brazil

Background: Nutritional imbalances during critical developmental periods, such as lactation, can induce metabolic alterations that impair cardiac mitochondrial function, compromising energy homeostasis and ATP production. Post-weaning moderate-intensity aerobic exercise may act as a non-pharmacological strategy to improve mitochondrial function and restore cellular REDOX balance. **Objectives:** Evaluate the effects of moderate-intensity continuous aerobic training on mitochondrial oxygen consumption, citrate synthase enzymatic activity (CS), and REDOX profile (NAD+/NADH ratio) in the cardiac tissue of rats subjected to early-life overnutrition during the suckling period. **Methods:** Male Wistar rats were standardized on postnatal day 3 into normal litters (N, 9 pups/dam) or overnourished litters (O, 3 pups/dam), confirmed by LEE Index, during lactation. At weaning (postnatal day 21), animals were subdivided into non trained control and overnourished (NTC, NTO) and trained control and overnourished (TC, TO) groups. Trained rats underwent a 4-week individualized running program on a modified rodent treadmill (50% of maximal physical velocity, 60 min/day, 5 days/week). On day 54, the left ventricle was removed and isolated mitochondria were prepared by differential centrifugation. Mitochondrial respiration was measured using a Clark-type oxygen electrode with complex I substrates (glutamate/malate) followed by ADP stimulation. CS activity and cellular NAD+, NADH, and the NAD+/NADH ratio were assessed in spectrophotometer. Data were analyzed using Two-way ANOVA with Tukey's post-hoc test ($p<0.05$). Ethics Committee CEUA/UFPE: 03/2022. **Results:** Early-life overnutrition impaired mitochondrial function in the left ventricle, as regarding mitochondrial respiration, the basal state, state 2 (ST2), we observed that NTO animals had a higher respiratory rate compared to NTC animals ($p=0.029$). As for ADP-stimulation (ST3), resting state (ST4) and uncoupled state (maximal velocity of respiration in the CCCP presence) also showed no significant variations between the groups. In addition, the ratio between the ST3 and ST4 states was reduced in NTO animals compared to NTC animals ($p=0.04$). No significant differences were found in absolute NAD+ and NADH levels in all groups analyzed; however, a significant interaction was observed for the NAD+/NADH ratio in the group of NTO group compared with NTC group ($p=0.0362$). CS activity was higher when comparing the TC and NTC groups ($p=0.003$) but, when comparing the CS activity between NTC and NTO groups, it was observed that it showed a higher activity in the NTC group ($p=0.003$), analyzing the TC and NTO groups, we observed that the TC group increased CS activity ($p=0.02$). **Conclusion:** Early-life overnutrition impairs cardiac mitochondrial function efficiency and alters cellular aerobic and oxidative pathway. However, post-weaning continuous aerobic training serves as an effective therapeutic strategy to mitigate these disruptions, directly enhancing mitochondrial oxygen consumption and restoring cellular NAD+/NADH REDOX balance within the left ventricle. We would like to thank FACEPE, CNPq, and CAPES for their funding.

10.011FR **Effects of a Low-Protein or Obesogenic Diet during Pregnancy and Lactation on Body Mass, Fasting Glycemia, Food Intake and Indirectly Assessed Offspring Milk Consumption**. Vasconcelos BHA[1], Silva BA[2], Silva PHE[2], Lopes IGT[2], Bandeira VCA[2], Araújo FWC[1], Prieto SG[1], Rocha EP[1], Mousinho EM[1], Carreteiro EJC[1], Santos JVM[1], Vasconcelos DAA[1,2] [1]UFPE, Center of Health Sciences, Nutrition Dept, Recife – PE, Brazil. [2]UFPE-CAV, Vitória de Santo Antão – PE, Brazil.

Introduction: Both a low-protein diet and a high-fat diet during pregnancy and lactation are recognized as nutritional insults capable of programming the offspring for metabolic alterations in adulthood, according to the concept of the Developmental Origins of Health and Disease (DOHaD). However, the maternal metabolic profile resulting from these two models still lacks direct comparative characterization within the same experimental design. **Objectives:** To characterize the maternal phenotype of Wistar rats subjected to a low-protein or an obesogenic diet during pregnancy and lactation, regarding body mass, fasting blood glucose, food intake, and indirect maternal milk consumption. **Methods:** The study was approved by the Ethics Committee on the Use of Animals - UFPE (Nº 116/2024). Female Wistar rats were allocated into three groups (n=6/group): DCMat (Control Diet: 3.6 kcal/g, 19% PRO, 63% CHO, 18% FAT), DHMat (Low-Protein Diet: 3.6 kcal/g, 9% PRO, 73% CHO, 18% FAT), and DOMat (Obesogenic Diet: 4 kcal/g, 18% PRO, 43% CHO, 39% FAT + condensed milk), maintained on their respective diets from mating until the end of lactation (day 21). Maternal body mass was measured on days 1, 7, 14, and 21 of pregnancy and lactation; fasting blood glucose was measured on day 14 of pregnancy; food intake was monitored daily; and indirect offspring milk consumption was estimated from the change in offspring body mass (final minus initial weight) on days 14 and 21 of lactation. Data were analyzed by two-way ANOVA followed by Tukey's post hoc test, $p<0.05$. **Results:** Fasting blood glucose did not differ among groups, and maternal body mass did not differ during pregnancy. During lactation, however, DHMat dams showed reduced body mass compared with DCMat at all time points, while DOMat did not differ from DCMat. DOMat dams showed higher caloric and fat intake than DCMat throughout pregnancy and lactation, while DHMat dams showed lower protein intake than DCMat in both phases. The most notable finding concerned indirect milk consumption: on day 14 of lactation, DHMat offspring consumed less milk than DCMat offspring, with no difference for DOMat. By day 21, this pattern reversed, both DHMat and DOMat offspring showed significantly higher indirect milk consumption than DCMat offspring, indicating a late, compensatory rise in maternal milk demand associated with both dietary models. **Conclusion:** The low-protein and obesogenic models generate distinct maternal phenotypes compared with the control group regarding body mass and energy intake, without altering fasting glucose, and both drive a time-dependent, late increase in indirect milk consumption by the offspring, supporting their value as complementary experimental models for the study of maternal-fetal metabolic programming.

10.012FR **Maternal Protein Restriction Reprograms Placental Proteomic Networks and Ultrastructure: Insights into Early Developmental Adaptation**. Barata LA[1], Fioretto MN[1], Magosso N[1], Ferreira MR[2], Maciel FA[1], Felipe VAA[1], Ribeiro IT[1], Dos Santos DC[1], Justulin LA[1 1]IBB-Unesp-Botucatu, Dept Cellular and Molecular Biology, PPG in General and Applied Biology, Brazil. [2]Unesp-Botucatu, School of Medicine, Experimental Research Unit - Unipex, Molecular Genetics and Bioinformatics Lab, Brazil.

Introduction: The placenta is the central interface of the maternal–fetal unit, playing a pivotal role in fetal programming, epigenetic regulation, and the developmental processes that shape physiological responses throughout life. Maternal malnutrition is a major determinant of adverse developmental outcomes and is closely linked to the Developmental Origins of Health and Disease (DOHaD) paradigm. Among experimental models, Maternal Protein Restriction (MPR) is widely used to investigate how nutritional adversity disrupts placental function and programs offspring susceptibility to chronic diseases. **Objectives:** Here, we employed histological, ultrastructural, molecular, proteomic, and *in silico* approaches to comprehensively evaluate placental adaptations to MPR in rats. **Methods:** Sprague-Dawley rats (CEUA n°. 73761712240) were mated and, after confirmation of pregnancy, divided into two groups: control (CTR; 17% protein) and protein restriction (GLP; 6%). On gestational day 20 (GD20), placentas (n=5/group) were collected for morphological, proteomic, and ultrastructural analyses (n=2/group). Statistical analysis included normality testing, followed by Student's t-test or Mann-Whitney test. Data were expressed as mean ± standard deviation ($p<0.05$). For proteomic analyses, proteins were considered upregulated when $p\geq0.95$ and downregulated when $p\leq0.05$. **Results:** MPR reduced the anogenital distance of offspring in both sexes (male: 2.82 ± 0.20; female: 1.44 ± 0.16) indicating altered developmental trajectories. Although placental weight was unaffected, placental efficiency increased in female fetuses (7.73 ± 1.34), suggesting compensatory adaptations to nutrient restriction. Morphological analyses revealed significant reductions in both the labyrinthine zone ($p=0.027$) and total placental area ($p=0.025$), while ultrastructural evaluation demonstrated cytoplasmic disorganization, increased vacuolization, mitochondrial abnormalities, and endoplasmic reticulum alterations. Proteomic analyses identified extensive remodeling of pathways involved in hormonal signaling, protein quality control, energy metabolism, oxidative stress responses, and cellular structural organization. In addition, the enrichment data indicated overload cholesterol metabolism, glycolysis/gluconeogenesis, ribosomal components, cytoskeleton, and congenital and anemia developmental associated disorders. **Conclusion:** Collectively, these findings demonstrate that MPR profoundly disrupts placental structure and function while triggering adaptive mechanisms aimed at preserving fetal growth under adverse intrauterine conditions. However, the marked proteomic reprogramming required to sustain placental homeostasis may itself contribute to fetal programming and increase susceptibility to long-term metabolic and developmental disorders. **Acknowledgments:**: FAPESP, CAPES, IBB UNESP, DBMOL Lab, BGA.

10.013FR **Early life Protein Restriction Impairs GLP-1-Induced Insulin Secretion Despite Increased Intra-Islet GLP-1 Production**. Oliveira KM[1], Silva-Junior JA[2], Carvalho MS[1], Bem KCP[1], Barbosa HCL[1], Carneiro, EM[1] [1]Unicamp, Obesity and Comorbidities Research Center (OCRC), Brazil; [2]Universidad Miguel Hernández, Instituto de Investigación en Biotecnología y Salud

Introduction: The gastrointestinal tract is the primary entry point for nutrients and synthesizes hormones involved in metabolic regulation, including glucagon-like peptide-1, which exerts insulinotropic and trophic effects on pancreatic beta cells. Dietary modifications, such as protein restriction, can directly influence gut function and intestinal hormone production, particularly during early stages of life. Thus, prolonged post-weaning protein restriction may contribute to the development of metabolic diseases such as type 2 diabetes and obesity, later in life. **Objectives:** This study investigated intestinal and pancreatic GLP-1 production, and its effects on beta-cell function. **Methods:** 30-day-old male C57BL/6J mice were divided to either a control (C) group, fed a normoprotein diet (14% protein), or a restricted (R) group, fed a hypoprotein diet (6% protein). Data were analyzed using the Shapiro–Wilk test, followed by Student's t-test or Mann–Whitney U test, P-value<0.05. **Results:** Undernutrition phenotype in R mice was confirmed by lower plasma albumin and total protein levels, reduced body weight gain, and decreased feed efficiency compared with C mice. Protein restriction also increased insulin sensitivity during the insulin tolerance test, as indicated by a 33% increase in the glucose disappearance rate. R mice demonstrated higher glucose tolerance during both the oral and mixed-meal tolerance tests (MMTT). During the MMTT, R mice exhibited higher plasma GLP-1 concentrations at 0 and 10 minutes; however, plasma insulin levels were decreased at these time points, indicating that insulinemia did not increase in response to elevated GLP-1. Then, a glucose stimulated insulin secretion was performed to assess the direct action of GLP-1 on insulin secretion. Both groups had similar insulin secretion under non-stimulatory 2.8 mM glucose. At 11.1 mM glucose, insulin secretion was reduced by 40% in R mice compared with C mice. Incubation with 11.1 mM glucose and 10 nmol exendin-4, a GLP-1 receptor agonist, increased insulin secretion by 77% in C islets; however, this stimulatory effect was attenuated in R islets, which exhibited a 54% reduction compared with C islets. These findings were confirmed by reduced insulin and GLP-1R fluorescence intensity in the pancreases of R mice. Protein restriction atrophied both the pancreas and pancreatic islets in number and area. Finally, evaluation of intra-islet GLP-1 production showed that isolated pancreatic islets from R mice had increased proglucagon and proprotein convertase subtilisin/kexin type 1 gene expression indicating higher GLP-1 production which was confirmed by increased total GLP-1 content in isolated islets and a twofold increase in the GLP-1-positive area/islet area compared with C mice. **Conclusion:** Prolonged post-weaning protein restriction induced metabolic adaptations characterized by increased glucose tolerance, likely due to enhanced insulin sensitivity. Additionally, protein-restricted mice exhibited resistance to GLP-1 action on insulin secretion, as elevated plasma GLP-1 levels and increased intra-islet GLP-1 production failed to increase insulin secretion. Animal Ethics Committee Approval: CEUA/UNICAMP protocol nº 5564-1/2020.
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10.014FR **Developmental Exposure to Phthalates and Nanoplastics Disrupts Hypothalamic Neuroplasticity, Metabolic Homeostasis, and Glial Remodeling in Aging Male Rats**. Fioretto MN, Magosso N, Souza PV, Moreira MF, Rocha VA, Pinha VC, da Silva Maria VLR, Justulin LA, Scarano WR. IBB-Unesp, Dept Cellular and Molecular Biology, Institute of Biosciences, Sao Paulo State University, Botucatu, SP, Brazil.

Introduction: Plastic pollution is a major global environmental and public health concern. As plastics degrade, they generate microplastics (MPs) and nanoplastics (NPs) that can enter the body and act as carriers of endocrine-disrupting chemicals, including phthalates. Exposure during critical developmental periods may adversely affect fetal programming and the function of central regulatory organs, such as the hypothalamus, leading to long-term health consequences. **Objectives:** We evaluated the effects of maternal exposure (gestation and lactation) to a phthalate mixture (PM) and/or NPs and investigated their consequences on the hypothalamus of male rats during aging. **Methods:** Pregnant Sprague–Dawley rats were exposed to PM (20 µg/kg/day - T1 or 200 mg/kg/day – T2), 100 nm NPs (1 mg/kg/day – T3), or their combination (T4 and T5) from gestation to PND21. Offspring were maintained until PND540, when hypothalamic tissues were collected for histological, molecular, and *in silico* analyses. Data were analyzed for normality (Shapiro–Wilk test) and compared using one-way ANOVA or Kruskal–Wallis tests, followed by appropriate post hoc analyses. Significance was set at p <0.05. **Results:** Our results revealed no significant alterations in general hypothalamic morphology and histopathological parameters, in addition to remodulation by matrix metalloproteinases. In T1, BDNF protein expression was reduced (p=0.0301) while vimentin (p=0.0608) and SLIT2 (p=0.0117) were increased, suggesting impaired neurotrophic support, glial response, and axonal guidance. In T2, increased SLIT2 (p=0.0399) expression indicated the activation of adaptive mechanisms associated with axonal guidance. Exposure to NPs alone (T3) resulted in reduced GLUT4 (p=0.0038) and p27 expression (p=0.0166), together with increased BDNF (p=0.0089), vimentin (p=0.0053), and SLIT2 (p=0.0031), suggesting impaired glucose sensing and cellular homeostasis accompanied by compensatory responses involving neuronal plasticity, axonal remodeling, and glial activation. The co-exposure groups exhibited a distinct pattern, characterized by reduced SLIT2 (p=0.0027) expression in T4 and by decreased SLIT2 (p=0.0066) combined with increased vimentin (p=0.0130) in T5, indicating disruption of neuronal connectivity and persistent glial activation. *in silico* analyses (Enrichr and ShinyGO; adjusted p <0.05) corroborated the enrichment of the identified biological pathways and cellular components. **Conclusion:** Developmental exposure to PM and/or NPs altered hypothalamic neuroplasticity and metabolic response, suggesting glial activation, impaired glucose sensing, and disrupted neuronal organization, emphasizing specific changes not only in neurons but also in glial responses.

10.015FR **Saturated Fat-Rich Diet Enhances Histone H3-lysine9 Acetylation and Lipid Metabolism in the Liver Following Perinatal Protein Undernutrition**. Simões-Alves AC, de Mello APFAC, Nogueira VO, Leandro CVG, Fernandes MP, Pirola L, Morio B, Costa-Silva JH. UFPE, Academic Center of Vitória Lab Nutrition, Physical Activity and Phenotypic Plasticity, Vitória de Santo Antão – PE, Brazil. UFPE, Lab General Biochemistry, Academic Center of Vitória, Molecular Biology and Exercise, Universidade Federal de Pernambuco-, Vitória de Santo Antão – PE, Brazil. Université Claude Bernard Lyon1, Laboratoire de Recherche en Cardiovasculaire, Métabolisme, Diabétologie et Nutrition, INSERM, Oullins, Lyon, France

A nutritional transition to high-fat diets is a well-known risk factor for developing overweight and metabolic dysfunction in the liver. Here, we investigated the effects of a diet high in saturated fatty acids (HL) in rats previously malnourished during the perinatal period on the modulation of key enzymes in glucose and lipid metabolism and the involvement of the histone acetylation. Pregnant Wistar rats received either a control (C; 19% protein) or low protein (LP; 8% protein) diet during gestation and lactation. At weaning, pups received either C or HL diets up to 90 days of life. The LP-HL group showed an increase in the protein content and enzymatic activities of hydroxyacyl-CoA dehydrogenase (β-Had, +80% and +218%, respectively, $p<0.05$) and citrate synthase (+73% and +191%, respectively, $p<0.05$). This group also showed an increase in the enzymatic activity of glucose-6-phosphate dehydrogenase (G6PDH, +96%, $p<0.05$) and of fatty acid synthase (FAS, +455%, $p<0.05$) when compared to C-C group. A significant increase in PPARγ gene expression (151%, $p<0.05$) and decrease in SIRT1 protein (-52%, $p<0.05$), which were associated to increased acetylation of histone H3-lysine 9(H3K9,> 6-fold , $p<0.05$ were also observed in the LP-HL group. Taken together, these data suggest that a switch to a diet high in saturated fatty acids at weaning in previously malnourished rats, strongly modulate liver lipid metabolism with a predominance of fatty acid anabolism. Higher histone acetylation in this situation might play a role possibly via the reduction of the histone deacetylase SIRT1. **Key words: Epigenetic. Malnutrition. Metabolism. Saturated fatty acids.**

10.016FR **NADPH Oxidase Participates of Intrauterine Growth Retardation and Nephrogenesis Impairment Induced by Maternal Inflammation**. Constantino TS, Veras AC, Farias JS, Lima NKS, Aires RS, Silva-Filho LF, Sant'Helena BRM, de Queiroz DB, Paixão AD, Vieira LD UFPE, UFRPE, IELUSC, UPE

Introduction: Maternal inflammation induces intrauterine growth retardation (IUGR), impairs nephrogenesis and programs hypertension at adult life. Albeit reactive oxygen species (ROS) have a physiologic role in gestation and organogenesis, enhanced ROS production mediated by NADPH oxidase activation may lead to adverse intrauterine development. **Objectives:** To investigate the role of NADPH oxidase in IUGR and nephrogenesis impairment induced by maternal endotoxemia in rats. Methods Lipopolysaccharide (LPS) was subcutaneously administered (0.5 mg/kg, sc) in pregnant rats at days 13, 15, 17 and 19 of gestation, in the absence and presence of the treatment with the NADPH oxidase inhibitor apocynin throughout entire gestation (100 mg/kg, drinking water). Experimental protocols were approved by the Animal Research Ethical Committee (CEUA-UFPE n. 42/15). **Results**: Maternal LPS administration induced IUGR evidenced by lower birthweight in parallel to elevation of NADPH oxidase activity in the placenta. LPS administration also decreased the (Na++K+)ATPase activity in the placenta, and impaired nephrogenesis, as evidenced by enlargement of nephrogenic zone, reduction of cell proliferation, and increased the ratio of Bax/Bcl-2 protein content. The apocynin treatment prevented LPS-induced IUGR, reduced superoxide anion production, recovered placental (Na++K+)ATPase activity, along with recovery of some normal nephrogenesis parameters, as nephrogenic zone and Bax protein content. On the other side, in control conditions, apocynin impaired renal fetal cell differentiation. **Conclusion:** Maternal endotoxemia leads to activation of placental NADPH oxidase which impacts fetal development and nephrogenesis. Therefore, it must be considered a promising target to prevent intrauterine programming of diseases.

10.017FR **Preconception and Gestational High-Fat Diet Differentially Affect Reflex Ontogeny and Somatic Maturation in Male and Female Rat Offspring: A Sex-Specific Developmental Study**. Chagas MAC, Dutra MLV, Souza DM, Aquino JS UFPB, Experimental Nutrition Lab João Pessoa, Paraíba, Brazil. [2]UFPB, , João Pessoa, Paraíba, Brazil.

Introduction: Maternal high-fat diet consumption impairs offspring neurodevelopment, but the effects of exposure during the preconception period remain unclear. Reflex ontogeny and somatic maturation are important indicators of early neurodevelopment and may be differently affected according to offspring sex. **Objective:** To investigate the effects of maternal dyslipidemia induced by a high-fat diet during preconception and gestation on reflex ontogeny and somatic maturation in male and female rat offspring. **Methods:** Twenty-four female rats were assigned to four groups (n=6/group): Control (C), HF (high-fat diet during preconception and gestation), HF-C (high-fat diet during preconception followed by control diet during gestation), and C-HF (control diet during preconception followed by high-fat diet during gestation). During lactation, all dams received the control diet. Reflex ontogeny and somatic maturation were assessed from postnatal day (PND) 1–21 in 10 male and 10 female offspring per group. Somatic maturation included body growth, pinna detachment, eye opening, incisor eruption, auditory canal opening, and fur appearance. Reflexes evaluated were palmar grasp, righting, vibrissa placing, cliff avoidance, negative geotaxis, acoustic startle, and aerial righting. **Results:** At PND1, male offspring from HF and C-HF dams showed greater nasoanal length than controls ($p<0.01$), whereas females were unaffected. HF females exhibited earlier pinna detachment than C-HF females ($p<0.001$). Eye opening occurred earlier in C-HF males than in controls ($p<0.05$). Fur appearance was accelerated in HF-C males compared with C and C-HF males ($p<0.05$). In females, cliff avoidance emerged earlier in HF-C than in C-HF offspring ($p=0.05$). Negative geotaxis was delayed in both sexes from HF and HF-C groups compared with controls. The aerial righting reflex was accelerated in C-HF males compared with control and HF males, while no changes were observed in females. **Conclusion:** Maternal exposure to a high-fat diet during preconception and gestation differentially affects offspring neurodevelopment according to sex. Alterations in reflex ontogeny and somatic maturation were more pronounced in males, suggesting greater male vulnerability to maternal metabolic disturbances. **Acknowledgments:**: The authors thank CAPES for **Financial support** and scholarship funding. Animal Research Ethical Committee Number: CEUA 5496250422. **Financial support:** CAPES, Brazil (Finance Code 001). M.L.V. Dutra received a graduate scholarship from CAPES.

11. Clinical Pharmacology, Pharmacokinetics, Pharmacogenomics and Toxicology

11.001 **Toxicological Evaluation of the Ruthenium Complex FOR0777G Using the HET-CAM Assay**. Costa SGA[1], Soares JJF[2], Silva FAO[2], Oliveira ACX[3], Andrade FRS[2], Lima NCB[2], Alves RS[3], Marinho AD[4], Jorge RJB[2], Manigat W[2], Júnior FSG[2], Pereira WG[2], Sousa EHS[2], Lopes LGF[2], Monteiro HSA[2]. [1]UFC, Dept Pharmacy, Dentistry and Nursing, Brazil. [2]UFC, Dept Pharmacology and Physiology, Brazil Graduate Program in Pharmacology, Brazil. [3]UFC, Graduate Program in Morphofunctional Sciences, Dept Clinical and Toxicological Analysis, Brazil. [5]UFC, Center for Research and Development of Medicines (NPDM), Brazil.

Introduction: Ruthenium complexes have attracted significant attention due to their therapeutic potential in several diseases, especially because of their ability to release nitric oxide and act on cardiovascular disorders. However, toxicological evaluation is essential to ensure the safety and biocompatibility of these compounds. In this context, the Hen's Egg Test Chorio-Allantoic membrane (HET-CAM) test stands out as an alternative methodology to animal use, recognized by the Brazilian National Council for the Control of Animal Experimentation (CONCEA), allowing the analysis of irritative and toxic effects through the HET-CAM, presenting low cost, rapid execution, and good experimental sensitivity. Thus, this study aimed to investigate the effects of the compound FOR0777G on the HET-CAM assay, evaluating possible toxic effects associated with irritative processes. **Methods:** The ruthenium complex was synthesized at the Bioinorganic Laboratory (LABIO) of the Department of Organic and Inorganic Chemistry at the Federal University of Ceará, following the technique described by Manigat (2023). In the assay, phosphate-buffered saline (PBS) was used as the negative control, while 0.1 molar NaOH solution was used as the positive control, and the ruthenium complex was administered at a concentration of 3.16×10^{-5} mol/L . The evaluated criteria included hemorrhage, vascular lysis, and coagulation at treatment times t0, corresponding to the moment the compound was applied, t30 seconds, corresponding to the second evaluation, and t300 seconds, corresponding to the final analysis. The results were expressed according to the irritation score (IS), calculated using a specific formula, and the values obtained for the complex were compared with the positive and negative controls. At the end of the assays, the embryos were euthanized, with no requirement for ethics committee approval, and discarded according to the standards of the responsible center. **Results:** The FOR0777G-treated group (n=6), compared with the positive (n=6) and negative (n=6) control groups, showed no irritation on the chorioallantoic membrane at 0, 30, and 300 seconds. In addition, no signs of hemorrhage, vascular lysis, or coagulation were observed. The irritation scores (IS) obtained for FOR0777G were comparable to those of the negative control, indicating behavior similar to a non-irritating substance. **Conclusion:** The compound FOR0777G did not induce acute irritation in the chorioallantoic membranes, demonstrating low irritative potential and absence of deleterious vascular effects. Future studies should combine these findings with additional *in vivo* models to further investigate long-term local and systemic effects and broaden the evaluation of the compound's biocompatibility. **Financial support:** CAPES and CNPq.

11.002 **Bothrops Venoms Induce a Bell-Shaped Effect on Platelet Aggregation**. Catela B[1], Pagliarani J[1], Zani KM[2], Gaspar RS[1] [1]Unicamp, Extracellular Matrix Lab, Brazil. [2]IBu, São Paulo, Brazil.

Introduction: There are 30 known species of snakes from the *Bothrops genus* in Brazil, which are responsible for more than 80% of accidents involving snakes in Brazilian territory. The main treatment for snakebite is the bothropic antivenom, which is produced with venoms from 5 species of snakes. While bothropic venoms are recognized for disrupting hemostasis, their effects on platelet function remains underexplored. It is also unclear if the antivenom neutralizes the platelet effects of bothropic venoms of different species. **Objectives:** To determine whether Bothropic venoms from 21 species could induce platelet aggregation and to assess the efficacy of the antivenom on the ones that showed a higher aggregation potential. **Methods:** Platelet aggregation was assessed in a 96-well plate assay with washed platelets from healthy donors. Platelets were added in each well with 11 venom concentrations, ranging from 2000µg/mL to 1,953125µg/mL and submitted to 1200 RPM orbital shaking at 37 degrees celsius for 10 minutes. The effect of the antivenom was assessed by performing a concentration-response curve in platelets stimulated with a single concentration of venom (6,25µg/mL) and 10 concentrations of the antivenom (from 32x to 0,0625x the original concentration, 5mg/ml) **Results:** 14 of the twenty one Bothrops venoms induced a concentration-dependent aggregation response characterized frequently by a bell-shaped curve where elevated concentrations (62,5µg/mL to 2.000µg/mL) resulted in a significant reduction of the initial effect. Based on these kinetics, species were categorized into distinct groups: Group A (*B. pauloensis*, *B. majaroensis*, *B. paranaensis* and *B. goyazensis*) achieved aggregation exceeding 90%, Group B (B. *alcatraz*, *B. erythromelas* and *B. fonsecai*) displayed sharp inhibition at higher doses, Group C (B. *matogrossensis*, *B. marmoratus*, *B. pubescens*, *B. leucurus*, *B. neuwiedi*, *B. diporus* and *B. insularis*) maintained moderate activity, and Group D (*B. lanceolatus*, *B. taeniatus*, *B. atrox*, *B. moojeni*, *B. alternatus*, *B. jararaca* and *B. jararacussu*) did not reach 50% platelet aggregation. Antivenom efficacy varied across species, for *B. alcatraz*, *B. erythromelas*, *B. insularis* and *B. marajoensis* a rightward shift in the curve indicates that higher concentrations are required to achieve inhibition, for *B. neuwiedi*, *B. pauloensis*, *B. matogrossensis*, *B. marmoratus*, *B. paranaensis*, *B. fonsecai*, *B. leucurus*, *B. goyazensis* and *B. diporus* there was a consistent increment of inhibition as the concentration increased. **Conclusion:** Bothrops venoms induce a concentration-dependent bell-shaped response on platelet aggregation and there is high interspecies variability. The antivenom is most effective against all species tested, except for B. pubescens, in higher doses than the recommended, and the indicated dose did not abrogate platelet aggregation in 95,2% of species tested. These findings reinforce the variability of bothropic venom composition and contribute to the understanding of how these venoms interact with platelet function.

11.003 **Optimization of Meropenem Pharmacokinetic/Pharmacodynamic Targets in Critically Ill Pediatric Patients: An Integrative Review**. Santos AKFS, Carvalho RMC, Macedo CL, Landim ECS, Santos YKA, Ramos PS, Marreiro VS, Praxedes MRS ESP-PB, Residência Multiprofissional em Saúde da Criança

Introduction: Meropenem is one of the main antimicrobials used to treat severe bacterial infections in pediatric intensive care units. However, physiological changes commonly observed in critically ill children may significantly affect its pharmacokinetic profile. Factors such as augmented renal clearance, fluid overload, hemodynamic instability, and organ dysfunction can lead to important variations in drug exposure, making it difficult to achieve pharmacokinetic/pharmacodynamic (PK/PD) targets. In this context, strategies aimed at optimizing meropenem therapy have gained increasing attention in pediatric critical care. **Objective:** To review the scientific evidence on PK/PD optimization strategies for meropenem in critically ill pediatric patients. **Methods:** An integrative review was carried out using the descriptors “Meropenem”, “Pharmacokinetics”, and “Intensive Care Units, Pediatric”. Searches were performed in PubMed, Scopus, and Web of Science, including studies published between 2021 and 2026. A total of 42 articles were identified. After applying the eligibility criteria and assessing the relevance of the studies, 10 articles were selected for analysis. The review included studies evaluating meropenem pharmacokinetics, target attainment, therapeutic drug monitoring, population pharmacokinetic models, and dosing strategies in critically ill pediatric patients. **Results:** The studies showed that meropenem exposure varies substantially among critically ill children, mainly due to differences in renal function, age, severity of illness, and changes in volume of distribution. Several authors reported that conventional dosing regimens may not consistently achieve PK/PD targets, particularly in patients with augmented renal clearance. Extended and continuous infusion regimens were associated with better target attainment in different clinical scenarios. In addition, therapeutic drug monitoring and pharmacokinetic modeling were frequently described as useful approaches to support dose adjustment and improve antimicrobial exposure. Overall, the findings indicate that a standardized dosing strategy may not be appropriate for all critically ill pediatric patients. **Conclusion:** The literature demonstrates that achieving adequate meropenem exposure in critically ill children remains a challenge. Approaches based on PK/PD principles, especially individualized dosing, prolonged infusion strategies, therapeutic drug monitoring, and population pharmacokinetic modeling, may improve target attainment and contribute to more effective antimicrobial therapy in pediatric intensive care units.

11.004 **Clinical Monitoring of Cardiovascular Risk in Patients Receiving Antipsychotic Therapy: A Narrative Review**.
Oliveira KS[1], Araújo JR[1], Araújo MLF[1], Alves ROF[1], Costa SGA[1], Carvalho JPAQ[1], Barbosa ISA[1], Canafístula LS[1], Pinheiro KS[1], Andrade FGA[1], Sampaio TL[2] [1]UFC, Faculty of Pharmacy, Dentistry and Nursing, Dept Clinical and Toxicological Analysis, Brazil; [2]UFC, Faculty of Pharmacy, Dentistry and Nursing, Dept of Clinical Analysis and Toxicological, PPG of Pharmaceutical Sciences, Brazil

Introduction: The use of antipsychotic medications has been associated in the literature with an increased risk of cardiometabolic alterations. The main complications include weight gain, hypertension, insulin resistance, and dyslipidemia, which are related to the development of cardiovascular diseases. In addition, these drugs may cause direct cardiac effects, such as QT interval prolongation on electrocardiography and arrhythmias. Typical antipsychotics are more strongly associated with extrapyramidal effects due to dopaminergic antagonism. In contrast, atypical antipsychotics, such as olanzapine, are more frequently linked to metabolic and cardiovascular alterations, mainly through antagonism of histaminergic H1 and serotonergic 5-HT2C receptors, mechanisms associated with increased appetite, disturbances in energy metabolism, and insulin resistance. Therefore, although essential in the management of mental disorders, these medications require careful attention to treatment-related risks. **Objective:** To compile evidence on cardiovascular and cardiometabolic alterations associated with antipsychotic use, with a focus on clinical monitoring strategies. **Methodology:** This narrative literature review addresses cardiovascular risks associated with antipsychotic medications, including studies published within the last 10 years. Priority was given to studies investigating the monitoring of these drugs, with emphasis on cardiometabolic effects and clinical assessment strategies. **Results:** A total of seven articles were identified, demonstrating that antipsychotic medications may be associated with both metabolic alterations and cardiovascular events. The analyzed studies revealed a disproportionality of cardiovascular adverse reactions associated with antipsychotics, both for the class as a whole and when comparing typical and atypical antipsychotics separately. The findings showed a disproportionality ratio of approximately 2.30 for both groups, suggesting an excess risk greater than expected. This finding was particularly evident for torsade de pointes and cardiac arrhythmias in patients treated with either type of antipsychotic. Another study found that the use of low doses of a typical antipsychotic was associated with an increased incidence of cardiometabolic events, including a higher risk of diabetes, when compared with low doses of an atypical antipsychotic. Furthermore, patient monitoring was found to remain insufficient in routine clinical practice. **Conclusion:** Although the cardiometabolic and cardiovascular risks associated with antipsychotic medications are well established, monitoring of these outcomes remains inadequate in clinical practice. Therefore, regular clinical and laboratory follow-up is essential, including assessment of body weight, body mass index, blood pressure, blood glucose levels, and lipid profile, aiming at the early detection of these alterations in patients receiving antipsychotic treatment.

11.005 **Toxicological Assessment of Pharmaceutical Surfactants in** *Caenorhabditis elegans* **Using Physiological and Behavioral Endpoints**. Silva VGO[1], Fagundes LS[1], Sá MEB[1], Poderoso VM[1], Araujo DS[1], Lisboa JS[2], Pacheco PGS[2], Trancoso CT[2], Araujo ZS[3], Cândido-Santos JH[4], Guimarães AG[5], Lira AAM[5] [1]UFS-São Cristóvão, Dept Pharmacy, Lab. of Clinical and Experimental Pharmacology, Brazil, [2]UFS-São Cristóvão, PPG in Pharmaceutical Sciences, Brazil, [3]UFS, Campus Lagarto, PPG in Applied Health Sciences, Brazil, [4]UFS-São Cristóvão, PPG in Health Sciences, Brazil, [5] UFS, Dept Pharmacy, Brazil.

Introduction: Surfactants are widely employed in pharmaceutical formulations due to their ability to enhance physicochemical properties. However, despite often being regarded as inert excipients, these compounds may exert concentration and exposure-dependent toxic effects. In this context, the nematode *Caenorhabditis elegans* is a well-established model organism for toxicological studies because of its high sensitivity to chemical stressors and suitability for assessing toxicity-related endpoints. **Objective:** To investigate the effects of pharmaceutical surfactants on survival, pharyngeal pumping, and body size in *C. elegans* . **Methods:** Worms were maintained on nematode growth medium (NGM) seeded with *E. coli* OP50. At the L1 stage, animals were exposed to M9 buffer (control) and to the following surfactants, all at a 5% concentration: polyvinyl alcohol (PVA), Tween® 80, Tween® 20, poloxamer 407, Cremophor®, propylene glycol, and Olivem® 300. Survival was monitored every 24 h for three consecutive days. Pharyngeal pumping and body size were assessed 48 h after exposure (n=10 worms/plate). All experiments were performed in triplicate. Statistical analyses were conducted using the Kruskal–Wallis test followed by Dunn's post hoc test, while survival data were analyzed using the log-rank test. **Results:** All surfactant-exposed groups exhibited significantly reduced survival compared with the control group ($p<0.01$), indicating toxicity under the tested conditions. Significant reduction in pharyngeal pumping was observed in the Tween® 80 ($p=0.0280$), Olivem® 300 ($p=0.0022$), and PVA ($p=0.0171$) groups relative to the control, indicating possible impairment of neuromuscular function and, consequently, feeding activity. No significant differences were detected in body size among the experimental groups ($p>0.05$). **Conclusion:** Exposure to pharmaceutical surfactants significantly affected survival and pharyngeal pumping in *C. elegans* without altering body size. Taken together, these findings suggest that surfactants can induce sublethal toxicity, affecting physiological and behavioral endpoints before the onset of detectable morphological alterations. Further studies are warranted to elucidate the mechanisms underlying surfactant-induced toxicity and to support the development of safer pharmaceutical formulations. **Acknowledgments:** The authors acknowledge the Federal University of Sergipe (UFS) and the National Council for Scientific and Technological Development (CNPq) for their support.

11.006 **Drugs of Abuse and Exogenous Intoxications of Forensic Interest in Brazil: Toxic Agent, Circumstances of Exposure, and Case Evolution, 2010–2025**. Sousa C, Melo R, Geraldino B Unirio, Centro Universitário Celso Lisboa,

Introduction: Exogenous intoxications are relevant to public health problems and are of forensic interest, especially when associated with substance abuse, violence, accidents, and deaths. In Brazil, the SINAN/DATASUS records allow for the analysis of toxic agents, exposure circumstances, and clinical evolution. Among these agents, drugs of abuse stand out due to their association with acute intoxications, social vulnerability, and fatal outcomes. **Objective:** To analyze exogenous intoxications of forensic interest in Brazil between 2010 and 2025, according to the toxic agent, exposure circumstances, and case evolution, with emphasis on drugs of abuse. **Methods:** A descriptive, retrospective study with a quantitative approach, based on secondary data from SINAN/DATASUS. Notifications of exogenous intoxication registered in Brazil between 2010 and 2025 were included. The variations analyzed were the toxic agent, exposure circumstances, sex, and clinical evolution. Descriptive statistical analysis was performed, with calculation of absolute and relative frequencies. **Results:** 2,358,325 notifications of exogenous intoxication were recorded. Medications were the main toxic agents, with 1,202,631 cases (51.0%), followed by drugs of abuse, with 294,550 notifications (12.49%). Suicide attempts were the main specific circumstance, with 1,052,518 records. Among the 19,409 deaths due to exogenous intoxication, 3,524 occurred due to abuse, corresponding to 18.16% of deaths. The occurrence of deaths in the abuse category was 1.15%, higher than that observed in suicide attempts, highlighting the greater severity of intoxications related to substance abuse. **Conclusion:** Drugs of abuse represent an important component of exogenous intoxications of forensic interest in Brazil, both due to the frequency of notifications and their significant contribution to deaths. The results reinforce the need for improvements in notification, in the integration between epidemiological surveillance, clinical toxicology and forensic investigation, as well as preventive actions related to the problematic use of the substance.
Keywords: exogenous intoxication; drugs of abuse; forensic toxicology; SINAN; epidemiology. Keywords: exogenous intoxication; SINAN; DATASUS; forensic toxicology; epidemiological surveillance.

11.007 **A Ferroptosis Resistance Gene Score Linked to KEAP1/NRF2 and Survival in Lung Adenocarcinoma**. Xavier EEP[1,2], Mota JA[1,3], Sales SLA[1,3], Oliveira KAF[1], Soares IF[1], Macêdo SMN[1], Fernandes MCR[1,4], Rocha DD[1], Furtado CLM[1,5], Scandolara TB[1,4], Pessoa CO[1,3]. [1]UFC, Lab Experimental Oncology, Brazil, [2]UFC, Undergraduate Program in Pharmacy, Brazil, [3]UFC, PPG Pharmacology, Brazil, [4]UFC, PPG Translational Medicine, Brazil and [5] UFMG, Dept Genetics, Ecology and Evolution, Brazil.

Introduction: Ferroptosis is an iron-dependent form of regulated cell death driven by lipid peroxidation and is associated with therapy resistance in lung adenocarcinoma (LUAD). Genes such as SLC7A11, a central regulator of ferroptosis, SLC3A2, GSR, PRDX1, TXNRD1, PGD, ABCB6, PTGR1 and GPX2 sustain antioxidant defense and ferroptosis resistance. KEAP1, frequently mutated in LUAD, regulates NRF2, a transcription factor that activates many of these genes and has been linked to drug resistance. While ferroptosis-related gene signatures have been proposed for prognosis in LUAD, the impact of a KEAP1/NRF2-driven ferroptosis-resistant expression pattern on survival remains unclear. **Objectives:** We aimed to test whether a nine-gene ferroptosis resistance score is associated with overall survival (OS) in LUAD and reflects a therapy-resistant phenotype. **Methods:** Genes co-expressed with SLC7A11 (Pearson r≥0.4) were identified via UALCAN in the TCGA-LUAD dataset, selecting those with known roles in ferroptosis resistance or antioxidant pathways. RNA- sequencing data (mRNA z-scores) and clinical data for TCGA-LUAD were obtained through cBioPortal. The ferroptosis resistance score was calculated per tumor as the mean mRNA z-score of the nine selected genes. Cox proportional hazards models evaluated the score-OS association in univariate and multivariate analyses adjusted for age and sex, with tumor stage as a stratification variable, estimating hazard ratios (HR) and 95% confidence intervals (CI). Wilcoxon rank-sum test compared scores between KEAP1-mutant (KEAP1mut) and KEAP1-wildtype (KEAP1wt) tumors. Kaplan-Meier (KM) analyses used the median score as cutoff and combined KEAP1 status plus score groups. **Results:** Higher ferroptosis resistance scores were associated with worse OS (log-rank p=0.018; HR=1.28, 95% CI 1.08–1.51, p=0.004), and this association remained significant after adjustment for age, sex and stage stratification (HR=1.27, 95% CI 1.05–1.53, p=0.014). KEAP1mut tumors showed significantly higher scores than KEAP1wt tumors (p<2.2e-16), but KEAP1 mutation alone was not associated with OS (p=0.39). In KM curves combining KEAP1 status and ferroptosis score, KEAP1wt/high-score and KEAP1mut/high-score groups had similarly poor outcomes (p=0.955), suggesting OS is more closely related to a high ferroptosis- resistant expression state than to mutation status alone. **Conclusion:** A nine- gene NRF2-related ferroptosis resistance score predicts worse OS in LUAD. KEAP1 mutations appear to act mainly by elevating this score, while the high ferroptosis score more consistently reflects poor prognosis and may represent a therapy-resistant phenotype, warranting validation in independent cohorts with treatment response data. **Financial support:** This study was supported by INCTBIO2, PRONON, Brazilian Ministry of Health, FINEP, CNPq, CAPES and FUNCAP.

11.008 **Chronic Toxicity and Transgenerational Effects of Polymethyl Methacrylate (PMMA) in Alternative Animal Model**. Sá MBD[1], Amorim JCG[1], Santos RG[1], Lisboa JS[2], Moura PHM[2], Silva AS[2], Pacheco PGS[2], Barreto MS[2], Souza JB[2], Araújo ZS[3], Guimarães AG[2] [1]UFS, Dept Pharmacy, São Cristovão, Brazil. [2]UFS, Graduate Program in Pharmaceutical Sciences, São Cristóvão, Brazil. [3]UFS, Graduate Program in Health Sciences, Lagarto, Brazil.

Introduction: Plastics are materials composed of long polymer chains and are widely used in the manufacture of various types of products. The widespread use and improper disposal of these polymers in the environment lead to major environmental problems. Fragments smaller than 5 mm are called microplastics (MPs) and are considered emerging contaminants. Polymethyl methacrylate (PMMA) is a widely used thermoplastic due to its high durability and strength. However, chronic exposure in animals and humans, and its potential transgenerational effects, are not yet fully understood. In this context, *Caenorhabditis elegans* serves as an alternative animal model for environmental toxicity testing. ObjectiveThis study assesses the potential chronic toxicity of PMMA in the N2 strain of *Caenorhabditis elegans*. Methodology The nematodes were synchronized using alkaline lysis. L1 stage worms were transferred to NGM plates containing inactivated *E. coli* OP50, and approximately 24 worms per experimental group were exposed to concentrations of 10, 50, and 100 µg/L. Physiological and behavioral parameters were assessed using survival rate, swimming, pharyngeal pumping, defecation cycle, body size and egg production, all in triplicate. The progeny (L1) were transferred to new plates, constituting the F1 generation, and at the L4 stage, they were assessed for body size and swimming. This procedure was repeated, totaling 3 generations of the nematode. The results were statistically analyzed using GradPad Prism 8 software, applying a one-way ANOVA with Tukey's post-hoc test. Results The analysis showed that PMMA was able to significantly alter the defecation cycle of the nematodes (10 µg/L: $p<0.001$; 100 µg/L: $p<0.0001$). In addition, there was a significant difference in the F1 generation at 10 µg/L for body size ($p<0.0001$) and swimming ($p<0.01$) when compared to the control. When compared to the parent generation, F1 showed a difference in body size ($p<0.0001$), while for swimming, F1 and F2 had $p<0.001$ and $p<0.01$, respectively. At 50 µg/L, F1 and F2 showed differences, relative to the control, in body size ($p<0.05$) and swimming ($p<0.001$; $p<0.05$). The F1 ($p<0.001$) and F2 ($p<0.01$) generations showed differences when compared to the F0 generation. At 100 µg/L, F1 showed a difference in swimming ($p<0.01$) compared to the control, and $p<0.05$ compared to the parent generation, and F2 in body size ($p<0.01$). **Conclusion:** The results suggest toxicity in a key physiological parameter of C. elegans, as well as possible transgenerational effects, which vary by concentration and generation, on the parameters evaluated. **Financial support** This study received **Financial support** from the Sergipe State Foundation for Research and Technological Innovation (FAPITEC)- 07/2025.

11.009 **PK/PD Modeling and Monte Carlo Simulation of β-Lactams Against Pseudomonas aeruginosa and Acinetobacter baumannii Isolates from Hospitalized Patients**. Araujo MLF[1], Ananias CF[1], Fernandes MO[1], Freitas AGS[1], Oliveira KS[1], Pinheiro NM[2], Pontes ER[1], Costa MDR[1], Duque BR[2], Sousa PCP[2], Teixeira IMM[2], Lima DTF[2], Dantas FJL[2], Sampaio TL[1] [1]UFC, Faculty of Pharmacy, Dentistry and Nursing, Dept Clinical and Toxicological Analysis, Brazil; [2]UFC, Faculty of Pharmacy, Dentistry and Nursing, PPG of Pharmaceutical Sciences, Brazil.

Introduction: *Pseudomonas aeruginosa* and Acinetobacter baumannii are major causes of hospital-acquired infections and are highly capable of developing resistance to antimicrobials, including carbapenems. Although the minimum inhibitory concentration (MIC) and susceptibility testing provide relevant information on antimicrobial activity, these parameters do not account for the influence of pharmacokinetic and pharmacodynamic (PK/PD) factors on the efficacy of the therapeutic regimens used. In this context, PK/PD modeling combined with Monte Carlo simulation can help estimate the probability of therapeutic success for different antimicrobial regimens. **Objective:** To evaluate the likelihood of therapeutic success of different regimens containing β-lactams against clinical isolates of Pseudomonas aeruginosa and Acinetobacter baumannii from hospitalized patients. **Methodology:** A total of 121 clinical isolates of *Pseudomonas aeruginosa* and Acinetobacter baumannii collected between January and December 2023 at a university hospital were evaluated. Based on dosing regimens previously defined according to institutional clinical protocols, Monte Carlo simulations were performed using PK-Sim software for the antimicrobials piperacillin/tazobactam, meropenem, ceftolozane/tazobactam, aztreonam, and ampicillin/sulbactam. The PK/PD evaluation was based on the probability of achieving the target (PAA) and the cumulative response fraction (FCR), considering reference values of 40% fT>MIC for meropenem and 50% fT>MIC for the other β-lactams. **Results:** A limited susceptibility profile was observed, with the percentage of susceptible isolates ranging from 0–59% in *P. aeruginosa* and from 0–23% in A. baumannii. The MIC_{50}/MIC₉$_0$ values for meropenem were ≤4/≤32 µg/mL in P. aeruginosa and ≤32/≤32 µg/mL in A. baumannii, indicating a high frequency of isolates with high MICs. Meropenem showed the best predictive PK/PD performance among the antimicrobials evaluated. The regimens of 2 g every 8 hours and 1 g every 8 hours achieved AAP values close to 100%, though these were limited to the lower minimum inhibitory concentrations (MICs). Similarly, the ampicillin/sulbactam combination against A. baumannii showed high PAA at the 9 g every 4 hours regimen for an MIC of 1 µg/mL, with a progressive reduction in efficacy as the MIC increased. None of the simulated regimens achieved ideal CRF values (>90%), a result associated with the high frequency of isolates with higher MICs, in which PAA values were substantially reduced. **Conclusion:** The results highlight limitations of the evaluated β-lactam regimens in relation to the susceptibility profile of the isolates studied. The findings suggest that some treatment regimens may be inadequate against microorganisms with high MICs and reinforce the usefulness of PK/PD modeling combined with Monte Carlo simulation as a tool to support the optimization of antimicrobial therapy.

11.010 **Weight Loss Pens: the Multisystemic Impact of GLP-1 Analogs on the Liver and Pancreas**. Costa AC[1], Lima ES[1], Moraes TDB[1], Montenegro GMF[1], Silva ALT[2], Costa MMC[3], Guimarães CRA[1] [1]Unichristus, Brazil, [2]UFC Brazil, [3]UNESA Brazil

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) originated in the 1980s with the identification of the native hormone and became firmly established in the 1990s through the development of metabolically stable molecules. According to recent literature, this class of drugs was initially developed for the treatment of type 2 diabetes mellitus; however, its pharmacological evolution has transformed the clinical management of obesity and related metabolic disorders. In this context, GLP-1 analogs have shown promising results in the management of systemic comorbidities, including a potential positive impact on the progression of chronic liver diseases such as steatohepatitis and cirrhosis. Despite the substantial benefits reported in patients' quality of life, the widespread popularity and indiscriminate use of these so-called “weight-loss injection pens” have raised concerns within the medical community due to the occurrence of severe adverse effects. Experimental studies and pharmacovigilance analyses suggest a potentially concerning association between sustained GLP-1 receptor stimulation and an increased risk of acute pancreatitis and pancreatic neoplasms. Given this dual scenario, the present study aims to review the multisystemic effects of GLP-1 analogs, with particular emphasis on their impact on the liver and pancreas, in order to determine whether their widely reported metabolic benefits outweigh potential long-term organ-related risks. This qualitative integrative literature review was conducted between January and May 2026 using the keywords and descriptors “GLP-1 receptor agonists,” “adverse reactions,” and “misuse.” Scientific articles published between 2021 and May 2026 were retrieved from the PubMed database and included if available in full text in Portuguese, English, or Spanish. The reviewed studies reinforce the positive effects of these medications in the treatment of patients with diabetes and obesity, demonstrating improvements in body weight and insulin resistance. However, rare but documented adverse events, such as acute pancreatitis, have been reported in the literature. Evidence also indicates that switching between different GLP-1 receptor agonists may contribute to a higher incidence of adverse effects, particularly when appropriate dose-adjustment protocols are not followed, as observed in cases of self-medication. In conclusion, greater protocol standardization, together with careful dose adjustments during treatment, is essential to ensure patient safety. Further research is needed to better characterize the safety profile of this class of medications, thereby guiding clinical practice and improving patient outcomes.

11.011 **Pharmacological Potential of an Isatin-Derived Oxime against Cellular Oxidative Damage Induced by Subchronic Exposure to Organophosphate Pesticide**. Batista WT, Comis Neto AA, Luzardo BFSL, Gomes J, Rodrigues ES, Fontoura EA, Strebs BL, Rosa SG, Pinton S. Unipampa-Uruguaiana, RS, Brazil.

Introduction: The intensive use of organophosphate pesticides such as malathion raises public health concerns due to continuous exposure to low doses. In addition to the classical inhibition of cholinesterases, the bioactivation of malathion generates excessive reactive oxygen species (ROS), leading to cellular damage and lipid peroxidation. Oximes have been studied to counteract these toxic effects. Cl-HIN, (3Z)-5-Cloro-3-(Hidroxiimino)indolin-2-ona, an isatin-derived oxime, has shown promising protective activity in acute models; however, its effects under repeated-dose exposure still require investigation. **Objectives:** To investigate the protective effects of Cl-HIN against oxidative stress and hepatic damage induced by repeated malathion exposure in Wistar rats by evaluating ROS generation, lipid peroxidation, and AST/ALT activities. Materials and **Methods:** Male Wistar rats (N=9-10/group) were treated daily for 20 consecutive days and randomly allocated into four experimental groups: Control (distilled water i.p. + canola oil i.g.); Cl-HIN (5 mg/kg i.g.); MAL 1 (malathion 1 mg/kg i.p. + canola oil i.g.); and MAL 1 + Cl-HIN. The experimental protocol was approved by the Animal Ethics Committee of UNIPAMPA (#3497040526). After euthanasia, liver samples were homogenized. ROS levels were determined using the DCFH-DA fluorescence assay, and lipid peroxidation was assessed by measuring malondialdehyde (MDA) levels through the thiobarbituric acid reactive substances (TBARS) assay. Total protein content was quantified using the Bradford method. The activities of AST and ALT enzymes were determined in serum using commercial biochemical kits (Bioclin-Quibasa). Data were analyzed using one-way ANOVA followed by Tukey's post hoc test. **Results:** Repeated exposure to malathion significantly increased hepatic ROS production compared to the control group ($p=0.0255$). Simultaneously, malathion induced lipid peroxidation, evidenced by a significant increase in MDA levels in liver tissue ($p=0.0344$). Co-treatment with Cl-HIN successfully prevented the increase in both ROS generation and lipid peroxidation, maintaining these biomarkers at levels similar to those of the control group ($p=0.0033$ and $p=0.0054$ vs MAL 1, respectively). Cl-HIN administered alone did not cause significant changes in any of the evaluated parameters. Additionally, no significant differences in AST and ALT levels were observed following either malathion exposure or Cl-HIN treatment. **Conclusion:** Repeated exposure to low doses of malathion induces early oxidative stress in the liver of rats by accelerating radical generation and causing damage to membrane lipids without detectable changes in AST and ALT activities. The oxime Cl-HIN exerts a potent antioxidant protective effect, preventing the onset of organophosphate-induced cellular oxidative injury.

