08 Respiratory and Gastrointestinal Pharmacology

08.001 Structural Modification in the LASSBio-448, a Phosphodiesterase 4 Inhibitor, increase the relaxant potency from guinea pig trachea in a model of allergic chronic pulmonary inflammation. Silva MCC[1], Oliveira IVS[2], Costa AC[3], Vasconcelos LHC[4], Lacerda-Júnior FF[3], Ferreira PB[1], Nunes IKC[5], Lima LM[5], Barreiro EJL[5], Cavalcante FA[6], Silva BA[7] [1]UFPB - PPgPNSB, [2]UFPB - PIVIC/CNPq, [3]UFPB - PIBIC/CNPq, [4]DFP-UFPB, [5]UFRJ – PPgFQM/LASSBio®, [6]UFPB - PPgPNSB/DFP, [7]UFPB - PPgPNSB/DCF

Introduction: Asthma is an inflammatory disorder of the airways, associated with hyper-responsiveness and symptoms as wheezing, shortness of breath, chest tightness and cough (GINA, 2018). Phosphodiesterase 4 (PDE4) is target of new drugs to treat asthma and reduction of emesis is major challenge in the development of these drugs (Niu, PLoS One, v. 8, p. e82360, 2013). LASSBio-448, a PDE4 inhibitor, was the prototype for LASSBios-1611, 1612, 1613, 1623, 1625 and 1628 (Nunes, Thesis, UFRJ, 2013). The aim was to evaluate the relaxant activity of these derivatives on guinea pig trachea in a model of allergic chronic pulmonary inflammation (ACPI). **Methods:** *In vivo* sensitization was performed in guinea pig (*Cavia porcellus*, 300-350 g) with ovalbumin solution in NaCl 0.9% (Tibério, Am. J. Respir. Crit. Care Med., v. 155, p. 1739, 1997). *In vitro*, trachea was suspended in organ baths on appropriate conditions and isometric tensions were registered by force transducers. Epithelium integrity was verified using arachidonic acid 10^{-4} M on trachea pre-contracted with carbachol (CCh) 10^{-6} M (Tschirhart, J. Pharmacol. Exp. Ther., v. 243, p. 310, 1987). Relaxant activity was assessed by cumulative addition of LASSBios-448, 1611, 1612, 1613, 1623, 1625 or 1628 (10^{-12}-3 x 10^{-4} M) over CCh-induced tonic contraction. E_{max} and pCE_{50} 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:** LASSBio-448 relaxed guinea pig trachea with ACPI CCh-contracted, in both the presence (E_{max} = 119.0 ± 8.1; pCE_{50} = 4.98 ± 0.17) or absence (E_{max} = 130.5 ± 6.0; pCE_{50} = 4.88 ± 0.19) of functional epithelium. As well as LASSBios-1611, 1612, 1613, 1623, 1625 and 1628 showed a concentration-dependent relaxant efficacy on trachea, in both the presence (E_{max} = 116.7 ± 9.5, 123.8 ± 8.3, 122.1 ± 7.1, 127.6 ± 5.0, 112.3 ± 1.3 and 117.0 ± 7.4%, respectively) or absence (E_{max} = 118.3 ± 8.2, 115.2 ± 4.9, 118.9 ± 6.1, 124.6 ± 1.9, 119.9 ± 4.9 and 119.4 ± 7.8%, respectively) of functional epithelium. Already in relation to relaxant potency, the LASSBios-1611, 1612, 1613, 1623, 1625 and 1628 increased the potency when compared to LASSBio-448, in both the presence (pCE_{50} = 6.49 ± 0.11, 4.79 ± 0.19, 5.73 ± 0.19, 5.16 ± 0.16, 6.45 ± 0.12 and 5.22 ± 0.21, respectively) or absence (pCE_{50} = 7.70 ± 0.13, 4.95 ± 0.06, 6.23 ± 0.29, 6.70 ± 0.14, 5.26 ± 0.14 and 5.85 ± 0.24, respectively) of functional epithelium. When compared to each other, the LASSBio-1625 was the most potent in the presence of epithelium, suggesting an epithelium-derived relaxing factors release; and the LASSBios-1611 and 1623 were the most potent in the absence, indicating an effect directly on smooth muscle. **Conclusions:** Among the derivates, LASSBio-1611 is the most potent in relaxing guinea pig trachea with ACPI, in the absence of functional epithelium, being the mechanism in a target on smooth muscle itself. In a next step, it will be evaluated PDEs pathway as possible action mechanism, to assign probably antiasthmatic action. **License number of ethics committee**: Ethical Committee on Animal Use/UFPB (018/2015) **Financial support**: CAPES, CNPq

08.002 Gastroprotective effect of Artepillin C, **Drupanin**, **Aromadendrin-4'-O-methyl-ether and kaempferide isolated from the Brazilian green propolis**. Costa P[1], Almeida MO[2], Lemos M[2], Arruda C[2], Casoti R[2], Somensi BL[1], Boeing T[1], Mariott m[1], da Silva RCMVAF[1], de Souza P[1], dos Santos AC[1], Bastos JK[2], da Silva LM[1], de Andrade SF[1] [1]Univali – Ciências Farmacêuticas,[2]FCFRP-USP – Farmacologia e Toxicologia de Produtos Naturais

Introduction: Brazilian green propolis (BGP) is extensively used to improve health and prevent diseases in worldwide. Therefore, this study evaluated the antiulcer potential of three prenylated *p*-coumaric acid derivatives and two flavonoids from BGP, respectively named: 3,5 diprenyl-4-hydroxycinnamic acid (artepillin C), 3-prenyl-4-dihydroxycinnamoiloxy cinnamic acid (baccharin), 3-prenyl-4-hydroxycinnamic acid (drupanin), aromadendrin-4'-O-methyl-ether and kaempferide. **Methods:** The compounds were characterized by nuclear magnetic resonance and mass spectrometry. Their gastroprotective effects were evaluated against ethanol/HCl- and indomethacin-induced ulcer in mice. Further, histological, histochemical, oxidative and inflammatory parameters were analyzed at ulcerated tissue. Their acid antisecretory activities also were also assessed (approval number in CEUA-UNIVALI: 034/17p). **Results:** Baccharin did not reduce the ethanol/HCl- induced ulcer at 30 mg/kg (p.o), whereas the minimum oral gastroprotective doses of artepilin C, drupanin, aromadendrin-4'-O-methyl-ether and kaempferide were 0.3, 0.3, 3 and 3 mg/kg, respectively. Besides, artepilin C, drupanin, aromadendrin-4'-O-methyl-ether and kaempferide promoted gastroprotective action with a dose ten times lower in ethanol/HCl-induced ulcer, by intraperitoneal administration. Moreover, artepilin C (0.3 mg/kg), drupanin (0.3 mg/kg), aromadendrin-4'-O-methyl-ether (3mg/kg) and kaempferide (3 mg/kg) protected the gastric mucosa against indomethacin-induced ulcer by oral route. The gastroprotection was accompanied by normalization of superoxide dismutase, catalase and glutathione-*S*-transferase activities and reduction in myeloperoxidase activity in the gastric mucosa. Moreover, the compounds aromadendrin-4'-O-methyl-ether and kaempferide increased the gastric mucin content; whereas artepilin C reduced the TNF amount. Furthermore, artepilin C, drupanin, aromadendrin-4'-O-methyl-ether and kaempferide decreased volume, pH, total acidity and pepsin activity of the gastric juice from rats. **Conclusion:** Together, our findings showed a diversified mode of action elicited by artepilin C, drupanin, aromadendrin-4'-O-methyl-ether and kaempferide on the gastroprotection and contribute to explain the anti-ulcer activity reported for green propolis extract in the folk medicine.
License number of ethics committee: CEUA-UNIVALI: 034/17p **Financial support**: São Paulo Scientific Foundations-FAPESP, CNPq, CAPES, UNIVALI and Aster BioChem.