11.012 **Racial and Ethnic Influences on Post-Transplant Complications in a 634-Recipient Allogeneic Hematopoietic Cell Transplant Cohort Using Cyclosporine and Tacrolimus**. Pessoni JG[1], Costa-Junior LC[2,3], Leão AM[4,5], Izu M[3], Tavares RC[3], Maradei SC[3], Moreira MC[3,6], Nogueira MC[3], Lerner D[3], Bino FG[7,5], Moriel P[8], Fernandez TS[4], Santos PC[1,2] [1]EPM-Unifesp, Department of Pharmacology, São Paulo, Brazil, [2]FMUSP, Postgraduate Program in Medical Sciences, São Paulo, Brazil, [3]INCa, Bone Marrow Transplant Center, Rio de Janeiro, Brazil, [4]INCa, Cytogenetic Laboratory, Cell and Gene Therapy Program, Rio de Janeiro, Brazil, [5]Unigranrio, Duque de Caxias, Brazil, [6]UFRJ, Bone Marrow TransplantProgram, Rio de Janeiro, Brazil, [7]UFRJ, Division of Nephrology, Rio de Janeiro, Brazil, [8]Unicamp, Faculty of Medical Sciences, Campinas, Brazil

Allogeneic hematopoietic cell transplantation (HCT) is a curative therapy for various hematologic diseases, but it is frequently associated with early complications, such as acute graft-versus-host disease (GVHD) and acute kidney injury (AKI). Cyclosporine and tacrolimus are widely used in GVHD prophylaxis, requiring strict therapeutic monitoring to balance immunosuppressive efficacy and toxicity. This retrospective cohort study evaluated clinical, demographic, laboratory, and transplant-related factors associated with acute GVHD and AKI in 634 allogeneic HCT recipients followed between 2002 and 2023 at the Bone Marrow Transplant Center of the National Cancer Institute (INCA). Clinical and laboratory data were extracted from electronic medical records, and uni and multivariate analyses were performed to identify independent factors associated with the outcomes. Acute GVHD occurred in 60.1% of patients, while AKI was observed in 46.8% of recipients in the first 21 days after starting calcineurin inhibitors. The use of cyclosporine, older age, unrelated donor transplant, and a diagnosis of lymphoma/multiple myeloma were associated with a higher risk of acute GVHD. Self-reported brown and black patients had a lower chance of GVHD compared to white patients. For AKI, higher body weight, AST >40 U/L, albumin >3.5 g/dL, and brown race/color were associated with a higher risk. The findings reinforce the high frequency of early complications after HSCT, as well as that self-reported race/ethnicity was associated with GVHD and AKI, suggesting potential variability in post-transplant complications and highlighting the importance of risk stratification and individualized monitoring in the post-transplant period.

11.013 *In vitro* **Metabolism of Violacein, a Molecule with Antimalarial Therapeutic Potential, Using Human, Rat, and Mouse Liver Microsomes**. Calemi DBA[1], Guldoni LF[1,2], Godoi AB[1,3], Minuti G[1], Carnevale Neto F[4], Hispagnol GF[5], Pilon AC[5], Costa JL[1,3,6], Hyslop S[1], Antunes NJ[1] [1]FCM-Unicamp, Depto Farmacologia, Campinas, SP, Brasil, [2]UNOESTE, Lab Toxinologia e Estudos Cardiovasculares, Programa de Graduação em Ciências da Saúde, Brasil, [3]Unicamp, Centro de Informação e Assistência Toxicológica, Brasil, [4]Washington University, Centro de Pesquisa Metabolômica do Noroeste, Depto Anestesiologia e Medicina da Dor, Seattle, EUA, [5]Unesp, Depto Bioquímica e Química Orgânica, Instituto de Química, Brasil, [6]Unicamp, Faculdade de Ciências Farmacêuticas, Brasil.

Malaria has a profound impact on the health and quality of life of populations living in poverty and vulnerable conditions. In parallel, the increasing resistance to currently available antimalarial drugs highlights the urgent need for the development of new, safer, and more effective therapeutic strategies. In this context, violacein has emerged as a promising candidate due to its potent antiplasmodial activity against the mature asexual stages of the Plasmodium parasite, demonstrating strong potential as an antimalarial drug candidate. However, to date, there are no reports in the literature regarding studies that investigate the metabolism of violacein. This study aimed to evaluate the *in vitro* metabolism of violacein and, consequently, determine its metabolic stability in human (HLM), mouse (MLM), and rat (RLM) liver microsomes using liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS). Additionally, the metabolites generated in HLM and RLM were identified using liquid chromatography coupled with high-resolution mass spectrometry (LC-HRMS), complemented by *in silico* predictive analyses. The half-life (t1/2) of violacein was 36, 81, and 216 minutes in RLM, MLM, and HLM, respectively. The *in vitro* intrinsic clearance (CLint, *in vitro*) values were 38.4, 17.0, and 6.4 µL/min/mg in RLM, MLM, and HLM, respectively. The in vivo intrinsic clearance (CLint, *in vivo*) estimated was 93.7, 67.0, and 6.6 mL/min/kg, respectively. A slow elimination profile was observed in HLM, an intermediate elimination in MLM, and a rapid elimination in RLM, indicating greater metabolic stability of violacein in HLM and MLM compared to RLM, and highlighting interspecies differences in the metabolism of this compound. These findings were corroborated by the metabolite identification results, which showed a significant reduction in the percentage of remaining violacein in RLM, associated with a higher abundance of metabolites. Four violacein metabolites were identified in HLM and RLM, including two metabolites formed by reduction (phase I), one by glucuronidation of aromatic alcohols (phase II), and one by sequential reduction (phase I) followed by glucuronidation (phase II). This information is essential for selecting the most appropriate animal model for the future *in vivo* pharmacokinetic and metabolism studies. Keywords: malaria; violacein; pharmacokinetics; *in vitro* metabolism; LC-MS/MS; *in silico* prediction; drug development

11.016 **Acute Toxicity Evaluation of Compound LOE2208 by Up-and-Down Method (OEC D425) in NOD-SCID Mice.**

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Introduction: Developing new Active Pharmaceutical Ingredients (APIs) is crucial due to high cancer mortality. The isoflavonoid LOE2208 modulates microtubule activity and induces apoptosis in different cancer cell lines, with IC50 0,8 to 6 uM. To advance its preclinical development, evaluating acute toxicity is mandatory. **Objective:** To evaluate the acute toxicity of LOE2208 using the Up-and-Down Procedure (UDP) (OECD 425). **Methodology:** NOD-SCID mice (IACUC No. 129261224) were used to align with the immunodeficient model planned for subsequent *in vivo* efficacy assays. The compound was diluted in a vehicle (DMSO, EtOH, PEG400, propylene glycol, water) and administered intraperitoneally (IP) with a dose factor of 5. Doses exceeding the maximum volume for a single administration were fractionated (up to 6 h interval). Testing initiated with a vehicle control and one animal at 69 mg/kg, adjusting doses every 48 hours based on survival/morbidity. Animals were monitored for 14 days, then euthanized (ketamine/xylazine) for hematological, biochemical, and histopathological analyses (Butantan Institute). Daily body weight was monitored. Statistics were performed using GraphPad Prism 8.0.1. **Results:** The UDP trial concluded upon meeting stopping criterion A (three consecutive survival events at the highest dose) following the dose sequence: 69, 109, 175, 175, 175, and 175 mg/kg (fractionated administrations from 109 mg/kg upwards, with the fractionated dosage of a vehicle-treated animal) with an LD50 value > 175 mg/kg due to the solubility limit. Clinical signs included transient diarrhea and auricular venous engorgement at 3 animals of 175 mg/kg. Animal weight remained stable (17 +/- 2 g; $p = 0.0346$, F-test). Hematology at 175 mg/kg showed a significant reduction in WBC (0.86-1.07 vs. standard 2.68 x10^3/uL, $p < 0.01$), HGB ($p < 0.01$), HCT ($p < 0.05$), VCM ($p < 0.01$), and HCM ($p < 0.05$), alongside increased CHCM ($p < 0.01$) and RDW (16.4-16.6% vs. standard 14.4%, $p < 0.001$). RBC increased ($p < 0.05$) and PLT showed no significant change ($p > 0.05$). Biochemical analysis (TGP, TGO, Urea) showed no statistically significant differences ($p > 0.05$, ns) compared to baseline reference standards (TGP: 32.0 U/L; TGO: 201.0 U/L; Urea: 65.5 mg/dL), with individual values remaining within or below normal ranges. Pathological findings were mild and comparable across groups, limited to mononuclear infiltrates (lungs/liver), hepatocyte degeneration (two animals at 175 mg/kg), and renal cortex congestion (one at 109 mg/kg, one at 175 mg/kg), which were attributed by pathologists to the euthanasia method. **Conclusion:** LOE2208 demonstrated a favorable acute safety profile up to 175 mg/kg in NOD-SCID mice with no biochemical toxicity. The observed leukopenia at the highest dose is consistent with its microtubule-targeting mechanism, supporting its progression to *in vivo* efficacy trials.

11.017 **Clinical Response to Cannabidiol in a Pediatric Cohort with Autism Spectrum Disorder: A Randomized Placebo-Controlled Trial**. Canquerino YK, Feliz MC, Cunha JM. UFPR, Curitiba, Sector of Biological Sciences, Dept. of Pharmacology, PPG Pharmacology, Brazil.

Introduction: Autism Spectrum Disorder (ASD) is a neurodevelopmental condition characterized by persistent deficits in social communication and restricted, repetitive patterns of behavior. Current pharmacological interventions approved for ASD are limited to managing comorbidities like irritability, often presenting significant side effects and limited efficacy for core symptoms. Cannabidiol (CBD) has emerged as a promising therapeutic candidate. Full-spectrum extracts, which include terpenes and minor cannabinoids, are hypothesized to be superior to isolated CBD due to the synergistic entourage effect, potentially offering a better safety and efficacy profile. However, robust evidence from randomized controlled trials (RCTs) in the Brazilian pediatric population is still needed to isolate pharmacological effects from the high placebo response typical in this group. **Objectives:** To evaluate the efficacy and safety of a CBD-rich full-spectrum cannabis extract compared to placebo in reducing behavioral symptom severity and improving executive functions in children and adolescents with ASD. **Methods:** This is a Phase II, randomized, double-blind, placebo-controlled trial with a 1:1 allocation ratio and a subsequent open-label crossover extension. One hundred participants (aged 7-17 years) with a confirmed diagnosis of ASD (CID-11: 6A02) will be recruited. Participants will receive either CBD full-spectrum oil (50 mg/mL; 20:1 CBD:THC ratio) or an organoleptically matched placebo for 12 weeks. Dosing will start at 0.5 mg/kg/day, with weekly titration up to a maximum of 20 mg/kg/day (capped at 600 mg/day). Clinical assessment includes ADOS-2, CARS, SRS-2, ABC-C, CGI-S/I, and SDSC. Executive functions (working memory, inhibitory control, and cognitive flexibility) will be assessed via a direct neuropsychological battery. Safety will be monitored through serial hematological and biochemical tests (liver and renal function). **Results:** It is anticipated that the CBD-treated group will exhibit a statistically significant reduction in irritability and agitation scores (ABC-C) and improved social responsiveness (SRS-2) compared to the placebo group. Positive impacts on sleep architecture (measured via actigraphy) and executive performance are also expected. The double-blind design is essential to mitigate measurement bias and distinguish true pharmacological efficacy from natural symptom fluctuation. **Conclusion:** This study aims to provide high- quality clinical data on CBD for ASD in Brazil, contributing to evidence-based clinical guidelines and the future implementation of precision medicine in neurodevelopmental disorders. **Financial support:** Biominerales Pharma LLC (CR Wellness), CNPq.

11.019 **Subclinical Inflammatory and Endothelial Alterations in Patients Victim of Scorpion Envenomation by** *Tityus stigmurus*. Araújo LM[1], Lopes NC[1], Souza RN[2], Almeida IM[1], Maia KM[3], Magalhães KN[3], Vasconcelos Neto H[3], Landim MJS[4], Oliveira GN[3], Albuquerque PLMM[7], Gonzalez RC[8], Meneses GC[1], Silva-Júnior GB[6], Daher EDF[2], Martins AMC[1] [1]UFC, Faculty of Pharmacy, Dept Clinical and Toxicological Analysis, PPG Pharmacology, Brazil. [2]UFC, Faculty of Medicine, PPG Medical Sciences, Brazil. [3]Dr. José Frota Institute, Toxicological Information and Assistance Center, Brazil. [4]Dr. José Frota Institute, Lab Unit, Brazil. [5]UNIFOR, Faculty of Pharmacy, Brazil. [6]UNIFOR, Faculty of Medicine, PPG Medical Sciences, Brazil. [7]Charles Darwin University, Biomedical Sciences, Australia. [8]UECE, Prof. Dias da Rocha Natural History Museum of Ceará, Brazil.

Scorpion envenomation represents a significant public health concern in Brazil, accounting for approximately 65% of all venomous animal-related accidents in 2025. Children are at a higher risk of developing severe clinical manifestations and may require antivenom therapy, whereas adults generally experience mild local symptoms, such as pain and paresthesia. However, it remains unclear whether envenomation by scorpions of the genus Tityus stigmurus can induce subclinical systemic alterations in adults. Therefore, the present study aimed to investigate subclinical systemic changes in adult victims of Tityus stigmurus envenomation through the assessment of biochemical parameters, inflammatory markers, and endothelial biomarkers. A total of 80 adult patients with scorpion stings treated at the CIATox Fortaleza, located at Dr. José Frota Institute, were included in the study. Hematological, renal, hepatic, and cardiac evaluations were performed, including measurements of creatine phosphokinase (CPK), CK-MB, and troponin levels. Routine laboratory analyses were conducted at NULAB-IJF, whereas inflammatory and endothelial biomarkers were quantified using sandwich ELISA assays at LBFBC-UFC. The species Tityus stigmurus was identified in 82.5% of cases (n = 66). Females predominated (59.3%), and the mean age was 36 ± 11 years. Most accidents occurred in Fortaleza (95.1%), with a median interval of approximately 2 hours between the sting and hospital admission. The most frequently affected anatomical sites were the hands (35.0%), followed by the feet and legs (17.5% each).Clinical manifestations were predominantly local, with pain reported by 97.5% of patients and paresthesia by 86.4%. Pain was classified as mild in 49.4% of cases and as moderate or severe in 49.4%. Nausea was reported by 6.2% of patients and erythema by 7.4%. All patients were classified as having mild envenomation, with no clinically evident systemic manifestations. Regarding therapeutic management, 71.6% of patients received analgesics, primarily dipyrone (54.3%) and ketoprofen (49.4%).No significant abnormalities were observed in routine laboratory parameters. Interleukin-6 (IL-6) was detectable in 18.8% of patients (n = 17), suggesting a subtle degree of systemic inflammatory activation. Patients with detectable IL-6 levels exhibited significantly higher Angiopoietin-2 (Ang-2) concentrations compared with those with undetectable IL-6 levels ($p = 0.006$). Similarly, the Ang-2/Ang-1 ratio was significantly higher in the detectable IL-6 group than in the undetectable IL-6 group ($p = 0.003$). Spearman correlation analysis demonstrated a moderate positive correlation between Ang-2 and IL-6 levels ($\rho = 0.549$, $p = 0.022$), suggesting an interaction between endothelial activation and systemic inflammatory responses.These findings indicate the presence of subtle systemic alterations involving inflammatory and endothelial pathways, even in patients classified according to Brazilian Ministry of Health criteria as having mild Tityus stigmurus envenomation

11.020 **Role of TLR4 Polymorphisms and Gut–Brain Axis Signaling in the Therapeutic Response to Natalizumab in Multiple Sclerosis**. Gimenes BD[1,2], Trefilio LM[1,3], Fernandes GG[1], Mesquita IA[1], Cardoso RC[1,2], Matos MD[1 3], Duarte LA[5,6], Pavani GK[1], Pereira VCSR[4], Domingues VB[4], Fernandez KA[4], Schmidt FR[4], Alves-Leon SV[5,6], Montes GC[1,2,3], [1]UERJ, NeuroPharmacoGenetics Lab, Brazil; [2]UERJ, PPG in Clinical and Experimental Physiopathology, Brazil; [3]UERJ, PPG in Biosciences, Brazil; [4]UERJ, Pedro Ernesto University Hospital, Brazil; [5]UFRJ, Clementino Fraga Filho University Hospital, Brazil; [6]UFRJ, Translational Neuroscience Lab, Brazil

Introduction: Multiple Sclerosis (MS) is a chronic autoimmune disease of the central nervous system, characterized by demyelinating lesions caused by autoreactive lymphocytes that cross the blood-brain barrier (BBB) and promote neuroinflammation. Increasing evidence suggests that gut microbiota dysbiosis contributes to MS pathophysiology through gut-brain axis signaling and activation of innate immune pathways. Lipopolysaccharide (LPS), a bacterial product derived from gram-negative microbiota, activates Toll-like receptor 4 (TLR4), promoting inflammatory responses associated with blood–brain barrier dysfunction and neuroinflammation. Natalizumab (NTZ) is a monoclonal antibody that blocks the migration of active immune cells through the BBB. Although highly effective, approximately 25% of patients show inadequate therapeutic response. Genetic variations in TLR4 may contribute to interindividual variability in NTZ efficacy. **Objectives:** To investigate the contribution of TLR4 genetic variants, inflammatory signaling, and gut–brain axis mechanisms to the therapeutic response to natalizumab in multiple sclerosis. **Methods:** We selected 119 patients treated with NTZ at HUPE-UERJ and HUCFF-UFRJ. Peripheral blood samples were collected for DNA extraction, SNP Genotyping (rs10759931 and rs2737190). A functional assay was conducted using peripheral blood mononuclear cells from genotyped healthy individuals. The cells were isolated and stimulated with LPS for 24 hours and TLR4 expression was evaluated by qPCR. In parallel, an experimental autoimmune encephalomyelitis (EAE) model is being standardized to investigate the interaction between TLR4 signaling, gut-brain axis mechanisms, and NTZ response. **Results:** Preliminary analyses demonstrated that the polymorphic AA genotype of rs10759931and rs2737190 are associated with a better response to NTZ, while the wild-type genotype (GG) prevails among non-responders. The functional assay revealed the GG genotype of rs10759931 is associated with a higher expression of TLR4 after LPS stimulation. **Conclusion:** TLR4 polymorphisms may influence NTZ efficacy in MS by modulating inflammatory pathways. These findings support the relevance of pharmacogenetic and gut-brain axis-related mechanisms in therapeutic response and contribute to personalized medicine strategies in MS. **Financial support:** FAPERJ and CNPq. CAAE: 64171122.7.0000.5259/69411517.2.0000.5258. CEUA: 029/2025.

11.022 *In vivo* **Pharmacokinetics Determination of the Anticancer Compound LOE420 by Mass Spectrometry: BioavaiLability and Biodistribution Study**. Bastos RS[1,2], Guimarães CJ[3,5], Sales SLA[1,2], Costa PMS[1,2], Pereira JVM[1,2], Mota JA[1,2], Gress LSB[1,2], Santos JEA[1], Maranhão SS[1,2], Barros-Nepomuceno FWA[1,4], Paier CRK[1,2], Moraes Filho MO[1,2], Pessoa CDÓ[1,2] [1]UFC, Lab. of Experimental Oncology, Drug Discovery and Development Center, Brazil; 2UFC, PPG in Pharmacology, Brazil; [3]Fiocruz, Institute of Pharmaceutical Technology, Brazil; [4]UNILAB, University for International Integration of the Afro-Brazilian Lusophony, Brazil; [5]FCECON, Amazonas State Cancer Control Center Foundation, Brazil

Introduction: According to INCA (National Cancer Institute) Brazilian cancer estimates for 2026-2028 trienium indicate the emergence of 780,000 new cases. Therefore, the continued discovery and research into new anticancer therapies remain necessary. The prototype LOE420 acts as a potent antimitotic tubulin and EGFR inhibitor, with IC50 values ranging from 0.06 to 1.21 μM in cancer cell lines. Currently, the antitumor drug prototype is advancing through *in vivo* preclinical studies, with the *in vivo* pharmacokinetic profile being one of them. **Objectives:** To evaluate the *in vivo* pharmacokinetic profile of the LOE420 in Wistar Rats using mass spectrometry. **Methodology:** This study was approved by the animal research ethics committee of NPDM (n°13310521-0). The mass spectrometer used was a Shimadzu® LCMS-8060. Male Wistar rats, 60 days old and weighing between 250 and 350 g, were provided by the animal facility. The experiment was performed in triplicate. The animals received a 2 mg/kg of LOE420, by IV bolus injection. The animals were euthanized at 10 time points (0-360 min), by decapitation (one animal per point). Heparinized blood was separated by centrifugation, and the following organs were found: brain, lung, heart, liver, kidneys, and adipose tissue. The tissues were ground and homogenized in a 1:10 ratio in PBS pH 7.4. Plasma and organ homogenates were subjected to a removal solution (50:50 ACN/MeOH). Concentration curves (0.02-10 μg/mL) were created with blank samples of all matrices. Precision, accuracy, and carryover (system-matrix suitability) to determine the lower limit of quantitation (LLOQ). The samples were verified by LC-MS/MS, with oven heating, for a run time of 4 min, using a 60:40 ACN:H2O with 0.1% AF. Data were analyzed using Excel 2023 with PKAnalix, using non-compartmental analyses based on the mean concentration-time curve, generating unit parameters representative (this is used in this type of analysis due to the non-population-based nature) of the N employed to determine T½ (h), CMax (mg/L) Cl (L/h.kg), AUC (h.mg/L), Kel and Vd (L/kg), as well as Tissue/Plasma ratio (%). **Results:** The analytical method showing adequate selectivity, linearity (R^2 = 0.9932 to 0.9995), precision, accuracy, and matrix effect, with a LLOQ in 2 ng/mL. Plasma AUC0-inf = 0.32, AUC0-6 = 0.19, Cmax = 0,65, Cl = 6.24, Vd = 53,26, T1/2 = 5.91 and Kel = 0.12. Brain parameters were unobtainable as levels fell below the LLOQ, after 5 minutes. AUC_{0}–inf values were 0.15 (lung), 0.16 (kidney), 0.10 (adipose tissue), 0.084 (liver), and 0.046 h·mg/L (heart). CMax values were 0.12, 0.17, 0.06, 0.14 and 0.075 mg/L. T½ was 4.53, 7.76, 12.65, 3.84, and 3.76 h, and the tissue/plasma ratio was 46.87, 50.00, 31.25, 26.25, and 12.78%. **Conclusion:** The analytical method showed that the LOE420 circulates moderately in the plasma and is distributed widely throughout the tissues, especially the kidneys and lungs, with slower elimination in adipose tissue.

11.023 **Behavioral, Biochemical, and Endocrine Stress Responses in Zebrafish Exposed to Azithromycin, Nimesulide, and their Combination**. Seibel RS[1], Almeida PA[2], Tamagno WA[3,1], Amaral FUI[2], Prado LDSD[2], Lampugnani JAD[4], Rutikoski GW[4], Alves C[5] , FaLabreti C[5] , Tibola GM[5] , Barcellos LJG[1,2,4] [1]UFSM, PPG Ciências Biológicas: Farmacologia, Universidade Federal de Santa Maria; [2]UPF, PPG Bioexperimentação, Universidade de Passo Fundo; [3]Purdue University, School of Health Sciences, West Lafayette, IN, United States of America; [4]UPF, Curso de Medicina Veterinária, Universidade de Passo Fundo; [5]IFRS, Instituto Federal do Rio Grande do Sul.

Introduction: The increasing consumption of pharmaceuticals and their improper disposal have contributed to the frequent detection of drug residues in aquatic environments, raising concerns about their effects on non-target organisms. Antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs) are among the most frequently detected compounds due to their widespread use and environmental persistence. Although not commonly prescribed together, Azithromycin (AZT), a broad-spectrum macrolide antibiotic, and Nimesulide (NIME), a selective COX-2 inhibitor NSAID, may coexist in aquatic environments due to combined disposal, potentially leading to additive or synergistic ecotoxicological effects. **Objectives:** This study evaluated the behavioral, endocrine, and biochemical stress responses induced by acute exposure to these compounds, individually and in combination, using adult zebrafish (Danio rerio). **Methods:** Adult zebrafish were randomly distributed into five experimental groups: control, vehicle (DMSO), AZT (12.5 µg/mL), NIME (0.4 µg/mL), and AZT + NIME. Fish were exposed to these concentrations for four consecutive days (15 min/day), individually or combined. Behavioral analyses included the Novel Tank Test (NTT), Light/Dark Test (LDT), and Social Preference Test (SPT) to evaluate anxiety-like behavior, locomotion, and social interaction. After exposure, whole-body cortisol was measured as an endocrine stress biomarker. Furthermore, oxidative stress as catalase (CAT), thiobarbituric acid reactive substances (TBARS), and non-protein thiols (NPT) and neurotoxicity (AChE activity) biomarkers were analyzed in both brain and whole-body samples. This study was approved by the Ethics Committee for Animal Use of the University of Passo Fundo (CEUA-UPF; protocol 002/2023). **Results:** Exposure to all treated groups (AZT, NIME, and AZT + NIME) reduced the time spent in the upper zone in the Novel Tank Test. Additionally, NIME and AZT + NIME exposure decreased locomotion, indicating anxiety-like behavior and hypolocomotion. In the LDT, combined exposure altered locomotion and increased light zone entries. No significant effects were observed in social behavior. Whole-body cortisol levels increased significantly in all exposed groups, indicating activation of the stress response. Biochemical analyses revealed alterations in oxidative stress biomarkers, including increased CAT activity and changes in NPT, especially in the combined group. Furthermore, exposure to AZT (alone or combined) increased AChE activity, suggesting neurotoxic effects. **Conclusion:** Repeated acute exposure to AZT and NIME, individually and combined, triggered significant behavioral, biochemical and endocrine stress responses in adult zebrafish. **Acknowledgements**: The authors would like to thank the University of Passo Fundo, for providing the laboratory structure and funding for this research. **Financial support:** CNPq (403048/2023-0 and 302167/2022-6) and CAPES (Finance Code 001).

11.024 **Beyond Addiction: Proteomic Evidence of Neurodegeneration Across Brain Regions in Alcohol Use Disorder**. Hoefel LPL[1,2], Almeida FB[1,3], Schons T[1], Ferreira CF[1], Rosa AR[1], Gomez R[1]. [1]UFRGS, PPG em Farmacologia e Terapêutica (PPGFT), UFRGS, Porto Alegre, RS; [2]UFRGS, PPG em Genética e Biologia Molecular (PPGBM), UFRGS, Porto Alegre, RS; [3]Hospital Moinhos de Vento, Faculdade de Ciências da Saúde Moinhos de Vento (FACSMV), Porto Alegre, RS

Introduction: Alcohol use disorder (AUD) is associated with complex molecular and neurobiological changes. However, the molecular mechanisms underlying these changes across distinct brain regions remain poorly understood. Notably, studies integrating proteomic alterations to distinguish shared and region- specific molecular signatures are limited. Thus, identifying common pathological pathways across distinct brain regions is essential for the development of systemic therapeutic targets. **Objectives:** To identify differentially expressed proteins and pathways in the brains of individuals with AUD compared to healthy controls (HC) using high-throughput proteomics and bioinformatics approaches. **Methods:** We compiled and analyzed nine proteomic datasets from postmortem human brain tissues of individuals with AUD and matched controls (62 AUD cases and 73 controls). After stratifying data by brain region (caudate nucleus, corpus callosum, and motor cortex), we identified and compared differentially expressed proteins (DEPs) to assess shared and region-specific proteomic signatures. DEPs were defined as proteins with a p-value < 0.05 (adjusted by False Discovery Rate, FDR) and |log2 Fold Change| > 0.5. Functional enrichment analysis was performed using Metascape to identify associated biological pathways and processes. **Results:** We identified 378 DEPs across the analyzed brain regions (119 in the corpus callosum, 232 in the motor cortex, and 27 in the caudate nucleus), of which 57% were downregulated. Functional enrichment analysis revealed overrepresentation of neurodegeneration-related pathways across all regions, particularly involving mitochondrial dysfunction, oxidative stress, and synaptic impairment. Parkinson's disease-related pathways were enriched in all analyzed brain regions, suggesting shared molecular mechanisms underlying alcohol-related neurobiological alterations. Specifically, proteins such as ENOA and TPIS emerged as markers of metabolic impairment, whereas PARK7 alterations highlighted a compromised antioxidant response. Although Venn diagram analysis showed no direct overlap of specific DEPs across all three tissues, functional enrichment analysis revealed a biological convergence, with distinct regional proteinsets consistently associated with common pathological processes, including mitochondrial dysfunction and neurodegeneration. Limitations of this study include technical heterogeneity among datasets and the observational nature of post-mortem analyses, which preclude direct causal inference. **Conclusion:** Our findings indicate that AUD is associated with molecular signatures resembling those of neurodegenerative diseases. This biological convergence suggests that neuroprotective strategies, particularly those targeting mitochondrial function, may represent promising therapeutic approaches for mitigating the systemic effects of AUD. These findings also provide a rationale for exploring the potential repurposing of neuroprotective agents in AUD treatment.

11.025 **Pharmacokinetic and Pharmacodynamic Evaluation of Nanoencapsulated Artemether**. Pereira LC[1], Silva MB[2], Miranda ALL[2] da Silva, RISde D[2], Pica K[3], Fialho MCP[4], Mosqueira VCF[4], Magalhães DRM[2], Azeredo FJ[3] [1]UFBA, Faculty of Pharmacy, Lab Pharmacokinetics and Pharmacometrics, PPG in Pharmacy, Brazil. [2]Fiocruz, Postgraduate Course in Biotechnology in Health and Investigative Medicine, Brazil. [3]University of Florida, College of Pharmacy, Center for Pharmacometrics and Systems Pharmacology, United States. [4]UFOP, School of Pharmacy, Galenic Development and Nanotechnology Lab, Brazil.

Introduction: Artemether, a semisynthetic derivative of artemisinin, is a clinically important antimalarial drug used to treat both uncomplicated and severe malaria. However, its pharmacokinetic limitations, such as low bioavailability, rapid elimination, and dose-dependent toxicity, have stimulated the development of novel drug delivery strategies. One approach involves encapsulating artemether in lipid nanocapsules, offering potential for controlled release and improved therapeutic outcomes. A detailed pharmacokinetic and pharmacodynamic evaluation is essential to understand the disposition of artemether in this nanocapsule formulation. **Objective:** The aim of this study was to characterize the pharmacokinetics and pharmacodynamics of artemether-loaded nanocapsules. Method: Pharmacodynamic data were generated from preclinical efficacy studies in mice infected with Plasmodium berghei. Treatment groups (n = 5/group) received oral doses of nanoencapsulated artemether, free artemether, at 20 mg/kg or vehicle control, and parasitemia and survival outcomes were assessed throughout the study. Pharmacokinetic data for artemether-loaded nanocapsules were obtained from a preclinical study in rats (n=3/group) following intravenous (5 mg/kg) and oral (15 mg/kg) administration. Additionally, pharmacokinetic data for free artemether retrieved from the literature were incorporated into the population pharmacokinetic (POPPK) model, which was developed using Monolix software. **Results:** Pharmacodynamic studies indicated no significant differences in efficacy between free and nanoencapsulated artemether. However, animals treated with nanoencapsulated artemether showed a 33% survival rate over a 30-day period compared with the other treatment groups. In the pharmacokinetic study, a two-compartment model with first-order absorption and linear elimination best described the artemether concentration-time profile. Nanoencapsulation significantly affected the PK parameters, leading to reduced clearance to 1.02 mL/h/kg (1.61 mL/h/kg for free Artemether) and central volume of distribution to 0.54 mL/kg (1.21 mL/kg for free Artemether), while increasing intercompartmental clearance to 2.9 mL/h/kg (0.79 mL/h/kg for free Artemether). **Conclusion:** Nanoencapsulation may offer a promising strategy to optimize the pharmacokinetic behavior of Artemether by decreasing its elimination and maintaining therapeutic efficacy. The findings of this study also emphasize the importance of pharmacometric models in evaluating the impact of such formulation approaches.

11.026 **Endothelial Biomarkers in Haff Disease-Related Acute Kidney Injury**. Santos PBS[1], Almeida IM[1], Araújo LM[1], Lopes NC[1], Aquino VHN[2], Costa MDR[3], Correia MN[4], Petruccelli KCS[5], Daher EDF[6], Silva-Júnior GB[7], Sampaio TL[3], Meneses GC[3], Martins AMC[1,3] [1]UFC, Faculty of Medicine, PPG in Pharmacology, Brazil; [2]UFC, Faculty of Pharmacy, Dept. of Pharmacy, Brazil; [3]UFC, Faculty of Pharmacy, PPG in Pharmaceutical Sciences, Brazil; [4]José Mendes Regional Hospital, Brazil; [5]UFAM, Faculty of Medicine, Brazil; [6]UFC, Faculty of Medicine, Dept. of Clinical Medicine, Brazil; [7]UNIFOR, Faculty of Medicine, Brazil.

Introduction: Haff disease (HD) is a rare syndrome of acute rhabdomyolysis associated with the consumption of contaminated fish or shellfish. Acute kidney injury (AKI) is a frequent complication, and endothelial and inflammatory pathways may contribute to renal damage beyond myoglobin-mediated toxicity. **Objectives:** This study aimed to investigate the association between endothelial biomarkers and rhabdomyolysis-related AKI in HD. **Methods:** In this retrospective study, 29 adults with HD from the Brazilian Amazon (2021–2023) were included. AKI was defined based on KDIGO criteria and reclassified using serum neutrophil gelatinase-associated lipocalin (NGAL ≥100 ng/mL) as a marker of subclinical kidney injury (Husain-Syed, Pract. Lab. Med., v.31, 2022). Whole blood samples were collected at hospital admission and throughout hospitalization. After centrifugation, serum was obtained and used for biomarker analyses. Non-conventional biomarkers - serum vascular cell adhesion molecule-1 (VCAM-1), angiopoietin-2 (ANG-2), and NGAL levels - were quantified by ELISA in admission serum samples, whereas conventional laboratory parameters were serially evaluated across five collection time points during hospitalization. Clinical and laboratory data were obtained from medical records. Comparisons were performed using Student's t-test or the Mann–Whitney test, while correlations were assessed using Spearman's coefficient. Statistical analyses were performed using R (R Core Team), adopting a significance level of $p<0.05$. **Results:** AKI occurred in 62% of patients based on KDIGO criteria. Conventional laboratory parameters and biomarker levels did not differ between AKI and non-AKI groups. However, biomarker-based reclassification suggested subclinical kidney injury in all patients. In non-AKI patients, VCAM-1 was strongly and inversely correlated with estimated glomerular filtration rate (eGFR) (rho = -0.83; p = 0.001), suggesting endothelial activation preceding clinically detectable renal dysfunction. Among AKI patients, creatine kinase was inversely correlated with eGFR (rho = -0.55; p = 0.021), whereas ANG-2 was positively correlated with creatine kinase (rho = 0.49; p = 0.046), indicating an association between rhabdomyolysis severity and endothelial destabilization. **Conclusion:** Endothelial dysfunction may contribute to renal injury in HD, even before conventional AKI criteria are met. Associations involving VCAM-1 and ANG-2 support endothelial activation as a potential mechanism linking muscle injury to kidney dysfunction in toxic rhabdomyolysis.

Keywords: creatine kinase, inflammation, novel biomarkers, subclinical kidney injury.

11.027 **Investigating the Effectiveness of Subcutaneous Administration of Unfractionated Heparin: A Detailed Analysis of Absorption and Therapeutic Response**. Lopes JRM; Oliveira SNMCG; Gorinstein IVL; Mourão PAS UFRJ Universidade Federal do Rio de Janeiro Lab Tecido Conjuntivo Instituto de Bioquímica Médica Leopoldo de Meis, Brasil.

Introduction: Unfractionated heparin (UFH) is widely used for the prevention and treatment of thrombotic disorders. Unlike low-molecular-weight heparins (LMWH), whose subcutaneous administration presents a more predictable pharmacokinetic profile, UFH administered through this route still lacks studies clarifying its absorption mechanisms. Although subcutaneous administration of UFH is already employed in clinical practice, particularly for porcine formulations, studies involving bovine UFH through this route remain scarce, highlighting the need to investigate its pharmacokinetic behavior considering potential future applications. Since UFH consists of heterogeneous mixtures composed of chains with different molecular weights, it is plausible that the distribution of these populations influences absorption and biological activity following subcutaneous administration. Therefore, understanding the influence of molecular weight on these parameters may contribute to the development of formulations with more predictable therapeutic profiles. Objectives To evaluate the pharmacokinetic and pharmacodynamic profiles of porcine and bovine UFH administered subcutaneously, investigating whether different molecular weight distributions influence the absorption and biological activity of these preparations. Additionally, this study aims to evaluate whether enrichment with specific fractions can modulate pharmacokinetic parameters and contribute to more predictable therapeutic profiles. Methods Porcine and bovine UFH preparations were separated into three fractions (F1, F2, and F3) using gel filtration chromatography on a BioGel P10 column. Molecular weight distribution was evaluated by HPLC, and structural characterization was performed by NMR. Fractions are being evaluated *ex vivo* using activated partial thromboplastin time (aPTT) assays to establish dose equivalence prior to subsequent subcutaneous administration in Wistar rats. Results Porcine and bovine UFH preparations were separated into three distinct fractions. HPLC analysis confirmed segregation into low-, intermediate- and high-molecular-weight fractions. The average molecular weights of the porcine UFH fractions were 12.39, 17.70, and 23.01 kDa, whereas those of the bovine UFH fractions were 11.97, 17.10, and 22.23 kDa for F1, F2 and F3, respectively. Fraction recovery yields were 4.75%, 47.96%, and 14.02% for porcine UFH and 8.64%, 41.22%, and 11.95% for bovine UFH, respectively. The incomplete mass recovery is consistent with expected losses during chromatographic fractionation, precipitation, and purification steps. NMR characterization revealed preservation of structural features among fractions, suggesting that the observed differences were predominantly associated with molecular weight distribution. Fractions are currently being evaluated using aPTT assays for dose equivalence determination. **Conclusion:** Preliminary findings demonstrate the generation and characterization of distinct UFH fractions with different molecular weight distributions. These findings reinforce the relevance of an indirect evaluation of the pharmacokinetic behavior of these formulations and may contribute to the development of more predictable therapeutic strategies.

11.028 **CYP2D6 Intermediate Metabolizer Status, Fluoxetine Phenoconversion, and Serotonin Toxicity at Therapeutic Doses: A Mechanistic Clinical Neuropharmacology Case Series**. Poian L. R., Chiavegatto S. ICB-USP, Dept Pharmacology, Brazil

Introduction: Serotonin syndrome, or serotonin toxicity, is a potentially serious adverse drug reaction associated with increased serotonergic activity in the central and peripheral nervous systems. Although classically related to overdose or the combination of multiple serotonergic agents, interindividual variability in antidepressant metabolism may also contribute to susceptibility to serotonin toxicity during standard pharmacological treatment. We report two consented cases of serotonin toxicity occurring during therapeutic-dose fluoxetine treatment for mood and anxiety symptoms, in which pharmacogenomic testing revealed CYP2D6 intermediate-metabolizer genotypes. **Methods:** Pharmacogenetic testing was performed by GnTech Exames S/A, Brazil, using the commercial PsicoGene® Start assay. Genomic DNA obtained from buccal-cell samples was analyzed by real-time PCR for CYP2D6 *1, *2, *4, *5 (deletion), *9, *10, *17, *39, *41, and duplication; CYP2C19 *1, *2, *3, *4, and *17. CYP2D6 diplotypes and predicted metabolizer phenotypes were assigned according to the enzyme activity score. The causal relationship between fluoxetine exposure and serotonin syndrome was assessed separately for each patient using the Naranjo Adverse Drug Reaction Probability Scale. The study was approved by the Research Ethics Committee (CAAE: 70388823.3.0000.5467), and both patients provided written informed consent. **Results:** Case 1 - was a 27-year-old male previously treated with escitalopram and olanzapine, whose regimen was changed to fluoxetine and low-dose haloperidol. After fluoxetine dose escalation from 20 to 40 mg/day, he developed limb tremor, myoclonus, hyperreflexia, tachycardia, and mild confusion. Symptoms improved after fluoxetine discontinuation and diazepam administration. Pharmacogenomic testing identified CYP2D6 *1/*4 and CYP2C19 *1/*2, consistent with intermediate metabolism for both enzymes. Case 2 - was a 30-year-old female with major depressive disorder and generalized anxiety disorder, previously treated with mirtazapine and pregabalin. After switching to fluoxetine, titrated to 40 mg/day, she developed gastrointestinal symptoms, body aches, tachycardia, insomnia, hand tremor, and myoclonus, which resolved after fluoxetine discontinuation. Genotyping showed CYP2D6 *1/*4, compatible with intermediate CYP2D6 metabolism, and CYP2C19 *1/*17, compatible with rapid CYP2C19 metabolism. Both cases received a score of 6, indicating a probable adverse drug reaction in the Naranjo Adverse Drug Reaction Probability Scale. **Conclusion:** Case 1 fulfilled both Sternbach and Hunter criteria, whereas Case 2 fulfilled Sternbach criteria but could not be confirmed by Hunter criteria because clonus or hyperreflexia were not documented. Causality assessment using the Naranjo Adverse Drug Reaction Probability Scale yielded a probable relationship in both cases. These findings suggest that CYP2D6 intermediate- metabolizer status may contribute to increased vulnerability to fluoxetine- related serotonin toxicity, particularly during dose escalation and in the context of serotonergic polypharmacy. Integrating pharmacogenomic testing with structured diagnostic criteria and causality assessment may improve recognition of antidepressant-induced serotonin toxicity in patients treated for mood disorders. **Financial support:** CAPES – Financing Code 001 to LRP and FAPESP 2023/17468-7

11.029 **A Starch-Based Bioabsorbable Dexamethasone-Loaded Implant Reduces Postoperative Pain and Inflammation in Mice**. Souza FMSR, Velozo ACL, Lemos PVF, Mäder[2] K, Villarreal CF. Gonçalo Moniz Institute, Fiocruz, Brazil, School of Pharmacy, UFBA, Brazil, Martin Luther University Halle-Wittenberg, Institute of Pharmacy, Germany.

Introduction: Pain and inflammation during the postoperative period remain major clinical challenges, as inadequate control of these processes may impair recovery, hinder tissue repair, and increase the risk of chronic pain development. Local drug-delivery systems capable of controlling inflammation and pain while reducing systemic exposure represent a promising therapeutic strategy. Starch-based implantable systems have emerged as versatile platforms for controlled drug delivery. **Objectives:** To investigate the pharmacological effects of a starch-based bioabsorbable dexamethasone-loaded implant in a mouse model of postoperative pain. **Methods:** Starch-based implants were prepared by hot-melt extrusion (HME) using a ZE 5 ECO extruder (Three-Tec GmbH, Seon, Switzerland), according to the method previously described (Esfahani G, J. Control. Release.,v. 358, p. 358, 2023). Male Swiss mice (25-30g) were subjected to a postoperative pain model induced by plantar incision in the right hind paw (de Lima FO, Int. J. Mol. Sci., v. 23, n. 19, 2022). At the time of surgery, a 3 mm implant containing either vehicle or dexamethasone was placed over the plantar muscle before skin closure. Systemic dexamethasone (0.5 mg/kg, s.c., once daily from surgery day until day 6) was used as the reference treatment. Mechanical nociceptive threshold was evaluated using the von Frey test, while paw edema was quantified by plethysmometry. Paw skin samples were collected 7 days after surgery for cytokine quantification by ELISA. **Results:** The dexamethasone-loaded implant significantly induced antinociceptive effects from days 1 to 5 after surgery ($p<0.05$). The implant demonstrated superior antinociceptive effects compared with systemic dexamethasone at early postoperative time points ($p<0.05$). Regarding inflammation, both dexamethasone treatments reduced paw edema compared with the blank implant group, although the dexamethasone-loaded implant promoted a more pronounced and sustained reduction in edema throughout the experimental period ($p<0.05$). Cytokine analysis demonstrated that the dexamethasone-loaded implant significantly reduced IL-1β levels in paw tissue at both evaluated time points, while systemic dexamethasone showed less pronounced effects ($p<0.05$). No significant alterations were observed for TNF-α levels ($p<0.05$). Interestingly, IL-10 levels were increased in the dexamethasone implant group ($p<0.05$), suggesting modulation toward an anti-inflammatory profile. **Conclusion:** The starch-based dexamethasone-loaded implant promoted prolonged antinociceptive and anti-inflammatory effects in a postoperative pain model, demonstrating superior efficacy compared with systemic dexamethasone in the evaluated parameters. These findings highlight the potential of starch-based implantable systems for local corticosteroid delivery as promising strategies for postoperative pain control while potentially minimizing systemic exposure.

11.030 **Single-Dose Oral Toxicity of Coumarin Nanocapsules for Leishmaniasis Treatment: A Preclinical Study**. Gonçalves IFS[1], Araújo AB[1], Almeida JJA[1], Almeida TS[1], Pereira PIO[1], Lopes, AJSB, Colares, NN, Rodrigues NLC[2], Teixeira, MJ[2], Leal LKAM[1] [1]UFC, PPGCF, [2]UFC, Lab. of Parasitology, Brazil.

Introduction: Leishmaniasis is a parasitic disease that poses a major health challenge in developing countries due to high incidence, morbidity, and socioeconomic burden. Current treatments are limited by toxicity and parasite resistance, emphasizing the need for alternative therapies. Coumarin-loaded nanocapsules (NanoCM) have shown promising *in vitro* leishmanicidal activity and may offer an innovative treatment strategy. However, comprehensive toxicological studies, including single-dose exposures, are essential for assessing *in vivo* safety and advancing preclinical development. **Objectives:** To evaluate the preclinical safety of coumarin-loaded nanocapsules through a single-dose acute oral toxicity study in female BALB/c mice, according to OECD Test Guideline No. 423, thereby supporting the development of an innovative nanodrug for leishmaniasis treatment. **Methods:** Female BALB/c mice received a single oral dose of NanoCM at 40, 60, or 80 mg/kg and were monitored for 14 days. Saline solution (0.9%) and blank nanocapsules (NB) were used as controls. Clinical signs of toxicity, mortality, body weight, hematological and biochemical parameters, and histological changes in major organs, including the kidneys, liver, lungs, and heart, were evaluated. **Results:**NanoCM administration at all tested doses resulted in no mortality, clinical toxicity, or significant changes in body weight over 14 days. Hematological parameters, including red blood cell counts (8.47–9.05 × 10^6/µL), hemoglobin (15.68–16.38 g/dL), hematocrit (49.4–51.2%), mean corpuscular volume (56–58 fL), mean corpuscular hemoglobin concentration (31–32 g/dL), and total leukocyte counts (3.33–5.76 × 10^3/µL), remained within expected physiological ranges for adult BALB/c mice. Platelet counts showed no relevant alterations, indicating preserved hematopoietic function. Serum biochemical values for ALT (36.8–61.8 U/L), AST (82.5–120 U/L), urea (33.6–43.7 mg/dL), creatinine (0.5 mg/dL), total cholesterol (53–61 mg/dL), and triglycerides (61–82 mg/dL) were within or near normal ranges, suggesting maintained hepatic, renal, and metabolic functions. Mild decreases in albumin (1.8–2.2 g/dL) and elevated glucose (184–276 mg/dL) may reflect nutritional, methodological, or handling- related stress rather than toxicity. Histological analysis of the kidneys, liver, lungs, and heart showed preserved tissue architecture with no treatment-related lesions. **Conclusion:** Single-dose oral administration of coumarin-loaded nanocapsules at doses of up to 80 mg/kg appeared safe in female BALB/c mice, with no clinical, hematological, biochemical, or histological evidence of toxicity. These findings support the continuation of preclinical studies and contribute to the development of safer and more effective therapeutic alternatives for leishmaniasis.

11.031 **Diesel Exhaust Particles Alter Mitochondrial and cAMP Signaling in Lung Epithelial Cells**. Carvalho AE[1,4,5], Manzano-Covarrubias AL[1,2], Cattani-Cavalieri I[1,3], Dolga A[1,2], Rafie K[1,2], Andrade MF[4,5], Schmidt M[1,2], Kennedy-Feitosa E[4,5] (1)University of Groningen, Molecular Pharmacology, The Netherlands; [2]University Medical Center Groningen, Groningen Research Institute for Asthma and COPD, The Netherlands; [3]Chapman University, Faculty of Pharmacy, Dept Biomedical and Pharmaceutical Sciences, United States; [4]UFERSA, Center for Biological and Health Sciences, Brazil; (5)UERN, Faculty of Health Sciences, Brazil

Introduction: Air pollution from diesel combustion is linked to the generation of diesel exhaust particles (DEP). DEP exposure induces inflammation, oxidative stress and cell death, contributing to a decline in lung function. CAMP signaling is critical for lung homeostasis. Despite its critical role, the impact of DEP on cAMP signaling and lung function still needs to be further defined. We aimed to elucidate the impact of DEP on human bronchial epithelial (BEAS-2B) and alveolar (A549) epithelial cell mitochondrial bioenergetics, oxidative stress and inflammation markers, cell death and components of cAMP signaling. **Methods:** Cells were exposed to DEP at different concentrations and periods of time. RSL3 was used as positive control. Ferroptosis inhibitor, ferrostatin (Fer-1, 5 μM), was added 1h before infection. Metabolic activity was assessed by MTT assay and xCELLigence. Lipid peroxidation was evaluated by malondialdehyde (MDA) quantification via thiobarbituric acid reactive substances assay. Components of cAMP signaling were examined by western blot, Rap pull-down, and real-time cAMP measurements using the GloSensor assay. Mitochondrial morphology was visualized with MitoTracker Deep Red. Bulk RNA sequencing was employed to identify transcriptomic changes in lung epithelial cells following DEP exposure. **Results:** DEP altered mitochondrial morphology and network integrity by decreasing the number of branches (p <0.0001) and branch length (p <0.05), reduced basal and ATP-linked respiration (p <0.0001). Glycolysis was also reduced by more than 50% (p <0.0001) together with glycolytic reserve decrease (p <0.0001). It also significantly increased (p < 0.05) gene expression of oxidative stress markers like heme oxygenases (HO-1 and HO-2) and superoxide dismutase-2, and inflammation markers such as interleukin-8 and interleukin-6. DEP exposure increased the mitochondrial scaffold A-kinase anchoring protein 1 and β2-adrenoceptor (mRNA/protein) levels. DEP decreased mRNA levels of adenylyl cyclase 9 and reduced cAMP levels stimulated by forskolin (AC activator) and fenoterol (β2-AR agonist). DEP induced ferroptotic cell death in BEAS-2B and A549 cells, as indicated by increased lipid peroxidation (BODIPYC11 and MDA). RNAseq revealed significant differential expression (p < 0.01) of inflammatory, cell death, EMT, and cAMP signaling pathways genes. Upregulated genes included IL6, CXCL8, IL1B, and TNF. Downregulated genes included SLC39A, GPX4, VDAC, TFRC, DRP1, BAX, MFN, NECTIN, and RAPGEF3. ADCY members showed variable regulation, while RAPGEF4 was upregulated in BEAS-2B but downregulated in A549. **Conclusion:** Data suggest DEP induced mitochondrial dysfunction, oxidative stress, inflammation, ferroptotic-like cell death, and broadly dampens cAMP signaling. These epithelial responses induced by air pollution may lead to lung dysfunction and contribute to loss of functional lung tissue. **Financial support:** CAPES/PDSE; GRIAC

11.032 **PBPK/PD Model of Levofloxacin: Translational Platform to Predict Tissue Distribution in Humans**. Santos LO[1,2], Santos FL[1,2], Lemos JLS[1,3], Olivo LB[1], Araújo BV[1,2,3] [1]UFRGS, Pharmacokinetics and PK/PD Lab., Brazil, [2]UFRGS, PPG Pharmaceutical Sciences, Brazil, [3]UFRGS, PPG Pharmacology, Brazil

Introduction: Levofloxacin (LVX) is a therapeutic option for the treatment of bacterial pneumonia, sinusitis, and complicated urinary tract infections (UTIs). As a fluoroquinolone, there is awareness of adverse effects that can be serious and potentially disabling. Additionally, literature data highlight the influence of efflux transporters on LVX's disposition. **Objectives:** The goal of this study was to describe LVX tissue exposure and evaluate whether the current dose regimens impact pharmacodynamic (PD) outcomes. Methods A whole-body PBPK model was developed in PK-Sim®, describing plasma and tissue concentration-time data for healthy and infected rats. LVX's disposition is strongly impacted by efflux transporters, such as ABCB1 and MATE1. The transporters were implemented to describe renal elimination as a combination of glomerular filtration and active tubular secretion. The model for healthy animals was scaled to infected ones by incorporating physiological changes. Validation was performed using the average fold error (AFE) of the concentration-time data and the fold error (FE) of the primary pharmacokinetic exposure parameters - area under the curve (AUC) and maximum concentration (Cmax). The model for infected animals worked as a translational platform to simulate free target-site concentrations of LVX in tissues such as the lung, brain, and kidney in humans. **Results:** The whole-body PBPK model performs well in both healthy and infected animals, with AFE between 0.98 and 1.72, and FE between 0.79 and 0.81. Both within the acceptance criteria of 0.5-2.0. Simulations showed that highly perfused organs with moderate efflux transporter expression, such as the lungs, have a better association between plasma and tissue exposure than organs with higher efflux transporter expression, such as the kidneys and brain. **Conclusion:** This platform provides relevant insights into LVX's disposition, as it is based on free tissue data. The link between tissue exposure and pathogen susceptibility allows the assessment of target-site concentrations of antimicrobials and supports better clinical decision-making.

11.033 **Validated LC-MS/MS Method for Quantifying Nicotine and Cotinine in Mouse Tissues: Application to Assess Nicotine Kinetics After Cigarette or e-Cigarette Exposure**. Santos, GCM, Rocha, BM, Oliveira, MEC, Santos, GRA, Carballo, LPF, Silva, PMR, Martins, MA. IOC-Fiocruz, Lab Inflammation, Brazil.

Introduction: Quantifying nicotine and its primary metabolite, cotinine, in tissue homogenates is essential for accurately interpreting data on the distribution, accumulation, and toxicity of this alkaloid in the organism after inhalation. This study aimed to develop and apply a liquid chromatography–tandem mass spectrometry (LC-MS/MS) method to quantify nicotine and cotinine in plasma, lung, and brain from mice exposed to cigarette smoke (CS) or e-cigarette (e-Cig) aerosol. **Methods:** Plasma, lung, and brain samples were prepared by protein precipitation and subjected to an isocratic elution under methanol/5 mM ammonium formate (65:35, v/v) in a C18 column. Detection was performed by positive electrospray ionisation (ESI) in multiple reaction monitoring (MRM) mode, using cotinine-d3 as the internal standard. Nicotine and cotinine were simultaneously quantified within 5 min to 3 h post-exposure. C57BL/6 mice (n = 5/group) were continuously exposed in a dosing mass box to aerosol of e-cigarette (e-liquid containing 20 mg/ml nicotine), or cigarette smoke (Marlboro Red® with filter, 10 cigarettes) for 1.5 h. Animal procedures were approved by FIOCRUZ CEUA (L- 002/2020- A 9). **Results:** This method provided routine analyses in about 3.5 min. Validation demonstrated acceptable accuracy, precision, carryover, matrix effect, reinjection reproducibility, and stability according to ANVISA criteria. Calibration curves were linear over the range of 1-125 ng/mL for all matrices. In plasma, we detected very low levels of nicotine and cotinine, except for e-Cig, which resulted in cotinine levels of 325 ± 93 and 135 ± 66 ng/ml (Mean ± SD) at 5 and 60 min post-exposure, respectively. In the lung, nicotine and cotinine levels peaked within 5 min, showing values of 75 ± 47 ng/g and 24 ± 17 ng/g after CS and 249 ± 105 ng/g and 146 ± 72 ng/g after e-Cig, for nicotine and cotinine, respectively. These values then decreased to 32 ± 23 ng/g and 10 ± 5 ng/g after CS, and to 31 ± 33 ng/g and 23 ± 31 ng/g after e-Cig 3 h post-inhalation. In the brain, nicotine and cotinine levels also peaked within 5 min, showing values of 144 ± 88 ng/g and 81 ± 50 ng/g after CS and 554 ± 157 ng/g and 733 ± 144 ng/g after e-Cig, for nicotine and cotinine, respectively. Values then decreased to 39 ± 8 ng/g and 42 ± 12 ng/g after CS, and to 77 ± 34 ng/g and 56 ± 35 ng/g after e-Cig 3 h post-inhalation. **Conclusion:** This validated LC-MS/MS method successfully mapped tissue kinetics, revealing that e-cigarette aerosol may induce significantly higher peak nicotine and cotinine levels than cigarette smoke.

11.034 *in silico* Screening admetSAR Profiles of the Nicotine: Human Using and Safety Aspects. Costa AEA[1], Lima EMR[2], Costa CR[2], Siervo JV[1], Taricano ID[3], Silva JLV[1] [1]FMO, [2]USP, [3]UNOESTE

Introduction: Nicotine is one of the naturally occurring tobacco alkaloids, acting as an addictive chemical in tobacco and maintaining smoking behaviors. Recently, the nicotine replacement therapy (NRT) has been used to treatment for cigarettes dependency and electronic-cigarettes (E-cigs), designed to deliver nicotine through aerosols without combustion, have been developed as an alternative to traditional cigarettes. However, emerging evidence suggests that nicotine may possess carcinogenic properties in mice and could be a potential carcinogen in humans. Thus, studies that collaborate to safety and profile pharmacokinetic of nicotine has been required. Aim: To analyse absorption, distribution, metabolism, excretion and toxicity profiles of the nicotine *in silico* screening. Methods: *in silico* assessment was performed using the admetSAR 3.0 software to predict pharmacokinetic (absorption, distribution, metabolism and excretion) and toxicity parameters for nicotine (smiles: CN1CCC[C@H]1C2=CN=CC=C2). Data were expressed as a percentage of probability (%). Results: Regarding the absorption, distribution, metabolism, and excretion (ADME) properties, nicotine demonstrated blood-brain barrier penetration (94.1 %), human intestinal absorption (94.4 %) and Caco-2 permeability (85.3 %). Nicotine had low CYP inhibitory and presented CYP substrate (1A2 = 63.1 %; 2B6 = 86.1 %; 2D6 = 70.8 %). Nicotine showed a renal clearance of 53.6 %. Predictive analysis indicated low probability of Ames mutagenesis (30,9 %) and carcinogenicity in rats (44.1 %).The data were consistent with literature, which report tobacco combustion, other than nicotine, are the causal agents for increased cancer risk in smokers. However, nicotine showed high repeated dose (88.2 %) or acute (98.3 %) oral toxicity. Thus, for example, the NRT, which includes chewing gum, transdermal patches, and intranasal spray, has been advocated to reduce smoking due to its lower risk of carcinogenesis associated with combustible tobacco and its well-established safety. Conclusion: These findings suggest and reinforce that nicotine is not carcinogenic and its use for humans need well-established safety. Keywords: Nicotine, ADME properties, *in silico* toxicology.

11.035 **Physiologically Based Pharmacokinetic-Pharmacodynamic (PBPK/PD) Modeling as a Tool for the Individualization of Antimicrobial Therapy in the Setting of Sepsis**. Olivo, LB[1]; Lemos, JLS[2]; Rodrigues, VJ[2]; Araújo, BV[1,2] [1]PPG Pharmaceutical Sciences, UFRGS; [2]PPG Pharmacology and Therapeutics, UFRGS

Background: : Sepsis causes profound pathophysiological alterations that significantly impact antimicrobial pharmacokinetics, particularly tissue distribution. Nevertheless, dose adjustment strategies remain largely guided by free plasma concentrations and simplified classifications, potentially leading to subtherapeutic dosing. **Aim:** This work investigated interstitial antimicrobial exposure in sepsis and its relationship with bacterial killing dynamics using physiologically based pharmacokinetic (PBPK) modeling and PBPK/pharmacodynamic (PBPK/PD) integration with human microdialysis data. **Methods:** Plasma and interstitial concentration-time profiles were collected from published human microdialysis studies for linezolid, cefpirome, vancomycin, and meropenem. PBPK models were first developed and validated in healthy virtual subjects, then extrapolated to septic patients by incorporating pathophysiological alterations, including reduced endothelial permeability and microvascular heterogeneity, into the virtual population. Free interstitial concentrations predicted by the models were subsequently coupled to an in vitro time-kill dynamic model to assess pharmacodynamic efficacy at the infection site. **Results:** PBPK/PD integration demonstrated that reduced tissueexposure does not necessarily imply pharmacodynamic failure. For linezolid, the standard 600 mg dose was effective against methicillin-resistant *Staphylococcus aureus* (MRSA) strains with MICs of 2–8 mg/L, despite predicted median plasma fAUC 0-24h of ~87 mg·h/L failing to achieve the classical target (fAUC/MIC>80) above 1 mg/L. For cefpirome, empirical dose doubling yielded only marginal gains in interstitial exposure, while standard regimens maintained antibacterial activity for MICs < 2 mg/L; notably, the lowest evaluated dose (500 mg) achieved the desired pharmacodynamic effect. For vancomycin and meropenem, PBPK/PD models indicated that standard empirical regimens sustained interstitial exposure with adequate antibacterial response against susceptible pathogens. For vancomycin, sustained bacterial reduction was observed against MRSA (MIC ≤ 2 µg/mL) despite interstitial exposures remaining below the classical plasma target ($fAUC_{0-24h}$/MIC ≥ 400). For meropenem, interstitial concentrations typically below 100 mg/L in septic shock and below 50 mg/L in sepsis still produced pharmacodynamic efficacy against pathogens with MICs up to 128 mg/L, contradicting strict interpretation of plasma %fT>MIC. **Conclusion:** Overall, this work challenges conventional dosing paradigms in sepsis, demonstrating that mechanistic PBPK/PD integration is essential for correctly interpreting antimicrobial efficacy by simultaneously considering the drug, the pathogen, and the host.

11.036 **Comprehensive Toxicological Assessment of Latanoprost: Safety Considerations for Expanded Therapeutic Use Beyond Glaucoma**. Picada JN[1,2],Bierhals AF1, Grivicich I2, Sousa JT2, Gomez R[1] [1]UFRGS, PPG Farmacologia e Terapêutica, Brazil, [2]ULBRA, PPG Biologia Celular e Molecular Aplicada à Saúde, Brazil.

Introduction: Latanoprost is the prostaglandin analogue active ingredient of an ophthalmic solution used to treat glaucoma. Its off-label cosmetic use has increased due to its ability to stimulate eyelash and hair growth, raising safety concerns. **Objectives:** This study aimed to perform a comparative assessment of underexplored toxicological parameters of latanoprost as an active substance and its ophthalmic formulation. **Methods:** Cytotoxicity was assessed in L929 fibroblasts using the MTT assay, and genotoxicity by the alkaline comet assay. Mutagenicity was evaluated through the Salmonella/microsome assay with five *S. typhimurium* strains, with and without metabolic activation. *In vivo* toxicity was further investigated using the nematode *Caenorhabditis elegans*. **Results:** The latanoprost ophthalmic solution exhibited higher cytotoxicity than latanoprost, based on IC50 values in L929 cells. Genotoxicity was observed only for the ophthalmic solution, whereas neither ophthalmic solution nor latanoprost showed mutagenic activity in the Salmonella/microsome assay. In *C. elegans*, the ophthalmic solution demonstrated higher toxicity and impaired development, as measured by nematode body length, whereas latanoprost caused toxicity above 70%. **Conclusion:** Latanoprost exhibited lower toxicity and did not induce DNA damage, whereas the latanoprost ophthalmic solution did, effects that may be attributable to the presence of the preservative benzalkonium chloride in the formulation. Overall, these results indicate that future latanoprost formulations should avoid benzalkonium chloride, while additional investigations are required to clarify the toxic potential of latanoprost. **Acknowledgments:** CNPq, CAPES, and FAPERGS.

11. General Pharmacology

11.001FR **Structure-Activity Relationship of Thymol and Carvacrol Isomers in Human Umbilical Arteries from Healthy Parturients**. Silva PEO, Pereira LRS, Cruz JF, Duarte MRS, Batista PR, Calixto GL, Morais LP, Sales VS, Sales EPN, Gonçalves SA, Cavalcante JMC, Silva FDS, Silva JA, Barbosa R URCA - Lab Physiopharmacology of Excitable Cells, Brazil

Introduction: Relating the chemical structure of natural compounds to biological activities allows us to characterize their mechanisms of action and identify differences in performance in experimental trials. In this context, *ex vivo* assays, especially in human umbilical arteries (AUH), are useful to characterize molecules with vasorelaxant potential. Thus, thymol (2-isopropyl-5-methylphenol) and carvacrol (5-isoproyl-2-methylphenol), phenolic monoterpenoids derived from plant secondary metabolism, are position isomers and, therefore, may present distinct pharmacodynamic performances in experimental trials with AUH. **Objective:** To investigate the vasorelaxant effect of thymol and carvacrol on potassium chloride (KCl 60 mmol/L) and serotonin (5-HT 10 µmol/L) evoked contractions in AUH. **Methods:** The collection of umbilical cord fragments was done with ethical approval (CEP/URCA N° 3.832.881) and free and informed consent of pregnant women (18-40 years), aged 34-40 weeks, and submitted to vaginal delivery or cesarean section; the transport of the samples in Krebs-Henseleit solution to the laboratory; the dissection and section of the AUH in small rings (3-5mm); and the assembly in a bath of organs filled with Krebs-Henseleit solution, at 37°C, pH 7.4 and gas mixture (95% O2/5% CO2), with isometric tension adjusted at 3 gf were performed. A stabilization period (90 min) was performed and the viability (contraction≥1 gf) of the AUH was tested by depolarization with KCl (60 mmol/L). For the mechanistic pathways, contractions were evoked by KCl (60 mmol/L) or 5-HT (10 µmol/L) and after obtaining the contractile plateau, thymol (1-5000 µM) and carvacrol (1-5000 µM) were added in an increasing and cumulative manner, separately. The percentages of thymol and carvacrol relaxation in each protocol were calculated and statistically analyzed. **Results:** Thymol and carvacrol were able to relax the pre-contracted preparations with KCl and 5-HT, with EC50 of 778.40 µM and 516.21 µM and with Emax of 104.80% and 98.51% for KCl; and EC50 of 648.58 µM and 630.72 and Emax of 88.38% and 80.73% for 5-HT. The statistically significant concentrations for the relaxation of the contractions evoked by KCl and 5-HT were 1000 µM for both. **Conclusion:** Thymol and carvacrol demonstrated a concentration-dependent vasorelaxant action by contractile pathways, in addition to presenting different pharmacodynamic parameters, suggesting that the region may impact the pharmacodynamic performances of the compounds.

11.002FR **Açaí Seed Extract Shows Antipsychotic-Like Effects in a Ketamine-Induced Schizophrenia Model**. Mattos JA, Caetano AC, Ferreira FS, Dias KM,1 Nascimento JM1, Soares LN, Lopes CFO, Trefilio LM, Fontes-Dantas FL, Tavares ACD, Villaça YA, Ognibene DT, Costa CA, Resende AC, Bem GF UERJ, Research Line in Neuropharmacology and Medicinal Plants (NFPM), PPG in Clinical and Experimental Pathophysiology (Fisclinex), Brazil

Introduction: Schizophrenia is an incurable mental disorder that affects approximately 1% of the global population. The disorder is associated with positive, negative, and cognitive symptoms. Current antipsychotics act mainly on positive symptoms and may cause significant adverse effects, as well as a reduction in patients' life expectancy. Thus, studies involving medicinal plants with neuroprotective potential represent a promising strategy. Our group studied açaí seed extract (ASE), which has anxiolytic and central antioxidant effects, suggesting its potential for treating schizophrenia. **Objective:** We aimed to investigate the effect of ASE on behavioral changes related to the positive, cognitive, and negative symptoms induced by ketamine administration. Furthermore, we will compare the effects of ASE with olanzapine, an atypical antipsychotic. **Methods:** Sixty 60-day-old male C57BL/6 mice were used and divided into the following groups: Control (water by gavage for 18 days and intraperitoneal saline from day 8 to day 18), Control+ASE (ASE 500 mg/kg/day by gavage for 18 days and intraperitoneal saline from day 8 to day 18), KET (water by gavage for 18 days and ketamine 20 mg/kg/day intraperitoneal from day 8 to day 18), KET+ASE (ASE 500 mg/kg/day by gavage for 18 days and ketamine 20 mg/kg/day intraperitoneal from day 8 to day 18), and KET+OLZ (olanzapine 2 mg/kg/day by gavage for 18 days and ketamine 20 mg/kg/day from day 8 to day 18). During the last three days, animals underwent the open field test (OF), Y-maze, and three-chamber test (SI) (CEUA 010/2025). **Results:** In the OF test, the KET group displayed consistent hyperlocomotion during both the 10-15 and 15-20 minute periods compared to the Control and Control+ASE groups ($p<0,05$). ASE reduced hyperlocomotion in the KET+ASE group compared with the KET ($p<0,05$) group, but activity remained higher than in controls and in KET+OLZ in the first experimental set. However, in a 15-20 minute period, the locomotor activity in the KET+ASE group is similar to that of the KET+OLZ group. In evaluating total distance covered during the test, we observed hyperlocomotion in the KET group compared with the control groups ($p<0,05$). In the KET+ASE group, there was a reduction in locomotor activity compared to the KET group ($p<0,05$). However, this group showed increased locomotor activity compared to the control and KET+OLZ groups. Notably, the KET+OLZ group showed lower locomotor activity than the control group, while ASE treatment did not. In the Y-maze and SI tests, no significant difference was observed between the control, KET, and KET+ASE groups. However, the KET+OLZ group showed reduced alternations and increased latency, likely reflecting its locomotor deficit. **Conclusion:** These findings suggest that ASE reduces ketamine-induced hyperlocomotion similarly to olanzapine, but without causing suppression of normal activity, supporting further investigation of its antipsychotic potential. **Acknowledgments:** CAPES, FAPERJ, and CNPq.

11.003FR **Anti-Inflammatory, Antioxidant and Antinociceptive Effects of the Hydroethanolic Extract from Piper sp. Leaves in Carrageenan-Induced Acute Inflammation in Mice**. Oliveira, SLMK[1], Azevedo VGS[1], Peixoto ABS[1], da Silva FGN[1], Lopes RF[2], Frota LS[3], de Morais SM[4], Assereuy AMS[1] [1]UECE, Instituto Superior de Ciências Biomédicas, PPG em Ciências Fisiológicas, Brazil; [2]UFAC, Lab Pesquisa em Fisiofarmacologia, Programa de Pós-Graduação em Biodiversidade e Biotecnologia da Rede BIONORTE, Brazil; [3]UECE, Lab Química de Produtos Naturais, PPG em Ciências Naturais, Brazil.

Introduction: Acute inflammation is characterized by vascular and cellular events associated with edema, leukocyte migration, oxidative stress and nociception. The genus Piper presents medicinal potential due to the presence of bioactive metabolites showing anti-inflammatory, antioxidant and analgesic activities. However, the pharmacological properties of Piper sp. remain poorly described. **Objectives:** To identify the phytochemical constituents of the hydroethanolic extract from Piper sp. leaves (EHFPsp) and evaluate its antioxidant, anti-inflammatory and antinociceptive effects in carrageenan- induced acute inflammation models in mice. **Methods:** The phytochemical profile of EHFPsp was determined by HPLC-DAD and the antioxidant activity by DPPH and ABTS assays. Male mice (n=8/group) received EHFPsp (25-200 mg/kg; p.o.) 1 h before carrageenan administration by intraplantar (300 µg/50 µL) or intraperitoneal (500 µg/100 µL) routes. Paw edema, nociceptive threshold and leukocyte migration were evaluated. Results were expressed as Mean ± S.E.M. and analyzed by ANOVA followed by Bonferroni's post hoc test ($p<0.05$). **Results:** Phytochemical analysis revealed the presence of gallic acid, chlorogenic acid, epicatechin, p-coumaric acid, kaempferol-3-O- rutinoside, ferulic acid and quercetin, with ferulic acid as the major compound. EHFPsp demonstrated antioxidant activity in DPPH and ABTS assays. In the carrageenan- induced paw edema model, EHFPsp (100 and 200 mg/kg) reduced the early inflammatory phase by 28.8% (160 ± 7.89 vs. carrageenan: 225 ± 12.09 AUC) and 22% (175 ± 13.50 vs. carrageenan: 225 ± 12.09 AUC), respectively. In the late phase, EHFPsp (50, 100 and 200 mg/kg) reduced edema by 46% (210 ± 16.48 vs. carrageenan: 390 ± 9.89 AUC), 58 % (165 ± 17.77 vs. carrageenan: 390 ± 9.89 AUC) and 63% (145 ± 9.81 vs. carrageenan: 390 ± 9.89 AUC), respectively. EHFPsp (100 mg/kg) increased the nociceptive threshold by 62% (23.30 ± 1.28 vs. carrageenan: 9.25 ± 0.47 g) and reduced total leukocyte migration by 50.9% (2700 ± 185.1 vs. carrageenan: 5500 ± 349.1 cells/mm^3) and neutrophils by 90% (442 ± 170.9 vs. carrageenan: 4538 ± 338.8 cells/mm^3). These findings demonstrate that EHFPsp presents antioxidant, anti- inflammatory and antinociceptive effects via reduction of inflammatory parameters associated with acute inflammation. **Conclusion:** EHFPsp presents a phytochemical profile rich in phenolic compounds and flavonoids and exhibits antioxidant, anti-inflammatory and antinociceptive effects in acute inflammation models induced by carrageenan in mice. **Acknowledgments:** Fundação Cearense de Apoio ao Desenvolvimento Científico e Tecnológico (FUNCAP). Ethical approval: The experimental protocols were approved by the Institutional Animal Care and State University of Ceará (CEUA-UECE No. 31032.003381/2025-00). Funding: Fundação Cearense de Apoio ao Desenvolvimento Científico e Tecnológico (FUNCAP).

11.004FR **Polysaccharides from *Genipa americana* Leaves: An Evaluation in the Rat Model of Arthritis Induced by Zymosan**. Azevedo VGS[1], Peixoto ABS[1], Araujo DFA[1], Da Silva Nascimento FG[1], Leite LMP[2], Pereira MG[2], Assreuy AMS[1] [1]UECE, Institute of Biomedical Sciences, PPG Physiological, Brazil; [2]FECLESC/UECE, Faculty of Education, Sciences and Letters of the Central Hinterland, Brazil

Introduction: Rheumatoid arthritis is a systemic inflammatory disease characterized by pain, synovitis, and leukocyte infiltration, whose conventional treatment may cause long-term adverse effects. *Genipa americana* L. (Rubiaceae), popularly known as jenipapo, is widely distributed throughout Brazil and predominantly found in the semi-arid region. Experimental studies demonstrated that the polysaccharide extract obtained from its leaves exhibits low toxicity and antioxidant, anti-inflammatory, antinociceptive properties in acute inflammatory models. **Objectives:** To evaluate the effect of polysaccharidic extract of *Genipa americana* (PE-Ga) in the model of zymosan-induced arthritis in the tibiotarsal joint of male Wistar rats. Methods: Leaves of *G. americana* were collected in the Custódio district, Quixadá-Ceará (voucher 4683, Herbário Prisco Bezerra, Universidade Federal do Ceará), washed, dried and crushed. Five grams of dry powder were depigmented (MeOH 1:50 w/v, 60 °C, 2 h), and the polysaccharides extracted in alkaline medium (0.1 M NaOH, 1:50 w/v), followed by precipitation (EtOH). Deproteinization was performed by precipitation with trichloroacetic acid (pH 3.0, 4 h, 4 °C), centrifuged (3500×g, 30 min, 25 °C), and the supernatant containing the PE-Ga was dialyzed and lyophilized (6% yield; 36% total carbohydrates, 0.8% proteins). The animals (n=6) received PE-Ga (3 mg/kg), saline or indomethacin (5 mg/kg) intravenously 2 h after arthritis induction by zymosan (500 µg/25 µl). Joint edema (caliper and photographs) and nociception (digital analgesimeter) were assessed before and up to 6 h after induction, as well as leukocyte migration in the articular fluid after euthanasia (6 h). Results were expressed as Mean ± S.E.M. and analyzed by ANOVA ($p<0.05$). **Results:** Zymosan reduced the nociceptive threshold (69.81 ± 7.35 vs. saline: 111.7 ± 3.97 g) and PE-Ga increased (up to 49%) this threshold from 4 h (AUC: 162 ± 9.60 vs. zymosan: 122 ± 8.34) to 6 h (219 ± 10.54 vs. zymosan: 112 ± 4.97 AUC). Indomethacin also increased the threshold between 4 and 6 h (192 ± 16.91 vs. zymosan: 112 ± 4.97 AUC). Zymosan increased joint diameter (7.83 ± 0.28 vs. saline 6.69 ± 0.06 mm) and PE-Ga reduced by 17% at 6 h (14.00 ± 0.17 vs. zymosan 16.83 ± 0.28 AUC) and the indomethacin by 14% (14.54 ± 0.26 vs. zymosan: 16.83 ± 0.28 mm). Zymosan increased total leukocytes (7670 ± 1141 vs. saline: 91.67 ± 27.13 mm^3) and neutrophil migration (6441 ± 1034 vs. saline: 110 ± 24.49 mm^3). PE-Ga (3 mg/kg) reduced these values by 67% (2567 ± 641.30) and 87% (840.20 ± 358.90), respectively, similar to indomethacin by 69% (2383 ± 338.50) and 90% (607.80 ± 125). **Conclusion:** PE-Ga showed anti-inflammatory and antinociceptive effects via reduction of the edema, hypernociception and leukocyte migration in zymosan-induced arthritis.

11.005FR **Synergic Healing Effect of *Delonix regia* Galactomanans and Platelet Rich Plasma in Mice Cutaneous Wounds**. Alves PGM[1], Lima IC[3], Oliveira SLMK[1], Falcão ES1, Mota MRL[2], Assreuy AMS[1] [1]UECE, Lab. of Physio-Pharmacology of Inflammation, PPG Physiological Sciences, Brazil, [2]UFC, Dept. of Clinical Odontology of UFC, Lab. of Oral Pathology, Brazil, [3]Universidade Christus, Brazil.

Introduction: The wound healing process is a physiological process which involves tissue reorganization and participation of cellular and molecular events to regenerate the damaged tissue. Galactomannans are hydrogel-like seed polysaccharides obtained from *Delonix regia* (Caesalpiniaceae), found in tropical countries like Madagascar and commonly used in food industry. Previous study on *D. regia* galactomannan (GM-Dr) demonstrated in mice anti- inflammatory and healing effects mediated by inhibition of pro-inflammatory cytokines (IL-1β, IL-6) and fibroplasia stimulation accompanied by TGF-β increase. **Objectives:** To evaluate the healing effect of the association GM-Dr + platelet rich plasm (PRP) in mice cutaneous wound model. **Methods:** Two cutaneous wounds were performed surgically (7mm diameter punch) at the dorsal region of female Swiss mice (25-35 g). Animal wounds received topical application of sterile saline (0.9% NaCl), platelet poor plasm (PPP), 1% GM-Dr or 1% GM-Dr combined (1:1) or alternated with platelet rich plasm (PRP) along 14 days. The wounds were analyzed for clinical inflammatory parameters: edema; hyperemia; exudate; vascular permeability (protein leakage); nociception (g); oxidative stress markers (reduced glutathione - GSH, malondialdehyde - MDA); and leukocyte infiltrate; and for healing signs: crust detachment; scar tissue formation; healing index (wound area); fibroblasts and collagen deposition). **Results:** Edema and hyperemia were inhibited by GM-Dr + PRP, being the combined therapy effective from the 2nd to the 7th day. Vascular permeability was also reduced by the combined therapy at the 2nd day. The nociceptive threshold was enhanced by the combined GM-Dr + PRP from 30 min to 7 days post-ulceration compared to control and PPP groups. The content of MDA was reduced (48-90%), but that of GSH was elevated (64-68%) by the combined GM-Dr + PRP from the 2nd to the 7th day compared to control group. Crust detachment and scar tissue formation were present in the groups GM-Dr + PRP (combined and alternated) from the 5th to the 7th day. The healing index was enhanced by GM-Dr + PRP compared to control and PPP from the 2nd to the 7th day, and until the 14th compared to control. At the wound site, GM-Dr + PRP reduced the leukocyte infiltrate of mono (70-70%) and polymorphonuclear (79-91%) from the 2nd to the 7th day, along with reduction in fibroblasts number from the 5th to the 7th day (53-39%) while total collagen deposition was enhanced at the 14th day (64%). **Conclusion:** The daily topical treatment of PRP and 1% GM-DR accelerates the healing process of excisional skin wounds in mice by modulation of inflammatory and healing parameters. These findings provide insights on the use of plant polysaccharides combined with regenerative endogenous molecules as wound healing therapy.

11.006FR **Polysaccharide-Rich Ointment of** *Caesalpinia ferrea* **Barks Inhibits Clinical Signs and Accelerates Skin Wounds Healing in Hyperglycemic Rats**. Lopes MR[1], Santos GA[1], Falcão ES[1], Leite LMP[2], Pereira MG[2], Mota MRL[3], Assreuy AMS[1] [1]ISCB-UECE, Lab Physiopharmacology of Inflammation, Brazil; [2]ISCB-UECE, Lab Polysaccharides Bioactives, Brazil; [3]UFC, Lab Oral Pathology, Brazil

Introduction: Wound healing in diabetic individuals is compromised by the occurrence of persistent inflammation. Since the current healing therapies for these individuals have limitations, plant polysaccharides emerge as potential alternative due to their various immunomodulator effects and low or absent toxicity. In particular, Caesalpinia ferrea or Libidibia ferrea is a native plant of Brazil Northeast, included in the List of National Medicinal plants of SUS interest (RENISUS) being popularly used to treat inflammatory conditions. The polysaccharides obtained from its stem barks have shown anti- inflammatory, antinociceptive and antioxidant effects in normal and hyperglycemic rats. These preclinical studies performed by our research group led to the formulation of an ointment containing C. ferrea polysaccharides (Patent N° BR 102017024814-3). **Objectives:** This study evaluated the effect of a dermal ointment containing 10% total polysaccharides of Caesalpinia ferrea (PLT-Cf) on cutaneous wounds of Wistar rats (160-200 g) with diabetes (≥200 mg/dL glucose) induced by alloxan (120 mg/Kg). Methods. Dorsal excisional wounds (7 mm; 4/animal) were surgically induced, treated with PLT-Cf, vehicle (lanolin, petrolatum and polyethylene gel) or reference ointment (Curaderm® and Fitoscar®) CEUA-UECE (31032.003360/2023-14) and evaluated on days (2-10) for parameters inflammatory (hyperemia, edema, exudate) and healing (area and healing index, crust detachment, scar tissue) clinical. The results were expressed as mean ± standard error of the mean (SEM) or median (min–max) and analyzed using two-way ANOVA ($p<0.05$). **Results:** Treatment with PLT-Cf reduced edema along the days 7 [0.8(0-2) vs. 0(0-0)] and 10: 0(0-0) vs. 0.8(0-2)], exudate on day 7 [0(0-0) vs. 0.6(0-2)], and hyperemia on day 10 [0(0-1) vs. 1.3(0-2)]. Besides, PLT-Cf reduced the wound area on days 5 (27.83 vs. 40.17), 7 (19.83 vs. 34.83), and 10 (3.00 vs. 14.00) and increased the healing index on days 2 (15% vs. 8%), 5 (31% vs. 21%), 7 (51% vs. 31%), and 10 (93% vs. 72%). In addition PLT-Cf increased crust detachment on days 5 (83% vs. 16%) and 7 (100% vs. 33%) and scar tissue formation on day 5 (83% vs. 33%). **Conclusion:** The ointment rich in polysaccharides from Caesalpinia ferrea stem barks possesses healing effect via attenuation of the healing inflammatory phase, suggesting its applicability to treat cutaneous wounds in diabetic patients.

12. Drug Discovery and Development

12.001 **Therapeutic Potential of a Promising N-Phenylacrylamide Derivative in the Treatment of Colitis**. Silva JVV[1,3], Araruna MEC[2], Barbosa YV[3], Farias AGC[1,2,3], Cavalcanti MAT[1], Menezes KJS[1], Leandro PF[1,3], Lima MKS[1,3] Fernandes HQA[1,3], Moura WCS[1,2,3], Lima AMAF[1,3], Oliveira MLA[1,3], Albino SL[1,2,3], Moura RO[1,2,3]. [1]UEPB, Lab Drug Devopment and Synthesis, Brazil; [2]UEPB, PPG in Pharmaceutical Sciences, Brazil; [3]UEPB, Dept Pharmacy, Brazil

Inflammatory bowel diseases (IBD) comprise ulcerative colitis (UC) and Crohn's disease (CD), which are auto-immune illnesses characterized by ulcerative and intense inflammation in the gastrointestinal tract. Current pharmacotherapy may include the use of amino salicylates and corticosteroids to mild and moderate forms, and biological therapy, such as monoclonal antibodies, to treat severe colitis. Nevertheless, these drugs are associated with significant side effects especially with long-term therapy. This can be overcome by searching for new molecules and more specific targets to securely reverse the disease. In the study of Silva, Pharmaceutics, v. 14, p. 188, 2022, (E)-2-cyano-N,3-diphenylacrylamide (JMPR-01) has demonstrated to be a potential anti-inflammatory compound, reducing inflammation *in vitro* and *in vivo* through immunomodulatory mechanisms. Therefore, the aim of this study was to evaluate the acute toxicity of JMPR-01 and its activity on the TNBS-induced acute colitis model. For this purpose, JMPR-01 (2000 mg/kg) was administered orally to female mice, and the animals were then evaluated for 14 days for any sign of toxicity. For the acute colitis, saline (10 mg/kg), prednisolone (2 mg/kg) or JMPR-01 (10 and 50 mg/kg) were administered 48, 24 and 1h before and 24h after intrarectal administration of 10 mg of TNBS (2,4,6-trinitrobenzenesulfonic acid) dissolved in ethanol 50%. The animals were euthanized, and the colon segment was removed to determine the ulcerative lesion area (ULA) for further healing percentage calculation. During 14 days of treatment with 2000 mg/kg neither death of the animals nor physiological alteration was observed, there was no significant alteration in water or food consumption, or in the morphology of the organs in comparison with the control. JMPR-01 at both doses significantly reduced the lesion area with a calculated healing percentage of 97.38% (10 mg/kg) and 94.03% (50 mg/kg), a response like that of prednisolone (95.51%). The wound score was reduced from 8.4 (untreated group) to 1.2 (JMPR-01, 10 mg/kg). The possible mechanism of action of its activity on colitis may include the modulation of pro- inflammatory cytokines and enzymes as shown in previous studies. Therefore, the findings suggest that JMPR-01 is a promising candidate for the treatment of colitis without acute toxicity. **Acknowledgments:** This study was supported by a CNPq fellowship awarded to Silva J.V.V., with additional financial support from CAPES and FAPESQ.

12.002 **Expression, Purification, and Validation of an in-House Recombinant Taq DNA Polymerase for PCR Applications**. Salviano RA[1,3]; Costa PMS[1,2]; Silva AS[1,3]; Desiderio GA[1,2]; Paier CRK[1,2]; Pessoa C[1,2] [1]UFC, Lab Experimental Oncology, Brazil, Drug Research and Development Center, Brazil; [2]UFC PPG Pharmacology, Brazil; [3]UFC Faculty of Pharmacy, Dentistry and Nursing, Brazil

Introduction: Taq DNA polymerase is a thermostable enzyme isolated from the bacterium -*Thermus aquaticus*.- Because of its high stability at elevated temperatures, such as those used during DNA amplification cycles, this enzyme is widely used in the polymerase chain reaction (PCR). Taq DNA polymerase also has considerable relevance in pharmacology, as it enables genetic analyses, the development of molecular tools, laboratory quality control, and studies aimed at the discovery and evaluation of new drugs. In this context, in-house production of the enzyme represents a promising strategy, since it reduces laboratory costs by decreasing dependence on commercially acquired enzymes. **Objective:** To produce a recombinant Taq DNA polymerase and validate its enzymatic activity. **Methodology:** The enzyme was expressed in *E. coli* BL21(DE3) pRARE after induction with IPTG. After 18 hours, the bacterial pellet was collected, resuspended in lysis buffer, and the lysate underwent cycles of heat shock and centrifugation to purify the enzyme. The produced protein was identified by SDS–PAGE, and its enzymatic activity was evaluated by PCR amplification of the human genes -*GAPDH*- and β-actin (-*ACTB*-). A commercial Taq DNA polymerase was used as an amplification control. **Result**: The enzyme was successfully produced recombinantly with a high degree of purity and a yield of 45 mg per liter of culture. In addition, the enzyme was able to amplify -*GAPDH*- and -*ACTB*- comparably to the commercial control. **Conclusion:** These results demonstrate the feasibility of in-house production of Taq DNA polymerase, representing an opportunity to reduce laboratory costs and to expand applications in molecular diagnostics, scientific research, and monitoring of biological contamination.

12.003 **Comparative Quantum Evaluation of Serotonin, DMT, 8-OH-DPAT, and 5-MeO-DMT Interactions with the 5-HT1A Receptor**. Dantas BLR, Silva MS, Silva FKO, Gavioli EC, Fulco UL, Bezerra KS, Silva-Junior ED UFRN, Dept Biophysics and Pharmacology, Brazil.

Introduction: Serotonin (5-HT) regulates mood, cognition, and behavior through distinct serotonergic receptors. Among them, the 5-HT1A receptor (5-HT1A-R) plays a central role in serotonergic neurotransmission and represents an important therapeutic target for neuropsychiatric disorders. In addition to 5-HT, new psychoactive compounds such as DMT, 5-MeO-DMT, and the selective agonist 8-OH-DPAT interact with the 5-HT1A-R. However, the molecular determinants governing ligand recognition and stabilization at this receptor remain incompletely understood. **Objective:** The present study aimed to comparatively evaluate, at the quantum level, the interaction energies of serotonin, DMT, 5-MeO-DMT, and 8-OH-DPAT with residues composing the orthosteric binding site of the 5-HT1A-R using density functional theory calculations. **Methods:** Computational analyses were performed using crystal structures of the 5-HT1A-R bound to 5-HT (PDB ID: 7E2Y), 5-MeO-DMT (PDB ID: 9KVG), DMT (PDB ID: 9KVI), and 8-OH-DPAT (PDB ID: 9VJG). Protein and ligand structures were prepared under physiological conditions, and interaction energies with orthosteric-site residues were calculated using the MFCC-DFT approach with the B97D functional and CPCM solvation model ε = 40). **Results:** The ligands exhibited the following total binding energies (in kcal·mol^{-1}) at the 5-HT1A-R, in decreasing order of interaction strength: 8-OH-DPAT (-56.00) > DMT (-48.84) > 5-MeO-DMT (-36.65) > 5-HT (-34.27). In the 5-HT/5-HT1A-R complex, the residues contributing most to the interaction energy (in kcal·mol^{-1}) were ASP116 (-11.41) > PHE361 (-3.83) > VAL117 (-3.75) > PHE362 (-2.69). The residues with the greatest contributions to the interaction energy (in kcal·mol^{-1}) in the 5-MeO-DMT/5-HT1A-R complex were ASP116 (-7.52) > VAL117 (-5.60) > PHE361 (-3.52) > PHE362 (-2.91). In the DMT/5-HT1A-R complex, the interaction energy profile (in kcal·mol^{-1}) followed the order ASP116 (-14.46) > VAL117 (-5.22) > PHE362 (-3.82) > TYR390 (-2.73). Finally, in the 8-OH-DPAT/5-HT1A-R complex, the energy interaction profile (in kcal·mol^{-1}) was ASP116 (-12.01) > PHE361 (-5.80) > VAL117 (-5.47) > TYR390 (-5.27). Comparative analysis revealed a common interaction core formed by ASP116, VAL117, PHE361, PHE362, and THR200 across all complexes. 5-HT and DMT shared interactions with THR121, LYS191, and ALA203, whereas DMT and 8-OH-DPAT displayed common interactions with CYS120, ILE189, TRP358, and TYR390. Exclusive interactions were observed for 5-HT (CYS119 and ILE129) and 5-MeO-DMT (ASN386). **Conclusion:** These findings improve the understanding of the structural and energetic determinants governing molecular recognition at the 5-HT1A receptor and provide valuable insights into ligand selectivity. The identification of conserved and ligand-specific interactions may support the rational design of novel serotonergic compounds with therapeutic potential. Funding: CAPES and CNPq.

12.004 **Computer-Aided Drug Design Applied to the Discovery of Potential Falcipain-2 Inhibitors Against Plasmodium falciparum**. Rios EO[1], Silva AVX[1], Silva KWL[2], Nascimento IJS[1] [1]CESMAC, Faculty of Pharmacy, Brazil, [2]Estácio, Faculty of Biological Sciences, Brazil

Introduction: Plasmodium falciparum is the species responsible for the lethal forms of malaria, and the growing resistance to traditional antimalarials makes the search for new therapies essential. Falcipain-2 (FP2), a cysteine protease involved in hemoglobin degradation in the parasite's digestive vacuole, is essential for parasite development, making it a promising target for inhibition. In this context, combining drug repurposing with Computer-Aided Drug Design constitutes a rational approach to identifying promising compounds. **Objectives:** To evaluate, through structure-based virtual screening, the potential of drugs approved by the Food and Drug Administration (FDA) as inhibitors of FP2 from P. falciparum. **Methods:** FDA-approved drugs were selected from the ZINC database to compose the screening library, and the crystallographic structure of FP2 (PDB: 6JW9) was obtained from the RCSB Protein Data Bank. Each compound was optimized in terms of conformation using ArgusLab. In addition, the target was prepared in GOLD software, in which the original ligand (E-64) and the water molecules were removed, and hydrogens were added. The ligands were processed in blocks of 100 and docked into the binding site under search efficiency settings of 200%, 125,000 maximum operations, with early termination turned off, using a fitscore ≥ 70 as the approval criterion. Finally, the visual inspection performed in Discovery Studio evaluated interactions with key residues Cys42, His174, and Gln36. The selected ones underwent individual bibliographic searches on antiplasmodial activity in PubMed, ScienceDirect, and Google Scholar. **Results:** Validation by redocking of the co-crystallized ligand resulted in RMSD = 1.28 Å. Of the 1613 FDA-approved drugs, 116 met the fitscore criterion. After the analysis of the interactions in Discovery Studio, only 8 presented hydrogen bonds with the key residues of the catalytic site. The bibliographic review of these 8 identified 3 with reported antiplasmodial activity, among them deferoxamine, iloprost, and venetoclax, while the others showed no prior evidence. Thus, these compounds could have promising antimalarial. **Conclusion:** Molecular docking screening against FP2 identified approved drugs as potential inhibitors of the target, with emphasis on deferoxamine, iloprost, and venetoclax, which have prior evidence of antiplasmodial activity. Because the mechanisms underlying their action against FP2 are distinct from those of enzyme inhibition, the drugs' activity against FP2 remains speculative and requires further investigation before any proposal for repurposing. **Acknowledgments:** The authors thank the National Council for Scientific and Technological Development (CNPq) for the financial support provided through the research grant awarded.

12.005 **Evaluation of the Antinociceptive Potential of Oxyethylariamides in Experimental Pain Model**. Valente AG, França PRC, Franco GRR, Silva IMF, Viegas-Junior C, Fernandes PD UFRJ, Institute of Biomedical Science, Lab Pharmacology of Pain and Inflammation, PPG Pharmacology and Medicinal Chemistry, Brazil, UFAL, Chemistry Institute, Medicinal Chemistry Research Lab, PPG Pharmaceutical Sciences, Brazil.

Introduction: Despite the variety of analgesic drugs currently available, pain treatment remains limited by insufficient efficacy and significant adverse effects. In this context, medicinal chemistry has focused on the development of novel compounds with potential antinociceptive activity and reduced toxicity. **Objective:** Therefore, the aim of this study was to evaluate the antinociceptive effects of the substances synthetized as PQM-337 and PQM-338. **Methods:** Female Swiss Webster mice (28-32g, n=5-6) were used in evaluation of toxicity, chemical (formalin-induced paw licking, FIL), and thermal (hot plate, HP) tests, effects of PQM-337 and PQM-338 (at 10 µmol/kg). In FIL, 1h after oral administration, mice received an intraplantar injection of 20 µL of formalin (2.5%) into the hind paw. This model consists of evaluating two distinct phases, a neurogenic phase (0-5 minutes) and an inflammatory phase (15-30 minutes), and the time the animal spends licking its paw in each phase is recorded. In HP model, mice were placed on a heated plate (55±0.5°C) and latency time was recorded every 30 minutes after the oral administration of the substances when the animals licked one of their paws, jumped, or showed an unexpected reaction. For toxicity assessment, animals were euthanized after 24 h for blood, organ, and bone marrow collection. Statistical analysis was performed using ANOVA followed by Tukey's test (*$p<0.05$). The protocol for animal use was approved by CEUA/UFRJ and received the numbers 31/19 and 28/20. Results were expressed as mean ± SD. **Results:** Although none of the tested substances inhibited the first phase of the FIL model, all showed an effect in the second phase: 1st phase: vehicle: 52.7±9.3 seconds; acetylsalicylic acid at 1110 µmol/kg (ASA): 19.6±4.1* seconds; morphine at 9 µmol/kg: 21.5±2.0* seconds; PQM-337: 46.2±6.2 seconds; PQM-338: 59.7±8.7 seconds; 2nd phase: vehicle 259.7±22.3 seconds; ASA: 63.2±15.9* seconds; morphine: 141±19* seconds; PQM-337: 134.4±21.5* seconds; PQM-338: 151.5±17.9* seconds. In the HP model, PQMs increased the latency time of the animals. Results were expressed in area under curve (AUC): vehicle: 869.9±517.7; morphine at 9 µmol/kg: 11,639.1±1,882.1*; PQM-337: 21,083.9±5,969.6*; PQM-338: 12,853.9±2,934.2*. There were no significant changes in hematological parameters, and the substances did not demonstrate toxicity in the bone marrow analysis when compared to the control group. Furthermore, no significant differences were observed in organ weight when compared to animal weight. **Conclusion:** The results suggest that the tested substances exhibit antinociceptive activity, indicating a possible antinociceptive effect. **Financial support:** CNPq, FAPERJ, Instituto Vital Brasil (donation of mice).

12.006 *In vitro* Evaluation of the Anti-Leishmania Potential of Isatin-Derived Cyanohydrazones Against *Leishmania infantum*. Albuquerque YS[1], Machado GR[1], Fernandes ALM[1], Ferreira RS[1], Cardoso LL[1], Santos ESFR[2], Lima-Junior CG[2], Keesen TSL[1] [1]UFPB, Immunology Lab Infectious Diseases, Brazil, [2]UFPB, Lab Medicinal Organic Synthesis, Brazil

Introduction: Visceral leishmaniasis is a chronic, systemic disease with a wide global distribution and high mortality, caused primarily in Brazil by the parasite *Leishmania infantum*. Currently, available treatments for this disease, such as Amphotericin B and pentavalent antimonials, have limitations, including parasite resistance and toxicity. In this context, isatin-derived cyanohydrazones stand out as promising bioactive compounds. **Objectives:** Thus, the present study aimed to evaluate the anti-Leishmania potential of isatin- derived cyanohydrazones against the promastigote and axenic amastigote forms of L. infantum, as well as their cytotoxicity in human erythrocytes. Methods: This research was approved by the Research Ethics Committee of the Health Sciences Center of the Federal University of Paraíba - CCS/UFPB (CAAE: 90688425.1.0000.5188). The anti-promastigote and anti-amastigote activities of the compounds were evaluated using the MTT colorimetric assay at concentrations ranging from 100 µM to 0.78 µM. Hemolytic activity was assessed by erythrocyte hemolysis at concentrations ranging from 100 µM to 0.78 µM. All *in vitro* assays were performed in three independent experiments, each conducted in triplicate, using Amphotericin B (AmB) as a positive control. Statistical analyses were performed using GraphPad Prism version 9.0 to calculate IC50, EC50, and HC50 values with 95% confidence intervals. **Results:** Initially, five molecules from this class were evaluated, and the compound with the best anti-promastigote activity was selected. ECN62 exhibited excellent inhibition of promastigotes, with an IC50 of 3.02 µM. In assays with axenic amastigotes of L. infantum, ECN62 exhibited an EC50 = 3.07 µM, whereas AmB showed an IC50 = 0.58 µM and an EC50 = 0.32 µM. ECN62 showed no hemolytic activity at the highest concentration tested, with an HC50 > 100 µM, whereas AmB exhibited an HC50 of 193.4 µM. The selectivity index of ECN62 was > 33.11 for promastigotes and > 32.57 for axenic amastigotes relative to human erythrocytes, whereas AmB exhibited selectivity indices of 333.45 and 604.37, respectively. The selectivity indices observed for ECN62 indicate preferential activity against the parasite over human erythrocytes, suggesting a promising therapeutic profile. **Conclusion:** ECN62 exhibited significant anti-Leishmania activity, highlighting isatin-derived cyanohydrazones as promising candidates for future studies on the treatment of visceral leishmaniasis.

12.007 **Synthesis, Characterization, and** *in silico* **Evaluation of Cyanoacrylate Derivatives for Treatment of Inflammatory Diseases**. Lima MKS[1], Silva JVV[1], Leandro PF[1], Farias AGC[1,2], Lima AMAF[1], Oliveira MLA[1], Fernandes HQA[1], Menezes KJS[1], Cavalcanti MAT[1], Albino SL[1,2], Silva JM[3], Moura RO[1,2] [1]UEPB, Lab Drug Development and Synthesis, Brazil [2]UEPB, PPG Pharmaceutical Sciences, Brazil [3]UFPE, PPG Pharmaceutical Sciences, Brazil

Inflammation is an essential biological response involved in tissue defense and repair. However, when it becomes chronic, it contributes to the development of several diseases. Although therapies such as non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids are available, their prolonged use is limited due to significant adverse effects. Therefore, the development of new drugs acting on different molecular targets represents a promising strategy. In this context, the present study aimed to synthesize, characterize, and evaluate, through *in silico* tools, the potential anti- inflammatory activity of three cyanoacrylate derivatives: JMS-16, JMS-17, and JMS-19, designed based on an N-phenylacetamide compound previously described by Silva, PR. Pharmaceutics, v. 14, p. 188, 2022. as presenting significant anti-inflammatory activity *in vivo*. For this purpose, molecular docking studies were performed using the GOLD software against two inflammatory targets obtained from the Protein Data Bank, NLRP3 (PDB ID: 7ALV) and Janus Kinase 1 (JAK1, PDB ID: 6BBU). The FitScore values of the derivatives were compared with those of the co-crystallized ligands, and the intermolecular interactions were analyzed in Discovery Studio. Pharmacokinetic properties were predicted using SwissADME. The compounds were synthesized via the Knoevenagel condensation reaction and characterized by infrared spectroscopy (IR) and nuclear magnetic resonance spectroscopy (^{1}H and ^{13}C NMR). In docking studies with NLRP3, all compounds showed higher FitScore values than the co- crystallized ligand (63.4043), especially JMS-16 (78.2182), which established intermolecular interactions with amino acid residues essential for maintaining the enzyme in its inactive conformation, similarly to the reference ligand. For the JAK1 target, only JMS-16 (79.0940) and JMS-19 (74.7017) outperformed the co-crystallized inhibitor (70.6921), both demonstrating good affinity for the enzyme active site. ADME predictions indicated favorable drug-likeness profiles for all compounds. In the synthesis stage, the compounds JMS-16 (acridine derivative), JMS-17 (benzene derivative), and JMS-19 (indole derivative) were obtained with satisfactory yields. IR characterization indicated the presence of characteristic bands, especially C≡N (2220–2232 cm^{-1}), C=O (1709–1724 cm^{-1}), and sp^2 C-H (3050–3067 cm^{-1}). The ^{1}H NMR spectra showed characteristic singlets corresponding to the C=C hydrogen at approximately 9 ppm, indicating successful molecular condensation. Meanwhile, the ^{13}C NMR spectra confirmed the presence of carbonyl (160–163 ppm) and nitrile (113–116 ppm) groups in the compounds. Therefore, the three derivatives demonstrated promising results from both synthetic and computational perspectives. Among them, JMS-16 and JMS-19 showed the best predicted affinity for both targets, suggesting potential for the treatment of inflammatory diseases and supporting further *in vitro* and *in vivo* studies. Acknowledgement: UEPB and CNPq. **Financial support:** CNPq.

12.008 **Preliminary** *in silico* **Evaluation of the Pharmacodynamic Profile of Isatin Derivatives as Potential N-Myristoyltransferase Inhibitors against Neglected Tropical Diseases**. Leandro PF1, Lima MKS1, Oliveira MLA1, Albino SL1, Moura WCS[1,2], Fernandes HQA1, Menezes KJS1, Silva JVV1, Cavalcanti MAT1, Farias AGC[1,2], Lima AMAF1, Moura RO[1,2], Nascimento IJS[1,2]. [1]UEPB, Lab Drug Development and Synthesis, Brazil; [2]UEPB, PPG in Pharmaceutical Sciences, Brazil. Neglected Tropical Diseases (NTDs) comprise a set of 20 infectious diseases that present high morbidity and prevalence in underdeveloped countries, whose populations lack vector elimination measures and access to health services. Currently, the best strategy to control the prevalence of these diseases is the search for new drugs and critical targets essential for survival of the disease-causing microorganisms. Pathogens such as Leishmania spp., Plasmodium spp., and T. brucei, possess in their organisms N-myristoyltransferase (NMT), an enzyme responsible for signal transduction and membrane integrity as an essential target for parasite survival. In view of this, a virtual screening was carried out using 12 derivatives of the isatin nucleus (1H indole-2,3-dione), a compound with potential against inflammatory conditions and NTDs, among them Leishmaniasis and Malaria, caused by protozoa transmitted by mosquitoes of the genus Lutzomyia sp. and Anopheles, respectively. The in silico evaluation was performed by molecular docking using the applications MarvinSketch 23.16.0, ArgusLab 4.0.1, GOLD 5.8.1, and Discovery Studio 2025, with RMSD < 2.0 Å for method validation and energy minimization by the semiempirical PM3 method, and molecular dynamics simulations through the software GROMACS® and Xmgrace® for the most promising derivatives. The proteins used, NMT from Leishmania major (LmNMT; PDB ID: 5A27) and Plasmodium vivax NMT (PvNMT; PDB ID: 4CAE), were obtained from the Protein Data Bank (PDB). Among the compounds tested by molecular docking, the molecule MAV-02 (-Cl) stood out, with Score values of 81.2542 and 83.9404 for LmNMT (co- crystallized ligand = 96.6518) and PvNMT (co-crystallized ligand = 112.2501), respectively. It was observed that the addition of the electron-withdrawing chlorine group makes the molecule more selective for the parasite enzyme through halogen bonding with the Met377 residue, as well as critical residues present in the LmNMT active site such as Val346, Tyr217, and Tyr345. For PvNMT, the molecule performs 3 π-π stacking interactions with the Tyr211 residue, found only in the protozoan enzyme. For molecular dynamics, the root mean square deviation (RMSD) parameter for both complexes proves to be ideal, with deviation curves below 2 Å during most of the simulation. The root mean square fluctuation (RMSF) shows few peaks, contributing to the stability of the complex. In simulation, the drug-PvNMT complex was able to perform up to three hydrogen bonds, superior to the MAV-02-LmNMT complex, which performed only two. Thus, although the tested molecule presents a lower score value than the co-crystallized ligands, its profile of intermolecular interactions demonstrates great anti-NTD potential, emerging as a promising candidate for a new drug in the therapy of leishmania and malaria, driving further studies in the development of versatile alternatives against different parasite species. **Acknowledgments:** UEPB. **Financial support:** UEPB, CNPq, FAPESQ/PB.

12.009 **Synthesis and Antimicrobial Activity of N-acyl-Hydrazones Derived from β-Lapachone**. Lima RRCF[1], Silva RF,[1] Pinheiro SM[1], Santos Filho J[2], Lima Júnior CG[3], Santos JRD[4], Lima EO[4] [1]UFPB, Center for Exact and Natural Sciences, Dept Chemistry, Lab Organic Synthesis and Biocatalysis, Brazil [2]UFPE, Technology and Geoscience Center, Chemical Engineering Dept, Lab Design and Synthesis Applied to Medicinal Chemistry, Brazil [3]UFPB, Center for Exact and Natural Sciences, Dept Chemistry, Lab Medicinal Organic Synthesis, Brazil [4]UFPB, Health Sciences Center, Dept Pharmaceutical Sciences, Lab Mycology, Brazil

Introduction: Antimicrobial resistance represents a major global health concern and underscores the urgent need for novel therapeutic agents. Natural products and their derivatives constitute a rich source of structurally diverse bioactive molecules. Among them, naphthoquinones such as β-lapachone, derived from lapachol, isolated from Bignoniaceae species, have attracted considerable interest owing to their redox-cycling properties and ability to generate reactive oxygen species (ROS), resulting in oxidative stress-mediated cellular damage. **Objectives:** To synthesize a novel series of β-lapachone-based N-acylhydrazone derivatives through molecular hybridization and evaluate their antimicrobial activity against selected bacterial and fungal strains. Methods: A bioisosteric molecular hybridization strategy was employed to design β-lapachone–N-acylhydrazone hybrids containing substituted benzhydrazide moieties (R = H, Cl, Br, OH, OCH_2O). Lapachol was extracted from the stem bark of Tabebuia avellanedae and converted into β-lapachone by acid-catalyzed cyclization using chilled concentrated H_2SO₄. Substituted benzhydrazides were synthesized via Fischer esterification of the corresponding benzoic acids followed by reaction with hydrazine hydrate. The target derivatives were obtained through condensation reactions under catalytic conditions. Structural characterization was accomplished by IR, HRMS, and one- and two-dimensional ^{1}H and ^{13}C NMR spectroscopy. Antimicrobial activity was evaluated according to the methodologies described by Cleland (Cleland, R. Antib. Lab. Med., v. 1, p. 739, 1991.), Eloff (Eloff, JN. Planta Med., v. 64, p. 711, 1998.), and CLSI (Clinical and Laboratory Standards Institute. CLSI M27-A3, 2008.), using gentamicin and fluconazole as positive controls. Minimum inhibitory concentration (MIC), minimum fungicidal concentration (MFC), and MFC/MIC ratios were determined against four bacterial and seven fungal strains. **Results:** The target hybrids were obtained in moderate to good yields (60–78%). Among the five derivatives evaluated, only the brominated analogue exhibited significant antimicrobial activity, inhibiting the growth of all tested microorganisms at concentrations ranging from 512 to 1024 μg/mL. The remaining compounds displayed limited efficacy under the experimental conditions employed. **Conclusions:** The molecular hybridization strategy successfully afforded a novel series of β-lapachone–N-acylhydrazone hybrids designed to integrate the biological attributes of both pharmacophoric units. The broad- spectrum activity observed for the brominated derivative highlights the potential of halogen-substituted β-lapachone analogues as promising lead structures for antimicrobial drug discovery. Further structural optimization and mechanistic studies are warranted to improve potency and elucidate the molecular basis of their antimicrobial activity. Funding: CNPq.

12.010 **Synthesis, Structural Characterization, and *in silico* Evaluation of the Leishmanicidal Activity of an Indole-Spiroacridine Derivative**. Oliveira MLA[1,3], Lima AMAF[1,3], Silva JVV[1,3], Leandro PF[1,3], Lima MKSL[1,3], Farias AGC[1,2], Fernandes HQA[1,3], Albino SL[1,2,3], Moura RO[1,2,3] [1]UEPB, Lab Drug Development and Synthesis, Brazil, [2]UEPB, Graduate Program in Pharmaceutical Sciences, Brazil, [3]UEPB, Dept Pharmacy, Brazil

Leishmaniasis is an endemic tropical disease caused by protozoa of the genus Leishmania spp. and transmitted by sandflies, manifesting in visceral, cutaneous, and mucocutaneous forms. Despite the availability of treatments, limitations related to parasite resistance, efficacy, and adverse effects still compromise the clinical management of the disease and reinforce the need for the development of new drugs. The objective of this study was to synthesize, characterize, and evaluate, using *in silico* tools, the leishmanicidal potential of the AMTAC-22.4 derivative. The compound was obtained from the Knovenagel condensation reaction between the acridine 9-carboxaldehyde core and the N-acylhydrazone derivative, and structurally characterized by FTIR (IRPrestige-21, Shimadzu®) and ^{1}H and ^{13}C NMR (Bruker Avance DRX Ultrashield® 600 MHz). For the *in silico* study, the web-based software SwissADME and XenoSite were used for pharmacokinetics, and the software MarvinSketch 23.16 and ArgusLab 4.0.1 were used for the preparation of the molecules. Molecular docking studies were performed using the AutoDock Tools (ADT) program on three pharmacological targets essential for parasite survival: L. infantum sterol 14-alpha-dimethylase (CYP51, PDB: 3L4D), L. infantum trypanothione reductase (TryP, PDB: 2JK6), and L. donovani topoisomerase I in complex with DNA (Topo 1, PDB: 2B9S). The compound was obtained as a yellow powder with a satisfactory reaction yield (44.07%) and exhibited a melting point above 310°C. IR characterization confirmed the presence of important functional groups, with bands suggestive of secondary N-H (3307.084 cm^{-1}), C=N (2234.984 cm^{-1}), C=O (1649.655 cm^{-1}), and aromatic C=C (1475.860 and 1329.906 cm^{-1}). The ^{1}H NMR data showed characteristic singlet peaks for N-H (11.75 ppm) and H-C=C (9.07 ppm), while the ^{13}C NMR spectrum exhibited absorption peaks for C=O (160.12 ppm), C=N (148.87 ppm), C≡N (115.72 ppm), and quaternary Csp^{3} (69.85 ppm). AMTAC-22.4 exhibited binding free energy (ΔG) values of -10.13 kcal·mol^{-1} for TryP, -8.21 kcal·mol^{-1} for CYP51, and -7.90 kcal·mol^{-1} for Topo I. For the CYP51 target, the compound exhibited a more favorable ΔG than fluconazole (-7.6 kcal·mol^{-1}), suggesting greater affinity for the active site. Significant interactions with enzyme residues and the heme group were also observed, indicating an interaction mechanism consistent with classical CYP51 inhibitors. Pharmacokinetic predictions indicated that the compound has a high probability of gastrointestinal absorption, does not cross the blood-brain barrier, is not a substrate of P-glycoprotein, and does not violate Lipinski's druglikeness rules. Thus, *in silico* studies indicate that the AMTAC-22.4 derivative exhibited high predicted affinity for CYP51 based on molecular docking, suggesting potential leishmanicidal activity and justifying future *in vitro* and *in vivo* studies. **Acknowledgments:** UEPB, UFPB. **Financial support:** FACEP and CAPES.