08.003 Bosentan, **the non-selective ETA/ETB receptor antagonist emerge as a valuable therapy for gastric wound healing**. Dal Lin FT[1], Ciapparini PG[1], Maria-Ferreira D[1], Luz BB[1], Kochem B[1], Nakao LS[2], Werner MFP[1] [1]UFPR – Farmacologia, [2]UFPR – Patologia Básica

Introduction: The incidence of gastric ulcers and its complications remains a worldwide health problem. Endothelins are one of the many signaling systems which might contribute importantly to gastric ulcer development. We have already demonstrated that bosentan, a dual ETA and ETB endothelin receptor antagonist, accelerates the gastric ulcer healing (Dal Lin et al., 49th SBFTE 2017). Importantly, the widespread use of antisecretory drugs, such as omeprazole, has been strongly associated with bone fractures, impaired B12 vitamin absorption and enteric infections. Thus, the present study sought to further investigate the mechanisms underlying the endothelinergic system modulation in gastric ulcer healing. **Methods:** Chronic ulcers were induced in male Wistar rats (~200 g) by serosal application of 80% acetic acid, and treatments starting 2 days after ulcer induction. Rats were orally treated with vehicle (water, 1 mL/kg), omeprazole (40 mg/kg) or bosentan (10 or 30 mg/kg), twice daily during 5 days. Gastric healing effect was evaluated through macroscopic ulcer area (mm^2) measurement. ETA and ETB receptor protein expression were determined by immunoblotting in naïve and vehicle-ulcerated stomach. Ulcer tissues were subjected to measurement of myeloperoxidase (MPO) activity and TNF-α and IL-1β levels (ELISA). Acute pylorus ligation in rats was employed to investigate the possible antisecretory effect of bosentan (10 mg/kg), using omeprazole (40 mg/kg) as control. All procedures were approved by the Local Ethical Committee (CEUA/BIO-UFPR; 1054). **Results:** At 7 days following ulcer induction, western blot analysis revealed that the relative levels of ETA and ETB receptor protein expression were significantly increased by 5.9 and 6.9-fold, respectively, in the vehicle ulcerated group, when compared to naïve group. Ulcer area was significantly reduced by omeprazole and bosentan (10 or 30 mg/kg) by 46, 38 and 34%, respectively, when compared to the vehicle ulcerated group (173.6 ± 12 mm^2). In agreement with the above, omeprazole and bosentan (10 or 30 mg/kg) treatments reduced MPO activity in ulcerated mucosa in 35, 59 and 54%, in comparison to the vehicle ulcerated group (22.9 ± 3.3 DO/mg of protein). Thus, the lower effective dose of bosentan (10 mg/kg) was chosen to carry out the following measurements. Furthermore, both omeprazole and bosentan (10 mg/kg) treatments promotes a 39 and 67% decrease in TNF-α levels in ulcer tissue (vehicle ulcerated group: 204.8 ± 31.8 pg/mg of protein). However, only bosentan (10 mg/kg) reduced IL-1β levels by 70% on ulcerated mucosa (vehicle ulcerated group: 42.2 ± 13.6 pg/mg of protein). Nevertheless, in sharp contrast to omeprazol, the volume, pH and total acidity of acid gastric secretion were unchanged by bosentan (10 mg/kg). **Conclusion:** Our demonstration that ETA and ETB receptors expression are increased in gastric ulcers, together to the bosentan inhibition of neutrophil infiltration, TNF-α and IL-1β and production, strengthen the relationship between endothelinergic system, inflammation and ulcerogenesis. Interestingly, we have demonstrated that bosentan accelerates successful the gastric mucosa healing without antisecretory mechanisms. Collectively, this property of bosentan can be considered for the treatment of gastric ulcer disease. **License number of ethics committee**: CEUA/BIO-UFPR; 1054 **Financial support**: CAPES, CNPq; 303875/2017-8

08.004 Antidiarrheal efficacy of sesquiterpene farnesol and its beta-cyclodextrin complex in rodents, Costa DS[1], Silva VG[1], Negreiros PS[2], Lima IBC[2], Souza LKM[1], Nogueira KM[1], Sousa FBM[1], Medeiros JVM[1], Santos RF[2], Oliveira RCM[1] - [1]UFPI – Biotecnologia, [2]UFPI – Farmacologia