12.011 **Physicochemical Stability Evaluation of Polymeric Nanocapsules Containing Copaiba Oil under Forced Stress Conditions**. Santos IB, Souza PHO, Formiga ALD, Xavier-Junior FH UFPB, Lab Biotecnologia Farmacêutica (BioTecFarm), Brazil

Introduction: Polymeric nanocapsules (PNCs) containing natural oils are promising systems for improving the stability and bioavailability of bioactive compounds. PNCs containing copaiba essential oil (CEO), rich in beta-caryophyllene (67.8%), may enhance therapeutic delivery and selectivity. Evaluating their physicochemical stability under forced stress conditions is essential to ensure formulation quality and performance. **Objective:** To evaluate the physicochemical stability of PNCs containing CEO under forced stress conditions. **Methodology:** PNCs were prepared by nanoprecipitation, in which the organic phase consisted of dissolving 30 mg of polycaprolactone (PCL), 20 mg of Lipoid S100, and 100 mg of copaiba oil in 6 mL of acetone; this solution was slowly injected into an aqueous phase containing 40 mg of Kolliphor® and 12 mL of Milli-Q® water. Hydrodynamic diameter (nm), polydispersity index (PDI), and zeta potential were determined by dynamic and electrophoretic light scattering (Zetasizer Lab, Malvern). The tests comprised: six consecutive freeze-thaw cycles (-20 °C / 25 °C, 24 h each); forced centrifugation (5,000 rpm, 30 min); and storage at 4, 25, and 37 °C for 15, 30, 60 and 90 days. **Results:** Initial characterization revealed a mean particle size of 216.9±1.0 nm, a PDI of 0.11±0.02, and a zeta potential of -32.4±1.1 mV. Following centrifugation, phase separation was not observed, and analysis was performed on the supernatant (181.6±2.4 nm; PDI 0.07±0.01; zeta -34.9±0.2 mV). In the temperature stability studies, PNCs stored at 25 °C exhibited relative variation in physicochemical parameters (218.6±5.3 nm; PDI 0.12±0.03; zeta -30.7±2.2 mV). At 37 °C, the nanosystem demonstrated a slight reduction in measured size values (218.9±5.1 nm; PDI 0.08±0.03; zeta -32.1±5.8 mV), whereas at 4 °C, greater variation in standard deviation was observed relative to the other conditions (208.0±5.2 nm; PDI 0.08±0.03; zeta -25.9±1.4 mV). The stability storage produced a non-significant modification after 60 days. In contrast, the freeze-thaw cycles induced progressive instability, with particle size increasing from 265±54 nm (cycle 1) to 1,447±373 nm (cycle 6), PDI reaching 1.0, indicating aggregation, and an absolute variation in zeta potential to 22.0±11.1 mV, compared with -25.3±0.4 mV at cycle 1. **Conclusion:** The PNCs demonstrated satisfactory physicochemical stability under centrifugation and thermal conditions evaluated for up to 90 days, particularly at 37 °C. The freeze-thaw cycles promoted significant colloidal destabilization, signaling the need for optimization with cryoprotective agents for long-term storage. The results support the viability of this nanosystem for potential biological applications.

12.012 **Virtual Screening of FDA-Approved Drugs as Potential N-Myristoyltransferase Inhibitors Useful Against Malaria**. Silva KWL[1], Rios EO[2], Silva AVX[2], Nascimento IJS[2] [1]Estácio, Faculty of Biological Sciences, Brazil, [2]CESMAC, Faculty of Pharmacy, Brazil

Introduction: Malaria is a disease of high worldwide prevalence caused by species of the genus *Plasmodium*. They have the enzyme *N*-myristoyltransferase (NMT), which catalyzes the addition of myristate to the *N*-terminal end of newly synthesized proteins. Because it is essential for parasite survival, it is a potential target for inhibition in the search for antimalarial drugs. In this context, drug repurposing combined with virtual screening represents a promising strategy against this tropical disease. **Objectives:** To identify potential NMT inhibitors among drugs approved by the Food and Drug Administration (FDA), using structure-based virtual screening. **Methods:** The crystallographic structure of NMT (PDB: 4CAE) was obtained from the RCSB Protein Data Bank, and a library of FDA-approved compounds was prepared from the ZINC database. Conformational analyses were performed in ArgusLab to select the most stable conformation. Molecular docking was conducted in GOLD, in which hydrogens were added and the original ligand and the water molecules were removed from the receptor; subsequently, the compounds, divided into blocks of 100, were docked into the binding site, adopting as the approval criterion a fitscore ≥ 90 under the settings: search efficiency 200%, 125,000 maximum operations, and early termination disabled. The interactions were analyzed in Discovery Studio, in which the compounds with hydrogen bonds with the key residues of the binding site His213, Ser319, Asn365, Tyr211, Phe105, and Leu410 were approved. Finally, an individualized bibliographic search of the articles on antimalarial activity was conducted in PubMed, ScienceDirect, and Google Scholar. **Results:** The protocol was validated by redocking of the co-crystallized ligand, RMSD = 0.3708 Å. Of the 1613 compounds submitted to molecular docking, 250 presented a fitscore ≥ 90, and 83 obtained hydrogen bonds with all the selected residues. A fitscore of ≥ 90 was defined due to the broad spectrum of the receptor. The bibliographic review revealed studies suggestive of antimalarial activity, with emphasis on losartan, irbesartan, iloprost (preclinical evidence), rosiglitazone, and methotrexate (clinical evidence). Although the drugs olaparib, azilsartan, telotristat, panobinostat, and isavuconazonium, showed little or no prior evidence, they exhibited high affinity scores and formed bonds with all residues, making them candidates for future investigations. **Conclusion:** The virtual screening applied to the search for NMT inhibitors identified drugs with an *in silico* profile favorable to repurposing for malaria therapy, with rosiglitazone, methotrexate, losartan, irbesartan, and iloprost standing out as candidate inhibitors of this enzyme. Further studies are recommended to investigate the *in vitro* antimalarial activity of the drugs olaparib, azilsartan, telotristat, panobinostat, and isavuconazonium. **Acknowledgments:** The authors thank the Research Support Foundation of the State of Alagoas (FAPEAL) for the financial support provided through the research grant awarded.

12.013 **Molecular Interaction Between Silymarin Flavolignans and Pancreatic Lipase: An *in silico* Study**. Ferreira ALN[1], Silva FRC[2], Bezerra VM[2], Magalhães EP[2], Aragão DA[2], Silva ME[2], Ribeiro LR[2], Carvalho JPAQ[1], Marinho ES[3], Marinho MM[3], Martins AMC[1], Menezes RRPPB[1]1UFC, Clinical and Toxicological Analysis Dept, Brazil. [2]UFC, PPG of Pharmaceutical Sciences, Brazil, Brazil. [3]UECE, Bioprospecting and Natural Resource Monitoring Lab, Brazil

Introduction: Obesity is a multifactorial disease associated with the development of metabolic syndrome, systemic inflammation, and oxidative stress. Despite the availability of pharmacological therapies, many anti-obesity drugs present limited efficacy and significant adverse effects, reinforcing the need to investigate new bioactive compounds. In this context, natural products with antioxidant and anti-inflammatory properties, such as silymarin, have attracted scientific interest. Silymarin, extracted from *Silybum marianum* L., contains flavonolignans with different pharmacological activities and may act on targets involved in lipid metabolism, such as pancreatic lipase. **Objectives:** This study sought to investigate the theoretical interaction of the main silymarin components with the pancreatic lipase enzyme, evaluating their anti-obesity potential. **Methods:** The chemical structures of isosilybin A, isosilybin B, silybin A, silybin B, silychristin, silydianin, taxifolin, and orlistat were obtained from the PubChem database and optimized using MarvinSketch and Avogadro software. The crystallographic structure of pancreatic lipase (PDB ID: 1LPB) was obtained from the Protein Data Bank. Molecular docking simulations were performed using AutoDock Vina software with the Lamarckian Genetic Algorithm and exhaustiveness 64. The protocol was validated by redocking with the co-crystallized inhibitor MUP. Fifty independent simulations were performed and poses with RMSD < 2.0 Å and binding affinity energy ≤ -6.0 kcal/mol were selected. Intermolecular interactions were analyzed using UCSF Chimera, Discovery Studio Visualizer, PyMol, and the PLIP server. **Results:** Silymarin compounds presented binding affinity values ranging from -10.5 to -8.6 kcal/mol, superior to orlistat (-7.4 kcal/mol) and the inhibitor MUP (-5.0 kcal/mol). Isosilybin A, silybin A, silybin B, silychristin, and taxifolin interacted near the catalytic site of the enzyme, involving important residues such as Ser152, His263, Phe77, Phe215, Tyr114, and Trp252. Hydrogen bonds, π-stacking, and hydrophobic interactions were observed, suggesting contributions to the stability of the formed complexes. Silychristin showed the best binding affinity (-10.5 kcal/mol). In addition, silybin A, silychristin, and taxifolin interacted directly with His263 and Ser152, essential residues for the catalytic activity of the enzyme. **Conclusion:** The results suggest that the major components of silymarin exhibit potential to modulate pancreatic lipase activity by interacting with key residues involved in triglyceride hydrolysis. Thus, silymarin demonstrates promising potential as a candidate for anti-obesity therapy, particularly due to the possible reduction in lipid absorption associated with its antioxidant and anti-inflammatory properties. **Acknowledgments:** UFC, FUNCAP.

12.014 **Anti-Inflammatory Activity of the Compound (E)2-cyano-N-3-diphenylacrylamide (JMPR-01)**. Andrade MAJ[1], Rodrigues CVS[1], Costa TB[1], Silva PR[1], De Moura RO[2], Santos VL [11]UEPB, Lab Pharmacological Assays, Brazil, [2]UEPB, Lab Drug Design and Synthesis, Brazil.

To address the undesirable side effects inherent in existing therapies for the treatment of inflammatory conditions, the design and development of new molecules is essential. The compound (E)2-cyano-N-3-diphenylacrylamide (JMPR-01) was designed based on a prototype with anti-inflammatory activity already established through studies conducted by our group, using the molecular bioisosterism strategy to obtain this new phenylacrylamide derivative. In this context, the aim of this study was to evaluate the anti- inflammatory and toxicological profile of JMPR-01 through *in silico* , *in vitro*, and *in vivo* studies. Molecular docking was performed using AutoDock Tools with the following crystallographic structures: LT-A4-H, PDE4, 5-LOX, iNOS, CRTH2, COX-1, and COX-2. Safety was assessed using acute single-dose toxicity models (2000 mg/kg) and *in vitro* hemolytic activity (5000 µg/mL). A complete Freud's adjuvant (CFA)-induced paw edema test was also performed in mice. The experimental protocols were approved by the Animal Use Ethics Committee (CEUA) of UEPB (opinion no. 003/2021). *In vitro*, JMPR-01 demonstrated higher affinity for the enzymes LT-A4-H, PDE4, iNOS, and COX-2. In the acute toxicity test, there were no deaths or clinical signs of toxicity. It also demonstrated low hemolytic activity. In paw edema, the compound at a dose of 50 mg/kg promoted significant inhibition (54%) of edema starting at 4 hours ($p<0.01$), and at a dose of 100 mg/kg, significant inhibition of inflammation (65%) occurred starting at the second hour ($p<0.01$). **Conclusion:** The compound demonstrated satisfactory anti-inflammatory activity *in vivo*, which may be partially related to the suppression of prostaglandins, leukotrienes, and nitric oxide; it exhibited low toxicity *in vivo* and *in vitro*, proving to be safe and promising as an anti-inflammatory drug. **Acknowledgments:** This study was supported by a CNPq fellowship awarded to Andrade M.A.J., with additional financial support from CAPES.

12.016 **Formulation and Characterization of Resveratrol-Loaded Cubosomes for Improved Therapeutic Efficacy**. Santos GRA[1], Santos GCM[1,2,3], Pimentel RS[1,3], Bernardi A[1,2,3], Martins MA[1,2,3] [1]Fiocruz, Lab Inflammation, Brazil. [2]Fiocruz, Preclinical Pharmacokinetic Platform, Brazil. [3]Fiocruz, PPG Biologia Celular e Molecular, Brazil.

Introduction: Resveratrol is a polyphenolic compound with potent anti- inflammatory and antioxidant properties, found in foods such as grapes and berries. Although it exhibits significant biological activities, this compound presents unfavorable pharmacokinetic properties due to its low bioavailability, short half-life, and rapid metabolism. Therefore, the aim of this study was to develop and characterize resveratrol-loaded cubosomes (Cub RSV) to stabilize its pharmacological activity and enable its therapeutic use. **Methods:** The Cub RSV formulation was prepared by incorporating the organic phase, comprising phytantriol and resveratrol, into an aqueous Pluronic® F-127 solution. Initially, the organic and aqueous phases were separately homogenized under magnetic stirring (600 rpm, 45°C) for 10 min. Subsequently, the mixture was subjected to cavitation-induced shearing using a probe sonicator (Q55 Sonicator®, QSonica, USA) for three 15s cycles. Formulated cubosomes were characterized in terms of particle hydrodynamic diameter, polydispersity index (PdI) and zeta potential by dynamic light scattering (DLS). After ultrafiltration centrifugation, the resveratrol content in cubosome formulations was determined by liquid chromatography coupled to mass spectrometry (LC-MS/MS) using a method developed in-house (linear range 5-500 ng/mL). Data are presented as mean ± SD, with statistical significance set at $p \leq 0.05$. **Results:** Cub RSV exhibited a hydrodynamic diameter of 158.1 nm, a low polydispersity index of 0.1 and a zeta potential of -14.6 mV. Furthermore, the formulation showed a resveratrol content of 92.0 ± 3.0 % and an entrapment efficiency of 97%. **Conclusion:** Overall, the developed Cub RSV exhibited favorable physicochemical properties, including nanoscale size, low polydispersity, and high resveratrol entrapment efficiency. These results indicate successful drug incorporation and suggest that the formulation is a promising nanocarrier for enhancing resveratrol delivery and bioavailability.

12.017 **FTIR Spectroscopic Characterization of Folate-Functionalized Liposomes Encapsulating 5-Fluorouracil for Targeted Colorectal Cancer Therapy**. Andrade FGA, Barroso MKA, Petrilli R, Eloy JO UFC, Faculty of Pharmacy Dentistry and Nursing, CEDEFAR/GPNANO, Brazil

Introduction: Colorectal cancer (CRC) is the third most commonly diagnosed malignancy and the second leading cause of cancer-related death worldwide. 5-Fluorouracil (5-FU), a pyrimidine analog antimetabolite and key component of first-line CRC regimens such as FOLFOX and FOLFIRI, has its therapeutic outcomes constrained by a short biological half-life (5–20 min) and significant systemic toxicity. Folate receptor-targeted liposomes represent a promising drug delivery strategy, combining the biocompatibility and low immunogenicity of lipid-based systems with selective intracellular uptake mediated by folate receptor overexpression on tumor cells. Fourier-transform infrared spectroscopy (FTIR) is a well-established analytical tool for characterizing liposomal systems, enabling confirmation of drug encapsulation and surface functionalization. **Objectives:** To assess, by FTIR, the molecular interactions between 5-FU, the lipid matrix, and folic acid in folate- functionalized liposomes, confirming drug encapsulation and surface conjugation. **Methods:** Folate-functionalized liposomes were prepared by the ethanol injection method using DSPC, cholesterol, and DSPE-PEG2000 at a molar ratio of 55:45:2.5. Lipids were dissolved in ethanol and the organic phase was injected dropwise into phosphate-buffered saline (PBS, pH 7.4) under magnetic stirring at 60 °C for 30 min. Five lyophilized samples were analyzed: free 5-FU, 5-FU-loaded liposomes (IE 5-FU), folate-functionalized 5-FU-loaded liposomes (IE Fol 5-FU), blank folate-functionalized liposomes (IE Fol Blank), and blank liposomes (IE Blank). FTIR spectra were recorded on a Jasco FT/IR-4100 spectrometer over the 4000–600 cm^{-1} range and processed with OriginPro software. **Results:** Free 5-FU exhibited characteristic absorption bands at 3146 cm^{-1} (N-H, imide), 1645 cm^{-1} (C=O stretch), 1348 and 813 cm^{-1} (pyrimidine ring and C-H vibrations), and 1238 cm^{-1} (C-F stretch), confirming the structural integrity of the drug (Heydarian R. Int. J. Pharm., v. 671, p. 125262, 2025). After encapsulation (IE 5-FU), the N-H band at 3146 cm^{-1} was absent and the C=O band shifted to 1665 cm^{-1} with reduced intensity, indicating drug entrapment within the lipid matrix. The band at 1056 cm^{-1} (P=O) confirmed phospholipid integrity (Ezekiel C. Pharmaceutics, v. 13, p. 821, 2021). In the IE Fol 5-FU and IE Fol Blank samples, folate functionalization was evidenced by Amide I (~1650 cm^{-1}, C=O stretch) and Amide II (~1540 cm^{-1}, N-H and C-N vibrations) bands, consistent with amide bond formation between folic acid and DSPE-PEG (Moghimipour E. Eur. J. Pharm. Sci., v. 114, p. 166, 2018). The IE Blank sample displayed a lipid carbonyl band at 1735 cm^{-1}, and the absence of the 3146 cm^{-1} signal in blank formulations validated matrix purity as a negative control. **Conclusion:** FTIR analysis confirmed 5-FU encapsulation within the lipid matrix and successful folic acid conjugation, as evidenced by characteristic spectral shifts and amide bond formation. These findings support the physicochemical integrity of the folate- functionalized liposomal system and provide a foundation for subsequent in vitro cytotoxicity and drug release studies targeting CRC therapy. **Acknowledgements:** The authors thank CEDEFAR/GPNANO.

12.019 **Deciphering α1A-Adrenoceptor Molecular Recognition Through Quantum Interaction Energy Analysis**. Silva MS, Gavioli EC, Fulco UL, Bezerra KS, Silva-Junior ED. UFRN, Dept Biophysics and Pharmacology, Brazil.

Introduction: In addition to regulating motor activity in the genitourinary tract, the α1A-adrenoceptor (α1A-AR) has also been implicated in cardiac remodeling and memory-related processes. However, the therapeutic application of α1A-AR ligands remains limited by poor subtype selectivity. In this context, quantum-level approaches such as MFCC-DFT may provide valuable insights for the rational design of novel selective α1A-AR ligands. **Objective:** The present study aimed to evaluate, at the quantum level, the interaction energies of different α1A-AR ligands with residues composing the receptor binding site using MFCC-DFT calculations. **Methods:** Computational analyses were performed using Cryo-EM structures of the α1A-AR bound to the agonists adrenaline (PDB ID: 8THL) and A61603 (PDB ID: 8THK), and to the antagonist dozazosin (PDB ID: 9M4Q). Protein structures were prepared in Discovery Studio with structural correction, protonation at physiological pH using PropKa, and CHARMm minimization. Ligands were evaluated for their ionization states under physiological pH conditions in MarvinSketch. Orthosteric-site residues within 2-10 Å of each ligand were selected, and interaction energies were calculated using the MFCC-DFT with dielectric constant ε = 40. **Results:** The ligands exhibited the following total binding energies (in kcal·mol-1) at the α1A-AR, in decreasing order of interaction strength: doxazosin (-72.02) > A61603 (-63.67) > adrenaline (-43.69). In the adrenaline/α1A-AR complex, the residues contributing most to the interaction energy (in kcal·mol-1) were ASP106 (-10.95) > PHE312 (-4.71) > VAL107 (-4.15) > PHE288 (-3.81) > TYR316 (-2.48) > PHE289 (-2.04) > TYR184 (-1.72) > SER188 (-1.72) > TRP285 (-1.71). The residues with the greatest contributions to the interaction energy (in kcal·mol–1) in the A61603/α1A-AR complex were: ASP106 (-9.67) > PHE288 (-7.09) > PHE312 (-6.37) > VAL107 (-6.03) > SER192 (-4.60) > PHE289 (-2.85) > TYR184 (-2.63) > ILE176 (-2.28) > TYR316 (-2.19). Finally, in the doxazosin/α1A-AR complex, the energy interaction profile (in kcal·mol–1) followed the order ASP106 (-11.91) > ILE178 (-6.45) > TRP102 (-5.79) > VAL107 (-5.56) > PHE312 (-4.91) > PHE288 (-3.53) > ALA103 (-3.23) > LYS309 (-2.84) > GLN177 (-2.40) > PHE308 (-2.09). Comparative analysis revealed a common interaction core formed by ASP106, VAL107, PHE312, and PHE288 across all complexes. Agonist complexes shared residues such as TYR316, PHE289, and TYR184, whereas the selective α1A- AR agonist A61603 exhibited exclusive interactions with SER192 and ILE176. The antagonist doxazosin also displayed exclusive interactions with α1A-AR, including ILE178, TRP102, ALA103, LYS309, GLN177, and PHE308. **Conclusion:** These findings improve the understanding of the structural and energetic mechanisms underlying α1A-AR molecular recognition and may support the rational design of novel selective ligands with therapeutic potential. Funding: CAPES and CNPq.

12.020 *In vitro* and *in silico* Evaluation of the Spiro-Acridine AMTAC-18 as a Potential Antileishmanial Compound.

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Leishmaniasis is a widespread parasitic disease in tropical and subtropical countries, characterized by a broad spectrum of clinical manifestations associated with considerable morbidity and mortality. Its current therapeutic arsenal is limited due to factors such as high toxicity, increasing drug resistance, and high cost, emphasizing the urgent need for novel antileishmanial drugs. In this context, the acridine nucleus presents itself as a potential scaffold for the development of new chemotherapeutic drug candidates. Therefore, this study aimed to evaluate the leishmanicida activity of a spiro-acridine derivative (AMTAC-18) through *in vitro* and *in silico* approaches In *in vitro* assays against *Leishmania infantum* promastigotes, quantified by Neubauer chamber counting, AMTAC-18 obtained a good IC50 of 2.34 µM. Cytotoxicity evaluation in Vero cells and O+ human erythrocytes, using MTT assay or spectrophotometric analysis, respectively, resulted in a CC50 of 18.32 µM (SI = 7.82) and HC50 > 916.4 µM (SI > 391.62). *in silico* evaluation by molecular docking were conducted using Chimera® 1.17.3, Gold 2022.3.0, MarvinSketch 23.16, and ArgusLab 4.0.1 softwares, targeting 3D structures of trypanothione reductase (TyR) from L. infantum (PDB 4APN), sterol 14α- demethylase (CYP51) from L. donovani (PDB 3L4D), and triosephospate isomerase (TFI) of L. mexicana (PDB 1IF2). AMTAC-18 presented fitness score values of 62.77 (3L4D), 65.21 (4APN), and 53.73 (TFI). In particular, for CYP51, AMTAC-18 exhibited comparable affinity to fluconazole (co-crystallized ligand, fitness = 64.90), highlighting the conventional hydrogen bond interactions between NH spiro-acridine at Met459 and π-alkyl interactions with Val356, Pro209, and Met459. These findings suggest that this spiro-acridine derivative holds promise as a potential leishmanicidal agent, possibly acting through inhibition of sterol biosynthesis in Leishmania, which provides an opportunity for further in-depth studies.

12.021 **Development of a Functional Screening Platform Targeting the Mitotic Kinesin Eg5 for Anticancer Drug Discovery**. Desiderio GA[1,2], Salviano RA[1], Silva AS[1], Mota JF[1], Macêdo SMN[1], Castro CM[1], Mota JA[1,2], Gress LSB[1,2], Feijó-Neto JRF[1], Sousa GC[1,3], Sales SLA[1,2], Almeida MCM[1,4] Costa PMS[1], Pessoa C[1,2,3], Paier CRK[1,2,4] [1]UFC, Lab. Experimental Oncology, Brazil [2]UFC, PPG Pharmacology, Brazil [3]UFC, Northeast Biotechnology Network, Brazil [4]UFC, PPG Translational Medicine, Brazil

Introduction: Kinesin Eg5 (KIF11) is a mitotic motor protein essential for bipolar spindle assembly and maintenance during cell division. Pharmacological inhibition of Eg5 disrupts spindle formation, leading to mitotic arrest and cell death, highlighting this protein as a promising target for anticancer therapy. In this context, biochemical screening platforms are valuable tools for the rapid identification of bioactive molecules, supporting the discovery and early characterization of novel antimitotic agents with potential therapeutic applications. **Objectives:** To develop and validate a low-cost screening platform for identifying natural and synthetic inhibitors of kinesin Eg5 ATPase activity. **Methods:** The recombinant ATPase domain of human Eg5 was produced in *E. coli* BL21(DE3) pRARE cells following IPTG induction. The soluble fraction was purified by immobilized metal affinity chromatography (IMAC) and size exclusion chromatography (SEC) using an ÄKTA Start™ system (Cytiva). Protein purity was assessed by SDS-PAGE, and concentration was determined using a NanoDrop Lite Plus spectrophotometer (Thermo Fisher Scientific). Compounds were incubated with Eg5 and ATP for 20 min at 25°C. ATP hydrolysis was quantified by measuring inorganic phosphate release using a commercial colorimetric kit after 30 min, with absorbance recorded at 340 nm in a microplate reader. **Results:** The recombinant human Eg5 ATPase domain was successfully obtained with purity greater than 90%. Seven compounds were evaluated at three or more concentrations, including two reference inhibitors (compounds 6 and 7). Compounds 2 and 3 reduced enzymatic activity by 11–20% at concentrations ≥15 µM and ≥125 µM, respectively, whereas compounds 1, 4, and 5 showed no significant inhibitory effect under the tested conditions. Reference inhibitors reduced enzymatic activity by approximately 60% and 22–46%, respectively. The assay demonstrated excellent reproducibility and robustness, presenting technical CV values below 3% across independent experiments, a signal-to-background ratio of 2.60 ± 0.16, a dynamic range of 0.60 ± 0.05 absorbance units, and a mean Z'-factor of 0.87 ± 0.04. **Conclusion:** The validated platform proved highly robust, sensitive, and reproducible for detecting changes in Eg5 ATPase activity, demonstrating excellent suitability for screening applications. Additionally, the assay efficiently discriminated active and inactive compounds, supporting its applicability in the identification and characterization of novel antimitotic agents targeting Eg5. Taken together, these findings establish the platform as a reliable, accessible, and cost-effective tool for early-stage antimitotic agent discovery and anticancer drug development programs.

12.022 **Pradimicin-IRD-Loaded PLGA Nanoparticles: A Novel Approach to Colorectal Cancer Treatment**. Gomes MAM, Miguel RA, Passos JS, Lotufo LVC, Lopes LB ICB-USP, Dept Pharmacology, Graduate Program in Functional and Molecular Biology, Brazil

Introduction: Conventional treatment of colorectal cancer (CRC) with 5-fluorouracil (5-FU) is impaired due to its low oral bioavailability and short plasma half-life, requiring intravenous administration at high doses, leading to undesired systemic effects and poor patient compliance. This scenario highlights the needs for new pharmacological interventions. Here, we employ a nanotechnological approach for the delivery of pradimicin-IRD (PRM), a natural molecule with antitumoral activity capable of inducing DNA damage, cell cycle arrest and apoptosis in a p53-independent manner. More specifically, poly (lactic-co-glycolic acid) (PLGA) nanoparticles (NPs) were developed to encapsulate PRM, either alone or in combination with 5-FU. **Methods:** Drug synergism between free PRM and 5-FU was calculated using the Chou-Talalay method to guide coo-encapsulation ratios. Single (only PRM) and co-loaded (PRM+5-FU) NPs were obtained via the emulsion/solvent evaporation method. *In vitro* release kinetics was evaluated using Franz diffusion cells, and the drugs were quantified using UV-HPLC. Cytotoxicity against HCT-116 and SW480 colon adenocarcinoma cell lines was assessed by MTT assay after treatment for 72h. Irritative potential was evaluated via the HET-CAM assay. **Results:** PRM and 5-FU demonstrated strong synergistic antitumor activity at a 1:1 molar ratio (n = 3), resulting in a combination index (CI) of 0.235. Unloaded, single, and co-loaded NPs exhibited diameters ranging from 158 to 182 nm, low polydispersity (PDI ≤ 0.1), negative zeta potential (-27 to -34 mV) (n = 3), and spherical morphology when examined by electron transmission microscopy. Approximately 40% of PRM was released over 72h (n = 2). Cell treatment with both single or co-loaded NPs increased drug IC50 values by 3-fold compared to the free solutions (n = 3). Importantly, encapsulation was highly efficient in mitigating the drug's irritative vascular effects (lysis, hemorrage and coagulation) in the HET-CAM assay (n = 1). **Conclusion:** We successfully developed stable PLGA NPs that can co-encapsulate a highly synergistic drug combination. The reduction in *in vitro* cytotoxicity aligns with the observed modified release (~40% at 72h) and might suggest lysosomal trapping typical of weak bases. The mitigation of irritative vascular effects supports the potential applicability of this nanoformulation for delivery of cytotoxic drug combinations. **Acknowledgements:** This work was financially supported by FAPESP (Processes 2018/13877-1, 2024/17768-3 and 2025/02119-2) and CAPES (Finance Code 001). Ethics Committee Code: 1376/2024.

12.024 **Antifungal Potential, Cytotoxicity, and *in silico* Analysis of (-)-Carveol Against *Sporothrix brasiliensis* Strains**. Piancó MESV[1], Moura DEG[2], Lima LO[3], Silva LA[3], Medeiros CIS[3], Alexandre HMS[3], Silva EVA[4], Souza LDG[4], Gonçalves JCR[3], Sobral MV[3], Barbosa-Filho JM[3], Lima EO[3], Guerra FQS[3] [1]UFPB, Graduate Program in Natural and Synthetic Bioactive Products (PPgPNSB), Brazil [2]UFPB, Undergraduate Program in Pharmacy, Brazil [3]UFPB, Graduate Program in Natural and Synthetic Bioactive Products (PPgPNSB), Brazil [4]UFPB, Graduate Program in Dentistry (PPGO), Brazil

Introduction: Sporotrichosis is a subcutaneous fungal infection caused by fungi of the *Sporothrix genus*, affecting humans and animals through traumatic inoculation into the skin. In Brazil, *Sporothrix brasiliensis* is the species with the highest incidence and is mainly associated with zoonotic transmission. Although conventional antifungal agents are available, limitations related to toxicity and increasing reports of resistant strains have encouraged the search for new compounds with antifungal potential. In this context, natural metabolites have been investigated as promising alternatives against pathogenic fungi, highlighting (-)-Carveol as a potential candidate. **Objective:** To evaluate the antifungal activity of (-)-Carveol against *S. brasiliensis* strains, investigating its mechanism of action, cytotoxicity, pharmacokinetic properties, and molecular interaction with the CYP51 enzyme. **Methods:** The mechanisms of action of (-)-Carveol on the fungal cell wall and plasma membrane were investigated by broth microdilution assays using sorbitol and exogenous ergosterol, based on changes in MIC values. Cytotoxicity was assessed in human keratinocytes (HaCaT) using the MTT reduction assay. Results were expressed as mean ± SEM and analyzed by one-way ANOVA followed by Dunnett's test ($p < 0.05$). Pharmacokinetic and toxicological properties were evaluated *in silico* , including physicochemical analysis according to Lipinski's rule of five. Additionally, molecular docking was performed against the *S. brasiliensis* CYP51 enzyme, using itraconazole as the control drug to evaluate molecular interactions and binding affinity. **Results:** (-)-Carveol exhibited antifungal activity with a fungicidal effect against the evaluated strains. Sorbitol and ergosterol assays demonstrated that the compound does not act directly on the fungal cell wall nor through binding to ergosterol in the plasma membrane, suggesting an alternative mechanism of action. In the cytotoxicity analysis using HaCaT cells, (-)-Carveol promoted a concentration-dependent reduction in cell viability, while maintaining viability above 50% at concentrations of 256 and 512 µg/mL. *in silico* analyses indicated high intestinal absorption, favorable pharmacokinetic properties, and the absence of predicted hepatotoxicity, mutagenicity, and tumorigenicity. Molecular docking revealed interaction of (-)-Carveol with *S. brasiliensis* CYP51, although with lower affinity than itraconazole, suggesting a possible interaction with the same molecular target involved in ergosterol biosynthesis. **Conclusion:** (-)-Carveol demonstrated promising antifungal potential against *S. brasiliensis*, associated with favorable *in silico* pharmacokinetic and toxicological properties, as well as interaction with the CYP51 enzyme. However, the cytotoxicity observed in human keratinocytes highlights the need for further studies, including nanoformulation approaches, to optimize its applicability and support future *in vivo* validation.

12.025 **Subchronic Toxicity Assessment of Docetaxel-Loaded Lipid Nanoparticles: A Comparative Study Focusing on the Male Reproductive System of Rats**. Inácio, JM[1]; Carvalho, FV[1]; Geronimo, G[1], Paula, E[1], Rodrigues da Silva, GH[2] [1]Unicamp, Dept Biochemistry, Institute of Biology, Brazil. [2]CNPEM, Brazilian Biosciences National Lab, Brazil.

Introduction: Docetaxel (DTX) is a cornerstone chemotherapeutic agent for solid tumors, but its clinical use is limited by systemic and reproductive toxicity. Nanostructured Lipid Carriers (NLCs) have been developed to improve drug biodistribution and therapeutic efficacy; however, their effects on highly proliferative tissues remain poorly understood. **Objective:** This study aimed to evaluate the toxicity profile of docetaxel-loaded nanostructured lipid carriers (NLC-DTX) compared with Taxotere®, focusing on systemic effects and toxicity to the male reproductive system. **Methods:** Male Sprague–Dawley rats (n = 6 / group) were subjected to intraperitoneal administration of NLC-DTX or Taxotere® following a subchronic toxicity protocol. Different dose levels were evaluated to determine the maximum tolerated dose, after which the systemic and reproductive effects of a sublethal dose were investigated through hematological analyses, organ assessment, and sperm morphology evaluation. A 14-day recovery period was also included to assess the reversibility of toxic effects. **Results:** The results revealed that encapsulation markedly altered the safety profile of DTX. While Taxotere® was well tolerated at doses of 10.0 and 5.0 mg/kg, the NLC-DTX formulation caused complete mortality at these concentrations, so that 2.5 mg/kg was the survival threshold established for the subchronic protocol. Even at this reduced dose, NLC-DTX exhibited greater toxicity than Taxotere®, as evidenced by hematological alterations and persistent thymic atrophy after the recovery period. In the reproductive system, although both treatments induced epididymal atrophy, NLC-DTX induced a significantly higher incidence of sperm abnormalities. These findings support the hypothesis that encapsulation modifies drug distribution, suggesting that sustained release prolongs exposure of the seminiferous epithelium to DTX, thereby exacerbating impairment of spermatogenesis compared with the free drug. **Conclusion:** Although nanostructured delivery systems are promising tools for chemotherapy, caution is warranted regarding the balance between therapeutic efficacy and preservation of reproductive function. The greater toxicity observed for NLC-DTX suggests that its sustained release prolongs *in vivo* exposure to DTX, thereby compromising the organism's homeostatic regenerative capacity. Further studies correlating pharmacokinetic behavior with antitumor efficacy are needed to establish the balance between therapeutic benefits and toxicological risks associated with this nanostructured strategy.

12.026 **Sedative and Anesthetic Activity of the Essential Oil of** *Cymbopogon winterianus* **in** *Penaeus vannamei*. Meira-Graziela M[1], Schmidt D[1], Wasielesky Junior W[2], Cardozo AP[2] Giesta LB[2], Menossi O[3], Pedrosa VF[2], Toigo YL[4], Baldisserotto B[1] Heinzmann BM[1] [1]UFSM, Fish Physiology Lab, Brazil. [2]FURG, Shrimp Farming Lab. [3]FURG, Lab Immunology and Pathology of Aquatic Organisms. [4]UFRGS.

Introduction: Monoterpenoids, the main constituents of essential oils (EOs), have central nervous system depressant activity and are promising natural anesthetics for aquaculture. The EO of *Cymbopogon winterianus*, rich in citronellal, geraniol, and citronellol, has shown anesthetic properties in aquatic species and may reduce handling stress in shrimp farming. **Objectives:** To evaluate the sedative and anesthetic effects of *C. winterianus* EO in adult *Penaeus vannamei*. **Methods:** EO was extracted by hydrodistillation using a Clevenger apparatus and analyzed by gas chromatography. Shrimp fasted for 12 h were exposed to 0 (control), 200, 300, 400, 500, or 600 µL/L EO. Because the EO was diluted in ethanol (1:10), an ethanol control (5400 µL/L) was included (N = 8 per treatment). Sedation, deep anesthesia, recovery time, and survival (48 h) were evaluated. Data were analyzed by one-way ANOVA followed by Tukey's test ($P < 0.05$). **Results:** Sedation induction time decreased significantly ($P = 0.0014$), from 283.5 ± 37.2 s at 200 µL/L to 95.0 ± 52.5 s at 500 µL/L. Deep anesthesia induction also decreased significantly ($P < 0.0001$), from 934.4 ± 417.6 s to 219.5 ± 49.6 s. Recovery time differed among treatments ($P = 0.0017$), although no differences were observed among 400, 500, and 600 µL/L. Control and ethanol groups showed no signs of sedation or anesthesia. **Conclusion:** *C. winterianus* EO is an effective anesthetic for *P. vannamei*. Concentrations of 500 and 600 µL/L provided rapid induction with similar recovery times, supporting its potential as a safe natural alternative to reduce handling stress in shrimp farming. **Financial support:** CAPES and CNPq.

12.027 **Evaluation of the Tripanocidal Effect of the Combination Between Benznidazole and Antimicrobial Peptides Analogs Derived from the M-PONTx-Dq4e Fragment [1-10]**. Martins BVB[1], Magalhães EP[1], Martins BMS[1], R LR[1], da Silva Júnior PN[1], Sampaio BCC[1], Silva BP[2], Adelino SM[2], Ferreira ALN[2], Carvalho JPAQ[2], Lima AKP[2], Marques BMC[2], Amorim AC[2], de Menezes RRPPB[1], Martins AMC[1] [1]UFC, Faculty of Pharmacy, Dept Clinical and Toxicological Analysis, PPG Pharmacological Sciences, Brazil. [2]UFC, Faculty of Pharmacy, Dept Clinical and Toxicological Analysis, Brazil.

Introduction: Chagas disease occurs in more than 21 countries, in both rural and urban areas. In Brazil, benznidazole (BZN) is the primary drug available for treatment; however, it requires a long course of treatment, which hinders treatment adherence and is associated with severe adverse effects and limited efficacy. In this context, antimicrobial peptides (AMPs) emerge as a promising alternative due to their well-studied antiparasitic properties. Pharmacological synergy refers to an increase in therapeutic effect when two or more substances are used in combination, compared to their isolated effects, leading to a reduction in the administered dose, fewer adverse effects, and greater treatment efficacy. **Objectives:** Thus, the purpose of this study was to evaluate the tripanocidal effect of the combination between benznidazole and antimicrobial peptides analogs derived from the M-PONTx-Dq4e fragment [1-10], present in the venom of the *Dinoponera quadriceps* ant, on trypomastigote forms of *Trypanosoma cruzi* Y strain. **Methods:** The chosen compounds were peptide P37 ([R3,R8,R10], R = arginine) + BZN and P39 ([R4]) + BZN. A 96-well plate count assay was performed on treated and untreated trypomastigote forms, using concentrations based on the IC50/2: P37 (4,56 µM; 2,28 µM; 1,14 µM; 0,57 µM; 0,29 µM; 0,15 µM; 0,075 µM; 0,0375 µM); P39 (6,78 µM; 3,39 µM; 1,70 µM; 0,85 µM; 0,43 µM; 0,22 µM; 0,11 µM; 0,055 µM); and BZN (238,95 µM; 119,48 µM; 59,74 µM; 29,87 µM; 14,93 µM; 7,47 µM; 3,73 µM; 1,87 µM). The experiments were conducted in triplicate (n = 3), with counts taken after 24 hours. The data were analyzed using Combenefit software, a tool that allows for the visualization and analysis of the quantification of drug combination effects using the Bliss independence model. **Results:** Synergistic effects were observed at different concentrations for all peptides, particularly in combinations involving low peptide concentrations paired with different concentrations of BZN. The greatest synergistic effects observed were in the combinations P37 + BZN (2,28 µM + 59,74 µM; 2,28 µM + 14,93 µM; 2,28 µM + 1,87 µM; 1,14 µM + 29,87 µM); and P39 + BZN (0,22 µM + 1,87 µM; 3,39 µM + 14,93 µM; 3,39 µM + 1,87 µM; 0,22 µM + 7,47 µM). These findings suggest that the drug dose may be reduced when used in combination. **Conclusion:** The evaluated peptides exhibited tripanocidal activity and have potential for use in combination with benznidazole in the treatment of Chagas disease. However, further studies are needed to assess the cytotoxicity of these combinations to ensure safety during therapeutic administration. This study was funded by CNPq Process Number 409925/2025-0; CNPq Process Number 306113/2023-6; and Capes. Keywords: Chagas disease; Antimicrobial Peptides; Pharmacological synergy.

12.028 *In vivo* and *In vitro* Anti-Inflammatory Activity of CBD-Derived Terpene-Cinnamoyl-Acyl-Hydrazone Molecules. Paiva JPB[1], Lontra ACP[1], Souza, MK[2], Franco GRR [2], Gontijo VS [2], Viegas-Jr C[2], Fernandes PD[1] [1]ICB-UFRJ, Program of Reserch and Drug Discovery, Lab. of Pharmacology of Pain and Inflammation, Brazil; [2]UNIFAL, Lab. of Research in Medicinal Chemistry, Brazil.

Inflammation is a complex pathological condition characterized by an exacerbated immune response involving the activation of immune cells and the release of pro-inflammatory mediators. Current therapies for inflammatory diseases are mainly based on steroidal and non-steroidal anti-inflammatory drugs (NSAIDs), whose prolonged use is associated with important adverse effects. Therefore, the development of safer and more selective anti-inflammatory agents remains an important therapeutic challenge. Cannabidiol (CBD) has attracted considerable attention due to its anti-inflammatory and immunomodulatory properties. However, its clinical application is limited by poor aqueous solubility, low oral bioavailability, and rapid metabolic degradation. In this context, structurally modified CBD analogues have emerged as promising alternatives to improve pharmacokinetic and pharmacological properties, including metabolic stability, selectivity, and bioavailability. Thus, this study aimed to evaluate the *in vitro* and *in vivo* anti-inflammatory potential of Novel CBD-Based Terpene-Cinnamoyl-Acyl-Hydrazone Analogues. Female Swiss Webster mice (28–30 g, n = 6–8) were orally treated with the analogues PQM-290 or PQM-291 at doses of 1, 3, and 10 µmol/kg. One hour later, animals received carrageenan (0.5%, 1 mL) or saline (NaCl 0.9%) injection into the subcutaneous air pouch (SAP). After 24 h, the animals were euthanized and SAP exudates were collected for leukocyte counting. RAW 264.7 macrophages were maintained in a humidified atmosphere containing 5% CO_2 at 37°C and stimulated with LPS (1 µg/mL) in the presence or absence of the analogues (1, 3, or 10 µM). After 24 h, supernatants were collected for cytokine quantification. Results are expressed as mean ± SD and analyzed by ANOVA followed by Tukey's test (*$p<0.05$). Carrageenan induced intense leukocyte migration (135.7±30.3x10^3 cells/µL) compared to saline (3.5±1.5x10^3 cells/µL). Dexamethasone (6.5 µmol/kg) reduced cell migration to 58±20x10^3*cells/µL. PQM-290 also reduced migration, 1 µmol/kg: 83.6±14.9*x10^3 cells/µL; 3 µmol/kg: 129.8±40.7x10^3 cells/µL; and 10 µmol/kg: 98.75±14.3x10^3 cells/µL. PQM-291 showed reductions, 1 µmol/kg: 92±18.8*x10^3 cells/µL; 3 µmol/kg: 83.9±7.3*x10^3 cells/µL; and 10 µmol/kg: 85.5±33.6*x10^3 cells/µL. *In vitro*, RAW 264.7 control cells produced 228.8±80.1 pg/mL TNF-α, while LPS stimulation increased production to 7,753.3±382 pg/mL. PQM-290 reduced TNF-α levels to 7,237±878.5 pg/mL (1 µM), 6,603±155.4*pg/mL (3 µM), and 5,566.5±824.8*pg/mL (10 µM). PQM-291 reduced TNF-α production to 7,809.29±301.1 pg/mL (1 µM), 6,678.1±1190.4 pg/mL (3 µM), and 5,215.1±902*pg/mL (10 µM). These findings suggest that the structural analogues PQM-290 and PQM-291 exhibit anti-inflammatory activity by reducing carrageenan-induced leukocyte migration and TNF-α production *in vitro*.

12.029 **Liposomal Coencapsulation of Piplartine and Fenretinide Aiming the Treatment of Non-Invasive Breast Cancer**. Melo GB, Lopes LB ICB-USP, Dept Pharmacology, Graduate Program Functional and Molecular Biology

Approximately 25% of breast cancer cases are classified as Ductal Carcinoma in Situ (DCIS), a non-invasive form of the disease that still presents significant therapeutic challenges. In this context, nanomedicine has emerged as a promising strategy to overcome limitations associated with conventional therapies, including poor selectivity, invasiveness, and systemic toxicity. In this study, liposomes (LPs) were developed for the intraductal co-delivery of antitumoral drug combinations aiming at the localized treatment of non- invasive breast cancer. Initially, piplartine, an alkaloid with recognized antitumor activity, was combined with fenretinide at different molar ratios to evaluate potential synergistic effects against breast cancer cells. Drug interactions were assessed using the Chou–Talalay method to determine the combination index (CI). Synergistic effects were observed for piplartine (PL) and fenretinide (FE) combinations at 1:1 and 2:1 molar ratios (PL:FE). Subsequently, liposomal formulations were optimized by varying the proportions of soy phosphatidylcholine (PC), propylene glycol (PG), and the incorporated drugs, using the film hydration method followed by sonication for particle size reduction. Liposomes composed of 10% PC and PG, containing 0.25% PL and 0.12% FE (2:1 PL:FE), and subjected to three sonication cycles (50 s ON / 30 s OFF), exhibited an average diameter of approximately 150 nm with a polydispersity index of 0.25. Transmission electron microscopy confirmed a spherical morphology, while drug entrapment efficiency exceeded 99%. The cytotoxicity of the formulations was further evaluated in breast cancer cell lines to investigate the effect of piplartine encapsulation. Piplartine- loaded liposomes showed enhanced cytotoxicity in MCF-7 cells compared to the free drug solution, with IC50 values of 7.5 μM and 10.5 μM, respectively. More pronounced effects were observed for liposomes co-encapsulating piplartine and fenretinide, which reduced the IC50 by approximately two-fold compared to the PL solution. Overall, these findings demonstrate the potential of this nanosystem to improve antitumor activity while enabling localized drug delivery, representing a promising strategy for the treatment of non-invasive breast cancer.

12.030 **Preparation, Characterization and *in vitro* Evaluation of Liposomes Containing an Antitumor Prototype from the Pterocarpan Class**. Sousa GC[1,2], Maranhão SS[1,3], Vieira Neto JB[1,3], Bastos RS[1,3], Desiderio GA[1,3], Falcão JS[4,5], Lapa DP[4,5], Costa PRR[4,5], Caleffi GS[4,5], Pessoa C[1,3]. [1]UFC, Lab. of Experimental Oncology, Brazil, [2]UFC, PPG Biotechnology, Brazil, [3]UFC, PPG Pharmacology, Brazil, [4]UFRJ, Lab. of Bioorganic Chemistry, Research Institute of Natural Products Walter Mors, Brazil, [5]UFRJ, PPG Chemistry of Natural Products, Brazil.

Introduction: Prostate cancer is one of the most common solid tumors in men and poses therapeutic challenges due to progression to aggressive forms and resistance to conventional treatments, which highlights the need for new therapeutic approaches. In this context, compounds of the pterocarpan class have shown antitumor potential but may present pharmacokinetic limitations that hinder their application. Liposomal systems emerge as a promising strategy to improve solubility, stability and controlled release, potentially enhancing the therapeutic performance of bioactive molecules. Objectives To develop and characterize a stable liposomal nanoformulation containing a pterocarpan compound (LOE2208), aiming for its application in *in vivo* studies in a prostate cancer model. Methods The liposomal formulation was composed of LIPOID S 100, cholesterol, DSPE-PEG-MAL, and phosphatidylserine, into which the compound LOE2208 was incorporated. Liposomes were produced by the thin-film hydration method. Hydrodynamic size, polydispersity index (PDI) and zeta potential were determined using a Zetasizer Nano-ZS. Formulations were frozen in PBS:sucrose, lyophilized and subsequently reconstituted in PBS. Encapsulation efficiency (EE%) was determined by HPLC after separation of free compound by filtration. Stability was evaluated after 30 days of storage in a desiccator at room temperature, with reassessment of physicochemical parameters and EE%. The release profile was analyzed in an orbital shaker, and the cytotoxic effect was tested on the PC3 cell line using resazurin assay, with a 72 h incubation; LOE2208 was tested at 80 µM–0.04 µM and docetaxel at 10 µM–0.0025 µM. Results The formulation presented a nanoscale size of 84.68 ± 1.10, low PDI (0.2 ± 0.01), negative zeta potential (-2 ± 0.20) and encapsulation efficiency greater of 93%. Physical stability was satisfactory, with better preservation of parameters at a PBS:sucrose ratio of 1:5. The liposomal formulation showed controlled release of the pterocarpan, with 49.2% released at 24 h and 96.9% at 76 h. The free compound showed an IC50 of 1.33 µM, while the liposomal formulation showed an IC50 of 2.1 µM. The blank liposome showed no cytotoxicity, with IC50 > 80 µM. **Conclusion:** The developed liposomal formulation proved to be a promising strategy for antitumor application, with physicochemical stability, good encapsulation efficiency, prolonged release and retention of cytotoxic activity. These findings support advancement of the system to preclinical studies in a prostate cancer model.

12.031 **New Synthetic Morita-Baylis-Hillman Compounds as Candidates for the Treatment of Visceral Leishmaniasis**. Ferreira RS[1], Fernandes ALM[1], Cardoso LL[1], Lamec DTF[1], Albuquerque YS[1], Machado GR[1], Almeida FS[1], Santos ESFR[2], Lima-Junior CG[2], Keesen TSL[1] [1]UFPB, Dept Cell and Molecular Biology, Lab Immunology of Infectious Diseases, Multicenter Graduate Program in Physiological Sciences (PMPGCF), Brazil. [2]UFPB, Dept Chemistry, Lab Medicinal Organic Synthesis, Brazil.

Introduction: Visceral leishmaniasis is the most severe form of leishmaniasis and constitutes a major public health problem, especially in endemic regions of Brazil. Although drugs are available for the treatment of the disease, current therapeutic options present important limitations. In this context, synthetic compounds derived from the Morita-Baylis-Hillman (MBH) reaction have demonstrated promising activity against Leishmania species, representing a relevant strategy for the development of more effective, safe, and selective therapies. **Objective:** To evaluate the *in vitro* biological activity of five novel synthetic compounds against *Leishmania infantum*. **Methods:** The compounds were tested at concentrations ranging from 3.12–400 μM and 0.78–100 μM, in triplicate and across three independent experiments, to determine cell viability in promastigote forms (IC50) and axenic amastigote forms (EC50), as well as cytotoxicity in human erythrocytes (HC50), using the MTT colorimetric assay. Amphotericin B (AmB) was used as the positive control, while the negative control consisted of untreated cells. Statistical analyses were performed using GraphPad Prism software. **Results:** In promastigote forms, the MBH compounds showed IC50 values of ≥ 400 μM (AIN43), 20 μM (AIN01), 19.91 μM (AIN51), 16.97 μM (AIC52), 12.05 μM (AIN53), and 8.16 μM (AIN41), whereas Amphotericin B exhibited an IC50 of 0.75 μM. In axenic amastigote forms, EC50 values were ≥ 400 μM (AIN43), 136.4 μM (AIN01), 11.46 μM (AIN53), 4.48 μM (AIN51), 4.24 μM (AIC52), and 0.85 μM (AIN41), while Amphotericin B showed an EC50 of 0.32 μM. In human erythrocytes, none of the compounds exhibited hemolytic activity at the highest concentration tested (HC50 ≥ 400 μM), whereas Amphotericin B presented cytotoxicity of 193.4 μM. Results were expressed as 95% confidence intervals, with the negative control considered, and $p < 0.05$ compared to controls. **Conclusion:** The results demonstrate that this class of synthetic compounds exhibits potential anti-Leishmania activity, particularly the adduct AIN41 (EC50 = 0.85 μM) against axenic amastigote forms, the intracellular stage responsible for maintaining infection and its clinical manifestations. The compound showed a selectivity index ≥ 470-fold relative to its cytotoxicity in human erythrocytes (HC50 ≥ 400 μM), highlighting its potential as a promising prototype candidate for the development of new therapies against visceral leishmaniasis. Ethical Approval: Research Ethics Committee for Human Subjects of the Health Sciences Center/UFPB (CAAE: 90688425.1.0000.5188). **Financial support:** Research Support Foundation of the State of Paraíba (FAPESQ-PB). **Acknowledgments:** The authors thank the Research Support Foundation of the State of Paraíba (FAPESQ-PB), the Federal University of Paraíba (UFPB), and the research groups LABIDIC and LASOM-PB.

12.032 **Trypanothione Reductase as a Target in Drug Repurposing Strategies** *against L*. (*L*.) *amazonensis*. Melchert SSL, Passero LFD, Souza FF, Honorio KM, Laurenti MD. [1]FMUSP, Lab of Pathology of Infectious Diseases, PPG Experimental Pathophysiology, Brazil, [2]IEAMAR-Unesp, Brazil, [3]EACH/USP, Brazil.

Introduction: Leishmaniasis comprises a complex of parasitic diseases caused by protozoa of the genus Leishmania and represents a major public health concern. Current therapies are limited by toxicity, parasite resistance, high costs, and poor therapeutic adherence. In this context, drug repurposing represents a promising strategy for identifying new therapeutic applications for previously approved compounds. Associated with this approach, molecular docking enables the prediction of interactions between small molecules and target proteins, supporting the rational screening of candidate compounds. Trypanothione reductase (TryR) plays an essential role in maintaining redox homeostasis in *Leishmania*, catalyzing the reduction of oxidized trypanothione into its reduced form, which is fundamental for the neutralization of reactive oxygen species. **Objectives:** Identify drug repurposing candidates with potential leishmanicidal activity through inhibition of TryR, using molecular docking and *in vitro* biological evaluation. **Methods:** 95 FDA-approved drugs with potential interaction with reductase enzymes and without previous reports of activity against *Leishmania* spp. were screened. The crystallographic structure of TryR complexed with the BVN ligand (PDB: 6ER5) was used for molecular docking analyses. For each compound, five independent poses were generated and evaluated regarding interactions with the Arg222 and Arg228 residues, followed by the establishment of a ranking based on the predicted binding free energy using the GNINA score. After ADMET analyses, five drugs were selected for *in vitro* evaluation: ethacrynic acid, carbamazepine, clozapine, naltrexone, and quinidine. **Results**: In the biological assays, all drugs presented a selectivity index (SI) higher than that of miltefosine, except for ethacrynic acid after 24h. Clozapine showed remarkable activity against promastigotes, with EC_{50} values of 6.08±1.02µg/mL and 10.55±1.63µg/mL after 24h and 72h, respectively. Quinidine also demonstrated high activity, with EC_{50} values of 13.56±1.21µg/mL and 6.38±1.18µg/mL in the respective periods. In intracellular amastigotes, a marked reduction in EC_{50} values and increased SI were observed, particularly for carbamazepine, clozapine, and quinidine, with SI values of 291.4, 155.5, and 133.2 after 24h, and 672.43, 161.43, and 313.1 after 72h, respectively. In contrast, miltefosine exhibited SI values of 15.6 and 23.5 after 24h and 72h. Antiparasitic activity did not fully correlate with the docking prediction ranking, highlighting the influence of multiple biological and pharmacological factors. Additionally, the greater activity observed against intracellular amastigotes suggests the influence of the oxidative and nitrosative macrophage microenvironment, which may potentiate parasite susceptibility to compounds interfering with TryR-dependent redox mechanisms. **Conclusion:** Overall, the findings reinforce TryR as a promising pharmacological target for drug repurposing against *L*. (*L*.) *amazonensis*, especially in models that preserve the parasite–macrophage interaction. Furthermore, the integration of *in silico* and *in vitro* approaches enabled the identification of clozapine, quinidine, and carbamazepine as promising candidates for future mechanistic and preclinical studies.

12.033 **Maximizing Benznidazole Solubility: Optimization of Polymeric Solid Dispersions via Desirability**. França BCS, Amorim IS, Borba LMR, Ferreira IGS, Ferreira AS, Rolim Neto PJ UFPE

Introduction: Benznidazole (BNZ) is the drug of choice for the treatment of Chagas disease and has been used for over 50 years; however, its low solubility, coupled with its crystalline structure, remains a pharmacokinetic challenge. The use of solubility-enhancing techniques, such as the preparation of solid dispersions, has proven to be a promising tool for the amorphization of samples and the consequent improvement of solubility. Experimental tools such as Quality by Design (QbD) are used in this context to optimize the process through statistical analysis of variables. **Objectives:** To evaluate the factors influencing BNZ solubility by preparing polymeric solid dispersions (SDs) using multilevel experimental design and to determine which one exhibits the highest desirability. **Methods:** Solid dispersions of BNZ and two polymers (POLY) (Soluplus® and PVP K30) were obtained in the ratios (RAT) of 1:1, 1:2, and 1:3 using the solvent evaporation method (70% alcohol). All experimental runs were performed in triplicate (n = 3). The evaluated responses were aqueous solubility (S), crystallinity index (CI) determined by X-ray diffraction, and the area under the dissolution curve (AUC). A multilevel factorial design was used for the statistical analysis within the QbD framework. Regression models were fitted for each response variable and evaluated using analysis of variance (ANOVA). Model significance and the effects of the formulation variables were assessed using F-tests and p-values. The goodness-of-fit of the models was evaluated using the coefficient of determination (R^2) and the adjusted coefficient of determination (adjusted R^2). Multi-response optimisation was performed using Derringer's desirability function to identify the optimal formulation. **Results:** The results indicated that all three dependent variables were statistically significant, with p-values less than 0.032 for all. For CI, the F-value was 29.70 for the model, with R^2 of 0.9956 and R^2(adj) of 0.9938; only RAT showed statistical significance (F=38.95). For S, the p-value was 0.00 and F was 32.51, R^2 0.9313, and R^2(adj) 0.9026. There was statistical significance for RAT (F=26.99), POLY (72.19), and RAT*POLY (18.20). For AUC, the p-value was 0.00, with F = 31.89, R^2 = 0.9300, and R^2(adj) = 0.9008. Statistical significance was observed for RAT (F = 15.06), POLY (114.24), and RAT*POLY (7.54). Optimization via desirability calculation indicated the BNZ:Soluplus mixture in a 1:3 ratio as the best, with a desirability of 0.6384. **Conclusion:** The statistical results of the experimental design indicate significance for the three factors, demonstrated by the F and p-value, and with the fit described by R^2 and R^2(adj). While for CI only the ratio was significant, for S and AUC the polymer, the ratio, and the interaction between the two were significant. The desirability factor indicated SD BNZ:Soluplus in a 1:3 ratio as the best option for increasing solubility.

12.034 **A Novel cinnamoyl-N-acylhydrazone Compound Attenuates Ulcerative Colitis by Reducing Intestinal Inflammation in Mice**. Lontra, ACP[1], França, PRC[1], Paiva, JPB[1], Castro, FBF[1], Souza, ML[2], Franco, MRR[2], Viegas-Junior, C[2], Fernandes, PD[1] [1]UFRJ, Institute of Biomedical Science, Lab. of Pharmacology of Pain and Inflammation, PPG of Morphological Sciences, Brazil. [2]UNIFAL, Lab. of Research in Medicinal Chemistry, Brazil.

Introduction: Ulcerative colitis is a chronic inflammatory disease affecting the colon. Its pathogenesis is not fully elucidated, but it is known to involve several conditions, such as dysregulation of the immune system response and alterations in intestinal microbiota. The main symptoms of this disease include stools with blood, increased intestinal motility, abdominal pain, and weight loss, furthermore, many patients do not adapt to current treatments available due to severe adverse effects. Therefore, aiming a therapeutic alternative approach, a new cinnamoyl-N-acylhydrazone compound, PQM-276, was synthesized and its effects in the treatment of this disease were analyzed. **Objective:** Evaluate the effects of treatment with PQM-276 in an experimental model of ulcerative colitis in mice. **Methods:** Female and male K-18 hACE2 mice (20-25g) were used. Ulcerative colitis was induced using DSS (Dextran Sulfate Sodium, 2.5%) for 7 consecutive days. The experimental groups consisted of a control group (access to water) and groups with ulcerative colitis (access to DSS) treated orally with vehicle, 5-aminosalicylic acid (5-ASA, 326 µmol/kg) or PQM-276 (1, 3 or 10 µmol/kg) on days 2, 4 and 6. On day 7, euthanasia was performed, and colon samples were collected for cytokine quantification using ELISA method. Results are represented as mean ± SD. Statistical analysis was performed using ANOVA followed by Dunnett's test (*$p<0.05$ vs Vehicle; #$p<0.05$ vs Control). **Results:** Treatment with PQM-276 did not affect the colon length of animals with ulcerative colitis. Control: 8.6±0.6 cm; Vehicle: 6.4±0.3#cm; 5-ASA: 7.3±0.7*cm; PQM-276: 1, 3 and 10 µmol/kg: 6.6±0.3 cm; 6.9±0.4*cm; 7±0.7*cm respectively. PQM-276 reduced IL-1β levels in colon. Control: 0.63±0.83 pg/µg of tissue; Vehicle: 7.0±1.42#pg/µg of tissue; 5-ASA: 3.08±1.37*pg/µg of tissue; PQM-276: 1, 3 and 10 µmol/kg: 6.38±1.73*pg/µg of tissue, 5.32±0.99*pg/µg of tissue, 4.26±1.33*pg/µg of tissue, respectively. PQM-276 also reduced IL-6 levels: Control group: 0.3±0.8 pg/µg of tissue; Vehicle: 5.11±1.67#pg/µg of tissue; 5-ASA: 3.61±1.05*pg/µg of tissue; PQM-276: 1, 3 and 10 µmol/kg: 4.77±2.2 pg/µg of tissue, 1.16±0.42*pg/µg of tissue and 3.39±1.05*pg/µg of tissue, respectively. **Conclusion:** PQM-276 showed promising therapeutic effects in the treatment of ulcerative colitis in mice by preventing colon shortening length and reducing levels of inflammatory cytokines (IL-6 and IL-1β).

12.035 *in silico* **Evaluation of LOE2208 and Its Derivatives Reveals Predicted Interactions with Tubulin Protein and Suitable ADMET Profiles**. Lima JM[1,2], Da Costa RF[3,4], Bezerra EM[3,4], Viera-Neto JB[1,2], Falcão JS[5,6], Lapa DP[5,6], Costa PRR[5,6], Caleffi GS[5,6], Pessoa C[1,2]. [1]UFC, Lab. of Experimental Oncology, Drug Research and Development Center, Brazil; [2]UFC PPG Pharmacology, Brazil; [3]UFERSA, Lab. of Computational Physics, Brazil; [4]UFERSA, PPG Science and Engineering of Materials, Brazil; [5]UFRJ, Lab. of Bioorganic Chemistry, Research Institute of Natural Products Walter Mors, Brazil; [6]UFRJ, PPG Chemistry of Natural Products, Brazil.

Introduction: The identification of small molecules that interfere with mitotic progression remains a promising strategy for cancer treatment. Computer-Aided Drug Design (CADD) enables the prediction of molecular targets and pharmacological properties, supporting the development of novel anticancer agents. LOE2208 is a synthetic isoflavonoid analogue and previous studies reported antiproliferative activity and the ability to induce G2/M cell cycle arrest in tumor cells, showing similar effects of microtubule-destabilizing agents that bind to the Colchicine domain. However, the molecular targets responsible for its biological activity and its ADMET properties remain to be elucidated. **Objectives:** To characterize the ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) profile of LOE2208 and 15 rationally designed derivatives, and to investigate the potential binding interactions of these molecules with the α/β-tubulin heterodimer. Methods: Pharmacokinetic, toxicological, and drug-likeness profiles were predicted using multiple platforms, including ADMET Predictor® 13 (Simulation Plus) and open-access servers such as pkCSM, Deep-Pk, SwissADME, ADMETlab 3.0, and ProTox 3.0. Structure-based blind docking was performed using the crystal structure of two αβ-tubulin dimers (PDB: 4O2B) and CB-Dock2, a platform that identifies multiple cavities on the protein surface and performs rigid docking using AutoDock Vina v.1.2.0. Colchicine, Nocodazole and Taxol were utilized as reference ligands. Ligands were ranked by binding energy (Vina score, kcal/mol), and molecular interactions were analyzed using LigPlot+ and PyMol. **Results:** LOE2208 demonstrated a favorable drug-like profile with no Lipinsk, Ghose and Vebber Rules violations and an low overall ADMET risk score of 2.07. Predictions indicated high oral absorption, significant blood-brain barrier (BBB) penetration and high permeability in PAMPA assays. The metabolic profile suggested predominantly oxidative clearance through multiple CYP450 isoforms, notably CYPs 1A2 and 3A4. Toxicity models predicted a safe mutagenic profile (Ames negative) but flagged potential microsomal instability and cardiotoxicity. Three derivatives presentend overwall ADMET Risk comparable to or lower than the lead molecule, being those Deriv-7 (Risk 1.0), Deriv-12 (Risk 2.09) and Deriv-14 (Risk 2.06). Molecular docking best poses placed LOE2208 at the colchicine-binding domain at the interface of both αβ-tubulin dimers (Vina scores: -8.4 and -8.6 kcal/mol), with key contacts at the αT5 loop (SER178, THR179, ALA180) and β-H8 helix (ASN249, LYS254), critical residues for microtubule destabilization. Among the derivatives, candidates 3, 7, 8, 12, and 14 showed enhanced binding affinities (up to -9.3 kcal/mol), with derivatives 7, 8, and 12 exhibiting superior interactions with the β subunit, more closely mimicking colchicine's binding mode. **Conclusion:** Computational analyses indicated that LOE2208 and its derivatives present favorable early drug-like properties and interact with the colchicine-binding site of α/β-tubulin. Deriv-7 displayed the most favorable balance between predicted binding affinity and ADMET profile. These findings support further experimental validation of this series of compounds as potential antimitotic agents. **Financial support:** INCTBIO2, PRONON/Brazilian Ministry of Health, FINEP, CNPq, CAPES, and FUNCAP.

12.036 **Preclinical *in vivo* Tests of LOE2026, a Combrestastatin a-4 (CA-4) Analogue Compound, in Zebrafish Embryos and a Xenograft Murine Model Derived from Human Colorectal Cancer Cells**. Motta LCB[1], Raymond J[2], Benedetto MC[2], Woyome VS[1], de Brito Neto JV[1], Nepomuceno FWB[1], Miguel EC[3], Vieira JHA[3], Sampaio, TL[4], Fernandes MO[4], Duarte, ASG[5], Lima LM[6], Pessoa CO[1], de Moraes MO[1], Paier CRK[1] [1]UFC, Lab. of Experimental Oncology, Brazil, [2]Institut Pasteur of Montevideo (IPMon), Lab Animal Biotechnology Unit, Uruguay, [3]UFC, Biomaterials Lab, Brazil, [4]UFC, Lab. of Clinical and Toxicological Analyses, Brazil, [5]UFC, Morphology Dept, Brazil, [6]UFRJ, Lab. of Evaluation and Synthesis of Bioactive Substances, Brazil.

Introduction: Colorectal cancer remains one of the leading causes of cancer-related death worldwide, and therapeutic resistance continues to limit treatment efficacy and patient survival. In this context, LOE2026, a combretastatin A4 analog, was developed to overcome the toxicity and stability limitations of the parent compound. Previous *in silico* studies predicted that LOE2026 inhibits tubulin polymerization and interacts with the epidermal growth factor receptor (EGFR). In addition, *in vitro* analyses demonstrated its antiproliferative activity against tumor cell lines, including those resistant to anti-EGFR therapy. **Objective:** To evaluate the toxicity of LOE2026 in zebrafish embryos and a murine model, as well as to investigate its antitumor efficacy in immunodeficient mice bearing HCT-116 human colorectal cancer xenografts. **Methods:** This project was approved by CEUA under protocols 80230823-0 (UFC), 81230823-0 (UFC), 4645080322 (UFC), and 006-25 (IPMon). Zebrafish embryos were exposed to LOE2026 at 20, 30, and 40 nM for 96 h, and survival, hatching rate, body length, yolk sac size, and malformations were evaluated using negative (reconstituted water), vehicle (0.5% DMSO), and positive (3,4-dichloroaniline) controls. Acute toxicity was assessed in NOD-SCID mice using the OECD 425 Up-and-down protocol following intraperitoneal (i.p.) administration of 17,5-175 mg/kg to estimate the LD50. Antitumor efficacy was investigated in HCT-116 xenograft-bearing immunodeficient mice treated with 10 mg/kg intratumoral (i.t.) LOE2026 or vehicle on alternate days, and tumor growth was monitored by digital caliper measurements. **Results:** In zebrafish embryos, LOE2026 showed a favorable safety profile, with survival rates of 98,3%, 100%, and 96,6% at 20, 30, and 40 nM, respectively, hatching rates above 90%, and malformation rates below 10%, with no significant differences compared with the negative control. In the murine acute toxicity assay, the estimated LD50 was 59.03 mg/kg, while 41 mg/kg was the highest tolerated dose evaluated in the Up-and-Down protocol. Following the limited efficacy observed after intraperitoneal administration and evidence of compound accumulation in adipose tissue, intratumoral administration was evaluated. Treatment with 10 mg/kg LOE2026 significantly delayed tumor growth, producing a 38.6% reduction compared with the vehicle group by day 10 ($p < 0.05$), with even greater inhibition on days 12 and 14 ($p < 0.0001$), without significant changes in body weight. **Conclusion:** Collectively, these findings demonstrate that LOE2026 exhibits a favorable preclinical profile, combining low embryotoxicity in zebrafish with significant antitumor activity in a xenograft model of resistant colorectal cancer. These results support the translational potential of LOE2026 as a promising multi-target candidate for the development of novel therapeutic strategies against colorectal cancer. **Funding:** This study was supported by INCTBIO2, PRONON, Brazilian Ministry of Health, FINEP, CNPq, CAPES, and FUNCAP.

12.037 **Multifunctional Nanocarriers for Local Treatment of Breast and Cervical Cancer: Development and *In vitro* Cytotoxicity**. Santos AA[1], Passos JS[1], Araki K[2], Lopes, LB[1] [1]ICB-USP, Dept Pharmacology, Brazil. [2]IQ-USP, Dept Fundamental Chemistry, Brazil.

Introduction: Breast and cervical cancer represent two highly prevalent tumor types among women, with mortality rates directly associated with the human development index. Delays in diagnosis, as well as difficulties in accessing healthcare systems for treatment, are important factors that reduce the chances of cure. These factors are compounded by general challenges related to tumor therapy, including systemic toxicity, low selectivity, and resistance to conventional chemotherapeutic agents. In this work, we propose combining local administration routes with nanotechnology for the personalization of treatment for these tumors, aiming to improve drug localization in cervical tissue and mammary ducts to increase cytotoxicity and selectivity. **Objectives:** This study aims at developing lipid nanocarriers (NLCs) functionalized with hyaluronic acid for incorporation of paclitaxel and potential application in the local treatment of non-invasive of breast and cervical cancer. **Methodology:** : In this initial stage of the study, we developed NLCs using the emulsification-sonication method. Variations in the composition of the solid lipid, the ratio between solid and liquid lipids, and the type/concentration of hydrophilic surfactants, as well the concentration of hyaluronic acid (HA) for surface functionalization) were evaluated. The nanocarriers were characterized by assessing particle size and zeta potential. The effects on the viability of keratinocytes (as a non-tumor cell model) and MCF-7 breast cancer cells were assessed after treatment for 72 h. **Preliminary Results:** Different solid-to-liquid lipid ratios (w/w), ranging from 7:3 to 5:5, were evaluated using tristearin or compritol as solid lipids and tricaprylin or linoleic acid as liquid lipids. The 5:5 ratio was selected for subsequent experiments. Due to improved physicochemical characteristics, compritol and tricaprylin were selected as the oily phase, while phosphatidylcholine and 2% polysorbate 80 were selected as hydrophobic and hydrophilic surfactants, respectively. NLC surface modification was performed including a cationic surfactant (0.1% w/w) and hyaluronic acid. Treatment of MCF-7 breast cancer cells and keratinocytes with the unloaded NLC did not reduce cell viability in the concentration range studied, suggesting that they should not cause adverse effects per se. Further assays are under way to assess drug incorporation effects.

12.038 **Cannabigerol-Loaded Nanostructured Lipid Carriers for Potential Application in Autism Spectrum Disorder**. Carvalho, FV[1]; Rodrigues da Silva, GH[2]; Paula, RM[3]; Rocco, SA[2]; de Paula, E[1]. [1] Unicamp, Dept of Biochemistry, Institute of Biology, Brazil. [2]CNPEM, Brazilian Biosc. Natl Lab, Brazil. [3]Unicamp, Fac. Pharmaceutical Sciences, Brazil.

Introduction: Autism Spectrum Disorder (ASD) is a neurodevelopmental condition of increasing Public Health interest in which pathophysiology the endocannabinoid system is involved, making phytocannabinoids potential therapeutic candidates for its treatment. Cannabigerol (CBG) exhibits neuroprotective, anti-inflammatory, and antioxidant properties; but its low aqueous solubility and propense to oxidation may compromise its therapeutic potential. In this context, encapsulation in nanostructured lipid carriers (NLC) is a strategy to improve CBG stability and enable controlled drug delivery. **Objective:** This study aimed to optimize an NLC-formulation for cannabigerol using a Design of Experiments (DoE) approach. **Methods:** NLC containing CBG associated with antioxidants were developed using DoE to analyze the effect of total lipids, surfactant, CBG, and antioxidant over particle size, polydispersity index (PDI), and zeta potential (ZP). An HPLC method was established for CBG quantification. Physicochemical characterization included dynamic light scattering (DLS), transmission electron microscopy (TEM), X-ray diffraction (XRD), differential scanning calorimetry (DSC), CBG content determination, and photostability evaluation. The *in vitro* release profile of free and encapsulated CBG was also investigated. **Results:** Butylated hydroxytoluene (BHT) was the selected antioxidant to be incorporated in the NLC. 19 formulations from the combination of the 4 investigated variables were analyzed by DoE; higher total lipid and CBG concentrations increased particle size, whereas higher surfactant concentrations reduced PDI and negatively affected ZP. NLC presented: 180-270 nm mean diameters, low PDI (<0.20) and ZP >|20| mV, indicating systems with potential colloidal stability. TEM analysis revealed spherical nanoparticles with regular morphology and no evidence of aggregation. XRD disclosed the lower crystallinity of the lipid matrix compared with pure excipients and physical mixtures. *In vitro* release kinetics studies demonstrated rapid release of free CBG, while NLC promoted its sustained release, with the Weibull model providing the best fit for the release kinetics. **Conclusion:** CBG-loaded NLC exhibited suitable (nanoscale dimensions, homogeneity, structural integrity) features and promoted the sustained release of CBG. These findings support the potential of NLC as a promising delivery platform to improve CBG stability and contribute to its future therapeutic application in ASD.

12.039 **Lipid Nanoparticle Containing Simvastatin and Adenosine-Loaded Hydrogel Improves Wound Healing: Evaluation of Skin Penetration, Biocompatibility, and Therapeutic Efficacy in HaCat Cells and Mice**. Daré RG, Rocco VM, Marques B, Akamine EH, Lopes LB ICB-USP, Dept Pharmacology, Brazil

Introduction: Chronic wounds remain a major clinical challenge due to impaired angiogenesis, persistent inflammation, and delayed re-epithelialization. Simvastatin and adenosine have shown pro-healing properties, but the therapeutic application of simvastatin is limited by poor skin retention and systemic side effects when not locally retained. **Objectives:** Our group previously developed nanostructured lipid carriers co-loading simvastatin and adenosine (NLC-SA) with suitable physicochemical properties and enhanced skin retention (Daré RG. Eur. J. Pharm. Biopharm., v. 205, 114533, 2024). The present study aimed to incorporate the NLC-SA into a hydrogel and evaluate its therapeutic potential for diabetic wounds. **Methods:** Chitosan–pectin hydrogel was optimized by varying polymer ratios (1-1.5% chitosan; 1-2.5% pectin) and mixing speed (1,000-10,900 rpm). NLC-SA were incorporated by dispersing nanoparticles in the pectin phase, then mixing with chitosan. Formulations containing 20-100% nanoparticle dispersion were evaluated, and aqueous dispersion was compared with lyophilized NLCs. Lyophilization was optimized using different cryoprotectants. Hydrogels were characterized for rheological behavior, stability, and *in vitro* drug release. Skin penetration was assessed using injured porcine skin. Biocompatibility was evaluated in NIH-3T3 and HaCaT cells, and by chorioallantoic membrane (CAM) assay. Keratinocyte repopulation and PDGF-B expression were assessed in HaCaT cells. *In vivo* efficacy was evaluated in a streptozotocin-induced diabetic mouse wound model over 21 days. **Results:** The optimized hydrogel (1.5% chitosan, 2.5% pectin) required high-speed mixing (10,900 rpm) for stability. Hydrogels prepared with dispersed NLCs showed phase separation, whereas lyophilized NLCs with PEG 8000 preserved nanoparticle characteristics (144 nm; PDI 0.274) and produced homogeneous hydrogels with pseudoplastic behavior. The formulation containing 100% NLCs showed the highest viscosity and stability. Hydrogel incorporation significantly reduced drug release (adenosine ~10.7% vs. ~57% from NLCs alone at 48h). *ex vivo* studies showed increased drug retention in injured skin. The NLC-loaded hydrogel reduced simvastatin cytotoxicity in fibroblasts and keratinocytes and was classified as non-irritant in the HET-CAM assay. Scratch assay showed enhanced keratinocyte repopulation (~60% vs. ~35% in control). In diabetic mice, the hydrogel improved wound closure (~95% vs. ~85% in untreated diabetic animals) and promoted re-epithelialization. **Conclusion:** Incorporation of NLC-SA into a chitosan–pectin hydrogel generated a stable and biocompatible formulation capable of sustained drug release and enhanced dermal retention. The system promoted keratinocyte migration and improved wound healing in diabetic mice, supporting its potential as a topical therapy for diabetic wounds.

12.040 **Drug Discovery: PAD4 Inhibitors as a Novel Pharmacological Approach for the Treatment of NET-mediated Inflammatory Diseases**. Augusto PSA, Costa VF, Miguel PEG, Lavorini LS, Melo IFS, Leandro MO, Cunha TM, Cunha FQ [1]FMRP-USP, Depto Farmacologia, Lab Inflamação e Dor, PPG em Farmacologia, Brasil, [2]FMRP-USP, Depto Bioquímica e Imunologia, Lab Inflamação e Dor, PPG em Imunologia Básica e Aplicada, Brasil

Introduction: Pharmacotherapy options for inflammatory diseases are still limited. Neutrophil extracellular traps (NETs) triggered acute and chronic inflammatory diseases, despite their physiological functions. PAD4 is one of the key enzymes of NET formation by mediating histone citrullination. Therefore, discovering PAD4 inhibitors has potential to be a pharmacological approach to prevent NET formation and consequently reduce tissue damage in acute and chronic inflammatory diseases. We have screened PAD-4 inhibitors HITs from commercial chemical libraries englobing a broad chemical diversity, including isolated natural products, terpenes and alkaloids. **Objectives:** to evaluate *in vitro* and *in vivo* PAD4 inhibitors activity of HITs screened. **Methods:** Neutrophils of heathy volunteers were isolated by Percoll gradient, pre-treated with 11 different PAD4 inhibitors HITs, in a range from 3 nm to 1000 nM, or GSK-484, a standard PAD4 inhibitor, and stimulated with ionomycin. Free DNA levels were measured for 6 hours using nucleic acid stain. We confirmed PAD-4 dependent NET formation using Western Blot and ELISA for citrullinated histone (H3Cit) and immunofluorescence for H3Cit and myeloperoxidase (MPO). Supernatants were collected to measure cytokines released. Similar protocols were applied in mice neutrophils isolated from bone marrow of WT and PAD4 KO C57 BL 6 mice. For *in vivo* protocols, mice were pre-treated with the inhibitors named iPAD4-E or iPAD4-F (lower IC50) at the concentration of 1 mg/kg, 3 mg/kg and 10 mg/kg, and GSK-484 10 mg/kg 1 h before LPS administration (15 mg/kg) or cecal ligation and puncture (CLP). Survival rate was followed up for 7 days. Samples were collected 12 h after LPS administration or 24 h after CLP surgery to measure NET released, tissue damage and cytokine levels. **Results:** HITs were effective in reducing NET induced by ionomycin in a concentration-dependent manner and were classified by IC50. Also, some of them demonstrate activity in a post-treatment assay. HITs demonstrated no cytotoxicity measured by free-DNA and LDH levels. Selected HITs failed in reducing NET formation in PAD4-KO isolated neutrophils. Western Blot and immunofluorescence confirmed PAD4 inhibitory activity in both human and mouse neutrophils. Selected HITs also reduced PAD4 related cytokines releasing in isolated neutrophils (TNF-α and IL-1β) in a concentration-dependent manner. Pre-treatment with iPAD4-E or F reduced NET releasing, heart, lung, liver and kidney damage, and cytokine levels in plasma samples (TNF-α, IL-6 and IL-1β) in a dose-dependent manner in endotoxemy and CLPS models. Pre-treatment and therapeutic administration of iPAD4-E or F improved survival rate also in dose-dependent manner in the same experimental models. **Conclusions:** HITs were screened *in vitro* assay and demonstrated activity *in vivo* experimental models. We are currently testing iPAD4 drugs in psoriasis and rheumatoid arthritis models validating the pharmacology effect in acute and chronic inflammatory diseases. **Acknowledgments:** São Paulo Research Foundation – FAPESP, Ribeirão Preto Medical School (FMRP-USP) and Center for Research in Inflammatory Diseases (CRID).

12.041 **Nanocarrier-Based Delivery of the Semi-Synthetic Digoxin Derivative BD-15: A Safer Therapeutic Strategy for Alternating Hemiplegia of Childhood**. de Andrade MM[1], Passos JS[1], Fernandes, PH[1] Barbosa LA[2], Lopes LB[1], Scavone C[1] [1]ICB-USP, Dept, of Pharmacology, Brazil. [2]UFSJ-Dona Lindu Central-West Campus, Brazil

Alternating Hemiplegia of Childhood (AHC) is a rare, complex neurological disorder affecting one in a million people worldwide, marked by paroxysmal episodes, progressive motor and cognitive decline, and high mortality. Caused by ATP1A3 mutations that disrupt critical brain ionic balance via the α3-Na+,K+-ATPase isoform (α3-NKA), AHC remains incurable, highlighting the urgent need for novel therapeutic strategies. In this context, the semi- synthetic compound BD-15, a digoxin derivative, stands out for its selectivity toward the neuron-specific α3-NKA isoform and its neuroprotective effects at low doses. However, unfavorable pharmacokinetic properties, such as high lipophilicity and poor blood-brain barrier (BBB) permeability, hinder its clinical application. To overcome these limitations, this study proposes developing and characterizing BD-15-loaded nanostructured lipid carriers (NLCs) and evaluating their physicochemical properties, cytotoxicity, and pharmacological effectiveness using *in vitro* models to support the advancement of AHC treatment. Accordingly, BD-15-loaded NLCs (1% w/w) functionalized with polysorbate 80 were prepared via hot homogenization. Dynamic light scattering (DLS) revealed an average particle size of 253.9 ± 33.07 nm, a narrow size distribution (PDI < 0.25), and a negative zeta potential of - 9.20 ± 2.50 mV. Morphological evaluation by TEM revealed well-dispersed, spherical particles whose dimensions aligned with light scattering data. The incorporation of BD-15 into the lipid matrix did not induce additional cytotoxicity compared to empty NLCs, as assessed by MTT and LDH assays ($p = 0.1141$), supporting the safety and biocompatibility of the nanoformulation. To investigate the neuroprotective effects of these NLCs, primary neuron-glia cultures from neonatal Wistar rats were pre-treated with BD-15-loaded NLCs and challenged with LPS, and inflammatory and oxidative stress markers were analyzed by Western blotting. These preliminary findings suggest that BD-15-loaded NLCs are safe and stable, warranting further investigation into their neuroprotective potential and possible relevance to AHC and other ATP1A3-related disorders.

12.042 **Scalable Liposomal Platform for Efficient Encapsulation and Oral Delivery of Angiotensin-(1–7): Proof of Concept in Acute Gouty Arthritis**. Mendes S[1], Matosinhos RC[2], Saúde-Guimarães DA[2], Santos RAS[1], Frézard F[1]
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Introduction: Bioactive peptides, such as the renin-angiotensin system peptide Angiotensin-(1–7) (Ang-(1-7)), show therapeutic potential, but rapid degradation and low bioavailability limit their application. Liposomes offer a promising strategy for peptide protection and delivery; however, efficient encapsulation of hydrophilic molecules remains challenging. **Objective:** To develop and characterize a stable and scalable liposomal platform for the efficient encapsulation and oral delivery of Ang-(1-7), and to evaluate its anti-inflammatory activity in acute gouty arthritis. **Methods:** The platform was prepared via ethanol injection, using soybean phosphatidylcholine and sodium cholate (97:13, w/w) in a 1–15 L bioreactor, under controlled agitation at 20–30 °C and under aseptic conditions. Lipids dissolved in ethanol were injected into phosphate buffer at a 1:5 (v/v) organic-to-aqueous phase ratio, leading to liposome formation. Ang-(1-7) was remotely loaded into liposomes at 4 mg/mL by incubation at 60 °C for 2 h. The LAng-(1-7) formulation was characterized for hydrodynamic diameter, polydispersity index (PDI), zeta potential, particle concentration, particle-size distribution, and morphology by cryogenic transmission electron microscopy (cryo-TEM). Stability was assessed at 30 °C, and peptide encapsulation efficiency was determined fluorimetrically. As a proof of concept, C57BL/6 mice (n = 8/group) received oral LAng-(1–7) (30 μg/kg) 1 h before intra-articular injection of monosodium urate (MSU) crystals. After 6 h, joint lavage was analyzed for neutrophil infiltration and IL-1β, IL-6, and TNF levels. Indomethacin (3 mg/kg), free Ang-(1–7), and empty liposomes served as controls. **Results:** The formulation exhibited a hydrodynamic diameter of 180 ± 2.1 nm, PDI of 0.120 ± 0.024, zeta potential of -12 ± 2.8 mV, and 55% encapsulation efficiency. Cryo-TEM confirmed spherical vesicles with mixed lamellarity. After four months at 30 °C, no significant changes in physicochemical parameters were observed, and more than 50% of initially added peptide remained encapsulated. In MSU-induced acute arthritis, oral LAng-(1–7) significantly reduced neutrophil infiltration and IL-1β, IL-6, and TNF levels compared with the negative control, with no significant differences from indomethacin. Free Ang-(1–7) and empty liposomes did not significantly reduce neutrophil infiltration. **Conclusion:** The platform was produced through a simple and scalable process without requiring post-production particle-size reduction, yielding a nanoscale, low-polydispersity formulation with physicochemical stability for four months at 30 °C. Oral LAng-(1–7) attenuated MSU-induced joint inflammation, reducing neutrophil infiltration and pro-inflammatory cytokines. These findings provide proof of concept for the oral delivery of Ang-(1-7) and support further development of this reproducible and scalable liposomal platform for peptide-based therapies. **Keywords:** Liposomes; Peptide encapsulation; Angiotensin-(1–7); Acute gouty arthritis; Oral delivery.

12.043 **Nanostructured gamma-Decanolactone Enhances Oxidative Stress Resilience in *Caenorhabditis elegans*: A Model for Healthy Aging**. De Andrade EM, De Souza VL, Garofalo CB, Farias MSR, Santos PA, Pereira P. UFRGS-Institute of Basic Health Sciences, Dept Pharmacology, Lab Neuropharmacology and Clinical Toxicology, PPG in Pharmacology and Therapeutics. Brazil

Introduction: Population aging is associated with increased prevalence of oxidative stress-related and neurodegenerative disorders, particularly in rapidly aging regions such as southern Brazil. Nanostructured delivery systems have emerged as promising strategies to improve the stability, bioavailability, and therapeutic efficacy of bioactive compounds. Gamma- decanolactone (GD), a naturally occurring lactone, has demonstrated antioxidant and neuroprotective properties; however, its biological effects in nanoformulated systems remain incompletely characterized.**Objectives:** To evaluate the toxicological safety, antioxidant activity, and stress resilience effects of nanostructured gamma-decanolactone using *Caenorhabditis elegans* as an experimental model for healthy aging. **Methods:** GD-loaded lipid nanoparticles were formulated using Precirol ATO and sunflower oil and characterized regarding particle size, polydispersity index, and zeta potential. Wild-type and transgenic *C. elegans* strains were employed to assess toxicity, oxidative stress modulation, and behavioral performance. Survival, reproduction, locomotion, intracellular reactive oxygen species (ROS) levels, and stress resistance under hydrogen peroxide- and heat-induced conditions were evaluated. Fluorescence-based assays were used to quantify antioxidant responses and ROS accumulation. **Results:** GD-loaded nanocarriers exhibited a mean particle size of 153.4 nm, polydispersity index of 0.114, and zeta potential of -21.9 mV, demonstrating high colloidal stability and formulation homogeneity. Exposure to GD-nanocarriers did not significantly affect nematode survival, reproductive capacity, or locomotor activity, supporting a favorable toxicological profile. Fluorescence analyses revealed activation of endogenous antioxidant defense pathways associated with reduced intracellular ROS accumulation. Under oxidative and thermal stress conditions, GD-nanocarriers significantly improved survival and neuromotor performance, suggesting activation of hormetic stress-response mechanisms linked to enhanced cellular resilience. **Conclusion:** Nanostructured delivery improved the biological efficacy and antioxidant potential of gamma-decanolactone in *C. elegans*. The observed reduction in oxidative stress and enhancement of stress resilience support the potential application of GD-loaded nanocarriers as candidate neuroprotective and healthy aging-promoting strategies. Furthermore, the integration of nanotechnology, natural compounds, and *C. elegans* establishes a cost-effective and ethically relevant preclinical platform for screening nanoformulated bioactive compounds targeting age-associated dysfunctions. Funding: CAPES and CNPq. Ethics Committee Approval: Not applicable. **Acknowledgments:** The authors acknowledge the use of public computational platforms and biological databases employed in this study.

12.044 **Safety and Neurobehavioral Evaluation of a Donepezil–Thalidomide Hybrid in** *Caenorhabditis elegans*. Arantes LP, Montijo RB, Cordova GL, Campos JP de, Santos AL, Morais RC de, Damasceno ACR, Colombo PC, Ortiz CJC, Viegas Júnior C UEMG, Passos, Research Group in Biochemical Pharmacology and Toxicology, Brazil. UNIFAL, Lab of Medicinal Chemistry, PPG Chemistry, Brazil

Introduction: Neurodegenerative diseases are complex and multifactorial disorders for which current therapies are largely symptomatic and do not prevent disease progression. Given the involvement of multiple molecular pathways, the development of multitarget-directed ligands has emerged as a promising strategy to simultaneously modulate different biological targets. Molecular hybridization has been widely employed in the rational design of such compounds. Based on the anti-inflammatory properties of thalidomide and the acetylcholinesterase (AChE) inhibitory activity of donepezil, a new series of thalidomide–donepezil hybrids was designed by the Medicinal Chemistry Research Laboratory (PeQuiM) at UNIFAL. Preliminary studies identified these compounds as potential neuroprotective agents, demonstrating *in vitro* AChE inhibition and *in vivo* anti-inflammatory effects, with PQM-189 emerging as the most promising candidate. **Objectives:** This study aimed to investigate the toxicological and neurobehavioral effects of chronic exposure to the donepezil–thalidomide derivative PQM-189 in Caenorhabditis elegans, using phenotypic and biochemical endpoints. **Methods:**:Wild-type (N2) worms at the L1 larval stage were exposed to PQM-189 at 5, 10, 25 and 50μM on NGM agar plates seeded with *E. coli* OP50 until adulthood. Dimethyl sulfoxide (DMSO) was used as vehicle and control (final concentration of 0.01%). Survival and larval development were assessed at 24, 48 and 72h after the onset of exposure using an optical microscope. Pharyngeal pumping rate, defecation cycle length, and the number of body bends and thrashes were evaluated in L4 larvae. AChE activity was measured in worm lysates at the same developmental stage using the Ellman method and normalized to total protein content determined by the Bradford assay. Parametric data were analyzed using one-way ANOVA, followed by Tukey's post hoc test for multiple comparisons. Statistical significance was set at $p < 0.05$. **Results:** Under the conditions tested, PQM-189 did not induce significant changes in survival, larval development, and behavioral parameters. The 25 and 50 μM concentrations showed approximately 20% reduction in AChE activity compared to the vehicle; however, variability among groups indicates that additional replicates are needed. No difference was observed between the two concentrations. **Conclusion:** These findings suggest that PQM-189 does not exert toxicity at the evaluated concentrations, supporting its potential safety. It also appears to have AChE inhibitory potential, consistent with *in vitro* assays, but more replicates are needed to confirm this effect. *In vitro* findings are not always reproduced *in vivo* due to biological complexity. Future studies will explore the effects of the compound in *C. elegans* models of neurodegenerative diseases.

12.045 **Development of an LC-HRMS Method for the Analysis of Sickle Cell Disease New Drug Candidates in Pharmacokinetic Studies**. Cerqueira LB[1], Serafim YKBS[2], Custódio RPC[3], Rocha GP[3], Pontarolo R[1], Santos JL[2], Campos ML[3] [1]UFPR, Dept of Pharmacy, Brazil, [2]Unesp, Campus Araraquara, School of Pharmaceutical Sciences, Brazil, [3]UFMT, Campus Sinop, Healthy Sciences Institute, Graduate Program in Health Sciences, Brazil.

Introduction: Sickle cell disease is a severe hereditary condition primarily affecting individuals of African descent, leading to significant health complications. Current treatment options are limited, necessitating the urgent development of new therapies. The induction of fetal hemoglobin (HbF) has emerged as a promising strategy, and studies indicate that selective inhibition of histone deacetylases (HDACs) can increase HbF levels. The drug development pipeline includes pharmacokinetic studies, which require bioanalytical methods to quantify the compounds and to search for potentially harmful metabolites. **Objectives:** To develop a method capable of quantifying new molecules in plasma while exploring possible metabolites. **Methods:** The new histone deacetylase inhibitors (PTF and PBFF) were obtained from the Drug Research and Development Laboratory at UNESP. The equipment consisted of an Acquity UPLC H-Class (Waters) coupled to a Xevo G2-S (Waters) Q-TOF mass spectrometer. The mobile phase consisted of ultra-pure water and acetonitrile, both containing 0.1% (v/v) formic acid. Separation was performed on a BEH Shield RP18 column (1.7 µm, 100 mm × 2.1 mm), and the m/z range was set from 80 to 800. The spiked samples were processed by precipitation with organic solvent, followed by centrifugation and evaporation, and then reconstituted in mobile phase for injection into the system. **Results:** Direct infusion of a 500 ng/mL solution achieved signal intensities of approximately 1.7×10^7; and 3.8×10^6 for PTF and PBFF, respectively. The mass spectra showed the [M+H]+ ion at m/z 310.1020 for PTF and at m/z 322.1346 for PBFF, both with mass errors below 3 ppm. Chromatographic analysis after sample preparation achieved an adequate signal-to-noise ratio at 100 ng/mL for both compounds using only 100 µL of sample, which is compatible with preclinical studies in small animals. The retention times were 3.56 min for PTF and 2.26 min for PBFF in a 7-minute run. **Conclusion:** Achieving appropriate detection limits is a critical challenge in drug development. For our two new HDAC inhibitors, we have developed a highly sensitive bioanalytical method using a very low sample volume. This method will be validated and applied in further pharmacokinetic studies. **Financial support** was provided by Fundação de Amparo À Pesquisa do Estado de Mato Grosso (FAPEMAT) Grant #513/2023 and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) Grant #405760/2024-8. **Acknowledgments:** The authors thank CAPES, CNPq, and FAPEMAT for their support.

13. Pharmacology Education

13.001 **Problem-Based Learning and the Flipped Classroom as Innovative Tools in Pharmacology Teaching in Biomedical Sciences**. Silva GS, Dorneles GL, Correa ILO, Nascimento AR, Gonçalves YS, Castro PFS UEG, UnU Goiânia – Eseffego, Goiânia, Brazil

Introduction: This is a qualitative, pedagogical, and multifactorial study conducted with a Biomedical Sciences class at a public university in Goiânia, Goiás. The objective was to evaluate the effectiveness of active methodologies in the Pharmacology teaching-learning process, aiming to develop technical and critical competencies in healthcare students. **Methods:** Data were collected in May 2026 via a structured questionnaire employing a 5-point Likert Scale to measure pedagogical impact. The instrument integrated two main axes: the Multidimensional Engagement Scale, which evaluates students' behavioral (participation), emotional (interest), and cognitive (mental effort) dimensions, and the Professional Competencies Inventory based on the National Curriculum Guidelines for Biomedical Sciences, focusing on clinical reasoning, decision-making, and teamwork. The questionnaire was organized into sections: Student profile; Autonomy in the Flipped Classroom; Technical competencies in Problem-Based Learning (PBL); and Perceived value in the transition from the traditional to the active model. It was administered at the end of the semester to assess students' development. The data were tabulated and analyzed using Microsoft Excel 2025® and NotebookLM®, a Google tool for AI-assisted document analysis from user-provided documents. Research Ethics Committee approval number: 8,236,624. **Results:** Among the 18 students enrolled in Pharmacology for Biomedical Sciences, 16 completed the questionnaire (an 88.9% response rate). In general, all responses indicated satisfaction with the practical application of the PBL and Flipped Classroom methods. One notable finding was that 56.3% of the students in the analyzed sample had only encountered the Flipped Classroom in other subjects. Additionally, 75% agreed with the statement that the sense of responsibility for the subject is greater when the Flipped Classroom practice is adopted, and 100% agreed with the statement that the PBL teaching model provided a more realistic understanding of the clinical cases studied in Pharmacology. Finally, the statement indicating better content absorption from adopting the PBL and Flipped Classroom teaching practices received only 12.5% neutral responses, with most students agreeing. **Conclusion:** The adoption of these practices promotes a deeper understanding of the content, stimulates active participation, and strengthens collaboration among students, contributing to improved content retention. **Financial support:** Universidade Estadual de Goiás (UEG).

13.002 **Innovative Pedagogical Tools for Gamification in Pharmacology Education: Construction, Evaluation and Student Perception**. Gonçalves YS, Moreira EM, Monteiro IPG, Fontes MLS, Silva GS, Pires ARL, Castro PFS UEG - UnU Goiânia – Eseffego

Introduction: Gamification utilizes game elements in non-game contexts to enhance engagement and motivation. This active methodology facilitates content comprehension and retention through interactive processes. **Objectives:** This study aimed to evaluate the effectiveness of gamification within the teaching- learning process of pharmacology, focusing on the development of technical and critical skills in biomedicine students. **Methods:** The methodology involved the application of two educational games for content review one week prior to the course examination in a class of 18 students. The first game, “Fact or Fake”, utilized the NotebookLM tool to generate true or false statements based on the syllabus. Students evaluated these statements using green (true) or red (false) visual signals. The second game, “Farmaco Tapple”, employed a 42-card deck featuring pharmacological themes; the class was divided into three groups, with each group having 10 seconds to alternately respond to the designated theme. Following the activities, a structured questionnaire containing objective and open-ended questions was administered to investigate student perceptions regarding gamification as a review tool. Research Ethics Committee approval number: 8.236.624.0. **Results:** Out of the 18 students enrolled, 16 completed the questionnaire (an 88.9% adherence rate). Among the respondents, 100.0% agreed that gamified elements helped identify gaps in prior knowledge; 93.8% stated that the games encouraged active participation and rendered dense content less exhausting; 81.3% reported increased motivation to assume responsibility for their own learning; 93.8% expressed a preference for hybrid learning methods; 75.0% reported improved information retention compared to traditional methods; 87.5% affirmed that the games facilitated comprehension; and 68.8% felt the dynamics reduced exam-related anxiety. Additionally, 93.8% considered “Fact or Fake” superior to expository lectures for consolidating clinical reasoning, while 81.3% highlighted that “Farmaco Tapple” was more effective than conventional methods for memorizing pharmacological classes. **Conclusion:** The findings demonstrate a highly positive perception among undergraduate biomedicine students regarding the integration of gamification into pharmacology education, highlighting its potential to optimize active learning. **Financial support:** Universidade Estadual de Goiás (UEG).

13.003 **Creation and Impact of the Academic League of Pharmacology of the State University of Goiás: An Experience Report**. Nascimento AR, Silva GS, Monteiro JCL, Silva MCB, Reis BC, Fontes MLS, Gonçalves YS, Jacobina KF, Lima OM, Matheus EM, Castro PFS. UEG, UnU Goiânia – Eseffego, Goiânia, Brazil

Introduction: Academic leagues play an important role in integrating teaching, research, and outreach activities, contributing to the scientific and professional development of health science students. In this context, the Academic League of Pharmacology of the State University of Goiás (LAFAR-UEG), the first academic league of the Biomedicine course at the institution, was founded in May 2025 with the purpose of deepening knowledge of pharmacology and encouraging student leadership through academic and outreach activities. This study aimed to report the experience of creating LAFAR-UEG and its impact on the academic and scientific development of its founding members. Methods: This is an experience report based on perceptions voluntarily shared by members of the league's founding board. The reports addressed the process of creating and structuring LAFAR-UEG, the positions held by the participants, and the contributions of this experience to their academic, scientific, and personal development. The league was structured by ten founding members distributed among the sectors of presidency, treasury, scientific board, marketing and products board, and public relations secretariat, under faculty coordination. **Results:** Participants highlighted that involvement in the league contributed to greater engagement in research and outreach activities, a deeper understanding of pharmacology, and scientific development. Gains related to leadership, communication, academic organization, and teamwork were also reported. Activities developed by the league included drafting the league statute, planning classes, organizing outreach activities, selecting new members, and participating in scientific events. The reports also demonstrated personal growth, strengthened ties with the university, and expanded academic and professional perspectives among the participants. **Conclusion:** This experience demonstrated that academic leagues can play a relevant role in the education of health science students by fostering scientific development, student leadership, and the integration of teaching, research, and outreach. **Financial support:** Universidade Estadual de Goiás (UEG).

13.004 **Development and Acceptance Evaluation of a Didactic Board Game as an Active Learning Tool for G Protein-Coupled Receptor Pharmacology**. Almeida KBS[1], Souza JB[1], Barreto MS[1], Santana ALS[2], Louzada RN[2], Lima YRS[2], Gomes VS[2], Guimarães AG[1] [1]UFS, Dept. of Pharmacy, Lab. of Clinical and Experimental Pharmacology, Brazil; [2]UFS, CCBS, Brazil

Introduction: G protein-coupled receptors (GPCRs) represent one of the most pharmacologically relevant receptor families, mediating the effects of numerous drugs in clinical practice. Despite their importance, the complexity of GPCR signaling pathways poses significant challenges for undergraduate students in Pharmacology courses. Active learning strategies, including educational games, have demonstrated effectiveness in promoting meaningful learning by encouraging engagement and critical reasoning. **Objectives:** To develop a competitive didactic board game on metabotropic G protein-coupled receptor signaling for undergraduate health sciences education and to evaluate its acceptance among the target audience. **Methods:** Game content was grounded in peer-reviewed literature on GPCR pharmacology. Card illustrations and the game board were hand-drawn using IbisPaint, after which the card illustrations were incorporated into the card layout in Canva, later resulting in a physical set of 84 cards accompanied by the Membrane Board, a die, and a rules booklet. A playtest session was conducted in May 2026 with 22 undergraduate Pharmacy students enrolled in the Pharmacodynamics course at Universidade Federal de Sergipe. After that, participants answered a 17-item opinion questionnaire using a 4-point Likert scale. **Results:** The resulting game, Gê!, covers six GPCR signaling pathways, namely opioid Mu (μ), muscarinic M2, adrenergic alpha-1, beta-1, beta-2, and beta-3 receptors, each organized as a card set of four cards: Receptor, Drug, Mechanism of Action, and Pharmacological Effects, complemented by Action cards that introduce strategic elements, reinforcing engagement throughout gameplay. Players must assemble complete card sets and verbally explain the pharmacological content within a time limit defined by a die roll, with the game ending when the first player completes three card sets or when the draw pile is exhausted. In the playtest, 100% of students agreed that the game dynamics kept them motivated, that the experience was enjoyable and stimulating, and that they would recommend the game to other students. All participants agreed that the game was an effective complement to lectures and that they would like other topics to be taught through educational games. Regarding learning outcomes, 100% agreed that the game helped them associate receptor, drug, mechanism of action and pharmacological effect in an integrated manner, and that the oral explanation of card sets helped consolidate information. Content alignment with the course syllabus reached 100% agreement. The use of color coding to distinguish the six signaling pathways received 90.9% agreement, and items regarding game rules clarity and card content comprehension each reached 95.5% agreement. **Conclusion:** Gê! is an educational tool that addresses a conceptually challenging topic through an active and playful approach. Acceptance evaluation results indicate strong acceptance and perceived learning among undergraduate students, supporting its potential as a complement to traditional teaching in GPCR pharmacology.

13.005 **Developing Scientific Literacy Through Neuropharmacology Education and Research Training in Middle Grade Students**. Fonseca RD[1], Costa SF[2], Machado LHR[2], Nin MS[3], Barros HMT[4] [1]UFCSPA, Lab. Neuropsychopharmacology, PPG Health Sciences: Pharmacology and Toxicology, Brazil. [2]UFCSPA, Lab. Neuropsychopharmacology, Brazil. [3]UFCSPA, Dept. of Pharmacosciences, Lab. Neuropsychopharmacology, Brazil. [4]UFCSPA, Dept. of Pharmacosciences, Lab. Neuropsychopharmacology, PPG Health Sciences: Pharmacology and Toxicology, Brazil.

Introduction: Neuroscience represents an interdisciplinary field capable of stimulating curiosity, critical thinking, and scientific literacy among young learners. Early exposure to neuroscience education may enhance students' understanding of brain function, behavior, health, and effects of drugs while fostering interest in Science, Technology, Engineering, and Mathematics (STEM) careers. University-based advanced placement programs provide a unique environment in which middle-grade students can engage with authentic scientific practices beyond the traditional school curriculum. **Objective:** Describe the application of an educational methodology for the training of junior scientific initiation students in ethopharmacology. **Methods:** Two junior students (O1, O2), without previous experience, underwent a three-step training for video analysis with an experienced observer through: (1) Interactive presentation of ethological concepts regarding behavioral analysis of rodent preclinical models in psychopharmacology; (2) Joint observation of Open Field Test (OFT) video fragments to identify and discuss key behavioral concepts (e.g., thigmotaxis); (3) **Introduction:** to the use of Behavsoft® and independent analysis. Behavsoft® is a program developed by our research group that allows for the computer-assisted analysis of predefined behaviors in videos of animal models. For training evaluation, students analyzed 10 OFT videos randomly selected from the laboratory's own repository to guarantee blindness to treatment and sex conditions. Each video was analyzed in two distinct moments, with an interval of at least 7 days to evaluate intra-class correlation (ICC) coefficients. **Results:** Intra-rater ICC (test-retest) showed strong agreement for walking frequency (O1: 0.96; O2: 0.93) and center frequency (O1: 0.92; O2: 0.82). Inter-rater ICC analysis indicated excellent coefficients in the initial test session for both walking frequency (0.94) and center duration (0.94). In the retest session, however, some inter-rater coefficients decreased, notably for center duration (0.16). Grooming episodes were consistently measured between observers across both sessions, maintaining moderate coefficients (0.64 to 0.53). **Conclusion:** Students showed great engagement with the activity. Quantitative results also indicated that students could understand the biological meaning of OFT, consistently identifying animals with anxiety-related behaviors. Through beginner research training for data collection in ethopharmacology and the connections with ethics, scientific communication, and laboratory exposure, students may develop foundational competencies in translational scientific thinking. Our initiative can bridge secondary education and higher education, promoting early talent and equitable access to scientific opportunities. All experimental procedures with animals were approved by UFCSPA's Animal Research Ethics Committee (CEUA/UFCSPA 213/2022).

13.006 “**ConsCIÊNCIA DOS MEDICAMENTOS”: Educational Game for Health Education on the Use and Disposal of Medications**. Silva VS[1,4], Reis MDS[2,4], Lins MP[3,4], Ferro JNS[1,2] [1]UFAL, PPG Ciências Farmacêuticas, Brasil, [2]UFAL, PPG Ciências da Saúde, Brasil, [3]UFMT, PPG Ciências da Saúde, Brasil, [4]INCT Neuroimunomodulação, Brasil

The improper use and disposal of medicines constitute important public health, socioeconomic, and environmental problems. In this context, schools play an indispensable role as strategic spaces for the development of educational practices aimed at health promotion. Thus, playful activities are valuable tools capable of fostering critical learning and greater student engagement in relevant social issues. Therefore, this study aimed to develop and apply a digital educational game as a didactic-pedagogical resource on the rational use and proper disposal of medicines with students in the final years of elementary school. The game, entitled “ConsCIÊNCIA DOS MEDICAMENTOS”, was developed on the free Genially® platform and structured into four stages, each containing four questions. The stages included different question formats, including (1) true or false, (2) multiple choice, (3) two truths and one lie, and (4) sentence completion with alternatives. The questions addressed everyday situations related to self-medication, the influence of the media on medicine consumption, bacterial resistance, medication intoxication, and the environmental impacts resulting from improper disposal, topics of great relevance to society. The activity was carried out in person at a public state school in Maceió, Alagoas, during the elective course "Construindo ConsCiências", involving 20 students from the 6th to the 9th grades of elementary school. The game was presented in the classroom using a television, with the students organized into groups of up to four participants, who recorded their answers and had their scores monitored using printed score sheets. The activity lasted approximately one hour, was mediated by the teacher, and concluded with the calculation of the final score and the awarding of a prize to the winning group. The results demonstrated good acceptance of the activity, with students showing interest in the game dynamics and achieving satisfactory scores throughout the game. The implementation of the game made it possible not only to identify prior knowledge but also to stimulate discussions after each answer, promoting the clarification of doubts and allowing students to critically reflect on everyday situations involving family members and friends, sharing experiences and relating the content addressed to their own lives. However, it was observed that some participants were shy when discussing the topic, while others remained distracted during certain moments of the activity. Despite these limitations, the strategy encouraged group participation, stimulated dialogue, and brought scientific content closer to situations present in the students' daily lives. Thus, the educational game proved to be an effective didactic-pedagogical tool for making the teaching-learning process more dynamic, contributing to the strengthening of health education and environmental awareness in the school environment.