Introduction: Diarrheal diseases nowadays comprise a public health problem that affects developing countries, with distinct etiologic agents and one of struggles involving this fact is the lack of potential agents to treatment different types of diarrhea (AWE, J ETHNOPHARM, 137, 148, 2011). The search for new sources of treatment for diarrheal diseases is based on the use of natural products such as terpenes and derivatives, among them farnesol, a sesquiterpene found in several essential oils of red fruits, flowers and as a secondary metabolite obtained within the pathway of synthesis of mevalonate, already having several pharmacological activities described, such as antinociceptive, antitumor, antimicrobial, neuroprotective and hepatoprotective (LAPCZYNSKI, FOOD CHEM TOXICOL, 46, 149, 2008). **Aim:** To investigate the antidiarrheal activity of sesquiterpene farnesol (FOH) and β–cyclodextrin complex (FOH-BCD) in rodents. **Methods:** This study was approved by local Ethics Committee Research (CEUA/UFPI 367/17). Antidiarrheal activity of was evaluated for castor oil-induced diarrhea and *enteropooling*. Swiss Mice (25-30 g) were pretreated with FOH or FOH-BCD (6.25; 12.5; 25 and 50 mg/kg, *p.o*.) or loperamide (5 mg/kg, *p.o*.), and after 1 h, was administered castor oil (10 ml/kg, *p.o*.) Animals were placed in cages lined with filter paper and observed for 3 h for the presence of diarrhea defined as watery (wet), unformed stool. Besides, were sacrificed and small intestine was isolated and volume of intestinal contents was measured by graduated tube. Intestinal motility was evaluated using activated charcoal. Mice (Swiss strain, 25-30g) received castor oil and 30 minutes later they were treated with FOH or FOH-BCD (50 mg/kg, *p.o*). After 1 h, all animals were received 0,2 mL of charcoal activated (10% charcoal suspension in 5% gum acacia *p.o*). 20 minutes later, animals were sacrificed, and the distance covered by the activated charcoal in the small intestine was measured and were performed the opioid and cholinergic modulation. **Results:** FOH and FOH-BCD (6.25; 12.5; 25 and 50 mg/kg) were reduced significantly ($P<0.05$) the frequency of defecation (56.61, 62.99, 78.92 and 70,58% respectively for FOH; 55.55, 67.56, 76,71 and 79,65 % respectively for FOH-BCD), also decreased severity of diarrhea (54.20, 60.48, 75.98 and 72.03% respectively for FOH; 48.32, 62.00, 75.07 and 77.81 % respectively for FOH-BCD) and total number of wet feces produced upon administration of castor oil as in enteropooling, where in all doses significantly reduced ($P<0,05$) intestinal content except 6.25 mg/kg in FOH or FOH-BCD (10.16, 40.67, 47.45 and 66.10% respectively for FOH; 15.25, 50.84, 42.37 and 71.18 % respectively for FOH-BCD). FOH and FOH-BCD reduced significantly the gastrointestinal transit ($P <0.05$) compared to control, however it did not provide opioid action because naloxone did not reverse the FOH or FOH-BCD effect. Nevertheless, FOH and FOH-BCD provide anticholinergic action, because both reverted the effect caused by bethanecol. **Conclusions:** In this study, we observed the antidiarrheal effect by FOH and FOH-BCD against castor oil with reduction of defecation, inhibition of diarrheal faeces with anticholinergic action. Antoher studies will be executed for investigated another mechanisms involving Farnesol. **License number of ethics committee**: CEUA-UFPI 367/17 **Financial support**: CAPES/FAPEPI/UFPI

08.005 Evaluation of antidiarrheal effect of ethanolic extract of *Terminalia fagifolia* Mart.& Zucc. (Combretaceae) leaves in mice. Silva VG[1], Negreiros PS[2], Costa DS[1], Silva TIN[2], Chaves MH[3], Gomes JPS[3], Nunes PHM[4], Oliveira RCM[1] [1]UFPI – Biotecnologia, [2]UFPI – Farmacologia, [3]UFPI – Química, [4]UFPI – Biofísica e Fisiologia