13.007 **The "MicroMuseu Somos Mar": A Portable, Interactive, and Accessible Totem for Marine Pharmacology and Environmental Education**. Nogueira CN[1], Oliveira AGNA[2], Sahm BB[3], Silva JYG[1], Brito TL[1], Costa-Lotufo LV[3], Longo G[4], Lima MMX[2], Wilke DV[1] [1]UFC, Graduate Program in Pharmacology, Fortaleza, CE, Brazil. [2]UFC, Graduate Program in Architecture, Urbanism and Design, Fortaleza, CE, Brazil. [3]USP, Graduate Program in Pharmacology, São Paulo, SP, Brazil. [4]UFRN, Dept Oceanography and Limnology, Natal, RN, Brazil.

Introduction: Marine environments offer unique metabolic pathways and chemical structures with high biomedical potential. Connecting marine conservation with human health requires promoting ocean literacy focused on bioprospection, highlighting marine microorganisms and natural products as primary sources for drug discovery. Translating these complex biotechnological concepts into early childhood education demands specialized pedagogical strategies that convert cellular and molecular dynamics into tangible, multisensory experiences to foster scientific literacy. **Objectives:** To develop and evaluate the "MicroMuseu Somos Mar", a portable, interactive totem-shaped educational artifact aimed at promoting marine environmental education and disseminating research on marine natural products as sources of pharmacological products. **Methods:** Scientific content, including organisms's imagery and research data, was shared by scientists from ProspecMar Network. Structurally, the artifact features three depth levels: the panoramic beach landscape, the marine environment with its macro-organisms, and the microbial/molecular domain. The modular structure integrates interactive strategies: an Arduino-controlled electronic mapping panel of collection sites, a pop-up book with red-light optical filters to reveal hidden data, simulated bacterial cultures in Petri dishes, monocular viewfinders displaying marine bacteria, acrylic tactile photographs, interactive "life bubbles" with image of marine animals and respective data on the reverse, thematic postcards, and augmented reality (AR) photographs. The artifact was evaluated with 100 six-year-old children, assessing qualitative interaction and engagement. Afterward, a free-drawing activity on poster boards registered the children's mental models. **Results:** The modular architecture successfully facilitated the artifact's portability, assembly, and spatial transition across the three conceptual depth levels. During evaluation, the totem prompted active exploration, where the multisensory interfaces and AR technologies effectively captured the children's attention. This interactive approach successfully introduced core concepts of marine biodiversity, environmental conservation, and biotechnology. By interacting with the simulated cultures and digital media, the participants connected macroscopic marine organisms to their microscopic structures and underlying biomedical applications. Furthermore, analysis of the subsequent free-drawing session indicated that the children assimilated these core concepts, frequently depicting marine habitats alongside different marine animals, illustrating the concept of biodiversity. **Conclusion:** The "MicroMuseu Somos Mar" represents an application where education, technology, and design converge into a portable tool for scientific dissemination. By contextualizing marine biodiversity through its ecological and pharmacological relevance, this artifact contributes to scientific literacy and environmental consciousness, especially, from early childhood. **Financial support:** This work was supported by CNPq (grant No. 408549/2024-6), FAPESP (grant No. 2025/27006-6), CAPES (Finance Code 001).

13.008 **Gamification Inspired by Television Game Shows for Pharmacology Teaching: An Experience Report with Four Educational Strategies**. Nin MS UFCSPA, Lab Neuropsicofarmacologia, Depto Farmacociências, Brazil.

Introduction: Pharmacology learning is often perceived by students as challenging due to the large volume of content and the need to integrate basic concepts with clinical applications. In this context, gamification strategies may increase engagement and promote learning, as competition, active participation, and collaboration provide benefits, particularly for cognitive learning. **Objectives:** To describe the implementation of a set of gamified activities developed for a Pharmacology course and to assess perceptions of engagement, content review, and learning. **Methods:** This is an experience report developed through successive offerings of Pharmacology courses in different undergraduate programs over a ten-year period. Four gamified activities inspired by television game shows were designed, tested, selected, and progressively refined with the purpose of content review. The first, called “Pharmacological Treasure Hunt”, used clues and challenges distributed throughout the campus to promote collaborative problem-solving in a fully active-learning approach. The second, “Farmacolojão Show”, consisted of a team-based competition involving questions and answers with different levels of difficulty. The third, “Pharmacological Trivia”, involved the development of questions by small groups of students, which were subsequently applied to their classmates in a competitive trivia format. The fourth, “Pharmacological Temptation”, used progressively more difficult questions requiring rapid decision-making and continuous review of pharmacological concepts, combined with intense movement throughout the classroom. For the first time, these four activities are being implemented within a single class, allowing a relative assessment of satisfaction and learning at the end of the course. **Results:** Throughout previous semesters, the activities showed acceptance among students, with a noticeable increase in participation, peer interaction, and involvement during content review sessions. Greater student protagonism was observed when compared with traditional review methods, in which content was revisited through guided study sessions and tutoring activities. **Conclusion:** The combined use of different games proved to be a valuable approach for Pharmacology teaching, promoting engagement, participation, and content review. The adoption of multiple game mechanics makes it possible to explore different cognitive and social skills, contributing to a more dynamic and meaningful learning process. As a limitation, difficulties in time management and the need to ensure that competition does not trigger conflicts among students should be considered. At the end of the current semester, a survey will be administered to the class in which students will report their perceptions regarding satisfaction and learning associated with the activities.

13. Immunology, Microbiology and Parasitology

13.001FR **Analysis of the Antimicrobial Activity of the Ruthenium-Arene Complex Against** *Streptococcus mutans* **Strains**. Sousa SLO[1], Pinheiro AA[3], Oliveira MI[6], Alves EA[1], Malveira EA[4], Holanda AKM[5], Vasconcelos MA[2], Teixeira EH4[4] [1]UFC, Integrated Lab Biomolecules, Dept Pathology and Legal Medicine, Brazil [2]UECE, Faculty of Education of Itapipoca, Brazil [3]UFC, PPG Patholgy, Brazil [4]UFC, PPG Biotechnology of Natural Resources, Brazil [5] UFC, PPG Chemistry, Brazil [6]UFSC, Dept Chemistry, Brazil

Introduction: Dental caries is a multifactorial, diet-modulated, non- communicable disease in which bacteria of the species *Streptococcus mutans* are among the main microorganisms involved in its etiopathogenesis due to their high ability to adhere to dental surfaces, form biofilms, and tolerate acidic environments. Thus, in the search for new strategies for the control and prevention of dental caries, metal-based compounds have attracted interest because of their biological properties. Among them, photoactivatable ruthenium complexes, especially those coordinated to the aromatic ligand p-cymene , have shown promising potential. **Objectives:** The present study aimed to evaluate the antimicrobial activity of the ruthenium-arene complex [Ru(η^6-p-cym)(La-κ^2O,S)(Cl)] (3a) against *Streptococcus mutans* UA130 and UA159 strains. **Methods:** The assays were performed using the broth microdilution method to determine the Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC). Additionally, the experiments were conducted under two experimental conditions in the presence and absence of blue light (465 nm). The strains were exposed to concentrations of the complex ranging from 500 to 7.8 µg/mL. **Results:** Complex 3a showed activity against both strains. For *S. mutans* UA130, MIC and MBC values in the presence of light were both 15.6 µg/mL, whereas in the absence of light the MIC was 7.8 µg/mL and the MBC was 15.6 µg/mL. For *S. mutans* UA159, MIC and MBC values were 31.25 µg/mL under both experimental conditions. Therefore, it can be concluded that the ruthenium-arene complex 3a demonstrated antimicrobial activity, highlighting its potential for future investigations aimed at developing strategies for controlling microorganisms associated with dental caries. **Acknowledgments:** CAPES, CNPq and UFC.

13.002FR *In vitro* and *in silico* Evaluation of Hydroxylated Chalcone Derivatives as Antibiofilm Alternatives against *Staphylococcus aureus*. Alves MF[1], Cunha HAS[1], Fiorin BC[2], Menegatti ACO[1] [1]UFPB, João Pessoa, Dept Molecular Biology, Brazil. [2]UEPG, Uvaranas, Dept Chemistry, Brazil.

In the context of antimicrobial resistance mechanisms, *Staphylococcus aureus* stands out for its high capacity to form biofilms, structures that confer protection to bacterial cells and hinder conventional treatments. Part of this matrix is composed of membrane-associated surface proteins, which are fundamental for the adhesion and colonization of host cells. In this context, this study evaluated, through *in vitro* and in silico approaches, the antibiofilm potential of 15 hydroxylated chalcone derivatives against *Staphylococcus aureus* (ATCC 25178). In the *in vitro* assays, the bacterial strain was standardized to 0.5 on the McFarland scale (1.5×10^8 CFU/mL), diluted in tryptic soy broth (TSB) supplemented with 1% (v/v) glucose, and incubated in the presence of the compounds at 500 µg/mL for 18–24 hours at 37 °C. Biofilm formation was quantified by staining with 0.2% safranin and reading the absorbance at 530 nm. The compound solvent was used as a reference control, tetracycline as a positive control, and uninoculated medium as a negative control. To investigate possible mechanisms of action of the compounds, a molecular docking study was carried out with the enzyme Sortase A (SrtA), using the crystal structure available in the Protein Data Bank (PDB ID: 1T2W). The simulations were conducted in the GOLD software and the Goldscorekinase template was selected to evaluate the generated poses, and a consensus docking strategy was employed using the ChemScore and GoldScore fitness functions. Chlorogenic acid was used as a reference compound for comparing binding energies and intermolecular interactions. The *in vitro* results demonstrated percentages of biofilm formation inhibition ranging from 42.7% to 92.2%. Compound C5 showed the highest activity, promoting a reduction of 92.2 ± 4.2%, with a performance superior to that of tetracycline. Among the most promising compounds, C5, C17, and C24 presented affinity scores of 26.77, 25.73, and 23.54, respectively, while chlorogenic acid presented a score of 26.26. Docking analyses indicated that C5 established intermolecular interactions similar to those observed for chlorogenic acid. Its binding to Sortase A was favored by hydrogen bonds with residues Arg197 and Ala104, in addition to π-alkyl and van der Waals interactions with Gly172, Ile182, Ser116, Glu105, and Ala118, corroborating its high antibiofilm activity observed *in vitro*. In conclusion, the *in vitro* and *in silico* analyses revealed that hydroxylated chalcones show promising potential as antibiofilm agents. Among the evaluated compounds, C5 stood out for its potential interaction with Sortase A, an enzyme responsible for anchoring surface proteins, which may contribute to the reduction of bacterial adhesion and biofilm formation in *Staphylococcus aureus* .

13.003FR **Antimicrobial Activity of the Extract Obtained from** *Zingiber officinale* **Roscoe Residues Enriched with Gingerol Against** *Staphylococcus aureus* **and** *Pseudomonas aeruginosa*. Guilherme ACS, Almeida JBC, Souza SO, Silva AP, Sousa JCR, Lima CM UFS, Brasil

Introduction: Pathogenic microorganisms are a major concern, especially those with the ability to develop resistance to antimicrobials. As an alternative to infections caused by multidrug-resistant strains, the search for new compounds has been explored. Zingiber officinale stands out for its variety of pharmacological activities against these infections. **Objective:** To evaluate the antimicrobial potential of the extract obtained from the rhizomes of ginger residue enriched with gingerol against *Staphylococcus aureus* and *Pseudomonas aeruginosa*. **Materials and Methods:** The enriched ginger extract containing 6-gingerol and 6-shogaol was obtained from the residue of the oil extraction process, using the maceration and liquid-liquid partition extraction method. The enriched extract was subjected to quality control tests: phytochemical screening; quantification of 6-gingerol and 6-shogaol; antimicrobial effectiveness test against *Staphylococcus aureus* and *Pseudomonas aeruginosa*, using the solid medium diffusion technique. **Results:** The phytochemical screening of the enriched extract revealed the presence of phenolic compounds, flavonoids, and triterpenoids. Chromatographic analysis confirmed the presence of the main gingerols, [6]-, [8]-, and [10]-gingerol (180mg/mL). The extract did not show antimicrobial activity against *Pseudomonas aeruginosa* in the agar dilution assay, even at the highest concentration evaluated (1024 mg mL-1). In contrast, antimicrobial activity was observed against *Staphylococcus aureus* at a concentration of 1024 mg mL-1, while at a concentration of 512 mg mL-1 no inhibition of bacterial growth was observed. **Conclusion:** The gingerol-enriched Zingiber officinale extract showed selective antimicrobial activity against *Staphylococcus aureus* , with no effect on *Pseudomonas aeruginosa*, and stands out for its proposed sustainable reuse of plant waste. **Keywords:** secondary metabolites; antimicrobials; multidrug resistance; agro-industrial waste.

13.004FR **Antibacterial Activity of a Pentadentate Copper(II) Complex Against *Staphylococcus aureus* Strains**. Alves EA1, Soares PV1, Sousa SLO1, Malveira EA1, Santana FWP3, Holanda AKM3, Vasconcelos MA2, Teixeira EH1
1UFC, Integrated Lab Biomolecules, Dept Pathology and Legal Medicine, Brazil, 2UECE, Faculdade de Educação de Itapipoca, Brazil, 3UFC, Bioinorganic Lab, Dept Organic and Inorganic Chemistry, Brazil

Introduction: Antimicrobial resistance represents a major challenge to current healthcare systems, as the emergence of multidrug-resistant bacterial strains makes treating these infections difficult. In fact, methicillin-resistant *Staphylococcus aureus* (MRSA) strains are emerging as one of the main threats to antibiotic therapy in healthcare. Therefore, the search for new molecules with antibacterial activity has become imperative. In this way, metal complexes have gained prominence for presenting multiple mechanisms of action against bacterial colonization. Among these compounds, copper-based complexes stand out as promising antibacterial agents, given their intrinsic redox activity, stability, and ability to interact with multiple cellular targets. **Objectives:** Thus, the present study aimed to evaluate the antibacterial activity of the molecule [Cu(phen)2(2-meimN)](PF6)2 against the strains of *S. aureus* ATCC 25923 (methicillin-sensitive) and *Staphylococcus aureus* ATCC 700698 (methicillin-resistant). **Methods:** The antimicrobial analysis was evaluated using the broth microdilution method to determine the Minimum Inhibitory Concentration (MIC) and the Minimum Bactericidal Concentration (MBC). For the assays, the compound was diluted in 4% DMSO, in concentrations ranging from 240 to 3.75 µM (191.03 to 2.984 µg/mL). **Results:** The MIC value of [Cu(phen)2(2-meimN)](PF6)2 was 60 µM (47.76 µg/mL) for both strains tested (ATCC 25923 and ATCC 700698). Regarding MBC, for the resistant strain (ATCC 700698) the value was 240 µM (191.03 µg/mL), while for the sensitive strain, *S. aureus* ATCC 25923, no MBC value was detected. **Conclusion:** Given this scenario, copper metal complexes demonstrate promising antibacterial activity against *S. aureus*, potentially contributing to the development of new antimicrobial agents. **Acknowledgments:** The authors thank the Ceará Foundation for Support of Scientific and Technological Development (FUNCAP) and the Federal University of Ceará (UFC) for their financial and institutional support.

13.005FR **Chemical Characterization and Evaluation of the Antibacterial and Antibiofilm Activity of** *Cymbopogon flexuosus* **Essential Oil Against** *Staphylococcus* **sp. Isolated from Bovine Mastitis**. Zamboti B[1], Feijó FMC[2], Santos JS[3], Rodrigues THS[4], Carmo MK[5], Vasconcelos MA[6], Teixeira EH[1]. [1]UFC, PPG Biotechnology of Natural Resources, Brazil; [2]UFERSA, PPG Environment, Technology and Society, Brazil; [3]UFBA, PPG Teaching, Philosophy and History of Sciences, Brazil; [4]UVA, PPG Biotechnology, Brazil; [5] UFC, PPG Medical Microbiology, Brazil; [6]UECE, Faculty of Education of Itapipoca, Brazil.

Introduction: Bovine mastitis is the main disease affecting the global dairy chain, causing significant economic losses. In addition to its impact on production, the disease poses a risk to public health, as pathogens such as *Staphylococcus aureus* and other bacterial agents associated with bovine mastitis can be transmitted to humans through the consumption of contaminated milk or unpasteurized dairy products, as well as through the spread of antimicrobial resistance genes. The ability of these bacteria to form biofilms hinders treatment with conventional antimicrobials, favoring chronicity and infection recurrence. Thus, essential oils have emerged as promising therapeutic alternatives due to their complex chemical composition and multiple mechanisms of action. **Objectives:** The aim of this study was to chemically characterize the essential oil of Cymbopogon flexuosus, commonly known as "lemongrass", and to evaluate its antibacterial and antibiofilm activity against a Staphylococcus sp. isolate obtained from bovine mastitis. **Methods:** The chemical composition of C. flexuosus essential oil was analyzed by gas chromatography coupled to mass spectrometry (GC-MS). The Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) were determined by the broth microdilution method at concentrations ranging from 10% to 0.01% of the essential oil. Furthermore, the biofilm-forming capacity of the isolate was classified using the crystal violet method. The antibiofilm activity of the essential oil was tested at concentrations ranging from 10% to 0.01%. Biofilms were quantified by biomass measurement using crystal violet staining, cell viability by the resazurin colorimetric method, and enumeration of viable cells by counting Colony Forming Units (CFU/mL). **Results:** GC-MS analysis revealed that the main constituents of lemongrass essential oil were neral (32.75%) and geranial (52.28%), totaling approximately 85% citral. The Staphylococcus sp. isolate was classified as a weak biofilm former. The essential oil showed MIC of 0.07% and MBC of 0.16%. In the biofilm inhibition assays, a concentration-dependent reduction was observed, with significant inhibition at the highest concentration (10%), resulting in a 61.06% reduction in biofilm biomass. Cell viability was reduced by 20% at concentrations from 10% to 0.04%, and the number of CFU/mL was reduced by 1 to 5 log10 compared to untreated biofilms. **Conclusion:** The essential oil of C. flexuosus, rich in citral, demonstrated antibacterial and antibiofilm activity against a Staphylococcus genus isolate. These results indicate its potential as an experimental therapeutic agent for the control of staphylococcal mastitis, especially against biofilm-forming strains. Further studies on toxicity and *in vivo* efficacy are necessary to advance its clinical application. **Acknowledgments:** UFC, CAPES, LAMIV, LIBS, LMQPN.

13.006FR **Impact of Early Consumption of Ultra-Processed Foods on the Taxonomic Composition of the Gut Microbiota and Insulin Resistance Markers in School-Age Children**. Silva JVG, Clementino LCRF, Neves TAFV, Alves JLB, Martins VJB UFPB, PPG Nutritional Sciences, Brazil

Introduction: The importance of the first 1000 days for gut microbiota colonization and the detrimental effects of ultra-processed foods (UPFs) during this phase are well documented. However, it remains unknown whether the consumption of UPFs before 2 years of age leaves a microbial signature that persists into school age. Furthermore, the impact of UPFs on infant metabolism may be mediated by this alteration. Thus, investigating if early UPF intake persistently shapes gut microbiota and alters insulin resistance markers fills an important gap in the literature. **Objective:** To evaluate the impact of early UPF consumption on the taxonomic composition of the gut microbiota and insulin resistance markers in school-age children. **Methods:** A cross-sectional school- based study of 62 children, both sexes, aged 7 to 12 years, categorized according to early exposure to UPFs (before 2 years of age): unexposed (n=18) and exposed (n=44). Sociodemographic and early UPF exposure data were obtained through maternal reports using questionnaires. Anthropometry, glucose, insulin, and HOMA-IR, to measure insulin resistance and human feces for gut microbiota sequencing (16S rRNA). Clinical comparisons used t-test, Mann-Whitney, and Fisher's exact tests in SPSS. In R Studio, after data rarefaction, MaAsLin2 and LEfSe identified associations and biomarkers in taxonomic abundance at the genus level. **Results:** Demographic, anthropometric, and metabolic characteristics did not differ statistically between the groups ($p > 0.05$). In the taxonomic analysis, MaAsLin2 identified significant associations, and LEfSe confirmed the biomarkers. Children exposed to UPFs had an expansion of pathobiont bacteria, with higher *Prevotella* ($p = 0.016$; score = 3.91) and *Prevotella* 7 ($p = 0.024$; score = 3.40) genera. In contrast, the group unexposed to UPFs showed a higher abundance of a genus producing anti-inflammatory short-chain fatty acids (SCFAs), specifically *Odoribacter* ($p = 0.0017$; $q = 0.271$; score = -2.67). **Conclusion:** The unexposed group maintained a protective gut microbiota dominated by *Odoribacter* , an SCFA producer associated with protection against metabolic disorders. In contrast, exposure to UPFs replaced this protection with an expansion of *Prevotella* , a pathobiont that induces low-grade chronic inflammation and, consequently, insulin resistance. Therefore, we conclude that UPF consumption before 2 years of age is detrimental, as it leaves a persistent microbial signature that favors pro-inflammatory microbiota. Although no statistical differences were observed in insulin resistance markers, this alteration points to an early and silent metabolic vulnerability in these children. Ethical approval: CEP/UFPB No. 4.676.103. Financial support: FAPESQ (grant no. 009/2021, Term 3.044/2021) and PPSUS (Program of Research for the Unified Health System (grant no. 41903.612.28794.22092020, call no. 005/2020)). **Acknowledgments:** To the volunteers.

14. Pharmacology: Other

14.001 **Evaluation of the** *in vitro* **Antifungal Activity of 2-Benzyl-5-Methylbenz(d)oxazole against** *Nakaseomyces glabratus* (*Candida glabrata*) **isolates**. Dos Santos AC[1,2], Da Silva RBP[2], De Souza LDG[2,3], Da Silva EVA[2,3], Emídio JJ[1], De Sousa DP[1,4], Rocha WPS[2,3,4], Guerra FQS[1,2,3,4] [1]UFPB, Center for Health Sciences, PPG in Bioactive Natural and Synthetic Products, Brazil, [2]UFPB, Center for Health Sciences, Clinical Mycology Lab, Brazil, [3]UFPB, Center for Health Sciences, PPG in Dentistry, Brazil, [4]UFPB, Health Sciences Center, Dept Pharmaceutical Sciences, Brazil

Introduction: *Nakaseomyces glabratus* (formerly *Candida glabrata*) is an endogenous opportunistic fungus of high clinical relevance in immunocompromised patients and a major cause of leading hospital-acquired fungal infection. Current therapeutic options, limited to the azole, polyene, and echinocandin classes, present significant limitations, such as toxicity and the growing incidence of fungal resistance. Therefore, synthetic compounds have been explored in the search for new therapeutic alternatives. Among them, benzoxazole derivatives have emerged as promising options due to their diversity of pharmacological properties, particularly their antimicrobial activity. Thus, these issues associated with the limited knowledge of the pharmacological properties of a new benzoxazole derivative, 2-benzyl-5-methylbenz(d)oxazole (BMX), make it necessary to evaluate it as a potential candidate in the treatment against candidiasis. **Objectives:** To investigate the antifungal activity of BMX against *N. glabratus* isolates. **Methods:** 5 *N. glabratus* clinical isolates from the fungal collection of the Clinical Mycology Laboratory at UFPB and 1 *N. glabratus* ATCC 90030 were used in the assays. For this purpose, the Minimum Inhibitory Concentration (MIC) of BMX was determined by the broth microdilution technique, using amphotericin B (AMB) as a positive control. The MIC was defined as the lowest concentration of BMX capable of visually inhibiting fungal growth. Subsequently, the Minimum Fungicidal Concentration (MFC) was determined by plating on Sabouraud Dextrose Agar. The MFC is defined as the lowest concentration of BMX at which no fungal growth occurs in the culture medium. To investigate the possible mechanism of action of BMX, assays were performed with sorbitol (SORB) (osmotic protector) and exogenous ergosterol (ERG). **Results:** The assays demonstrated that BMX exhibited MICs ranging from 8 to 256 µg/mL, with a modal MIC of 32 µg/mL and MFC ranging from 32 to 1024 µg/mL. The MIC of AMB against the isolates ranged from 0.0625 to 0.250 µg/mL, with an MIC of 0.125 µg/mL for the ATCC strain. Furthermore, in the presence of SORB, the MIC of BMX was 32 µg/mL, and in the absence the same value was maintained for an isolate and the ATCC strain. In addition, in the presence of exogenous ERG, the MIC of BMX was 128 µg/mL, while in the absence a value of 32 µg/mL was obtained for one of the isolates. For the ATCC strain, a value of 64 µg/mL was obtained in the presence of ERG and 32 µg/mL in the absence. **Conclusion:** Based on the obtained data, as the MFC/MIC ratio was >4, BMX probably exhibits fungistatic activity against N. glabratus isolates. Furthermore, it probably interacts with ERG in the fungal membrane, as indicated by the increased MIC in the presence of exogenous ERG. Thus, BMX is a promising antifungal candidate against *N. glabratus*, justifying further *in vitro* and *in vivo* studies to confirm its antifungal potential. **Financial support:** CAPES (Financial code 001).

14.002 **Evaluation of the Wound-Healing Potential of Polymeric Films Containing an N-Acylhydrazone Derivative in a Wistar Rat Model of Excisional Skin Wounds**. Dantas VG[1], Nascimento BKL[1,2], Sousa BG[1,2], Silva JF[1], Chaves MJRS[1], Medeiros KA[1,3], Guedes GG[1,3], Oliveira TKB[4], Nonaka CFW[5], Araújo PHL[1], Damasceno BPGL[1,2,3], Cavalcanti ALM[1]. [1]UEPB, Lab for the Development and Characterization of Pharmaceutical Products, Brazil. [2]UEPB, PPG Pharmaceutical Sciences, Brazil. [3]UFPB, PPG Development and Technological Innovation in Medicines, Brazil. [4]UNIFACISA University Center, Brazil. [5]UEPB, PPG Dentistry, Brazil.

The skin wound-healing process involves inflammatory, proliferative, and tissue remodeling events and is directly influenced by inflammatory mediators. In this context, polymeric systems containing bioactive compounds have attracted considerable interest due to their potential to accelerate tissue repair. This study aimed to evaluate the wound-healing potential of polymeric films containing JR19, an N-acylhydrazone derivative previously reported to exhibit anti-inflammatory activity, either alone or in combination with silver sulfadiazine, in a Wistar rat model of excisional skin wounds. All experimental procedures were approved by the Ethics Committee on the Use of Animals of UEPB (CEUA/UEPB, protocol no. 030/2023). Male Wistar rats (200–300 g) were subjected to the induction of circular full-thickness dorsal skin wounds measuring 1 cm in diameter. The animals were randomly assigned to the following experimental groups: negative control (0.9% saline solution), positive control (betamethasone dipropionate combined with gentamicin), FQ (chitosan-based film), FJR19 (polymeric film containing JR19), and FJRSP (polymeric film containing JR19 associated with silver sulfadiazine). Topical treatments were applied immediately after wound induction and reapplied every two days for 21 days. Wound progression was monitored by photodocumentation on days 1, 2, 4, 7, 14, and 21 post-injury. Residual wound areas were quantified using ImageJ Pro 6.1 software. Data were expressed as mean ± standard error of the mean (SEM) and analyzed by one-way ANOVA followed by Tukey's post hoc test, with statistical significance set at $p < 0.05$. The FJR19 group demonstrated a significant acceleration of the wound-healing process beginning on the 4th day post-injury, exhibiting healing efficacy comparable to that of the positive control group and significantly superior to the negative control group up to the 7th experimental day. The FJRSP group promoted a significant reduction in residual wound area as early as the 2nd day post-injury, indicating an accelerated early healing response. However, no statistically significant differences were observed between the FJR19 and FJRSP groups from days 4 to 21. At the end of the experimental period, the lesions were almost completely re-epithelialized in all groups. These findings demonstrate that the polymeric films containing JR19 effectively accelerated the cutaneous healing process, especially in the early phases of tissue repair. The observed therapeutic effect is likely attributed mainly to the anti-inflammatory properties of the JR19 compound. Acknowledgments to CNPq, UEPB, the Laboratory for Drug Development and Synthesis, and the Laboratory for Development and Characterization of Pharmaceutical Products.

14.003 **Effect of Eucalyptol (1,8-CINEOL) on Human Umbilical Artery Dysfunction Associated with Gestational Diabetes Mellitus: An *ex vivo* Study**. Silva JA, Machado STS, Bastos CMS, Sousa MJS, Araújo ERL, Oliveira PES, Duarte MRS, Silva DFS, Pereira LRS, Silva AA, Sales EPN, Lacerda JML, Sales VS, Barbosa R URCA, Lab Physiopharmacology of Excitable Cells, Brazil

Introduction: Gestational diabetes mellitus (GDM) is a common metabolic condition during pregnancy, associated with alterations in fetoplacental vascular function and adverse maternal-fetal outcomes. Despite the available therapeutic approaches, none specifically target umbilical vascular reactivity, highlighting the need to investigate substances capable of modulating vascular tone under hyperglycemic conditions. In this context, Eucalyptol (EUC), a bioactive terpene with anti-inflammatory, gastroprotective, antimicrobial, and expectorant properties, whose vasodilator effect has already been described in guinea pig smooth muscle. However, its action on Human Umbilical Arteries (HUA) remains unexplored (note that this study is pioneering, as there is no existing research comparing DMG with natural products), especially under pathological conditions such as DMG. **Objective:** To investigate the effects of EUC on vascular reactivity in the AUH, under physiological conditions and in the presence of DMG. **Methodology:** Following approval by the Ethics Committee of the Regional University of Cariri (CAAE No. 6.841.548), fragments of human umbilical cords were obtained with the consent of the parturients. Segments of human umbilical cord were isolated and mounted in an organ bath for assessment of isometric tension. The effect of HUC on vascular tone was assessed by cumulative additions (1-3000 μM). The vasorelaxant response was analyzed following stimulation with K60 or 5-HT (10 μM) to evaluate electromechanical and pharmacomechanical coupling, respectively. Additionally, the involvement of Ca2+ channels in the vasorelaxing effect of EUC was investigated using CaCl2 and BaCl2 (0.1-20 mmol/L). **Results:** EUC (1-3000 μM) induced complete vasorelaxation (100%) in AUH-NG and AUH-DMG. Analysis of the mean effective concentration (EC50) revealed differences in sensitivity to EUC between the models. In AUH-NG, EC50 values were 928.69 ± 3.81 μM in the presence of K+ and 512.37 ± 5.24 μM in the presence of serotonin (5-HT). In contrast, segments from pregnant women with DMG showed increased EC50 values, at 1528.46 μM in the presence of K+ and 1279.48 μM in the presence of 5-HT, indicating lower sensitivity to EUC. Furthermore, in AUH maintained in Ca2+ free nutrient solution and depolarized with K+, it was observed that EUC (1-3000 μM) was able to significantly inhibit BaCl2 and CaCl2 induced contractions in both groups, when compared to the nifedipine control, a classic L-type calcium channel blocker. Suggesting that EUC may act through additional or broader mechanisms in blocking Ca2+ influx. **Conclusion:** In AUHs from pregnancies with DMG, the EUC exhibited changes in its pharmacological profile, suggesting a functional reorganization of vasorelaxant mechanisms and greater dependence on L-type Ca2+ channels. In both groups, the findings indicate the possible involvement of other calcium channel subtypes, such as VOCC-T (CaV3.2), VOCC-P/Q, and VOCC-R, in the observed vasorelaxant effect.

14.004 **Cortico-Hippocampal Network Involvement in Time-Dependent Fear Generalization**. Castro JC[1], Corrêa MS[2], Lopes LV[1], dos Santos ACQ[1], Lourenço WTB[1], Ferreira TL[1], Fornari RV[1] [1]UFABC, Lab. of Neurobiology of Memory, PG Neuroscience, Brazil. [2]Leibniz Institute for Neurobiology, Germany.

Introduction: Contextual fear conditioning is a key model for studying fear memories. Through systems consolidation, specific memories can become generalized through interactions between hippocampal and neocortical regions modulated by corticosterone (CORT). Previous findings in our laboratory showed a positive correlation between post-training CORT levels and fear responses in a novel context in animals trained with 0.6 mA footshocks and tested 14 days later. **Objectives:** We aimed to investigate the relationship between regional neuronal activation, post-training CORT release, and freezing levels in a novel context by quantifying c-Fos expression in the anterior cingulate cortex (aCC), prelimbic cortex (PrL), anterior insular cortex (aIC) and dorsal and ventral hippocampus subregions (dentate gyrus [DG], cornu ammonis [CA] 1, CA2 and CA3) during retrieval 14 days after moderate CFC. **Methods:** Brain samples from a previously published cohort of adult male Wistar rats (CEUA-UFABC #7479070916), trained with 0 or 0.6 mA and tested 14 days later in either the training context A (CtxA) or a novel context B (CtxB), were analyzed. Following exclusion of animals with inadequate histological quality, behavioral data were reanalyzed using the same animals included in the c-Fos analyses. Coronal brain sections (40 µm) were processed for Fos immunohistochemistry using a primary anti-c-Fos antibody (1:15,000) and the avidin–biotin–peroxidase detection method with diaminobenzidine visualization. The c-Fos-immunoreactive cell density (cells/mm^2) was quantified in each ROI using ImageJ, with values normalized to homecage averages. **Results:** Reanalysis of the behavioral dataset confirmed that animals trained with 0.6 mA exhibited significantly higher freezing than controls (Footshock effect: $F(1,20)=31.83$, $p<0.001$, $\omega^2=0.55$), whereas neither the Context effect nor the Footshock × Context interaction reached statistical significance in the reduced histological sample. Preliminary descriptive analyses indicated similar c-Fos levels across the analyzed ROIs. Exploratory correlation analyses further revealed a strong positive association between aCC and PrL c-Fos expression (Spearman's $\rho = 0.943$, $p = 0.017$), suggesting coordinated activation of medial prefrontal regions. **Conclusions:** These preliminary findings confirm the behavioral effect with animals trained at 0.6mA exhibiting greater freezing than controls, and suggest a coordinated activation of medial prefrontal cortex regions during remote memory retrieval. Immunohistochemical assays are currently ongoing to expand sample sizes, which are required to perform proper statistical inference and to verify potential correlations between Fos expression, post- training CORT release, and freezing levels in the novel or training context. The completion of these experimental groups may further elucidate the neural substrates underlying memory generalization, highlighting possible novel therapeutic targets for treating psychiatric disorders linked to maladaptive fear generalization. Funding: FAPESP(2025/10080-9).

14.005 **Vasodilatory Effect of (E,E)-Farnesol on Excitation–Contraction Coupling in Umbilical Vessels from Women with Preeclampsia**. Araújo ÉRL, Batista PR, Pereira LRS, Bastos CMS, Silva JA, Gonçalves SA, Silva PEO, Sales VS, Tavares AFC, Sousa MJS, Cavalcante JMC, Silva RER, Dias FJ, Sales EPN, Barbosa R. URCA - Excitable Cell Physiopharmacology Lab, Brazil.

Introduction: (E,E)-farnesol is a sesquiterpene alcohol found in plants, insects, and mammals, and may also be obtained through diet. Previous studies have described cardioprotective, antihypertensive, and vasorelaxant effects of (E,E)-farnesol, including in healthy fetoplacental vessels. However, studies involving natural products in human umbilical vessels from preeclamptic pregnancies remain scarce. Preeclampsia is a hypertensive disorder of pregnancy that directly affects umbilical vessels, compromising fetal health. **Objectives:** To demonstrate the relaxant effects of (E,E)-farnesol in umbilical vessels from preeclamptic pregnancies. **Methods:** After ethical approval (CEP/URCA No. 3.832.881), umbilical cord segments from pregnant women diagnosed with preeclampsia were collected after informed consent was obtained. The tissues were dissected to obtain arterial and venous umbilical rings (3–5 mm), which were mounted in organ baths under controlled conditions (Krebs–Henseleit solution, pH 7.4, 37 °C, carbogen). After a stabilization period (90 min), the rings were precontracted with KCl (60 mM) or serotonin (10 μM) to evaluate electromechanical and pharmacomechanical coupling, respectively. At the plateau phase (10–15 min), cumulative concentration–response curves for (E,E)-farnesol were obtained over a wide concentration range. **Results:** (E,E)-farnesol (1–1200 μM) completely relaxed KCl-induced vasoconstriction in both umbilical arteries (≥200 μM; two-way ANOVA: $p < 0.0001$) and umbilical veins (≥100 μM; two-way ANOVA: $p < 0.0001$). Similarly, serotonin-induced contractions were relaxed to the same extent. Analysis of the concentration required to produce 50% of the maximal response (EC50) demonstrated that the effect was significantly more potent in umbilical veins than in umbilical arteries during electromechanical coupling (EC50: 83.83 ± 12.22 μM vs. 295.50 ± 9.26 μM; t-test: $p < 0.0001$) and pharmacomechanical coupling (EC50: 172.0 ± 90 μM vs. 451.00 ± 3.63 μM; t-test: $p < 0.0001$). Furthermore, in both umbilical arteries and veins, (E,E)-farnesol was more potent in relaxing electromechanical coupling. **Conclusion:** Exogenous (E,E)-farnesol exhibits vasorelaxant properties through different pharmacological pathways relevant to fetoplacental circulation, supporting its potential as a promising molecule in cardiometabolic disorders associated with increased vasoconstriction of umbilical vessels, such as preeclampsia.

14.006 **Influence of Potassium Channels on the Vasorelaxant Effect of Carveol, *ex vivo*, in human umbilical veins**.
Pereira LRS, Batista PR, Cruz JF, Sousa MJS, Bastos CMS, Silva JA, Araújo ERL, Gonçalves SA, Silva FDS, Machado STS, Silva AA, Silva RER, Dias FJ, Calixto GL, Barbosa R URCA, Lab Physiopharmacology of Excitable Cells, Brazil

Introduction: (-)-Carveol (CAR) is a monoterpenoid abundantly found in essential oils of caraway, coriander, tangerine, and spearmint. Previous studies have demonstrated the vasorelaxant potential of CAR in rat aorta and human umbilical artery in a dose-dependent manner. Given this evidence of vasoactive regulation, exploring the effect of CAR on human umbilical veins (HUV), which are essential for fetoplacental circulation, constitutes a relevant strategy, since studies using natural products in HUV are still scarce in the literature and have great potential to foster the advancement of clinical research aimed at expanding vasodilator compounds for the gravid population. **Objective:** To evaluate the participation of potassium (K+) channels in the vasodilation promoted by CAR in HUV from normotensive parturients. **Methods:** After ethical approval (CEP/URCA nº 3.832.881), fragments of human umbilical cord (10 cm) from healthy parturients ≥18 years old were collected. Following dissection, venous rings (3–5 mm) were suspended in organ baths (37°C, pH 7.4, in a carbogenic mixture and Krebs-Henseleit solution) for isometric tension recording. K+ channel blockers: tetraethylammonium (TEA) - large-conductance Ca^2+-activated K+ channels; glibenclamide (GLIB) - ATP-sensitive K+ channels; 4-aminopyridine (4-AP) - voltage-dependent K+ channels, were pre-incubated (30 min), followed by contraction with serotonin (10 µM), and cumulative addition of CAR (1 – 5000 µM) every 5-15 min. Data are expressed as mean ± standard error of the mean. Statistical differences ($p < 0.05$) were calculated using SigmaPlot 12 (one-way ANOVA followed by Holm-Sidak test). Efficacy and potency were expressed as EMÁX and EC50, respectively. **Results:** In preparations exposed to K+ channel blockers, alterations in potency and efficacy parameters of the vasorelaxant activity of CAR were observed. All blockers used shifted the relaxation curve to the right, presenting statistically significant concentration from 300 µM onward ($p \leq 0.005$), resulting in an increase in the EC50 of CAR from 498.2 µM (absence of blockers) to 556.98 µM (TEA), 878.60 µM (GLIB), and 796.73 µM (4-AP). The blockers used did not decrease the EMÁX of CAR; however, in the presence of TEA, the administration of CAR showed 100% relaxation starting at the concentration of 3000 µM. **Conclusion:** The findings showed that CAR induces relaxation in HUV in the presence of K+ channel blockers. TEA, GLIB, and 4-AP promoted a significant increase in EC50, suggesting a partial participation of these channels in the vasorelaxant effect of CAR in HUV. Furthermore, TEA appears to improve the efficacy of CAR. Together, the findings point to CAR as a promising molecule to contribute to the development of more effective therapeutic strategies for gestational hypertensive conditions. **Financial support:** CAPES; CNPq; FUNCAP

14.007 **Therapeutic Potential of Polymeric Films Incorporating an N-Acylhydrazone Derivative in Burn Healing**. Silva JF[1], Nascimento BKL[1,2], Sousa BG[1,2], Dantas VG[1], Chaves MJRS[1], Medeiros KA[1,3], Guedes GG[1,3], Oliveira TKB[4], Nonaka CFW[5], Araújo PHL[1], Damasceno BPGL[1,2,3], Cavalcanti ALM[1] [1]UEPB, Lab for the Development and Characterization of Pharmaceutical Products, Brazil; [2]UEPB, PPG Pharmaceutical Sciences, Brazil; [3]UFPB, PPG Development and Technological Innovation in Medicines, Brazil; [4]UNIFACISA University Center, Brazil; [5]UEPB, PPG Dentistry, Brazil

Burns represent an important public health problem due to their high morbidity, susceptibility to infection, and substantial impact on quality of life. These injuries may result from thermal, chemical, electrical, or biological agents, leading to partial or complete skin destruction accompanied by an intense inflammatory response. In this context, the search for novel therapeutic systems that accelerate burn healing and minimize complications is highly desirable. Among the most promising approaches are chitosan-based polymeric films (CTS), a biodegradable, biocompatible biomaterial with intrinsic antimicrobial properties. The incorporation of JR19, a N-acylhydrazone derivative with previously described anti-inflammatory activity, may further enhance the therapeutic efficacy of these systems. Moreover, the association with silver sulfadiazine may broaden their antimicrobial spectrum. This study aimed to evaluate the healing and antimicrobial potential of chitosan-based polymeric films containing the N-acylhydrazone derivative JR19, either alone or in combination with silver sulfadiazine, for the treatment of second-degree burns. The films were prepared using the solvent evaporation method. Three systems were produced, including FQ (chitosan-based film), FJR19 (polymeric film containing JR19), and FJRSP (polymeric film containing JR19 associated with silver sulfadiazine). Antimicrobial activity was evaluated using the disk diffusion method against *Staphylococcus aureus* ATCC® 25923. For the healing evaluation, second-degree burns were induced in male Wistar rats using a metal device heated to 100 °C, which was applied to the skin for 20 seconds. The animals were randomly assigned to the following experimental groups: negative control (0.9% saline), positive control (1% silver sulfadiazine), FQ, FJR19, and FJRSP. Treatments were topically administered every two days over 21 days. The lesion area was evaluated by photodocumentation using ImageJ Pro 6.1 software. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test, with significance set at $p < 0.05$. The results demonstrated that only FJRSP exhibited antimicrobial activity against *Staphylococcus aureus*, as evidenced by the presence of an inhibition halo. Regarding wound- healing activity, the FJR19 and FJRSP films significantly reduced the burn area from the 7th day of treatment. These findings suggest that the enhanced healing effect is primarily associated with the anti-inflammatory properties of JR19. Overall, polymeric films containing JR19 demonstrated promising therapeutic potential for burn treatment by accelerating the healing process. The association with silver sulfadiazine conferred additional antimicrobial activity to the system. Acknowledgments to CNPq, UEPB, the Laboratory for Drug Development and Synthesis, and the Laboratory for Development and Characterization of Pharmaceutical Products.

14.008 **Terpinolene induces Vasodilation in Human Umbilical Arteries**. Silva FDS, Machado STS, Pereira LRS, Tavares AFC, Duarte MRS, Cruz JF, Sousa MJS, Sales EPN, Silva AA, Moraes LP, Araújo ERL, Sales SV, Barbosa R URCA, Lab Fisiofamacologia das Células Excitáveis, Brasil

Introduction: Hypertensive syndromes of pregnancy, especially pre-eclampsia, are associated with high maternal-fetal morbidity and mortality and alterations in vascular smooth muscle that compromise fetal blood flow. However, the available pharmacological options are still limited. In this context, the vasoactive potential of terpinolene (TERP), a monoterpene whose effects on vascular reactivity are still poorly understood, was investigated. **Objective:** To investigate the vasoactive effect of terpinolene in isolated human umbilical arteries (HUA) using ex vivo and *in vitro* approaches. **Methods:** After approval by the Ethics Committee of the Regional University of Cariri (no. 3,832,881), fragments of human umbilical cords were obtained with the consent of the parturients. The isometric tension of the human umbilical cord rings was recorded in an organ bath system under different pharmacological protocols. After the functional experiments, the tissues were submitted to histological analysis. The results were expressed as mean ± standard error of the mean (n = 10), using Student's t-test or two-way ANOVA, with $p < 0.05$. **Results:** When evaluating the effect of TERP on the active vascular tone of arterial rings, these were pre-contracted with serotonin (5-HT; 10 µM) or bradykinin (BK; 0.1 µM). TERP (1–3,000 µM) promoted concentration-dependent relaxation, with (Emax = 100%) at a concentration of 3,000 µM (EC50 = 980.57 ± 5.1 µM), with statistical significance from 100 µM ($p < 0.001$). BK (0.1 µM) induced maximal transient contraction in 5 min (4.85 ± 0.31 gf), which was reduced by 85.98% after pre-incubation with TERP (3,000 µM). The involvement of the protein kinase C (PKC) pathway was investigated using phorbol 12-myristate 13-acetate ester (PMA; 10 µM), which promoted time-dependent contraction, reaching a maximum tension of 1.306 ± 0.054 gf after 60 min. Pre-incubation with TERP (3,000 µM) suppressed this contractile response to 0.713 ± 0.040 gf. Additionally, the involvement of TRPC3 channels in the vasodilatory response induced by TERP was evaluated. Incubation of AUHs with PYR3 (10 µM), a selective TRPC3 channel blocker, significantly reduced TERP-induced relaxation (Emax = 21.9 ± 5.9% vs. control: 100 ± 6.03%). Histological analysis demonstrated the preservation of vascular architecture after incubation with TERP, with no evidence of edema, necrosis, or inflammatory infiltration. **Conclusion:** TERP promoted vasodilation in AUH, involving, at least in part, the modulation of the PKC pathway and TRP/TRPC3 channels, without significant morphological alterations. These findings suggest therapeutic potential of TERP for vascular alterations associated with hypertensive and metabolic syndromes of pregnancy.

14.009 **Integrated approach of Alternative Methods to Animal Use for the Preliminary Toxicity Assessment of Bioactive Compounds**. Alves AKL[1,2], Dantas MEA[1,2], Brito JM[1,3], Silva AP[1,3], Silva KKF[1,4], Dantas BB[1,5] [1]UFCG, Curimataú Cancer Observatory (OCC), Brazil; [2]PIBIC/UFCG; [3]UFCG, PPGCNBiotec, Brazil; [4]UFPB, Renorbio, Brazil; [5]UFCG, Academic Health Unit, Center for Education and Health, Brazil

Introduction: Studies on the toxicity of bioactive compounds are essential for their safe use in humans. In this context, the increasing ethical and scientific demand for the adoption of alternative approaches has driven the development of integrated strategies combining complementary methods to improve preliminary safety assessment while supporting the 5Rs principles (rethink, refuse, reduce, reuse and recycle). **Objective:** To propose an integrated approach of alternative methods to animal use for the preliminary toxicity evaluation of bioactive compounds. **Methodology:** The integrated approach consisted of three complementary assays, characterized by the use of negative and positive controls: (i) acute toxicity in Artemia salina, with exposure of nauplii to 0.9% NaCl and 8% DMSO for 24 h, followed by assessment of viability through motility; (ii) hemolysis assay, in which human erythrocytes (4%) were incubated with 0.9% NaCl and 10% SDS + 0.01 N HCl for 1 h, and the absorbance of the supernatant was measured at 540 nm; and (iii) HET-CAM, in which fertilized eggs of *Gallus gallus domesticus* were incubated until day 10, when the shells were opened to expose the chorioallantoic membrane and apply the controls (0.9% NaCl, 0.1 N NaOH, and 99.9% ethanol). The time of onset of vascular reactions was recorded over 5 minutes. Results Standardization of the assays established an integrated strategy for preliminary toxicity screening by combining complementary endpoints at different levels of biological organization, providing a broader toxicological assessment than isolated assays. The approach integrates whole-organism viability through Artemia salina motility, mammalian cell membrane integrity by the hemolysis assay, and tissue vascular responses by HET-CAM. The performance of each model was validated using positive and negative controls. In the A. salina assay, viability was 100.0±2.0% and 3.3±4.1% for the negative and positive controls, respectively ($p<0.05$). Hemolysis reached 1.4±0.8% and 100.0±7.7% for the negative and positive controls, respectively ($p<0.05$). In the HET-CAM assay, 0.1 N NaOH and ethanol produced MSc values of 18.83±0.2 and 17.67±1.0, respectively, whereas 0.9% NaCl yielded an MSc of 0.58±0.8. **Conclusion**: The integration of complementary alternative methods enables a more robust and biologically relevant preliminary toxicity screening by combining organismal, cellular and tissue endpoints, strengthening toxicological inference and supporting compound prioritization while contributing to the reduction of animal use in subsequent stages of toxicological evaluation. **Financial support** CNPq, CAPES, FAPESQ-PB. Ethical approval CEP/CES-UFCG (N° 6.728.938).

14.010 **Adjuvant Effect of Meldrum's Acid Derivatives on Antibiotic Activity against Multidrug-Resistant Bacteria**. Araújo IM, Silva AA, de Morais LP, Machado AJT, Almeida FF, de Matos YMLS, Gondin CNFL, Begnini IM, Rebelo RA, Coutinho HDM URCA, Brazil, FURB, Brazil

Introduction: Antimicrobial resistance is a major global health challenge that compromises the effectiveness of conventional antibiotics. In this context, compounds capable of restoring bacterial susceptibility have emerged as promising adjuvant strategies. Meldrum's acid derivatives have attracted attention due to their structural versatility and potential biological activities. **Objectives:** To evaluate the antibacterial and antibiotic-modulating activities of five Meldrum's acid derivatives (MAD1–MAD5) against multidrug-resistant strains of *Staphylococcus aureus* (SA 10) and *E. coli* (EC 06) and to investigate possible mechanisms involved in their modulatory effects. **Methods:** Minimum inhibitory concentrations (MICs) were determined by broth microdilution. The modulatory activity was evaluated using subinhibitory concentrations (MIC/8) of the derivatives combined with ampicillin, gentamicin, and norfloxacin. Membrane permeability was assessed using the SYTOX Green assay, and intracellular ATP levels were quantified by luciferase-based bioluminescence. Statistical analyses were performed using one-way ANOVA followed by Bonferroni's post hoc test. **Results:** None of the derivatives exhibited clinically relevant intrinsic antibacterial activity (MIC ≥ 1024 µg/mL). Against *S. aureus* 10 , ampicillin MIC was reduced from 256 µg/mL to 40.31 µg/mL (MAD 1), 50.8 µg/mL (MAD 2 and 3) 203.2 µg/mL (MAD 4) and 128 µg/mL (MAD 5). Gentamicin MIC was reduced from 40.31 µg/mL to 16 µg/mL (MAD 1 and 4), 20.16 µg/mL (MAD 2 and 5) and 25.4 µg/mL (MAD3). Norfloxacin MIC decreased from 101.59 µg/mL to 64 µg/mL (MAD 1, 2 and 3), and 80.6 µg/mL (MAD 5). No reduction in norfloxacin MIC was observed in the presence of MAD 4. Against *E. coli* 06 , the MIC of ampicillin, as well as its combination with Meldrum's acid derivatives, was ≥ 1024 µg/mL. Gentamicin MIC decreased from 80.63 µg/mL to 40.3 µg/mL (MAD 1), 50.8 µg/mL (MAD 2, 4 and 5) and 32 µg/mL (MAD 3). Norfloxacin MIC was reduced from 128 µg/mL to 64 µg/mL (MAD 1 and 2), 50 µg/mL (MAD 3), 80.6 µg/mL (MAD 4), and 101.59 µg/mL (MAD 5). Membrane permeability assays revealed limited alterations in *S. aureus* but increased permeability in *E. coli* , particularly for MAD1 and MAD3. Furthermore, intracellular ATP quantification demonstrated marked ATP depletion in *E. coli* treated with MAD 3, MAD 4, and MAD 5, whereas no significant changes were observed in *S. aureus* . **Conclusion:** Meldrum's acid derivatives acted as effective antibiotic adjuvants despite lacking intrinsic antibacterial activity. Their modulatory effects appear to be associated with alterations in membrane permeability, especially in *E. coli* . These findings support the potential application of Meldrum's acid derivatives as resistance-modifying agents capable of enhancing antibiotic efficacy against multidrug-resistant bacteria. **Financial support:** CAPES

14.011 **Relationship Between APOE Gene Polymorphisms and Neuropsychiatric and Neurodegenerative Disorders: Evidence from a Cohort in Ceará, Brazil**. Ferreira DMA[1,2], Souza TF[1,2], Guimarães APDS[1,2], Rosa R[3], Lima DP[3,4,5], Lima AB[5], Miyajima F[1,2] [1]Ficocruz-CE, Brasil, [2]ACMELab, Lab Analítico de Competências Moleculares e Epidemiológicas, Brasil, [3]UFC, Brasil, [4]Hospital Universitário Walter Cantídio, Brasil, [5]Hospital de Saúde Mental de Messejana, Brasil

Introduction: Apolipoprotein E (APOE) is involved in lipid transport and metabolism, playing a crucial role in the maintenance and repair of the central nervous system. Its genetic polymorphisms, particularly the ε4 allele, have been associated with susceptibility to and progression of several neurodegenerative and neuropsychiatric disorders. Therefore, investigating the distribution of APOE genotypes may contribute to a better understanding of the genetic profile of individuals with different neurological and psychiatric conditions. **Objectives:** To compare the frequency of APOE genotypes and alleles among patients with Alzheimer's disease (AD), Major Depressive Disorder (MDD), Bipolar Depression (BD), Bipolar Disorder (BD-I/BD), and cognitively healthy controls, as well as to evaluate their association with clinical and cognitive parameters. **Methods:** This comparative observational study was conducted at Walter Cantídio University Hospital (HUWC) and the Mental Health Hospital (HSM) and was approved by the Research Ethics Committee (Approval No. 7,504,021). Clinical and sociodemographic data were collected and stored in the REDCap platform. APOE genotyping was performed by quantitative polymerase chain reaction (qPCR) using TaqMan® probes (rs429358 and rs7412) on a QuantStudio™ 7 Pro system. Statistical analyses were conducted using SPSS software. **Results:** A total of 74 participants were recruited from HUWC and HSM, including 28 patients with AD (mean age: 69.9 ± 12.5 years), 15 with MDD (73.3 ± 6.6 years), 10 with Bipolar Disorder (66.2 ± 7.4 years), 6 with Bipolar Depression (67.8 ± 7.2 years), and 15 cognitively healthy controls (62.5 ± 10.2 years). In this sample from the state of Ceará, Brazil, the predominant genotypes were ε3/ε3 (55.4%) and ε3/ε4 (37.8%), with allele frequencies of 75.0% for ε3, 23.0% for ε4, and 2.0% for ε2. Genotype distribution was in Hardy–Weinberg equilibrium (p = 0.22). The overall frequency of ε4 carriers was 43.2%, with the highest proportion observed in the AD group (50.0%). However, no statistically significant differences were found in the frequency of ε4 carriers (p = 0.86) or in the distribution of APOE genotypes among the evaluated groups. **Conclusion:** The findings indicate a genetic profile similar to that reported in other Brazilian populations, with no significant association between the ε4 allele and the clinical groups evaluated. APOE genetic characterization represents a promising tool for advancing pharmacogenomics and precision medicine in Alzheimer's disease. Further studies with larger sample sizes and greater statistical power are necessary to validate these findings and support their clinical application.

14.012 **Biochanin A Promotes Wound Healing by Reducing the Inflammatory Response in Ovariectomized Mice**. Santos DN[1], Neres WS[1], Aragão JMDA[1], Nascimento ACS[1], Sant'ana ROS[1], Santos GJS[1], Souza MTS[3], Albuquerque-Júnior LC[2], Camargo EA[1], Grespan R[1]. [1]UFS, Pharmacology Lab the Inflammatory Process, Brazil, [2]UFSC, Pathology Departament, Brazil, [3]UFS, Pharmacy Dept, Brazil.

Introduction: Chronic wounds are a major global health problem associated with persistent inflammation and impaired healing. In aging women, estrogen deficiency contributes to delayed tissue repair, although hormone replacement therapy is limited by safety concerns. Phytoestrogens such as biochanin A (BCA) have emerged as potential alternatives due to their estrogen-like, anti-inflammatory, and antioxidant properties. Despite promising evidence, the effects of BCA on wound healing remain poorly understood. **Objective:** This study aimed to investigate the topical effects of BCA in a murine model of hypoestrogenic wound healing induced by ovariectomy. **Methods:** Female Swiss mice (25–30 g) underwent bilateral ovariectomy (OVX) or sham surgery, followed by a 30-day recovery period to allow establishment of a hypoestrogenic state. A 6 mm full-thickness excisional wound was created on the dorsum of each animal and the mice were randomly allocated into six experimental groups and housed individually: SHAM + Vehicle (**dimethyl sulfoxide (10%)**, and **propylene glycol (10%) in saline)**, OVX + vehicle, OVX + BCA (0.03, 0.09, or 0.27 mg/animal), and OVX + 17β-estradiol (E2; 0.009 mg/animal). Treatments were applied topically (30 µL) immediately after wound induction and once daily for 14 days. Samples were collected on days 3, 7, and 14 post-injury (n = 5–7 animals per group/time point), with additional histology (n = 3/group). Wound closure, myeloperoxidase activity, cytokines (TNF-α, IL-1β, IL-10), and histological parameters (re-epithelialization and collagen deposition) were evaluated. **Results:** Topical treatment with BCA did not alter the uterine weight of the animals, which remained significantly lower ($p < 0.001$) than that of the SHAM and OVX-E2 groups. Interestingly, the OVX-E2 group had a higher uterine weight on day 3 than the SHAM group ($p < 0.05$). BCA reduced lesion area on days 3 and 7 for all three tested doses compared to the OVX ($p < 0.001$, $p < 0.01$, or $p < 0.05$), with no differences at day 14. Based on these findings, the 0.03 mg dose was selected for subsequent experiments. On day 7, MPO activity decreased in SHAM, OVX-BCA (0.03 mg), and OVX-E2 compared to the OVX group. On day 3, TNF-α levels were reduced in OVX-BCA ($p < 0.001$) and OVX-E2 ($p < 0.05$), while IL-10 increased in SHAM and OVX-BCA ($p < 0.05$), IL-1β was unchanged. At day 14, BCA promoted complete re-epithelialization, a thicker granular layer, reduced dermal vascularity, and more organized type I collagen with longer, compact fibers compared to OVX. **Conclusion:** Topical BCA accelerated healing of hypoestrogenic wounds by reducing inflammatory parameters and improving tissue organization without inducing uterotrophic effects, supporting its potential as a therapeutic strategy for impaired wound healing associated with estrogen deficiency.

14.013 **Comparative Development and Characterization of PCL and PLGA Nanoparticles Co-Loaded with Itraconazole and Terbinafine**. Samuel AB[1], Cavalcante SB[1], Miguel RA[2], Gomes MAM[2], Passos JS[2], Lopes LB[2], Ishida K[1] [1]USP, Institute of Biomedical Science, Dept Microbiology, Lab. of Antifungal Chemotherapy, PPG Microbiology, Brazil, [2]ICB-USP, Dept Pharmacology, Lab. of Nanomedicine and Drug Delivery, PPG Funcional & Molecular Biology, Brazil

Introduction: Sporotrichosis is a neglected subcutaneous mycosis caused by Sporothrix spp. with increasing incidence in Brazil. Current treatment relies mainly on itraconazole (ITC) and terbinafine (TRB); however, the low aqueous solubility of these drugs, prolonged treatment regimens, and adverse effects may compromise therapeutic efficacy and patient adherence. Polymeric nanoparticles have emerged as promising drug delivery systems capable of improving drug solubility, bioavailability, and modifying release. Among them, polyε-caprolactone) (PCL) and poly(lactic-co-glycolic acid) (PLGA) are biodegradable polymers with distinct physicochemical properties that may influence nanoparticle performance. **Objective:** To prepare and to compare PCL- and PLGA-based nanoparticles co-loaded with ITC and TRB regarding their physicochemical characteristics and encapsulation efficiency. **Materials and Methods:** PCL nanoparticles were prepared by nanoprecipitation, whereas PLGA nanoparticles were produced using the single emulsion-solvent evaporation method. Formulations with different drug loads were characterized for particle mean diameter (Dz) and polydispersity index (PDI) by dynamic light scattering (DLS), and the zeta potential (Pz) was determined by electrophoretic light scattering (ELS). Encapsulation efficiency (EE) was determined indirectly by ultrafiltration, followed by quantification of the free drug by high-performance liquid chromatography (HPLC). **Results:** Both polymeric systems produced nanoparticles within the nanometric range. PCL nanoparticles loaded with 10 mg of ITC and 10 mg of TRB exhibited a Dz of 248.0 ± 13.7 nm, PDI of 0.358 ± 0.051, Pz of -28.6 ± 0.9 mV, and encapsulation efficiencies of 99.9% for ITC and 97.3% for TRB. PLGA nanoparticles exhibited Dz values ranging from 235.2 ± 3.0 to 250.3 ± 6.0 nm, PDI values between 0.097 ± 0.02 and 0.337 ± 0.04, and Pz values from -28.5 ± 1.34 to -35.5 ± 1.23 mV. The PLGA formulation containing 2 mg of ITC and 2 mg of TRB showed the most favorable physicochemical profile and preliminary EE values of 86.5% (ITC) and 68.5% (TRB), whereas the formulation containing 5 mg of each drug achieved higher preliminary EE values of 93.6% (ITC) and 85.2% (TRB). **Conclusion:** Both polymeric systems demonstrated physicochemical characteristics suitable for antifungal drug delivery. PCL nanoparticles exhibited excellent encapsulation efficiency even at a higher drug loading, whereas PLGA nanoparticles showed improved particle homogeneity and colloidal stability. These findings demonstrate that polymer selection influences nanoparticle physicochemical characteristics and support the continued development of biodegradable polymeric nanocarriers as promising therapeutic platforms for sporotrichosis treatment.

14.014 **Use of the Chorioallantoic Membrane in the Screening of Compounds with Antiangiogenic Potential: An Alternative Model to the Use of Animals**. Silva AP[1,3], Alves AKL[1,2], Dantas MEA[1,2], Brito JM[1,3], Silva KKF[1,4], Dantas BB[1,5] [1]UFCG, Curimataú Cancer Observatory (OCC), Brazil; [2]PIBIC/UFCG; [3]UFCG, PPGCNBiotec, Brazil; [4]UFPB, Renorbio, Brazil; [5]UFCG, Academic Health Unit, Center for Education and Health, Brazil

Introduction: The search for angiogenesis inhibitor compounds has increased in the context of diseases dependent on this process. In this scenario, alternative methods to animal use, such as the chorioallantoic membrane (CAM), stand out as promising tools for screening compounds with antiangiogenic potential. Objective To evaluate the chorioallantoic membrane of *Gallus gallus* domesticus embryos as an alternative model for screening compounds with antiangiogenic potential. **Methodology:** Fertilized eggs of *Gallus gallus domesticus* were incubated under controlled conditions (37.8±1.0°C and 55±5% relative humidity). On the 4th day of development, a controlled opening of the shell was made in the region of the air chamber, followed by sealing and returning to incubation. On the following day, the vehicle (DMSO), negative control (NaCl 0.9%) and standard drug (dexamethasone 4 mg/mL) were applied directly onto the chorioallantoic membrane using filter paper discs (6 mm). The vascular response was recorded by stereomicroscopy at 0 and 6h, and the angiogenic parameters (diameter, length, and branching) were quantified with ImageJ (v.1.54). Data were normalized considering baseline values (0h) as 100%. Statistical analysis was performed using Student's t-test, with differences considered statistically significant when $p<0.05$. **Results**: After 6h, treatment with dexamethasone promoted a significant reduction ($p<0.05$) in the angiogenic parameters compared to baseline (0h = 100%), with values of 54.5±8.2% for vascular diameter, 89.9±2.2% for length, and 73.3±8.1% for the number of branches, confirming its inhibitory effect on angiogenesis and the sensitivity of the model. The negative control (NaCl 0.9%) showed an increase in vascular parameters compared to baseline, with diameter of 121.6±2.6%, length of 119.2±2.7%, and branching of 115.1±2.5%, highlighting physiological growth of the vascular network during the experimental period. Regarding the vehicle, concentrations of 0.25% and 0.12% DMSO did not compromise the development of any of the vascular parameters evaluated ($p>0.05$), maintaining behavior compatible with physiological growth. In contrast, the concentration of 0.5% did not show a statistical difference compared to baseline values for any of the parameters analyzed, with values of 99.0±4.5% (diameter), 101.8±2.0% (length), and 101.1±4.1% (branching), suggesting absence of progression of angiogenesis and possible interference in the dynamics of vascular growth. **Conclusion:** The model studied constitutes a highly vascularized tissue, being viable for preliminary screening of compounds with antiangiogenic potential, due to its sensitive response to experimental stimuli and the action of a standard drug. However, interference of the vehicle was observed at certain concentrations, reinforcing the need for rigor in experimental standardization. **Financial support** CNPq, CAPES, FAPESQ-PB.

14.015 **Antimicrobial Activity and Pharmacological Modulation of the Compound 3,4-BZM Against Resistant Strains of MRSA and** *Candidozyma auris*. Jesus ICTR[1], Vieira MM[2], Emídio JJ[2], Souza DP[2], Castro RD[2] [1]UFPB, PPG in Dentistry, Brazil. [2]UFPB, PPG in Bioactive Natural and Synthetic Products, Brazil.

Introduction: Antimicrobial resistance represents a significant public health problem, stimulating the search for new bioactive molecules with antimicrobial and modulating potential. 3,4-dimethoxy-N,N-dioctylbenzamide (3,4-BZM), with the chemical formula C25H43NO3, emerges as a promising compound due to its potential for action alone or in combination with conventional antimicrobials against resistant microorganisms. **Objectives:** To evaluate the antimicrobial activity of 3,4-BZM, as well as its modulating potential associated with antibiotics and antifungals against the MRSA NTCC 13373 (MRSA) and *Candidozyma auris* (*C. auris*) strains. Additionally, to perform *in silico* prediction of the molecule's toxicity. **Methods:** The MIC was determined by the broth microdilution method using 96-well plates, according to the Clinical and Laboratory Standards Institute (CLSI) guidelines. Bacterial suspensions were prepared in Mueller-Hinton broth with a turbidity of 0.5 on the McFarland scale, equivalent to 5×10^5 CFU/mL, while fungal suspensions were prepared in Sabouraud Dextrose broth, equivalent to 2.5×10^3 CFU/mL. 100 µL of the microbial suspensions were added to each well containing serial dilutions of 3,4-BZM. Vancomycin and caspofungin were used as positive controls. After incubation for 24 hours at 37 °C for bacteria and 34 °C for fungi, the MIC was defined as the lowest concentration without visible growth. For the determination of MBC and MFC, aliquots from the wells corresponding to MIC, MIC_2, and MIC₄ were plated on Mueller-Hinton or Sabouraud Dextrose agar and incubated under the same experimental conditions. Antimicrobial modulation was evaluated using 3,4-BZM at a subinhibitory concentration (MIC ≥ 8) in combination with vancomycin, levofloxacin, amoxicillin, caspofungin, fluconazole, and amphotericin B. *in silico* toxicological analysis was performed on the ADMETlab 3.0 platform using the SMILES code obtained from the MolView software. **Results:** 3,4-BZM showed MIC and MBC/MFC of 200 µg/mL against MRSA and C. auris. In the modulating evaluation, a reduction in the MIC of vancomycin from 2 to 1 µg/mL and of amoxicillin from 20 to 10 µg/mL was observed against MRSA. For *C. auris*, the association with caspofungin reduced the MIC from 0.5 to 0.00312 µg/mL. No relevant changes were observed for levofloxacin and fluconazole. *in silico* analysis indicated a high probability of ocular irritation, skin sensitization, and hERG channel blockade, but a low probability of acute oral toxicity, hematotoxicity, immunotoxicity, and genotoxicity. **Conclusion:** 3,4-BZM demonstrated antimicrobial activity against MRSA and C. auris, as well as modulating potential when combined with conventional antimicrobials, especially caspofungin. Despite the predicted toxicological data, the results indicate pharmacological potential of the molecule for future antimicrobial studies.

14.016 **Anthocyanin Profile and Antioxidant Capacity of Syrah Winery By-Products from the Brazilian Cerrado**. Costa KCM[1], Pertuzatti PB[2], Giachini FR[1,3]. [1]ICB-UFG, Goiania, Brazil; [2]UFMT-Barra do Garças, Brazil; [3]UFMT-Barra do Garças, Institute of Biological Sciences and Health, Federal University of Mato Grosso, Barra do Garças, Brazil

Introduction: Viticulture in the Brazilian Cerrado occurs under unique climatic impacting on the production of phenolic compounds, particularly anthocyanins. During winemaking, a significant fraction of these compounds remains in subtilized by-products such as grape pomace and lees. Anthocyanins exhibit pronounced antioxidant capacity and modulate oxidative stress pathways involved in blood pressure regulation. **Objective:** To identify and quantify the anthocyanin profile of Syrah (Vitis vinifera) winemaking by-products cultivated in the Brazilian Cerrado and evaluate their antioxidant capacity. **Methods:** Syrah grapes and their winemaking by-products were collected from a winery in Cocalzinho de Goiás, Brazil, during the 2022 harvest. Extracts were obtained by ultrasound-assisted extraction using methanol, water, and formic acid. Total flavonoids, phenolic acids, and moisture were determined by spectrophotometric methods. Antioxidant capacity was assessed by FRAP and ABTS assays. Anthocyanins were identified and quantified by HPLC-DAD-ESI-MSn. **Results:** Winemaking by-products showed higher concentrations of phenolic compounds than fresh grapes. Total flavonoid contents were 150.6±4,26, 237.3±6,44 and 268.3±22,77 mg QE/100g for grapes, pomace, and lees, respectively; phenolic acids ranged from 60.7±3,04 to 95.7±2,86 mg caffeic acid/100g. Antioxidant activity determined by ABTS was highest in lees (6820.7±247,6 µmol Trolox/100 g), followed by pomace (5543.4±225,24 µmol Trolox/100 g) and grapes (5087.5±477,3 µmol Trolox/100 g). In the FRAP assay, grapes and pomace showed similar values and were higher than lees. HPLC-DAD-ESI-MSn analysis identified 25, 19, and 29 anthocyanin compounds in grapes, pomace, and lees, respectively. Malvidin, petunidin, peonidin, cyanidin, and delphinidin derivatives predominated, including glycosylated and acylated forms. Lees exhibited the greatest chemical diversity, including pyranoanthocyanins such as vitisins A and B and their derivatives. **Discussion**: The higher flavonoid and phenolic acid contents found in pomace and lees indicate that substantial amounts of bioactive compounds remain after winemaking. The elevated antioxidant activity of lees may be associated with its greater anthocyanin diversity. The predominance of malvidin, petunidin, and peonidin derivatives agrees with the phenolic profile typically reported for Syrah grapes, while the presence of vitisins reflects fermentation-induced transformations that increase pigment stability. **Conclusion:** Syrah winemaking by-products from the Brazilian Cerrado are rich sources of phenolic compounds and antioxidants. Their anthocyanin diversity, particularly in lees, highlights their potential for food, pharmaceutical, and nutraceutical applications, contributing to the sustainable valorization of winery residues.

14.017 **Performance of Large Language Models in Title and Abstract Screening of Preclinical Systematic Reviews**.
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Introduction: Preclinical systematic reviews play an important role in pharmacology by integrating heterogeneous animal evidence, evaluating the consistency of experimental effects, and supporting translational research. However, they remain labor-intensive, particularly during title and abstract screening, which often requires duplicate evaluation of hundreds or thousands of records. Large language models (LLMs) may streamline this step, but their performance in preclinical reviews requires validation. **Objectives:** To develop an LLM-based tool for title and abstract screening and evaluate its ability to retain relevant studies, produce reproducible decisions, and reduce screening workload. **Methods:** This study was preregistered at the OSF (osf.io/rzju8). We used title and abstract screening records from three pharmacology-related preclinical systematic reviews conducted by the BRISA Collaboration. One dataset was used for prompt engineering and workflow optimization, while two independent datasets were reserved for validation. We developed a web application connected to the OpenAI API ([brisa.bio.br](http://www.brisa.bio.br)) to apply standardized prompts and export screening decisions. For each record, the model received the review question and eligibility criteria and classified it for inclusion or exclusion. GPT-4o, GPT-5.2, GPT-5-mini, and GPT-5-nano were evaluated in repeated runs. Model decisions were compared with human screening and with studies selected after full-text assessment. The final included study list was used as the gold standard. **Results:** 4,013 deduplicated records were analyzed. In the validation datasets, LLMs selected fewer records for further screening than human reviewers, with AI-positive rates ranging from 37.9% to 61.2%, compared with 66.0% to 69.0% for human screening. Against the final included studies, GPT-5 models captured 90.3% to 100.0% of eligible records, whereas GPT-4o showed lower capture in one validation dataset. Test-retest reproducibility was high, with all validation-set model comparisons showing near-perfect agreement. Automation reduced estimated screening time by 93.5% to 98.9% across datasets. GPT-5.2 showed the best balance between capture and workload reduction, retaining 94.0% to 95.5% of final included studies while reducing the number of records selected for further screening by 34.5% to 42.6% in the validation sets. AI-included records excluded by humans were assessed by human full-text screening, and no additional eligible studies were identified. **Conclusion:** LLM-assisted screening can substantially reduce the workload of preclinical systematic reviews while retaining most studies included in the evidence synthesis. These findings support LLMs as valid alternatives for human reviewers in the title and abstract phase, although fully-automated analysis does lead to inadvertent exclusion of a small number of articles.

14.018 **Potential Hepatoprotective Effects of** *Helianthus tuberosus* **Polysaccharides in Acute Liver Damage**. Leal LE[1], Pilger BI[1], Cordeiro LMC[2], Acco A[1] [1]UFPR, PPG Pharmacology, Brazil, [2]UFPR, Dept Biochemistry and Molecular Biology, Brazil

Introduction: Acute hepatotoxicity is characterized by extensive hepatocyte injury, leading to rapid liver dysfunction. *Helianthus tuberosus* (Jerusalem artichoke or Tupinambo) is a tuber rich in polysaccharides, mainly inulin, which possesses several biological properties. However, few studies have investigated the effects of *Helianthus tuberosus* tuber polysaccharides (HTP) on acute hepatotoxicity models. **Objectives:** To evaluate the cytotoxicity of HTP in HepG2 cells and its hepatoprotective effects in acute hepatotoxicity induced by carbon tetrachloride (CCl4) in mice. **Methods:** *In vitro*: Cell viability was assessed in HepG2 cells by MTT assay after treatment with HTP (1–1000 µg/mL) for 24 and 48h. *In vivo*: Swiss male mice were randomly divided into three groups: 1) Naive; 2) Negative control (NC) treated with saline solution; and 3) HTP, treated at a dose of 200 mg/kg. The animals were pretreated with oral gavage once daily for 21 days. On the 22nd day, the animals, except those in the naive group, were subjected to intraperitoneal injection of CCl4 (0.1% in corn oil, 5 mL/kg). After 24 h of hepatotoxicity induction, blood and liver samples were collected for biochemical, oxidative stress, and inflammation biomarkers analyses. Data were expressed as mean ± SEM and analyzed by one-way ANOVA followed by Bonferroni's post hoc test, with $p < 0.05$ considered statistically significant. **Results:** HepG2 cells treated for 24 h with all concentrations of HTP maintained cell viability similar to that of the control group ($p<0.05$). At 48 h of treatment, cell viability was not altered ($p<0.05$). These results show that HTP has low toxicity to hepatic cells at 24 and 48 h. In mice, after CCl4 administration, HTP pre-treatment attenuated hepatomegaly, as demonstrated by a reduced liver index ($p=0.0068$). Plasma analyses showed that HTP decreased ALT ($p=0.0014$) and AST ($p=0.0002$) activities compared to the NC group, suggesting attenuation of hepatic injury, although ALP enzyme activity was not different between the HTP and NC groups ($p=0.5891$). Evaluation of oxidative stress parameters showed that HTP reduced ROS levels ($p=0.0313$) and lipid peroxidation ($p=0.0274$), and increased GSH levels ($p=0.0456$) and CAT activity ($p=0.0215$) compared to the NC group ($p<0.05$), suggesting an improvement in antioxidant defenses. No significant changes were observed in SOD and GST activities in the HTP group compared to the NC group ($p=0.5767$ and $p>0.9999$, respectively). Inflammatory cytokines IL-1β ($p=0.1688$), TNF-α ($p=0.4753$), and IL-6 ($p>0.9999$) were not significantly altered among the three groups. **Conclusion:** HTP did not present hepatic toxicity and mitigated acute hepatotoxicity through attenuation of hepatic dysfunction, oxidative stress and elevation of endogenous antioxidant defenses. **Financial support:** CAPES. Animal Research Ethical Committee Number: no. 1577.

14.019 **The Polysaccharides in Passion Fruit Peel Attenuate Acute Hepatotoxicity Through Redox and Metabolic Modulation**. Pilger BI[1], Leal LE[1], Cordeiro LMC[2], Brownlee I[3], Acco A[1] [1]UFPR, Dept Pharmacology, Brazil, [2]UFPR, Dept Biochemistry and Molecular Biology, Brazil, [3]Northumbria University, Dept Applied Sciences, England

Introduction: Acute hepatotoxicity represents a significant health problem and is associated with intense oxidative stress, inflammation, and metabolic alterations that can severely compromise liver function. In this context, natural compounds with antioxidant potential have been investigated as promising strategies for liver protection. **Objectives:** To evaluate the hepatoprotective effects of polysaccharides extracted from the peel of Passiflora edulis (passion fruit) in a model of acute hepatotoxicity induced by carbon tetrachloride (CCl4). **Methods:** Swiss male mice (n = 7/group) were treated orally for 21 days with saline solution (10 mL/kg; negative control) or polysaccharides extracted from the peel of P. edulis (Poli 200 mg/kg). At the end of the experimental period, hepatotoxicity was induced by intraperitoneal administration of CCl4 (0.1% in corn oil, 5 mL/kg). After 24 h of CCl4 administration, the animals were anesthetized, euthanized, and blood and liver samples were collected for biochemical, oxidative, inflammatory, and metabolomic analyses. Additionally, a naive group (n = 5) was included, which received neither treatment nor experimental induction. Data were expressed as mean ± SEM and analyzed by unpaired t test (or Mann-Whitney) and one-way ANOVA followed by Bonferroni's post hoc test, with $p < 0.05$ considered statistically significant. **Results:** Animals treated with Poli showed a significant reduction in relative liver weight ($p = 0.01$), as well as in serum markers of liver injury, ALT ($p = 0.02$) and AST ($p < 0.0001$), compared with the negative control group (CCl4). Furthermore, treatment significantly reduced levels of reactive oxygen species (ROS; $p = 0.04$), lipid peroxidation (LPO; $p = 0.03$), and IL-1β ($p = 0.03$), suggesting attenuation of oxidative stress and hepatic inflammatory response. Conversely, a significant increase in reduced glutathione (GSH; $p = 0.006$) and catalase (CAT; $p = 0.0015$) levels were observed in the treated group, indicating improved antioxidant capacity and possible hepatic functional recovery. No significant differences were observed for ALP, SOD, GST, IL-6, or TNF-α. Metabolomic analysis (Metaboanalyst® software) of mice plasma revealed a profile consistent with hepatoprotection, characterized by increased metabolites related to glutathione metabolism and antioxidant defense, including gamma-glutamyl, cystine, and serine, as well as reduced metabolites associated with oxidative stress, such as xanthine and oxidized lipid derivatives (FA 18:3+1O). From the 10 differential metabolites observed in the VIP score, only eicosenoic acid and inosine did not show significant differences. **Conclusion:** Taken together, these results suggest that polysaccharides from the P. edulis peel exert hepatoprotective effects associated with modulation of the redox state, reduction of lipid peroxidation, and hepatic metabolic reorganization. **Financial support:** CAPES, CNPq. Animal Research Ethical Committee Number: no. 1573.

14.020 **Effect of D-Limonene on the Attenuation of *Staphylococcus aureus* Virulence and Wound Healing in a *Tenebrio molitor* Model**. Pessoa DLR[1,2], Lima KKS[2], Torres LRD[2], Soares MS[2], Sousa MF[2], Arruda CS[2], Silva, EDM[2], Ferro TAF[2], Lima Neto LD[2], Mendes SJF[2]. [1]UFMA, Research and Graduate Lab in Pharmacology, Brazil. [2]CEUMA, Graduate Program in Applied Biosciences to Health, Brazil.

Introduction: *Staphylococcus aureus* is an opportunistic human pathogen with a high capacity to develop multi-resistance, being associated with severe skin infections and chronic wounds. Its pathogenicity is intensified by the production of biofilms and toxins, such as alpha-hemolysin (Hla), which causes tissue invasion and necrosis. D-limonene, a citrus monoterpene recognized as safe, exhibits antimicrobial and immunomodulatory potential, making it a promising candidate for alternative therapies against bacterial virulence. **Objectives:** To evaluate the impact of D-limonene on the growth, biofilm formation, and expression of virulence factors of *Staphylococcus aureus* , as well as to investigate its wound-healing effect *in vivo* in a skin infection model. **Methods:** The Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) were determined by microdilution. The biofilm biomass was quantified using crystal violet and its viability with the PrestoBlue reagent. The expression of the hla gene was analyzed via b-galactosidase assay (strain 8325-4 hla:lacZ). The hemolytic activity was tested on human erythrocytes. The *in vivo* model used Tenebrio molitor larvae (n=20/group) infected topically, monitoring survival, healing, and nitric oxide (NOx) production using the Griess assay. Statistical analyzes were performed using GraphPad Prism 5.0 software, employing two-way ANOVA followed by Tukey's test for mean comparison and the Kaplan-Meier method with the log-rank test for survival curves ($p < 0.05$). **Results:** D-limonene did not inhibit the growth or metabolism of the strains at the tested concentrations. In clinical isolates such as 0028 and 2111, there was an increase in the bacterial population by 94 ± 25% (5 mg/ml) and 158 ± 16.7% (10 mg/ml), respectively, with proportional increases in the metabolic rate. The biofilm formation in the ATCC 6538 strain was reduced by 70 ± 1.7% at 5 mg/ml, while the biomass of isolates 0028 and 2111 significantly increased by 217 ± 26% and 172 ± 27% at 10 mg/ml, respectively. The compound inhibited hemolytic activity in all strains in a dose-dependent manner and reduced hla expression by 92.5 ± 0.03% (at 5 mg/ml) and 71 ± 5.3% (at 10 mg/ml). In the *in vivo* model, topical treatment with 5 mg/ml promoted healing, with 70% of the larvae being wound-free on the third day. There was a 1.7-fold increase in NOx production in the infected larvae treated with 10 mg/ml compared to the infected control. **Conclusion:** D-limonene acts as an antivirulence agent by drastically inhibiting alpha-hemolysin and hla expression. Furthermore, it promotes the healing of infected wounds, an effect correlated with the positive modulation of nitric oxide production in the host.

14.021 **Establishment of a MASLD Mouse Model: Ultrasonographic, Biochemical, and Morphological Analysis**. Acco A[1], Leal LE[1], Longo-Filho A[2], Bejes HOC[1], Vilani JM[2], Ribeiro LS[1,3] [1]UFPR, Dept Pharmacology, Brazil; [2]UFPR, Veterinary Science Post Graduation Program, Brazil; [3]Unibrasil, Biomedicine course, Brazil

Introduction: MASLD (metabolic dysfunction-associated steatotic liver disease) is currently the leading cause of chronic liver disease worldwide. MASLD results from excessive lipid accumulation in the liver and may progress to advanced stages, such as cirrhosis and hepatocellular carcinoma. Despite its high incidence, treatment options remain limited, with no specific therapies targeting the liver condition itself. Therefore, establishing animal models for the investigation of new therapeutic approaches is essential. **Objectives:** The aim of this pilot study was to establish a MASLD model and characterize hepatic changes using ultrasonography, a non-invasive diagnostic method. In addition, we assessed whether these parameters differed between male and female mice. Biochemical and morphological parameters of the liver were also evaluated. **Methods:** Twelve C57BL/6 mice were used, including 6 males and 6 females, all maintained on a high-fat diet (HFD, 40% fat, Rhoster 19452) for 10 or 12 weeks, while Naïve groups (n=8 males and females) were maintained on regular chow. Body weight and food intake were measured three times per week. Throughout the study, three ultrasound (US) examinations were performed at weeks 4, 10, and 12 in animals under HFD. The procedures were conducted under sedation using a protocol adapted for rodents, aiming to evaluate hepatic and renal morphological parameters. After 10 weeks of dietary intervention, 3 animals of each sex were euthanized, and the remaining 6 animals continued the diet protocol until week 12. After euthanasia (inhaled isoflurane), liver, kidney, and blood samples were collected. Plasma was used for biochemical analysis. Data were analyzed using two-way ANOVA followed by Dunnett's test, or Student's t-test when applicable, using GraphPad Prism software, with $p<0.05$ considered statistically significant. **Results:** Ultrasonographic examinations did not reveal differences in liver size between male and female mice throughout the experimental period. Histological analysis, however, showed abundant lipid vesicles in the livers of HFD-fed mice of both sexes, confirming the presence of hepatic steatosis. Consistent with these findings, the livers of HFD-fed male and female mice had significantly lower weights than those of Naïve mice. There were no differences in HFD consumption or body weight gain between males and females. Likewise, plasma ALT and AST levels did not differ between the sexes at the end of the experiment. In contrast, alkaline phosphatase (ALP) activity was significantly higher in females than in males ($P = 0.0148$). **Conclusions:** The HFD successfully induced a murine MASLD model, with liver weight and histological analysis serving as reliable parameters for disease evaluation, whereas ultrasonography was not sufficiently sensitive to detect hepatic changes in this model. Overall, males and females exhibited comparable responses, with the exception of higher alkaline phosphatase (ALP) activity in females. These findings suggest that both sexes are suitable for use in future experimental studies of MASLD.

14. Scientific Methodology and Experimental Design in Biology

14.002FR **Involvement of Central Nitric Oxide in the Thermal Control of Rats During Physical Exercise**. Rocha LJ[1], Lopes RA[1], Noronha GL[1], Martins JA[1], Campos OC[2], Rodrigues QT[3], Silva KSC[3], Prímola-Gomes TN[4], Lacerda LT[1], Brandão CFCCM[1], Andrade MJO[5], Natali AJ[4], Szawka RE[3], Coimbra CC[3], Drummond LR[1] [1]UEMG, Dept Physical Education, Brazil; [2]UEMG, Dept Biological Sciences, Brazil; [3]UFMG, Dept Physiology and Biophysics, Brazil; [4]UFV, Dept Physical Education, Brazil; [5] UEMG, Dept Psychology, Brazil

Introduction: Running competitions are sporting events with a growing number of participants. In these situations, athletes experience significant thermoregulatory challenges. Animal models are widely used to study mechanisms related to fatigue and physical performance. **Objective:** To investigate the involvement of nitric oxide in thermoregulatory adjustments and performance during physical exercise in rats. **Methods:** The procedures were approved by the Ethics Committee on Animal Use of the Federal University of Minas Gerais (21/2015). Eight male Wistar rats (343,1 ± 8,3 g) at 16 weeks of age were used. The rats went through surgeries for the implantation of a chronic guide cannula in the right lateral cerebral ventricle and a temperature sensor in the abdominal cavity. After recovering from these surgeries, each animal was subjected to four exercise protocols at a constant speed at 60% of the maximum speed achieved in the incremental exercise until fatigue. On the day of the experiments, the rats were assigned to receive an intracerebroventricular injection of 2 µL of sodium nitroprusside (NPS) (2.1, 4.2, or 8.4 mmol) or saline solution. Tail skin temperature (Tskin) and abdominal temperature (Tabd) were recorded every minute during exercise. Data were analyzed using two-way repeated measures ANOVA and presented as means ± SEM (α=5%). **Results:** Intracerebroventricular injection of NPS at a dose of 8.4 mmol induced a greater increase in Tskin between minutes 13–16 and 26–29, as well as at fatigue (fatigue: 3.73 ± 0.27 °C vs. 2.46 ± 0.83 °C, $p < 0.05$), compared with the saline group. Consequently, it produced a smaller increase in Tabd between minutes 18 and 35 (min 35: 0.88 ± 0.22 °C vs. 1.66 ± 0.17 °C, $p < 0.05$). At the dose of 4.2 mmol, no difference in Tskin was observed between the NPS and saline groups (fatigue, 4.2 mmol: 3.25 ± 0.99 °C vs. saline: 2.46 ± 0.83 °C, $p > 0.05$). Likewise, the 2.1 mmol dose did not alter either Tskin (fatigue, 2.1 mmol: 2.93 ± 0.65 °C vs. saline: 2.46 ± 0.83 °C, $p > 0.05$) or Tabd (fatigue, 2.1 mmol: 2.28 ± 0.24 °C vs. saline: 2.22 ± 0.11 °C, $p > 0.05$) responses compared with the saline group. Intracerebroventricular injection of NPS did not alter exercise time (66.0 ± 6.8 vs. saline: 60.5 ± 6.7, $p > 0.05$), indicating no effect on physical performance ($p > 0.05$). **Conclusion:** Central injection of sodium nitroprusside increased heat dissipation, resulting in a smaller increase in abdominal temperature during exercise.

14.003FR **Discrimination of EMT-Associated Phenotypes in A549 Cells Using Raman Spectroscopy and Supervised Machine Learning**. Silva EC[1], Oliveira J[2], Figueiredo CG[1], Ferreira EGA[1], Souza ST[2], Ferro JNS[1] [1]ICBS-UFAL, Maceió, Alagoas, Brazil; [2]UFAL, Group of Optics and Nanoscopy (GON), Institute of Physics, Maceió, AL, Brazil

The epithelial–mesenchymal transition (EMT) is a finely regulated cellular mechanism triggered in response to cellular stress and is strongly associated with the development of several pathological conditions, including cancer, treatment resistance, and fibrosis. Pulmonary fibrosis, for instance, remains a condition with limited effective therapeutic options. Understanding the molecular and phenotypic alterations involved in this process remains a central challenge. In this study, we employed Raman spectroscopy combined with supervised machine learning algorithms (Principal Component Analysis–Linear Discriminant Analysis, PCA-LDA) to characterize and classify phenotypic transitions in A549 lung adenocarcinoma cells stimulated with TGF-β1 (fibrotic model) and IL-1β (inflammatory model), both relevant to EMT-associated pathways. The PCA-LDA model achieved an overall accuracy of 99.3% using leave- one-out cross-validation, demonstrating high sensitivity in detecting subtle biochemical alterations associated with cellular stress responses. Although exploratory PCA revealed that the major spectral variations were dominated by intrinsic cellular metabolism, the supervised approach successfully extracted treatment-specific molecular signatures. A significant increase in the 930 cm^{-1} band was identified as a global marker of cellular activation, reflecting cytoskeletal remodeling and vimentin-associated changes characteristic of EMT. Phenotypic distinction was further supported by specific spectral markers: the fibrotic phenotype (TGF-β1) showed an exclusive increase in the 1030 cm^{-1} band, associated with extracellular matrix synthesis and metabolic reprogramming, while the inflammatory phenotype (IL-1β) exhibited a significant reduction in the Amide I band (1660 cm^{-1}), consistent with protein degradation and oxidative stress. The alterations identified by PCA-LDA were corroborated by morphological, migratory, and vimentin expression changes, assessed through Giemsa staining, wound healing assay, and immunofluorescence analysis. Taken together, these results demonstrate that Raman spectroscopy combined with PCA-LDA constitutes a powerful, rapid, and label-free platform for identifying EMT-related phenotypic states, without the need for antibodies or additional reagents. This approach represents a promising strategy to advance the understanding of mechanisms underlying pathological conditions such as pulmonary fibrosis and to support the development of high-precision automated diagnostic tools for tumor microenvironment characterization.

14.004FR **Behavioral Characterization of Female Wistar Rats Subjected to D-Galactose-Induced Accelerated Aging**. Silva KRG[1], Pontual MMV[2], Lima RR[3], Aquino JS[4], Carvalho LRRA[4] [1]UFPB Course of Pharmacy, Health Sciences Center, João Pessoa, Brazil; [2]UNIPÊ, Course of Veterinary Medicine, Paraíba, Brazil; [3]UFPB, PPG in Gerontology, João Pessoa, Brazil; [4]UFPB, Experimental Nutrition Lab, João Pessoa, Brazil

Introduction: D-galactose (DGAL)-induced accelerated aging is a widely used experimental model associated with oxidative stress, chronic inflammation, and age-related functional decline. Although extensively characterized in male rodents, limited information is available regarding the behavioral effects of DGAL administration in females, despite known sex-related differences in aging biology and neurobehavioral responses. **Objectives:** To characterize the behavioral phenotype of female Wistar rats subjected to chronic DGAL administration and evaluate the suitability of this model for aging-related behavioral assessments in females. **Methods:** Female Wistar rats (10 weeks old) received D-galactose (200 mg/kg/day, subcutaneously) for eight weeks. At the end of the experimental period, animals were evaluated using a behavioral test battery consisting of the Open Field Test (OFT), Elevated Plus Maze (EPMT), Light-Dark Box Test (LDBT), and Sucrose Splash Test (SST). Behavioral tracking was performed using the EthoVision XT video-tracking system (Noldus Information Technology), while Splash Test parameters were scored manually. **Results:** In the OFT, DGAL-treated animals exhibited reduced total distance traveled, lower mean velocity, fewer zone transitions, and decreased time spent in the central area. In the EPMT, no significant differences were observed in the time spent in open or closed arms; however, DGAL-treated rats showed a lower frequency of head-dipping behavior, accompanied by reduced locomotor activity, as evidenced by lower distance traveled and velocity. In the LDBT, no significant differences were detected in the time spent in the light or dark compartments or in the number of transitions between compartments. Likewise, in the SST, no differences were observed in grooming duration, grooming frequency, or latency to the first grooming episode. **Conclusion:** Overall, DGAL administration induced a mild behavioral phenotype characterized primarily by reduced locomotor and exploratory activity, with limited effects on anxiety-like and depressive-like behaviors. These findings suggest that female rats exhibit only subtle behavioral alterations following chronic DGAL exposure, contrasting with the more pronounced phenotypes frequently reported in male rodents. The relative resistance of females to the development of a robust behavioral aging phenotype highlights the importance of sex as a biological variable in experimental aging research and suggests that DGAL-induced aging may be less pronounced in female rodents under the conditions evaluated.

14.005FR **Three-Dimensional Cold Porcelain Modeling as a Pedagogical Tool for Human Physiology Education**. Nóbrega VC, Cruz JC UFPB, Dept. of Biotechnology, PPG Physiological Sciences, Brazil

Understanding physiological processes requires the integration of different areas of knowledge, making learning complex and demanding active methodologies to address this challenge. However, Physiology is still frequently taught through traditional lecture-based approaches, which limit knowledge consolidation and the practical application of concepts. This study investigated the use of three-dimensional cold porcelain modeling as a pedagogical tool to enhance teaching and learning in Human Physiology through creativity and sensorimotor skills. A total of 48 undergraduate students enrolled in the Biotechnology program at the Federal University of Paraíba (UFPB), who were taking the Morphophysiology II course over three consecutive semesters, participated in the study. The project was approved by the Research Ethics Committee (CAAE: 91134025.5.0000.5188) and included interactive lectures on the use of art in physiology education and modeling techniques, theoretical content related to the respiratory or endocrine systems, a guided visit to the UFPB Museum of Morphological Sciences for immersion in the educational content, and, subsequently, the group-based construction of three- dimensional models over a two-week period. At the end of the activity, students presented their models, explaining the physiological mechanisms represented, and completed an evaluation questionnaire. Data were analyzed using descriptive statistics in GraphPad Prism 8 and presented as absolute and relative frequencies. Inferential statistical tests were not applied, as the objective of the study was to characterize students' perceptions regarding the use of three-dimensional cold porcelain modeling as an educational resource. Preliminary results indicated that, prior to the intervention, 62.5% of students considered their understanding of the subject to be good, while 75.1% perceived Physiology as a difficult discipline. After the experience, 93.8% reported that the methodology facilitated content comprehension; 97.9% stated that the guided museum visit contributed to their understanding of the topics addressed; 95.8% recognized that model construction enhanced learning; 95.8% highlighted the relationship between structure and function and the connection between theoretical concepts and real-world applications; 95.9% considered the experience to be an effective educational resource; and all participants reported that group work contributed to their learning. Furthermore, the models were used in science fairs and exhibitions, demonstrating accessibility and broad applicability beyond the university environment, as well as their potential to bridge academic knowledge and society. In conclusion, three- dimensional modeling promotes active learning and constitutes an effective educational resource in Human Physiology teaching, with educational benefits extending to both academic settings and outreach initiatives.

14.006FR **Evaluating Artificial Intelligence Tools for Bibliographic Surveys on Natural Product-Induced Immunogenic Cell Death**. Carneiro, IBS[1], Codellos, LL[2], Ladeia, LGF[3], Rodrigues, SIA[4], Wilke, DV[1] [1]UFC, PPG Pharmacology, Brazil. [2]UFC, Institute of Culture and Art, Brazil. [3]UNEB, Campus VI, Dept Human Sciences, Brazil. [4]UFC, Dept Biochemistry and Molecular Biology, Brazil.

Introduction: Cancer progression is associated with mechanisms that promote immune evasion and resistance to therapy. Immunogenic cell death (ICD) represents a promising strategy by combining tumor cell elimination with the activation of antitumor immunity through damage-associated molecular patterns (DAMPs). Natural products, particularly those from marine sources, have emerged as potential ICD inducers. Artificial intelligence (AI) tools may facilitate literature surveys, although concerns remain regarding reliability and hallucinations. **Objectives:** To develop an AI-assisted bibliographic research protocol for identifying natural product-induced ICD, evaluate the performance of different AI tools, and investigate the relevance of marine natural products in this field. **Methods:** Gemini 3.5, ChatGPT 5.5, and Microsoft Copilot were evaluated using a standardized prompt designed to retrieve open-access experimental studies on ICD induced by natural products published between 2021 and 2025. Searches were performed using unbiased accounts. Results were assessed according to article quantity, adherence to inclusion criteria, metadata accuracy, and hallucination occurrence. SciSpace, a specialized AI-based literature search platform, was used as a control group with access restricted to free resources. **Results:** SciSpace identified 51 publications, of which 18 met the established criteria. The remaining AI tools retrieved fewer studies but generally returned valid publications (15 articles for this research). ChatGPT showed the highest consistency and metadata accuracy, whereas Copilot presented occasional DOI and authorship errors. Gemini exhibited the highest incidence of hallucinations, including nonexistent articles. Altogether, 22 research articles were confirmed for the natural products. Identified compounds were classified as marine, plant- derived (curcumine, capsaicin, piceatannol, etc.), or fungal/bacterial/animal- derived products (narbomicine, violacein, etc.). The structured semantic search conducted using the selected software tool revealed that most frequently ICD-related mechanisms in these studies involved endoplasmic reticulum stress, reactive oxygen species generation, and cyclic GMP-AMP synthase/stimulator of interferon genes (cGAS/STING) signaling. Marine-derived compounds such as crassolide, lepadin A, chromomycin A5, MHO7, and MPM-1 emerged as promising ICD inducers. **Conclusion:** AI tools can support preliminary literature surveys when combined with critical human verification. While free versions may limit search comprehensiveness and accuracy, they remain useful for identifying relevant studies. Marine natural products constitute a promising and still underexplored source of ICD-inducing compounds with potential applications in cancer therapy. **Financial support**: CNPq 408549/2024-6, FAPESP 2025/27006-6, FUNCAP.

14.007FR **Validation of Experimental Streptozotocin-Induced Diabetes Mellitus Models in Rodents: Clinical, Biochemical, and Morphological Aspects**. Donato FF[1], Pires LAB[1], Sena VNF[1], Silva CPC[1], Vieira RR[2], Gil CD[2], Medeiros KCP[1] [1]UFRN, Lab. of Experimental Morphology, [2]Unifesp, PPG Structural and Functional Biology, Brazil

Introduction: Type 1 Diabetes mellitus (T1DM) is a chronic disease characterized by the absence of insulin synthesis due to the autoimmune destruction of pancreatic beta cells, leading to hyperglycemia and systemic impairment. This metabolic condition affects several organs, including the pancreas, causing morphofunctional alterations. Given its multifactorial etiological nature, the pathophysiology of T1DM is not yet fully elucidated, limiting pharmacological therapeutic possibilities. In this context, the study of experimental T1DM models is potentially useful for a better understanding of the disease pathophysiology and for evaluating possible therapeutic interventions based on these models. **Objective**: This study aimed to validate two experimental models induced by streptozotocin (STZ) in two types of rodents, rats and mice, based on morphometric analysis of the pancreas, as well as clinical and biochemical aspects. **Methods**: Forty male rodents were used, including 20 C57BL/6 mice and 20 Wistar rats, divided into four groups: CTR (rat control), DMR (diabetic rat), CTC (mouse control), and DMC (diabetic mouse). Mice received STZ (65 mg/kg i.p.) for 5 consecutive days, while rats received a single dose of STZ (50 mg/kg i.p.). The rodents were evaluated over an experimental period of 30 to 45 days. **Results**: Clinical results demonstrated increased water intake (polydipsia), increased food consumption (polyphagia), and weight loss in both diabetic groups (DMC and DMR) when compared to their respective controls (CTC and CTR). Hyperglycemia established at the beginning of the experiment was maintained throughout the experimental period (30–45 days), reaching 580 mg/dL in DMC and 420 mg/dL in DMR, compared with their respective control groups (CTC: 200 mg/dL and CTR: 100 mg/dL). Cholesterol levels remained elevated in the diabetic groups, with concentrations of 55 mg/dL in DMC and 75 mg/dL in DMR, while controls showed levels of 40 mg/dL. Triglyceridemia was also higher compared to controls, with concentrations of 175 mg/dL in DMC and 60 mg/dL in DMR. Control groups presented values of 50 mg/dL and 45 mg/dL for CTC and CTR, respectively. Regarding pancreatic morphology, representative islet atrophy was observed in both diabetic groups, in addition to the presence of a greater number of vacuoles within the islets in both groups (DMC and DMR). **Conclusion**: Thus, this study was able to validate two different in vivo models of STZ-induced Type 1 Diabetes mellitus in the rodent species most commonly used for experimentation, Wistar rats and C57BL/6 mice. Validation was confirmed through hyperglycemia, pancreatic islet atrophy and lesions, associated with classical metabolic alterations of T1DM, including polydipsia, polyphagia, and weight loss. This model will serve as a basis for future studies involving therapeutic interventions in experimental T1DM.

15. Neurobiology and Neuronal Diseases

15.001FR *in silico* **Evaluation of the Neuroprotective Potential of** *Alpinia zerumbet* **Extract Bioactive Compounds in Alzheimer's Disease**. Soares LN[1], Ferreira FS[1], Medeiros IV[2], Mattos JA[1], Nascimento JM[1], Dias KM[1], Lopes CFO[1], Caetano AC[1], Soares SCS[1], Dias CMN[1], Cunha MET[2], Ognibene DT[1], Costa CA[1], Resende AC[1] and Bem GF[1] [1]NFPM-UERJ, Research Line in Neuropharmacology and Medicinal Plants, PPG in Clinical and Experimental Pathophysiology (Fisclinex), Brazil, [2]UNINTA, Pharmacy Course, PPG in Health Sciences, Brazil

Introduction: Alzheimer's disease (AD) is a common neurodegenerative disorderand the main cause of dementia worldwide. It is marked by progressive memoryloss and cognitive decline. Since current treatments have key limitations, newtherapeutic strategies are needed. Medicinal plants are promising due to theirbioactive secondary metabolites, which have neuroprotective effects. Alpiniazerumbet is rich in phenolic compounds and flavonoids. These may act onmechanisms involved in AD. **Objective:** Investigate the pharmacologicalpotential of compounds in the hydroethanolic extract of Alpinia zerumbet (ALE)against AD using *in silico* approaches. **Methods:** ALE chromatographic analysiswas done using LC-DAD-MS. Extracted compounds were analyzed withbioinformatics platforms. Activity spectra were predicted to estimate thelikelihood of bioactivity. Toxicity was predicted using ProTox-II, which usedSMILES chemical structures to estimate toxicity and LD50. **Results:** The ALEextract LC-DAD-MS profile was suggestive of flavonoids, flavones, and phenoliccompounds, as previously described. These compounds were mainly trehalose,epicatechins, procyanidin B2, quercetin-3-O-glucuronide,kaempferol-3-O-glucoside, kaempferol-3-Glucoside-3" -rhamnoside, pinocembrin,and alpinetin. *in silico* analysis showed the investigated compounds havesignificant neuroprotective and anti-inflammatory potential, with lowpredicted toxicity. Several bioactive compounds, such as D-(+)-trehalose,epicatechin, procyanidin B2, quercetin-3-O-glucuronide, kaempferolderivatives, isorhamnetin-3-O-neohesperidoside, alpinetin, and pinocembrin,showed high probabilities for antioxidant, free radical scavenging, anti-inflammatory, and anti-dementia activities. Quercetin-3-O-glucuronide andisorhamnetin-3-O-neohesperidoside showed the highest free radical scavengingprobabilities (0.984 and 0.993, respectively). Epicatechin and procyanidin B2exhibited strong antioxidant potential. Toxicological predictions showed mostcompounds were classified as non-neurotoxic. Predicted LD50 values ranged from1.190 to 29.700 mg/kg, which mainly correspond to toxicity classes 4–6. Thissuggests low acute toxicity. Several compounds also demonstrated predictedblood–brain barrier permeability, including D-(+)-trehalose, epicatechin,procyanidin B2, quercetin-3-O-glucuronide, alpinetin, and pinocembrin. Thisreinforces their potential for central nervous system activity. **Conclusion:** Insummary, our results suggest that these phytochemicals may be promisingcandidates for treating neuroinflammation and neurodegenerative diseases, suchas Alzheimer's disease.

15.002FR **The Impact of Immersive Virtual Reality on Cortico-Muscular Coherence of Two Individuals with Parkinson's Disease, one with Essential Tremor and a Healthy Control – Case Study**. Flora JMG[1], Tourino FD[1], Rosa MVP[1], Silva GAB[1], Camargos MF[1], Brito FG[1], Fonseca LAS[1], Rodrigues IJS[1], Leite IHA[1], De Souza HLR[1], Brandão CFCCM[1], Andrade MJO[2], Drummond LR[1], Lacerda LT[1] [1]UEMG, Dept Physical Education, Brazil, [2]UEMG, Dept Psychology, Brazil

Introduction: The dopaminergic dysfunction present in Parkinson's Disease (PD), especially in those with freezing of gait (FoG), impairs motor processing and the functional coupling between motor cortex and muscles, resulting in reduced cortico-muscular coherence (CMC). It is well documented that resistance training (RT), cycling and immersive virtual reality (IVR) can improve motor processing. However, the possible synergistic effect of these interventions remains unexplored. **Objective**: To explore the effect of IVR on CMC in β-band during cyclergometer RT in 4 participants with different conditions: PD and FoG, PD (no FoG), essential tremor (no PD) and a healthy individual. **Methods**: In session 1, participants were characterized by age, FoG Questionnaire (FoG-Q), and Hoehn & Yahr (HY) scores. Maximum pedaling resistance (MPR) was determined via a 30 s test (15–20 km/h). Sessions 2 and 3 consisted of cyclergometer RT (CRT): 5 sets of 30 s at 80% MPR (15–20 km/h) with 30 s intervals, using a Tacx® magnetic roll for real-time speed tracking. IVR was integrated into either session 2 or 3, with 48h between sessions. During IVR, participants used a Meta headset to navigate a straight city avenue, while trying to avoid obstacles by moving the cyclergometer handlebar. Synchronized EEG and EMG data (OT Bioelettronica) were pre-processed with a 60 Hz notch filter and a 4th-order Butterworth band-pass filter. CMC in the β-band was calculated using Magnitude Squared Coherence between EEG-Cz and the EMG envelope (highest Root Mean Square), with 2 s windows and 50% overlap. Results are presented as area percentage above the analytical significance threshold (%SiT), defined as $CL=1-\alpha^{1/(N-1)}$ ($\alpha = 0,05$). **Results**: The participant with PD and FoG (male, 53 years; FoG-Q =19; HY = 3) achieved a %SiT = 12.0% (CRT only) and %SiT = 52.0% (CRT with IVR). The participant with only PD (male, 61 years; FoG-Q = 5; HY = 1), achieved a %SiT = 8.0% (CRT) and %SiT = 0.0% (CRT with IVR). The participant with essential tremor (male, 66 years; FoG-Q = 2; HY = 2), achieved a %SiT = 24.0% (CRT only) and %SiT = 6.0% (CRT with IVR). Finally, the healthy participant (female, 62 years; FoG-Q = 0; HY = 0), achieved a %SiT = 51.0% (CRT only) and %SiT = 35.0% (CRT with IVR). **Conclusion**: Combining IVR with CRT was associated with higher values of CMC in β-band for the participant with PD and FoG. However, in the other participants, the effect was the opposite, possibly due to a more complex motor task that shifts the coherence to higher frequency bands in subjects with more preserved capacity to modulate cortical activity. These results can be explained by alterations in cortical connectivity present in more severe PD cases, and suggests an enhanced neuromodulatory effect of combining IVR with CRT. Further studies are needed to evaluate if the findings of the present study can be extrapolated to general PD populations.