Introduction: The diarrhea is assessed as the second cause of death in children, accounting for around 1.5 million deaths / year in children under five. It is triggered by the formation of loose or aqueous feces when the small intestine and colon are ineffective in absorbing nutrients, fluids and salts from the liquid and in the contents of the upper intestine. Being the treatment centered on oral rehydration solutions and the use of antibiotics but the mortality rates are still significant, and the use of medicinal plants or compounds derived from them as a form of treatment is of great relevance. Among the most promising sources of natural products, we can highlight *Terminalia fagifolia* Mart & Zucc, popularly known as "chapadeiro," which is used in traditional folk medicine for its effective treatment of gastrointestinal disturbances, such as ulcer, gastritis, and diarrhea. Thus, the aim of the present study was to investigate the effect of ethanolic extract on antidiarrheal activity **Methods:** Initially, the antidiarrheal activity of ethanolic extract was evaluated in acute diarrhea model and enteropooling induced castor oil, where swiss mice were pretreated with ethanolic extract (EtOH-Tf 31. 25; 62. 5; 125 and 250 mg/kg, p.o.), and after 1 h received castor oil (10 mL/kg, p.o). The animals were then placed in lined cages and observed for 4 h, at the end of time, the severity of diarrhea, total weight of feces and measurement of intestinal contents (enteropooling) were evaluated. Ethics Committee of Animal Experimentation (CEEA/UFPI nº 365/2017). **Results:** ethanolic extract (31.25; 62.5; 125 and 250 mg/kg, p.o.) significantly reduced (**p*<0.05) total fecal mass (66; 70; 56 and 95% respectively) and especially the diarrheal stools (58; 66; 52 and 97% respectively), when compared with the control group (saline 10 mL/kg, p.o.). Loperamide-treated group also reduced (**p*<0.05) fecal mass (94%) and diarrheal stools (97%), compared to the control group. In all tested doses, was effective in reducing (**p*<0.05) the intestinal content (35; 32; 41 and 54%, respectively), when compared to the control. Loperamide also reduced the intestinal content (73%), when compared with the saline-treated group. **Conclusion:** Thus, it was concluded that the extract of *T. fagifolia* (EtOH-TF) leaves has remarkable antidiarrheal activity in low doses in mice at castor oil-induced diarrhea. **License number of ethics committee**: CEEA/UFPI nº 365/2017 **Financial support**: UFPI/CAPES

08.006 Evaluation of the antitussive and expectorant activities of carvone in mice.
Menezes PMN[1], Almeida RL[1], Brito MC[1], Duarte-Filho LAMS[1], Barbosa JM[1], Almeida PC[2], Silva BAO[1], Ribeiro LAA[1], Silva FS[1] [1]UNIVASF – Ciências Farmacêuticas, [2]UFRPE – Ciências Biológicas

Introduction: Carvone is chemically classified as a ketone, being a monoterpene, presented as the major component of the species *Lippia alnifolia*. Two forms of enantiomers can be found for carvone, the S- (+) form, present mainly in the essential oil of Alcaravia seeds of the *Carum carvi* species, as well as the R- (-) form present in the Mint species *Mentha spicata*. **Methods:** The animals were divided into 5 groups: saline 10 mL/kg (CN), morphine 5 mg/kg (CP) and carvone (10, 30 and 100 mg/kg) placed in a glass vat of 500 mL where they were subjected to nebulization by 0.4 M citric acid for 3 minutes, during which the number of coughs was counted. After 23h and 30 minutes the animals were treated according to the experimental groups and exposed to a second nebulization for counting and comparing the number of coughs. To evaluate the expectorant activity, 5 groups were separated: saline 10 mL/kg (CN), ambroxol 120 mg/kg (CP) and carvone (10, 30 and 100 mg/kg) containing 5 animals that were treated in the respective groups. After 30 minutes, the phenol red 500 mg/kg was administered intraperitoneally and after another 30-minute period the animals were euthanized and the bronchoalveolar fluid (BALF) was recovered with 2 mL of saline for spectrophotometric analysis. **Results:** During the first day of nebulization the animals of the CN had an average of 10.2 coughs, while in the CP group the mean was 6.6 coughs and for the groups 10, 30 and 100 mg/kg of carvone the averages were 6.0, 7.2 and 7.6 coughs respectively. On the second day of testing, the animals were treated and submitted to new nebulization. CN animals presented on average 8.6 coughs, CP with an average of 3.0 coughs, while the carvone groups 10, 30 and 100 mg/kg had a mean of 0.8, 1.0 and 2.2 coughs respectively. In the analysis of expectorant activity that was obtained by the saline-treated animals, the mean phenol red concentration in the BALF was 1.575 ± 0.07961 µg/mL, while for carvone 10 and 30 mg/kg was 5.986 ± 1.150 µg/mL and 4,139 ± 0.1987 µg/mL, respectively, representing a significant difference (t-test, $p < 0.05$). **Conclusions:** From the effective decrease of cough frequency in the experiments carried out, it is concluded that carvone has a good antitussive activity in mice. Moreover, carvone shows expectorant activity as the data provided from the analysis of phenol red in BALF suggests. New experiments are being carried out to investigate the possible pharmacological pathways that carvone may be performing. **License number of ethics committee**: 0003/080716 **Financial support**: CAPES, CNPq, UNIVASF