15.003FR **Impacts of an Enriched Environment on the Modulation of Oxidative Balance in the Hippocampus of Mice over 120 Days**. Santos KH[1,6,] Souza VL[1,2,3,] Ramos TL[3,4], Bezerra EFB[1,5], Fidelis DES[3,4], Fernandes MSS[3,4], Souto FO[3,4], Lagranha CJ[1] [1]CAV-UFPE, Lab General, Molecular and Exercise Biochemistry, [2]UFPE, Graduate Program in Neuropsychology and Behavioral Sciences, [3]UFPE, Keizo Asami Institute; [4]UFPE, Graduate Program in Biology Applied to Health, [5]UNIFACOL, Veterinary Medicine, [6]CAV-UFPE, Physical Education

Introduction: Brain aging is intrinsically linked to redox imbalances that compromise metabolic systems and the Central Nervous System (CNS). This study investigates how an enriched environment (EE) modulates the oxidative profilea nd its implications for hippocampal redox signaling. **Methods:** Female C57BL/6mice (21 days old) were assigned to: (1) Standard Environment (SE) or (2)Enriched Environment (EE). In the Enriched Environment, animals were stimulated to engage in physical activity through interaction with objects, ad libitum food access, increased social interaction, and a larger cage; through this diversification of stimuli, the animals received increased physical, cognitive, and social stimulation. Although the estrous cycle may introduce variability in enzymatic mechanisms, this study did not account for this factor; however, we assessed the Coefficient of Variation (CV) across several markers (carbonyls: 44–62%; GSSG: ~53–56%; GSH/GSSG: ~33–54%); further studies are needed for stronger conclusions. At 120 days, both hippocampal hemispheres were collected together with the dentate gyrus and subiculum, and oxidative markers were analyzed using Welch's t-test and the Mann-Whitney test ($p < 0.05$; CEUA-UFPE 0028/2024). **Results:** EE exposure significantly increased lipid peroxidation ($p < 0.0001$) but did not affect protein oxidation ($p = 0.8557$),indicating preserved protein integrity. Regarding antioxidant defenses, SOD activity and total thiol levels were significantly higher in the EE group ($p = 0.0163$ and $p = 0.0020$, respectively). No changes were observed in CAT, GST, orthe GSH/GSSG ratio ($p = 0.60$). **Conclusion:** The enriched environment triggers a beneficial adaptive response in the hippocampus. The elevation in lipid peroxidation, coupled with enhanced SOD activity and thiol levels without protein damage, suggests a hormetic mechanism. This adaptive signaling reinforces antioxidant defenses, promoting hippocampal resilience against age-related oxidative challenges. Acknowledgment: We also thank UFPE, CNPq, FACEPE and CAPES for providing scholarships. This study was financed in part by the CAPES - Finance Code 001. This study was partially funded by CNPq/INCT DOHaD(Proc #409165/2024-7).

15.004FR **Prevalence of symptoms of neuropsychiatric disorders in women exposed to domestic violence by an intimate partner**. Xavier MJS[3], Freitas GA[1,4], Silva GM[1,4], Souza BTBA[1,4], Azevedo ATF[1], Silva VFB[1], Cavalcante AM[1], Albuquerque SCSO[1], Santos MEB[1], Souto JJS[1,4], Abreu DFP[1], Oliveira ACGA[2], Santos NA[1,4] [1]UFPB, PPG Neurociência Cognitiva e Comportamento, [2]UNIPÊ, PPG Direito. Brasil, [3]UNINASSAU, Lab Percepção, Neurociências e Comportamento, [4]PPG Psicologia Social

Introduction: Domestic violence by intimate partners (DIP) constitutes a serious public health problem, considered a traumatic event and a chronic stressor. Victims of DIP may present a high prevalence of neuropsychiatric disorders. Objectives To analyze the prevalence of symptoms of neuropsychiatric disorders in women who are victims and non-victims of DIP. **Methods:** Thirty volunteers participated in the study, divided into a Study Group (SG, n = 15) and a Control Group (CG, n = 15), aged 24 to 54 years (M = 38.87; SD = 7.43 years). This was a non-probabilistic sampling. The Post-Traumatic Stress Disorder Checklist 5 (PTSC-5), the Life Events Checklist (LEC-5), and the Depression, Anxiety and Stress Scale (DASS-21) were used. The average time of exposure to violence was 11.03 years (SD = 8.82); most broke the cycle of violence (73.4%) between 2 months and 25 years (M = 3.93; SD = 6.39). Data analysis was performed using the Statistical Package for the Social Sciences (27) with a significance level of $p < 0.05$. **Results:** The Mann-Whitney U test indicated statistically significant differences between the groups for depression (U = 31,000; p = 0.003; r = -0.55), anxiety (U = 39,500; p = 0.002; r = -0.59), stress (U = 27,300; p = 0.002; r = -0.59), and Post-Traumatic Stress Disorder (PTSD) (U = 0.000; p = 0.001; r = -0.86). In the subgroup analysis of women exposed to VDPI, Spearman's correlation showed a positive correlation between PTSD and Depression (rho = 0.540; p = 0.04) with a moderate effect size; and between PTSD and Anxiety (rho = 0.722; p = 0.004) with a large effect size. PTSD and Stress (rho = 0.621; p = 0.01) with moderate effect size; Stress and Depression (rho = 0.640; p = 0.01) with moderate effect size; and Stress and Anxiety (rho = 0.783; p = 0.001) with large effect size. Positive correlations were also identified between the number of traumatic events and depression (rho = 0.526; p = 0.04); number of traumatic events and anxiety (rho = 0.821; p = 0.001); number of traumatic events and stress (rho = 0.595; p = 0.01); and number of traumatic events and PTSD (rho = 0.912; p = 0.001). **Conclusion:** Victims of violence presented a high prevalence of neuropsychiatric disorders, corroborating the research hypothesis and the literature. Violence against women (VDPI) not only generates immediate suffering but also establishes a stress-anxiety-depression cycle, making the psychological impact chronic and difficult to manage clinically. The findings may be related to amygdala hyperactivation, hypothalamic-pituitary-adrenal axis dysfunction, and reduced prefrontal cortex modulation of emotional responses. The results may support public health policies for victims of violence. This work was carried out with the support of the Coordination for the Improvement of Higher Education Personnel (CAPES). Research Ethics Committee number (CAAE 82068724.2.0000.5188).

15.005FR **Effects of Enriched Environment on the Hippocampal Oxidative Balance of Female Mice at 60 Days**. Mota IRFS[1,5], Souza VL[1,2,3], Ramos TL[3,4]; Bezerra EFB[1,5], Fidelis DES[3,4], Fernandes MSS[3,4], Souto FO[3,4], Lagranha [1]CAV-UFPE, Lab General, Molecular and Exercise Biochemistry, [2]UFPE, Graduate Program in Neuropsychology and Behavioral Sciences, [3]UFPE, Keizo Asami Institute; [4]UFPE, Graduate Program in Biology Applied to Health, [5]UNIFACOL, Veterinary Medicine, [6]CAV-UFPE, Physical Education

Introduction: The hippocampus is essential for memory and learning, but it presents a high vulnerability to REDOX imbalance. This study investigated the impact of an enriched environment (EE) on the modulation of oxidative balance in the hippocampus of 60-day-old female mice. **Methods:** Female C57BL/6 mice were maintained at 22°C ± 2 with Nuvilab CR1 feed and ad libitum water. At 21 days, they were distributed into: (1) Standard Environment (SE) (4-6/cage, 13×20×30 cm) and (2) EE with enrichment (6-10/cage, 18×34×41 cm), which provided physical and social stimuli. At 60 days, the animals were euthanized for hippocampal collection and analysis of oxidative markers using Welch's t-test and Mann-Whitney test ($p < 0.05$). CEUA-UFPE (0028/2024). **Results:** At 60 days, lipid peroxidation (MDA) was significantly elevated in the EE group (EE=0.887±0.089; SE=0.556±0.053; P<0.0126), whereas protein oxidation was significantly lower compared to SE (EE=97.980±4.402; SE=168.183±11.141; P<0.0008). Regarding antioxidant enzyme activity, SOD was higher in the EE group (EE=62.465±6.905; SE=34.229±6.608; P<0.0162) and GST activity was reduced (p=0.0109), while catalase (CAT) showed no significant differences (p>0.05). Finally, total thiol levels (sulfhydryls) were increased in the EE group (EE=0.01865±0.007021; SE=0.01293±0.005929; P<0.0001), with no significant changes observed in GSH levels (p>0.05). **Conclusion:** The enriched environment exerted adaptive neuroprotective effects at 60 days, preserving protein integrity and enhancing antioxidant defense via SOD and sulfhydryls. The increase in lipid peroxidation suggests an adaptive metabolic response compatible with the principle of hormesis. This indicates that EE exposure promotes hippocampal resilience through a controlled oxidative stimulus that triggers beneficial cellular adaptations, strengthening the brain's defense systems against potential stressors. **Acknowledgment**: The authors are thankful to FACEPE and CNPq for the financial support to acquire the equipment and reagents used in this work. We also thank UFPE, CNPq, FACEPE and CAPES for providing scholarships. This study was financed in part by the CAPES - Finance Code 001. This study was partially funded by CNPq/INCT DOHaD (Proc #409165/2024-7).

15.006FR **Association Between Screen Time and Sleep Quality in Children with Autism Spectrum Disorder: A Cross-Sectional Study**. Veloso CE, Drummond LR, Lopes RA, Augusto VG, Lima VVAF, Perina KCB UEMG-Divinópolis, Lab. of Experimental Exercise Physiology, PPG in Biosciences and Human Health, Brazil.

Introduction: The increasing exposure of children to digital screens has generated concerns due to its potential impacts on development and health, including sleep disorders. In children with Autism Spectrum Disorder (ASD), this relationship may be even more relevant due to characteristics such as sensory hypersensitivity, behavioral rigidity, and difficulties in organizing routines, factors associated with greater vulnerability to sleep disorders. Although studies point to an association between excessive screen use and poorer sleep quality in typically developing children, there is still a scarcity of research focused on the ASD population, especially in the Brazilian context. **Objective:** To evaluate the association between screen time and sleep quality in children with ASD, aged 2 to 12 years. **Methods:** This is an observational, cross-sectional, and quantitative study, conducted at an institution specializing in the care of children with ASD in Divinópolis, Minas Gerais. Participants were children with a prior diagnosis of ASD, aged 2 to 12 years, selected by convenience sampling. Their caregivers answered a sociodemographic questionnaire, including information on the routine use of electronic devices. Sleep quality was assessed using the Child Sleep Habits Questionnaire (CSHQ) and the Sleep Disorders Scale Child (SDSC). Data were analyzed using SPSS 23.0, with a significance level of 5%. The study was approved by the Research Ethics Committee of the State University of Minas Gerais (UEMG), Divinópolis Unit, under opinion number 6.656.662/2024. **Results:** Twenty-four children were evaluated, with a mean age of 6.79 ± 2.60 years, predominantly male (70.8%). Daily screen use was reported by 95.83% of the sample, with an average exposure of 3.41 ± 1.74 hours/day and predominant use at night (58.33%), with cell phones being the most used device (58.33%). The average score on the CSHQ was 56.33 ± 9.15 points, with 100% of the sample above the cutoff point for sleep disorders. On the SDSC, the average score was 56.50 ± 13.28, indicating sleep disorders in 95.83% of the sample, with a higher frequency of nocturnal hyperhidrosis (54.17%) and sleep-related breathing disorders (37.50%). No significant association was observed between screen time and sleep quality assessed by the CSHQ ($r = 0.038$; $p = 0.859$) and by the SDSC ($r = 0.042$; $p = 0.844$). **Conclusion:** High frequency of screen exposure and a high prevalence of sleep disorders were observed in children with ASD. However, there was no significant association between total screen time and sleep quality as assessed by the instruments used. Limitations include the use of a convenience sample, the cross-sectional design, and the use of instruments based on caregiver reports. Although no association was observed between screen time and sleep quality in this sample, studies with larger populations and objective measures may contribute to confirming these findings.

15.007FR **Functional Lateralization in the Posterior Insular Cortex Control of Conditioned Fear Responses in Rats**. Ferronato, MVS, Gomes-de-Souza, L, Reis-Silva, LL, Tavares, LRR, Crestani, CC FCFAr-Unesp, Lab Pharmacology, School of Pharmaceutical Sciences, São, Araraquara, Brazil.

Introduction: The insular cortex (IC) plays a key role in emotional regulation, and previous evidence suggests functional lateralization within this structure. However, the individual contribution of IC left and right hemispheres in fear- and anxiety-related behaviors remains poorly understood. **Objectives:** To investigate whether the regulation of fear- and anxiety-like behaviors by the posterior IC is lateralized, and whether interhemispheric interactions contribute to this process. **Methods:** Bilateral guide cannulae targeting the posterior IC were implanted via stereotaxic surgery (Protocol CEUA: 8809773336). Anxiety-like behaviors were assessed in the elevated plus maze (EPM) and open field (OF) tests following microinjections of vehicle, cobalt chloride [$CoCl_2$ (a reversible non-selective synaptic inhibitor)], or bicuculline (a GABAA receptor antagonist) into the left and/or right hemispheres of the posterior IC. Contextual fear conditioning (CFC) was subsequently performed, being the animals subjected to the same pharmacological treatments before the fear retrieval test. Fos expression in the IC following fear retrieval test was analyzed by immunohistochemistry in animals subjected to bicuculine treatment. **Results:** In the CFC test, inhibition of the left posterior IC with $CoCl_2$ significantly increased freezing behavior compared with the other groups ($F(3,30)=5.450$; $p=0.0041$). Conversely, activation of the right posterior IC via local treatment with bicuculline significantly reduced freezing behavior ($F(4,34)=7.692$;$p=0.0002$). This latter effect was completely abolished when bicuculline induced activation of the right hemisphere was combined with contralateral inhibition of the left hemisphere by local $CoCl_2$ microinjection ($p=0.0095$). No significant effects of the pharmacological treatments within the IC were observed in the EPM or OF tests. Immunohistochemical analysis revealed significant ipsilateral ($p<0.05$), but not contralateral ($p>0.05$), increase in the number of Fos-positive expression in animals subjected to unilateral treatment with bicuculine ($F(3,48)=5.407$;$p=0.0028$). **Conclusion:** These findings indicate a lateralized organization of the posterior IC control of contextual fear memory, with an inhibitory influence in expression of freezing behavior. Interhemispheric communication appears not essential for this modulation, while anxiety like behaviors remain unaffected. These findings highlight a specific and coordinated role of the posterior IC in fear-related processing.

15.008FR **Ventral Hippocampus Differentially Modulates Recruitment of Brainstem Catecholaminergic Cells During Acute and Chronic Restraint Stress**. Giatti LO[1,2], Crestani CC[1,2], Dunn T[2], Moore C[2], Packard BA[2], Chambers JB[2], Oliveira LA[1,2], Busnardo C[1,2], Herman JP[2,3] [1]FCFAr-Unesp-Araraquara, Lab Pharmacology, Araraquara, São Paulo, Brazil; [2]University of Cincinnati Dept Pharmacology, Physiology and Neurobiology; School of Medicine, Cincinnati, OH, USA; [3]Cincinnati VA Medical Center, Cincinnati, OH, USA

Introduction: The ventral hippocampus (vHip) modulates autonomic and neuroendocrine stress responses through polysynaptic pathways. Brainstem catecholaminergic nuclei, including the nucleus of the solitary tract (NTS) and rostral ventrolateral medulla (RVLM) in the medulla, participate in stress responses. However, it is not completely understood the regulation of medullary catecholaminergic centers by vHip during chronic stress. **Objectives:** To determine whether chemogenetic inhibition of glutamatergic neurons in the vHip modulates recruitment of catecholaminergic cells in the NTS and RVLM during acute and chronic restraint stress. **Methods:** Adult male and female Wistar rats received bilateral injections of inhibitory (hM4Di) or control (EGFP) viral vectors into the vHip and were exposed to acute or chronic (21-day) restraint stress. Twenty-four hours later, brains were processed for dual ΔFosB/TH immunofluorescence. Single- and double-labeled cells were quantified in the RVLM and NTS. Acute and chronic datasets were analyzed separately using two-way ANOVA (sex×DREADD), followed by Tukey's post hoc test. **Results:** Chemogenetic inhibition successfully silenced neurons within the vHip. During acute restraint stress, vHip inhibition increased ΔFosB/TH colocalization in the RVLM of males ($p=0.001$), whereas NTS ΔFosB/TH colocalization increased in both sexes ($p=0.05$). After chronic restraint stress, ΔFosB/TH colocalization in the RVLM was too sparse for statistical analysis. However, single-labeled TH+ cells increased in Gi-DREADD animals ($p=0.02$), whereas control males exhibited more single-labeled TH+ cells than control females ($p=0.05$). In the NTS, vHip inhibition increased ΔFosB/TH colocalization in both sexes ($p=0.0001$), whereas control females exhibited greater ΔFosB/TH colocalization than control males ($p=0.001$). Additionally, single-labeled TH+ cells increased in Gi-DREADD males ($p=0.0006$), whereas control females exhibited more single-labeled TH+ cells than control males ($p=0.002$). **Conclusion:** The vHip modulates recruitment of catecholaminergic cells within the RVLM and NTS during acute and repeated restraint stress in a nucleus- and sex-specific manner. Taken together, these findings support a role for the vHip in regulating brainstem catecholaminergic activation during both acute and chronic stress.

15.009FR **Central Irisin Administration Modulates Hypothalamic Energy Balance Pathways in Mice**. Bem KCP, Talpo TC, Nogueira GAS, Oliveira KM, Silva-Junior JA,Velloso LA, Barbosa HCL Unicamp, Obesity and Comorbidities Research Center (OCRC), Brazil

Introduction: Irisin is a myokine associated with the metabolic benefits of physical exercise and has been implicated in the regulation of energy homeostasis. Although irisin may exert central effects, its mechanisms of action within hypothalamic circuits involved in feeding behavior and metabolism remain poorly understood. **Objectives:** To investigate the effects of central irisin administration on metabolic parameters and hypothalamic transcriptional responses in adult mice. **Methods:** Nineteen-week-old male C57BL/6 mice maintained on a chow diet received intracerebroventricular (ICV) injections of irisin (7.5 µg/day) or saline for 7 days after stereotaxic cannulation. Food intake, body weight, adipose and muscle tissue mass were evaluated (n= 8/group). Hypothalamic transcriptomic profiling was performed by RNA sequencing (n = 4/group) followed by standard bioinformatic analysis. Additional quantitative PCR analysis was performed to evaluate genes related to irisin signaling and metabolic regulation (n= 8/group). For RNA-seq data, genes with adjusted $P < 0.05$ and $|log2FoldChange| > 0.8$ were considered differentially expressed. Data were analyzed using the Shapiro-Wilk test followed by Student t-test or Mann-Whitney U test ($P < 0.05$). **Results:** Irisin- treated mice exhibited a transient reduction in food intake during the first days of treatment ($P = 0.03$), without significant changes in body weight. Central irisin administration reduced epididymal white adipose tissue mass ($P = 0.02$), whereas skeletal muscle weights remained unchanged. Hypothalamic RNA- seq analysis detected 14,544 expressed genes and revealed extensive transcriptional remodeling in response to irisin treatment. Functional enrichment analyses identified pathways associated with signal transduction, neuroactive ligand-receptor interactions, glutamatergic synapses, and cAMP signaling. Among the most significantly regulated genes, transcripts involved in neuronal signaling and energy balance were identified. Specifically, the anorexigenic neuropeptide Pomc was upregulated, whereas Gabrd, encoding the delta subunit of the GABAA receptor, was downregulated, consistent with the transient reduction in food intake observed in irisin-treated mice. Complementary qPCR analyses further demonstrated reduced expression of Fndc5 (the irisin precursor; $P = 0.01$) and Pgc1a (its transcriptional coactivator; $P = 0.03$), together with increased expression of the glucose transporter Glut1 ($P = 0.01$). **Conclusion:** Central irisin administration modulates hypothalamic transcriptional programs associated with energy balance and metabolic regulation, promoting a localized reduction in adiposity and a transient decrease in food intake. These findings support a role for irisin in the central control of metabolism and reinforce its potential as a therapeutic target for metabolic disorders. Animal Ethics Committee Approval: CEUA/UNICAMP protocol n° 6818-1/20. **Financial support:** FAPESP n° 2021/01448-1 .

15.010FR **Behavioral and Nociceptive Changes Induced by Persistent Neuropathic Pain in Male and Female Rats**. Tavares LRR, Silva LLR, Ferronato MVS, Silva KS, Marinho JAN, Santos LO, Crestani CC FCFAr-Unesp, Lab Pharmacology, Araraquara, SP, Brazil

Introduction: Chronic neuropathic pain extends beyond nociceptive dysfunction and has been increasingly recognized as a sustained stressor capable of affecting behavioral, autonomic, and endocrine systems. Persistent nociceptive input may promote multisystem physiological adaptations, contributing to altered homeostasis and allostatic load. However, sex-dependent integrated responses to chronic pain remain incompletely understood. **Objectives:** To investigate whether persistent neuropathic pain induces sex-dependent behavioral and nociceptive adaptations in rats, supporting the concept of chronic pain as a multisystem stressor. **Methods:** Male and female rats underwent baseline nociceptive assessment using the electronic von Frey test and Rat Grimace Scale (RGS), followed by chronic constriction injury (CCI) of the sciatic nerve or SHAM surgery. Fourteen days after surgery, anxiety-like and exploratory behaviors were assessed using the elevated plus maze (EPM) and open field (OF) tests. Nociceptive responses were then reassessed, followed by nest-building evaluation to investigate motivated behavioral adaptation under persistent pain conditions. **Results:** CCI significantly reduced paw withdrawal thresholds in the ipsilateral paw in both sexes, as indicated by significant effects of condition [$F(1,40)=30.508$, $p<0.0001$], time [$F(1,40)=61.358$, $p<0.0001$], and time×condition interaction [$F(1,40)=73.040$, $p<0.0001$]. In the contralateral paw, CCI produced a more restricted effect, with a significant time×condition interaction [$F(1,40)=8.327$, $p=0.0063$], and post hoc analysis showed reduced thresholds in male CCI rats compared with male SHAM rats ($p=0.0213$), whereas no contralateral hypersensitivity was observed in females. In parallel, CCI increased RGS scores in both sexes, confirming sustained spontaneous pain behavior [condition effect: $F(1,40)=108.613$, $p<0.0001$], but females displayed greater affective expression of ongoing pain. In the EPM, CCI animals of both sexes exhibited anxiety-like behavior, reflected by reduced open-arm exploration, including a lower percentage of open-arm entries [$F(1,40)=16.37$, $p=0.0002$] and reduced time spent in the open arms [$F(1,40)=8.84$, $p=0.0050$]. In the OF test, CCI animals exhibited reduced exploratory and increased anxiety-like behavior, characterized by decreased time spent in the center [$F(1,40)=31.07$, $p<0.0001$], reduced total locomotion [$F(1,40)=35.10$, $p=0.0001$], and lower center locomotion. Nest-building behavior was also impaired by chronic pain, with CCI animals showing reduced nest quality [condition effect: $F(1,40)=94.38$, $p<0.0001$], indicating disruption of motivated and adaptive behavioral organization; an effect more intensely observed in females. **Conclusion:** These findings demonstrate that persistent neuropathic pain extends beyond sensory dysfunction, disrupting affective, anxiety-like, exploratory, and motivated behavioral domains in a sex-dependent manner. Together, these results reinforce the concept of chronic pain as a sustained stressor capable of reshaping behavioral adaptation under prolonged nociceptive burden.

15.011FR **Functional Lateralization of the Medial Prefrontal Cortex Reveals Distinct Contributions of CRF1 and CRF2 Receptors of Cardiovascular and Behavioral Responses to Conditioned Fear in Rats**. Gomes-de-Souza L, Busnardo C, Giatti LO, Ferronato MVS, Tavares LR, Crestani CC. FCFAr-Unesp, Lab Pharmacology, Araraquara, SP, Brazil.

Introduction: The medial prefrontal cortex (mPFC) is involved in the expression of conditioned responses, and recent findings of our group indicate that this control is lateralized. However, the local neurochemical mechanisms involved in control by the mPFC of conditioned responses is not completely understood. In this sense, local corticotropin-releasing factor (CRF) neurotransmission has been reported as an important local neurochemical mechanism involved in mPFC control of stress responses. However, a role of local CRF neurotransmission in lateralized control of conditioned responses by the mPFC has never been documented. **Objective:** To investigate the role of local CRF neurotransmission in the mPFC in controlling cardiovascular and behavioral responses to contextual fear conditioning, and whether this control is lateralized. **Methods:** Male Wistar rats had cannula-guide implanted either bilaterally or into the right or left hemispheres of the mPFC. For the conditioning, each animal was placed individually in the conditioning chamber and received six shocks (1,5mA/3s). Twenty-four hours after the conditioning session, the animals were submitted to femoral artery cannulation surgery for cardiovascular recording. The fear retrieval test was performed 48 hours after the conditioning session. Independent set of animals received microinjections into either the left, right or both hemispheres (bilateral) of the mPFC of vehicle (saline, 100nL), the selective CRF1 receptor antagonist CP356395 (5nmol/100nL) or the selective CRF2 receptor antagonist antisalvagine-30 (5nmol/100nL) 10 min before the fear retrieval test. **Results:** Antagonism of CRF2 receptor unilaterally into the left hemisphere ($F(2,14)=17.9$; $p=0.0001$) of the mPFC increased the expression of freezing behavior during re-exposure to the aversively conditioned context, whereas antagonism of this receptor in either the right ($F(2,12)=9.9$, $p=0.0028$) or left ($p=0.0285$) hemispheres reduced the tachycardic response. Treatment with CP376395 in the left hemisphere reduced the tachycardiac response ($p=0.0453$). **Conclusions:** These results provide further evidence for hemispheric specialization in mPFC control of conditioned responses, highlighting CRF signaling as a key neurochemical mechanism underlying this lateralized regulation. Our findings also indicate a dissociation between the neural control of behavioral and cardiovascular responses during contextual fear retrieval by mPFC CRF neurotransmission.

15.012FR **Prebiotics Enhance GPR43 and GPR109A Expression and Protect Against Hypothalamic Neuroinflammation in High-Fat Diet-Fed Mice**. Paiva IHR[1], da Silva RS[2], Peixoto CA[1] [1]IAM/Fiocruz - Lab Ultraestrutura, PPG em Biociências e Biotecnologia em Saúde, Brasil, [2]UFPE - PPG em em Ciências Biológicas, Brasil

Introduction: Obesity is associated with adipose tissue dysfunction, metabolic inflammation, gut microbiota dysbiosis, and hypothalamic neuroinflammation. High-fat diet (HFD) consumption promotes activation of inflammatory pathways, including TLR4/NF-κB signaling, contributing to insulin resistance and disruption of energy homeostasis. Short-chain fatty acids (SCFAs), such as acetate and butyrate, exert anti-inflammatory effects through receptors including GPR43 and GPR109A. However, the contribution of these receptors to the beneficial effects of prebiotics during obesity remains poorly understood. **Objectives:** To investigate whether fructooligosaccharide (FOS) and galactooligosaccharide (GOS) supplementation modulate GPR43 and GPR109A expression and attenuates hypothalamic neuroinflammation in mice with diet-induced obesity. **Methods:** Male C57BL/6 mice were fed either a standard diet (Control; n = 15) or a high-fat diet (HFD; n = 30) for 18 weeks. After obesity induction, HFD-fed animals were randomized into HFD and HFD+FOS/GOS groups (n = 15/group). FOS (0.3 g/animal/day) and GOS (0.4 g/animal/day) were administered in drinking water during the final six weeks of the protocol. Metabolic, biochemical, and inflammatory parameters were evaluated. Hypothalamic and epididymal white adipose tissue samples were analyzed by immunohistochemistry, immunofluorescence, and western blotting. Acetate and butyrate concentrations were quantified using commercial assay kits. Data were analyzed by one-way ANOVA followed by Tukey or Holm–Sidak post hoc tests. **Results:** FOS/GOS supplementation reduced body weight gain, waist circumference, food intake, and caloric intake in obese mice. Treatment improved glucose homeostasis, insulin resistance, serum lipid profile, and circulating inflammatory markers. In epididymal adipose tissue, prebiotics reduced inflammatory mediators and improved the expression of proteins involved in lipid metabolism and SCFA signaling. In the hypothalamus, FOS/GOS attenuated TLR4/NF-κB signaling, reduced TNF-α immunoreactivity, increased NeuN and pCREB expression, improved insulin signaling, and increased acetate and butyrate levels. Furthermore, prebiotic supplementation upregulated GPR43 and GPR109A expression compared with untreated HFD-fed animals. **Conclusion:** These findings demonstrate that prebiotic supplementation attenuates obesity-associated neuroinflammation and support the modulation of the microbiota–gut–brain axis as a promising therapeutic strategy for obesity. **Financial support** This work was supported by the Program-Instituto Aggeu Magalhães (IAM- PROEP#400208/2019-9), the Knowledge Generation Program of the Fundação Oswaldo Cruz (FIOCRUZ; #VPPCB-007-FIO-18-2-17), the National Council for Scientific and Technological Development (CNPq; #301891/2022-2), and the Pernambuco Science Support Foundation (FACEPE; BFP-0434-2.10/24). **Animal Research Ethical Committee Number:** All animal procedures were approved by the Animal Ethics Committee of the Aggeu Magalhães Institute (CEUA/IAM-FIOCRUZ), protocol number 190/2023.

15.013FR **Chemogenetic Activation of the Prelimbic–Infralimbic Circuitry Alleviates Dysfunction in Conditioned Fear Processing Following Traumatic Stress in Rats**. Crestani CC[1,], Ragonesi LM[1,] Dunn T[1,] Glorius A[1], Giatti LO[1,], Chambers J[1,] Packard B[1], Oliveira LA[1,], Herman JP[1] [1]University of Cincinnati; Dept Pharmacology, Physiology and Neurobiology; School of Medicine, Cincinnati, OH, USA; [2]FCFAr-Unesp, Lab Pharmacology, Araraquara, São Paulo, Brazil

Introduction: Preclinical studies show that traumatic stress, such as single prolonged stress (SPS), leads to hypofunction in the prefrontal cortex, particularly in the infralimbic (IL) region. Despite this piece of evidence, the underlying circuit mechanisms related remain unclear. Within the medial prefrontal cortex (mPFC), pyramidal neurons in the prelimbic (PL) cortex project to the IL, forming a microcircuit involved in fear processing. **Objectives:** We investigated whether activation of the PL→IL pathway is sufficient to reverse SPS-evoked deficits in fear memory processing. We also evaluated the effects of SPS and PL→IL circuit activation on corticosterone responses to acute stress. **Methods:** Using an intersectional DREADD (Designer Receptors Exclusively Activated by Designer Drugs) approach, we selectively activated IL-projecting PL neurons. Ten days after SPS exposure, animals underwent auditory fear conditioning, extinction, and reinstatement. Corticosterone response to an acute footshock was measured three days after the **Conclusion:** of these procedures. **Results:** SPS increased freezing during extinction (P=0.0176), consistent with impaired fear extinction. Notably, activation of the PL→IL circuit abolished this deficit (P=0.0007). Chemogenetic activation of the mPFC microcircuit also reduced cued fear retrieval in SPS-exposed animals (P=0.0321), and attenuated fear reinstatement (P=0.0386)—the latter effect occurring regardless of SPS history. SPS also blunted corticosterone responses to footshock (P=0.0297), but this endocrine effect was not reversed by PL→IL activation (P=0.0805). Nevertheless, circuit activation reduced corticosterone response to footshock in control animals (P=0.0435). **Conclusion:** These findings indicate that selective activation of IL-projecting PL neurons rescues trauma-induced impairments in fear extinction, likely by restoring disrupted mPFC circuitry. This effect appears specific to fear-related processes and does not extend to trauma-induced alterations in hypothalamic–pituitary–adrenal (HPA) axis reactivity.

16. Toxinology, Natural Products and Medicinal Chemistry

16.001FR **Development and Characterization of Starch Films Containing Red Propolis**. Sousa JCR[1], Souza SM[2], Guilherme ACS[2], Almeida JBC[2], Silva AP[2], Cardoso JC[2], Souza SO[1], Lima CM[1] [1]UFS-Lagarto. 2Universidade Tiradentes, Aracaju/Sergipe.

Introduction: Propolis is a heterogeneous mixture of varying color and consistency, formed by resinous and balsamic materials. Red propolis exhibits therapeutic actions, including antibacterial, anti-inflammatory, antioxidant, wound-healing, and antitumor effects. Propolis is available on the market in conventional pharmaceutical forms such as solutions, capsules, creams, and ointments; however, new products can be developed. **Objective:** The objective of the research was to develop starch films containing red propolis. Experimental: Propolis was subjected to ultrasonic extraction, dried, and analyzed for quercetin content. The starch film was prepared with 1 mg of red propolis for every 1.5 cm of film. The film was subjected to macroscopic evaluation, thermal characterization, and analysis of mechanical properties. **Results and Discussion**: The quantitative evaluation of the quercetin content obtained from the red propolis sample was 14.82 ± 1.00 µg/mL, which corresponds to 2.8% of the analyzed sample. The starch films and starch films with propolis showed satisfactory macroscopic characteristics. The thermal analysis data demonstrated that the starch film with propolis (SFP) exhibited four degradation stages: the first phase occurred between 29–265°C, with a mass loss (Δm1) of 10.74%; the second phase occurred in the temperature range of 265–323°C, with a mass loss of 35.69%; the third phase occurred between 323–368°C, with a mass loss of 31.78%; and the fourth phase occurred between 367–900°C, with a mass loss of 20.84%. The incorporation of red propolis into the film did not alter the decomposition profile of the films. The films containing propolis showed greater physical resistance. **Conclusion:** It is concluded that the red propolis meets the specifications recommended by current legislation, and the films showed adequate physicochemical characterization, suggesting that the propolis was compatible with starch.

**Keywords: **Red propolis, starch films, thermal and mechanical properties.

16.002FR **Investigation of the Lipid Composition of** *Cucumis anguria* **L. by Gas Chromatography–Mass Spectrometry (GC–MS)**. Jorge SAS, Lima SG, Brito LL, Sousa YRF, Silva Neta ER, Rocha MS. UFPI, Organic Geochemistry Lab, Brazil.

Introduction: *Cucumis anguria* L. (gherkin) is a vegetable widely consumed in Brazil and belongs to the Cucurbitaceae family, a group recognized for the presence of bioactive compounds with nutritional and pharmacological potential. Among these constituents, fatty acids play a fundamental role in maintaining biological functions, energy metabolism, and the oxidative stability of foods. Despite the importance of this species, studies on the composition of its saponifiable fraction remain limited (Silva; Clerici, Food Science and Technology, v. 45, 2025). **Objective:** To qualitatively characterize the fatty acids present in the saponifiable fraction of *Cucumis anguria* L. **Methods:** Fruits of *C. anguria* were collected, sliced, and lyophilized to remove moisture and preserve their chemical constituents. The lyophilized material was subjected to hexane extraction to obtain the lipid extract. The saponifiable fraction was obtained through transesterification according to a methodology adapted from Hartman and Lago (1973), producing fatty acid methyl esters (FAMEs). Samples were analyzed by gas chromatography coupled with mass spectrometry (GC–MS), allowing the identification of constituents based on mass spectra and retention indices. **Results:** The saponifiable fraction showed a yield of 78.4%, and 11 fatty acids were identified. A predominance of saturated fatty acids (84.68%) was observed, with palmitic acid (59.70%) as the major component, followed by stearic acid (11.77%), behenic acid (5.35%), lignoceric acid (4.36%), eicosanoic acid (1.79%), tricosanoic acid (0.95%), and myristic acid (0.76%). Unsaturated fatty acids accounted for 15.32% of the total composition and were mainly represented by oleic acid (9.37%), cis- vaccenic acid (2.78%), palmitoleic acid (2.32%), and linoleic acid (0.85%). The high proportion of saturated fatty acids suggests greater oxidative stability of the extract, a desirable characteristic for industrial applications. On the other hand, the presence of oleic and linoleic acids adds biological value to the sample, as these compounds are associated with cardiovascular health and the modulation of metabolic processes (Siddiqui et al., Pakistan Journal of Pharmaceutical Sciences, v. 38, p. 2238, 2025). **Conclusion:** The saponifiable fraction of *Cucumis anguria* L. exhibited a lipid profile characterized by the predominance of saturated fatty acids, especially palmitic acid, along with lower proportions of nutritionally important unsaturated fatty acids. These results contribute to the chemical knowledge of this species and indicate its potential for applications in the food, pharmaceutical, and biotechnological fields. **Acknowledgments:** The authors thank UFPI, the Organic Geochemistry Laboratory, Prof. Dr. Sidney Gonçalo de Lima, and M.Sc. Leonne Lopes Brito for their support in the development of this research.

16.003FR **Antinociceptive Effect of *Libidibia ferrea* Barks Polysaccharide-Based Orabase in a Rat Model of Traumatic Lesions of the Buccal Mucosa**. Anjos CJF[1], Araújo AM[2], Oliveira LPP[1], Maciel FMS3, Gadelha CJMU[2], Fonseca SGC[4], Assreuy AMS5, Mota MRL[2], Pereira MG[1] [1]UECE/ISCB, Hemostasis and Thrombosis Lab, PPG in Physiological Sciences, Brazil. [2]UFC, Oral Pathology Lab, PPG in Dentistry, Brazil. [3]UECE/FECLESC, Bioactive Polysaccharides Lab, Brazil. [4]UFC, Pharmaceutical Technology Lab, Brazil. 5UECE/ISCB, Lab Physiopharmacology of Inflammation, Graduate Program in Physiological Sciences, Brazil.

Introduction: Traumatic ulcers of the buccal mucosa are prevalent lesions associated with intense pain. Topical corticosteroids such as triamcinolone acetonide are the most prescribed pharmacological treatment, but may cause systemic adverse effects after prolonged use (e.g., adrenal suppression, peptic ulcer activation). *Libidibia ferrea* (Mart. ex Tul.), known as "Jucá", is widely distributed in the Brazilian Northeast and listed in the Brazilian RENISUS. Its bioactive polysaccharides, obtained from the bark, exhibit antithrombotic, anti-inflammatory, antinociceptive, and wound-healing properties in skin wounds of normoglycemic and diabetic rats. **Objectives:** To formulate an orabase containing the polysaccharidic extract of L. ferrea (PELf) and to evaluate its antinociceptive effect and systemic tolerability in traumatic ulcers of the buccal mucosa in rats. **Methods:** PELf was obtained from stem barks by methanolic and alkaline extraction, ethanol precipitation, dialysis and lyophilization (11.2% yield; 25.6% total carbohydrates, including 3.6% uronic acid; 12.8% total proteins; 1.64% polyphenols). The mucoadhesive orabase containing 10% PELf (Orabase-PELf) was formulated with anhydrous lanolin, polyethylene gel with petrolatum, citric pectin, sodium carmellose and gelatin; and the pH was checked before and after the experimental protocol. Female Wistar rats (200-250 g) were anesthetized (ketamine 80 mg/kg + xylazine 10 mg/kg, i.p.) and the traumatic ulcer was induced in the left buccal mucosa with a punch (6×2 mm). Animals received topical treatment (5 mg/kg, twice daily) for 14 days with Orabase-PELf, vehicle or Omcilon® (1 mg/g). Nociceptive threshold was measured using a digital analgesimeter at days: 1-D1, 3-D3, 5-D5, 7-D7, and 14-D14. Body weight (daily), and hematological and systemic markers of renal and hepatic function were assessed at D14. Mean ± SEM (n=6/group), analyzed by two-way ANOVA and Tukey's post-hoc test or multiple t tests; $p<0.05$. **Results:** The treatment with Orabase-PELf, showing acidic pH (D1: 5.34 and D14: 5.84), and with Omcilon® increased the nociceptive threshold compared to vehicle: Orabase-PELf at D1 (131.7 vs. 23.33 g), D3 (117.0 vs. 48.97 g), D5 (99.7 vs. 39.72 g) and D7 (74.08 vs. 35.56 g); Omcilon® at D1 (82.3 vs. 23.33 g), D3 (79.2 vs. 48.97 g) and D7 (68.83 vs. 35.56 g). However, Orabase-PELf showed higher nociceptive threshold compared to Omcilon®: D1 (131.7 vs. 82.3 g), D3 (117.0 vs. 79.2 g), D5 (99.7 vs. 56.9 g). Orabase-PELf promoted body weight gain of 7.2% (D0: 220 ± 22.35; D14: 235.8 ± 28.08 g), whereas Omcilon® induced weight loss of 7.8% (D0: 214.1 ± 13.04 g; D14: 197.5 ± 9.35 g). Orabase-PELf was well tolerated by animals, as indicated by the hematological and biochemical parameters analyzed. **Conclusion:** Orabase-PELf applied to rat buccal mucosa ulceration showed high tolerability by the animals and presents an antinociceptive effect, supporting its therapeutic potential for painful oral lesions. **Acknowledgments:** FUNCAP; CNPq. Ethics: CEUA-UECE, NUP 31032.004588/2025-93. **Financial support:** COGEFIT/FUNCAP - POBIMOP (nº 31032.003403/2024-42); IC BIT/FUNCAP; IC PIBIC/CNPq.

16.004FR **Cashew Nut Oil** (*Anacardium occidentale* **L.**) **as a Potential Anxiolytic-Like and GABAergic Neuromodulador in Zebrafish** (*Danio rerio*). Freire GA[1], Freitas YJS[2], Menezes JESA[2], Maciel JB[2], Santos HS[2], Martins CBR[1], Xavier Filho RRB[2], Canuto MJSF[1] [1]UFC, Lab Biochemistry and Pharmacology, Graduate Program in Pharmacology, Fortaleza, Ceará, Brazil; [2]UECE, Lab Chemical-Pharmacological and Environmental Bioassays, PPG in Natural Sciences, Fortaleza, Ceará, Brazil.

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Introduction: Zebrafish (Danio rerio) have been widely used as an experimental model for investigating compounds capable of modulating neurotransmission and behavior. This species shares important genetic and neurochemical similarities with mammals, including the GABAergic system, allowing the assessment of toxicity, behavioral responses, and mechanisms of action of novel bioative compounds. Cashew nut oil has demonstrated anti-inflammatory, antioxidant, and neuroactive properties in animal models, highlighting its potential as a neuroprotective nutraceutical and modulator of brain function and mood. **Objectives:** To evaluate the acute toxicity, locomotor activity, anxiolytic-like activity, and involvement of the GABAergic system of cashew nut oil in zebrafish. **Methods:** Adults zebrafish (n=6/group) received cashew nut oil at doses of 4, 20 and 40 mg/kg by intraperitoneal injection. Animals treated with 3% DMSO were used as the positive control. Acute toxicity was monitored for 96 hours. Locomotor activity was evaluated using teh light/dark test. To investigate the involvement of the GABAergic system, animals were pretreated with flumazenil (4 mg/kg), a GABA receptor antagonist. Data were analyzed by one-way ANOVA followed by Tukey´s post hoc test ($p<0.05$). The study was approved by Ethics Committee on Animal Use of the State University of Ceará (CEUA-UECE Nº 04983945/2021). **Results:** Cashew nut oil did not induce acute toxicity in adult zebrafish, and no mortality was observed during the 96 hours evaluation period (LD50>40mg/kg). In the open field test, the 4 mg/kg dose significantly reduced locomotor activity ($p<0.01$ vs. Control), suggesting a sedative-like effect similar to Diazepam. However, the 20 and 40 mg/kg doses did not significantly alter locomotion. In the light/dark test, all tested doses significantly increased the time spent in the light compartment of the aquarium ($p < 0.001$ vs. control), indicating anxiolytic-like activity. Pretreatment with flumazenil blocked the anxiolytic-like effect observed at the 4 mg/kg dose, suggesting the involvement of GABAA receptors in the neuromodulatory action of the oil. **Conclusion:** Cashew nut oil did not exhibit acute toxicity in adult zebrafish and demonstrated anxiolytic-like activity associated with modulation of the GABAergic system. Additionally, the 20 and 40 mg/kg doses did not impair locomotor activity, indicating a promising pharmacological profile for future studies targeting the central nervous system. **Financial support:** FUNCAP, CAPES, Embrapa SEG, and CNPq (#406690/2023-5 and #421078/2025-1).

16.005FR **Bioassay-Guided Screening of Plant Species from the Gurupi Biological Reserve Reveals Promising Sources of Anti-Inflammatory Compounds**. Costa FF[1], Rocha CQ[2], Reis AS[1] [1]UFMA, Lab Pathophysiology and Therapeutic Research, Brazil; [2]UFMA, PPG Chemistry, Brazil

Introduction: Inflammation is a biological response involved in tissue defense and repair, however, its persistence or dysregulation contributes to several diseases, highlighting the need for strategies to modulate inflammatory responses. Plant-derived products are promising sources of bioactive compounds, such as polyphenols, with immunomodulatory properties. The Amazon harbors remarkable plant biodiversity, and the Gurupi Biological Reserve, in the eastern Amazon, represents an important reservoir of plant species with unexplored pharmacological potential. Bioassay-guided screening of plant extracts and fractions enables the identification of candidates for drug development. **Objectives:** To identify plant species from the Gurupi Biological Reserve (Maranhão, Brazil) with anti-inflammatory potential as promising candidates for bioprospecting. **Methods:** Different parts of eight plant species from the Gurupi Biological Reserve (Maranhão, Brazil) underwent extraction and fractionation, yielding 16 samples. Total phenolic and flavonoid contents were quantified. All samples underwent initial cytotoxicity screening in RAW 264.7 macrophages using the MTT assay. Samples maintaining cell viability were evaluated for inhibition of nitric oxide (NO) production in lipopolysaccharide-stimulated macrophages using the Griess reaction. The most active samples were evaluated by serial dilution to determine the half-maximal inhibitory concentration (IC_{50}) for inhibition of nitric oxide production and the selectivity index (SI). Experiments were performed in triplicate, and statistical analyses were conducted using GraphPad Prism 8.0, with a 5% significance level. **Results:** Total phenolic content varied among samples, with the highest level detected in the acetate fraction of Lithraea brasiliensis leaves (689.89 ± 70.55 mg GAE g^{-1}), whereas the dichloromethane fraction of Tanaecium dichotomum leaves showed the highest flavonoid content (135.66 ± 3.75 mg QE g^{-1}). Following cytotoxicity screening, sample concentrations were adjusted and NO inhibition was evaluated. Of the 16 samples, 9 maintained cell viability above 80% and significantly reduced NO production ($p < 0.05$); among these, 7 showed an SI > 2. The acetate fraction of Lippia origanoides flowers showed the highest SI (>23.65), followed by the Tanaecium dichotomum flower extract (>10.9). **Conclusion:** Differences among species, plant parts, and fractions indicate an influence of phytochemical composition on anti-inflammatory activity. Samples with the highest phenolic and flavonoid contents were not necessarily the most active, suggesting that biological effects depend on specific chemical profiles rather than metabolite abundance. Bioassay-guided screening successfully identified promising candidates, particularly the Lippia origanoides flower acetate fraction and Tanaecium dichotomum flower extract. These findings highlight the pharmacological potential of plant species from the Gurupi Biological Reserve and support their further investigation as sources of bioactive compounds for inflammatory disorders.

16.006FR **Ethanolic extract of** *Trema micrantha* (**Cannabaceae**) **Leaves Reduces Mechanical Hyperalgesia in a Murine Model of Musculoskeletal Hyperalgesia**. Souza JA[1], Quintans-Júnior LJ[1], Passos FRS[1], Quintans JSS[1], Duarte MC[2], Santos LDS[2], Santos KVB[3], Reis WS[3], Lima YRS[3]. [1]UFS, PPG em Ciências da Saúde, 2PPG em Ciências Farmacêuticas, [3]UFS-LANEF

Introduction: Chronic musculoskeletal pain represents one of the central manifestations of fibromyalgia (FM), a condition of complex and multifactorial etiology, whose pharmacological management remains challenging. Medicinal plants represent an important source of biomolecules with therapeutic potential for chronic pain. *Trema micrantha*, a Cannabaceae native to the Americas, is traditionally used in the treatment of pain and inflammation. **Objective:** The present study evaluated the anti-hyperalgesic effect of the ethanolic extract of *Trema micrantha* (EETM) in a model of musculoskeletal pain. **Methods:** Female Swiss mice were used, under prior approval by the CEUA (nº. 7963190124/UFS). The Rota-rod test was previously performed to rule out possible myorelaxant and depressant effects and impairment of motor coordination induced by the extract. Thus, five experimental groups were used: vehicle (p.o.), diazepam (3 mg/kg, i.p.) and EETM (50, 100 and 200 mg/kg, p.o.). To investigate the anti-hyperalgesic effect in a chronic model, experimental groups (vehicle, p.o.; tramadol 4 mg/kg, i.p.; and EETM 100 mg/kg, p.o.) were submitted to the acid saline model (pH 4.0, 20 µL), administered into the gastrocnemius muscle, followed by assessment of mechanical hyperalgesia performed using a digital analgesimeter and immunofluorescence for c-Fos protein in the lumbar spinal cord and encephalic regions of the PAG and RVM. Data were analyzed by one- and two-way ANOVA, with Tukey's post-test and expressed as mean ± standard error of the mean ($p<0.05$). **Results:** In the Rota-rod test, no significant alterations in motor coordination were observed at any of the doses evaluated. In the chronic assessment of mechanical hyperalgesia, the EETM dose (100 mg/kg) promoted a significant increase in paw withdrawal threshold over the seven days of treatment ($p<0.0001$), compared to the vehicle group. EETM demonstrated a significant increase in nociceptive threshold during the first 5h after administration ($p<0.0001$), relative to the control group. In the immunofluorescence for c-Fos, a reduction in immunoreactive cells was observed in the spinal cord ($p<0.001$) and an increase in positive cells in the PAG and RVM ($p<0.0001$ and $p<0.01$, respectively), compared to the vehicle-treated group. **Conclusions:** The results show that EETM exhibits anti-hyperalgesic activity without impairment of motor function. EETM appears to have modulated central areas of pain processing, reducing neuronal activation in the spinal cord and increasing activity in the PAG and RVM, regions of the descending inhibitory system. The findings suggest the therapeutic potential of EETM in the management of FM and other chronic pain conditions. **Acknowledgements:** CNPq, CAPES and FAPITEC.

16.007FR **Embryotoxicity Assessment of Brazilian Cerrado Plants in the Zebrafish Model**. Andrade ICB[1 4], Lima AKS[2,4], Linhares KJS[3,4], Carneiro ERC[3,4], Lira-Júnior EP[3,4], Moraes IB[1,2,4] [1]UFOB, PPG Investigative Pathology, Brazil, [2]UFOB, PPG in Biochemistry and Molecular Biology, Brazil, [3]UFOB, Undergraduate Medical Programme, Brazil, [4]UFOB, Centre for Biological and Health Sciences, Brazil

Introduction: The use of plants for medicinal and nutritional purposes is closely linked to the identity of traditional peoples and communities worldwide. However, some species are endemic and remain underexplored in terms of their chemical composition and pharmacological properties. **Objectives:** Given that the Brazilian Cerrado harbours a rich yet poorly characterised biodiversity, this study aimed to investigate the embryotoxicity of fruit-bearing species such as cajuí (Anacardium humile), cagaita (*Eugenia dysenterica*), pacari (*Lafoensia pacari*), and jatobá (*Hymenaea stigonocarpa*) using zebrafish embryos as a model. **Methods:** Different extracts were prepared from specific parts of the plants: ethanolic extracts from the leaves of cajuí, cagaita, and pacari, and an aqueous extract from the floury pulp of jatobá. Zebrafish embryos were obtained from natural spawning of adult fish, and toxicity analysis was performed according to the OECD Test Guideline 236 (Fish Embryo Toxicity Test), with n = 20 embryos per group/concentration, in triplicate. A range of concentrations was tested for all extracts to estimate the LC50. Developmental and morphological parameters were also assessed, including oedema formation, tail detachment, and somite patterning, as well as hatching and survival rates. **Results:** The ethanolic extract of cajuí leaves delayed embryo hatching, particularly at concentrations above 400 µg/mL, showing a marked disruption in chorion rupture, which is essential for hatching. The ethanolic extract of cagaita leaves showed an LC50 of 129.04 µg/mL and induced cytotoxic and embryotoxic effects, including mortality, morphological alterations, and delayed hatching, especially at higher concentrations (> 400 µg/mL). Similarly, the ethanolic extract of pacari leaves presented an LC50 of 124.46 µg/mL and demonstrated dose-dependent embryotoxicity, with increased mortality, delayed hatching, and impaired embryonic development at elevated concentrations. In contrast, the jatobá fruit extract exhibited lower toxicity, with an estimated LC50 above 3200 µg/mL. However, developmental delay and reduced pigmentation were observed in individuals exposed to high concentrations (> 4000 µg/mL). **Conclusion:** These findings indicate that even plant species commonly used for medicinal purposes may present toxic effects and therefore require further investigation to ensure their safe use. The next step will involve compositional analysis using gas chromatography coupled with mass spectrometry (GC–MS) to identify major compounds and further characterize the extracts at the molecular level, correlating these findings with zebrafish embryotoxicity results to better understand their properties and potential applications.

17. Vision and Ophthalmology

17.001FR **Effect of Intimate Partner Violence on Women's Attentional Bias: An Eye-Tracking Study**. Souza BTBA[1,4], Freitas GA[1,4], Silva GM[1,4], Cavalcante AM[1,5], Albuquerque SCSO[1,5], Santos MEB[1,5], Xavier MJS[3], Souto JJS[1,4], Abreu DFP[1,5], Oliveira ACGA[2,6], Azevedo ATF[1], Silva VFB[1], Santos NA[1,4,5]. [1]UFPB, [2]UNIPÊ, [3]UNINASSAU, Lab Perception, Neurosciences, and Behavior, [4]PGP Social Psychology, [5]PGP Cognitive Neuroscience and Behavior, [6]PPG Law. Brazil.

Introduction: Intimate Partner Violence (IPV) is a serious public health issue that can cause neurophysiological, cognitive, and perceptual changes. Research related to IPV indicates changes in attention. **Objectives:** To analyze the attentional processes of victims of intimate partner violence through eye-tracking. **Methods:** Thirty female volunteers participated in the study, divided into an Experimental Group (EG, n=15, women exposed to IPV and diagnosed with Post-Traumatic Stress Disorder - PTSD) and a Control Group (CG, n=15, women who were never exposed to intimate partner violence NIPV), aged between 24 and 54 years (M= 38.87; SD=7.43 years), with normal or corrected-to-normal visual acuity. The sampling was non-probabilistic. Exposure to intimate partner violence was measured with the Intimate Partner Violence Scale. Eye movements were evaluated through a task with positive, negative, and neutral words, developed from the Affective Norms for English Words (ANEW-Br), using the Tobii TX300 eye tracker (300 Hz, binocular). All victims of violence (100%) showed a critical level of injury and physical violence; 80% had a critical level for health, sexuality, and property damage; and 40% had a critical level and 33.4% an alert level for behavioral control. The duration of exposure to violence ranged from 1 to 30 years (M= 11.03; SD= 8.82); most had broken the cycle of violence (73.4%) between 2 months and 25 years (M= 3.93; SD= 6.39). Data analysis was performed with the Statistical Package for the Social Sciences (27) with a significance level of $p < 0.05$. **Results:** The Kruskal-Wallis test demonstrated significant differences between groups for negative words in the number of fixations [X2 (1) = 8.856; p = 0.003] with a moderate effect size (U = 39,000; p = 0.02; r = -0.42); in the duration of the first fixation [X2 (1) = 3.807; p = 0.05] with a moderate effect size (U = 46,500; p = 0.05; r = -0.35); and in the duration of fixations [X2 (1) = 4.257; p = 0.03] with a moderate effect size (U = 44,500; p = 0.03; r = -0.37). **Conclusion:** Victims of intimate partner violence show sustained attention to negative words related to the traumatic experience, confirming the research hypothesis and the literature. Recalling traumatic experiences can generate acute emotional arousal, activating the fear circuit, which together with the symptoms of rumination and intrusion present in PTSD, contributes to the maintenance of attention to negative words. These results can support therapeutic interventions for victims of intimate partner violence. This work was carried out with the support of the Brazilian Coordination for the Improvement of Higher Education Personnel (CAPES). Human Research Ethics Committee number (CAAE 82068724.2.0000.5188)

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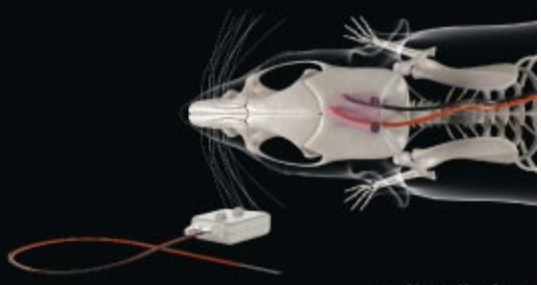
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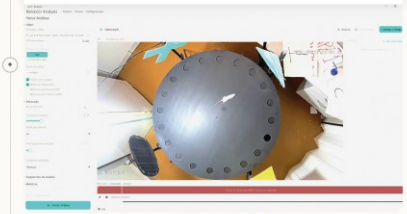
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