08.007 Spasmolytic activity of the monoterpene carvone: **a study of mechanism**.
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Introduction: Carvone is a monoterpene that has demonstrated several pharmacological activities: antihypertensive, anti-inflammatory, antipyretic, antinociceptive. **Objetives:** The aim of this work was to investigate the mechanism of action of Carvone on the spasmolytic activity in rat (*Rattus norvegicus*), isolated trachea (CARV). **Materials and Methods:** The experimental protocols were established in accordance with CEUA/UNIVASF (protocol # 0006/021014). Rat isolated trachea (n= 3 to 5) was incubated in 10 ml chambers in an organ bath system filled with a Krebs-Henseleit' solution at 37°C and constant oxygenation by 1h and tension settled for 1g. Cumulative concentrations of CARV (10^{-7} M a $3x10^{-3}$ M) were added after the induction of the contraction by 10 µM carbachol in order to investigate the spamolytic effect. To elucidate the CARV mechanism of action a set of experiments were performed both in the presence and absence of 2 mM 4-aminopyridine (4-AP), 5 mM tetraethylammonium (TEA), 3 µM glibenclamide (GLIB), 5 mM cesium chloride (CsCl), 10 µM N-nitro-L-arginine methyl ester (L-NAME), 10 mM indometacin (IND), 3 µM propanolol (PROP), 3 µM dexamethasone (DEX), 100 µM hexamethonium (HEX), and 1H-[1,2,4]-oxadiazol-[4,3-a]-quinoxalin-1-ona (ODQ, 1 µM). Data are presented as means ± standard error of the mean (SEM) and was analyzed using GraphPad Prism® Software (v.5). The concentration that caused 50% of the relaxation (expressed with confidence interval of EC_{50}) in rat isolated trachea was calculated by non-linear curve fitting. Statistically significant differences were calculated using non-parametric test t or one-way ANOVA and the post-hoc Tukey's multiple comparison test. **Results:** CARV inhibited the contraction induced by carbachol EC_{50} = 584 µg/mL (Confidence Interval CI - 428-796). The relaxing potential of CARV after contractions induced by carbachol in the presence of modulators of the pathway nitric oxide ODQ - EC_{50}= 643 µM (CI - 364-687) and L-NAME EC_{50}= 611 µM (CI - 466-748), neuronal nicotinic receptor antagonist HEX - EC_{50}= 655 µM (CI - 540-796), Kca, Kir, KATP, Kv channels TEA- EC_{50}= 861 µM (CI - 738-1006), 4-AP- EC_{50}= 1111 µM (CI -789-1564), GLIB - EC_{50}= 795 µM (CI - 678-933), CsCl - EC_{50}= 643 µM (CI - 481-860), pathway prostaglandins IND - EC_{50}= 1153 µM (CI- 536-2475), DEX - EC_{50}= 1160 µM (CI - 217-6185) and β-adrenergic PROP - EC_{50}= 1224 µM (CI - 663-2256) had not change when compared whith relaxation in the absence of these blockers.**Conclusions:** The Carvone present spasmolytic activity on activity in rat isolated trachea. These results suggest other studies are necessary to study other pathways related to relaxation, such as the participation of phosphodiesterases, channels for voltage-sensitive Ca^{2+}, SERCA and other pathways. **Keywords:** Carvone; Monoterpene; Spasmolytic; Isolated trachea. **License number of ethics committee**: 0006/021014 **Financial support**: FACEPE

08.008 Airway responsiveness is not altered by chronic treatment with paracetamol in rats. Ribeiro MTL[1], Abreu LB[2], Rocha ML[1], Castro PFS[2] [1]UFG – Farmácia, [2]UEG-Itumbiara

Introduction: Some studies relate the use of paracetamol with the exacerbation of asthma symptoms and other respiratory problems. Other studies are inconclusive or deny this correlation. This makes the association between paracetamol and airway hypersensitivity very controversial and still under debate. **Objectives:** To investigate the effect of chronic treatment with paracetamol on rats on the contraction and relaxation of isolated airways. **Methods:** Wistar rats were divided into 2 groups (n = 5-8). One group was treated for 2 weeks with paracetamol (400 mg/kg, v.o.) in drinking water and another control group (pure water). The animals were euthanized after two weeks, blood was collected for biochemical analyzes (ALT, AST, TBARs reaction) and tracheal rings were isolated and prepared in an organ bath to measure the isometric tension against contractile stimuli (concentration-effect curve for carbachol, KCl and Ca^{2+} stimulated with carbachol or KCl) and relaxants (isoprenaline, sodium nitroprusside and verapamil). **Results:** Liver enzymes ALT, AST and lipid peroxidation (TBARs) were significantly increased after paracetamol treatment. The airway tracheal smooth muscle response does not present any alteration, either to the contractile or relaxing stimulus for: cholinergic agonist, membrane depolarization, Ca^{2+} influx by the sarcolemma, internal release of Ca^{2+} from the sarcoplasmic reticulum, β-receptor agonist or NO donor-induced relaxation. **Conclusion:** Chronic treatment with paracetamol does not induce hyper or hyporeactivity of the airways isolated from rats. **Keywords:** Paracetamol, smooth muscle, trachea, asthma, oxidative stress. **License number of ethics committee**: 083/16 **Financial support**: CAPES, CNPq, FAPEG.

08.009 Pharmacological analysis of the ethanolic extract from the sweet-broom leaves (*Scoparia dulcis*) **upon the gastrointestinal tract motility**. Moura HM[1], Sousa EC[1], Moreira FAS[2], Sousa JA[3,4,5], Moura MCL[2], Ferreira LVA[2] [1]UNIFSA –Farmácia, [2]UNIFSA, [3]UNIFSA – Farmacologia, [4]Ulbra – Biosaúde, [5]UESPI – Farmacologia

Introduction: The gastrointestinal tract disorders (GTD) e.g. diarrhea and constipation, are among the most common disorders that harm the digestive system, which are rather frequent and wide-ranging on people, affecting millions' health. Exist several medicaments aimed to solve intestinal disorders available on the market, albeit the proven effects, these drugs bring with its therapeutic potential, a noticeable number of side effects. The indigenous people have always used of plants as an alternative treatment for diarrhea and constipation, between the vast kinds of plands and herbs found on Brazilian flora, *Scoparia dulcis* was always underscored for the lack of supporting research about its effects on the intestinal motility. For this reason, it was aimed to analyze the pharmacological effect of the ethanolic extract from sweet-broom leaves (*Scoparia dulcis*) upon the intestinal transit and the castor oil-induced diarrhea. **Methods:** This assessment occurred through two pharmacological tests, the intestinal transit model, where mice had pre-treatment (v.o) with vehicle (1mL/kg), loperamide (5mg/kg), ethanolic extract from *Scoparia dulcis* (EeSD) 500mg/kg and 30 minutes after that received 0,2 mL of activated carbon. Not more 30 minutes later, it was verified that the distance crossed by the carbon was from the pylorus to the proximal portion of the intestine. Through the castor oil-conducted diarrhea model, the mice were pre-treated with vehicle (1mL/kg), loperamide (5mg/kg) and EeSD (500mg/kg). 30 minutes after, the castor oil was administrated orally (0,1 mL/animal), afterwards the animals were separated in polyethylene boxes lined with paper, where the faeces were counted for the period of 2 hours. The obtained data were statistically analyzed through ANOVA oneway test, followed by the Turkey post-test, using the statistic program GraphPadPrism 7.0, the outcome was presented as mean ± (standard error of the mean). It was possible to verify that the EeSD 500mg/kg reduced the intestinal transit (33,5%), in an expressive value when compared to the vehicle (65,03%). This work was approved and recorded by the FSA Ethics Committee with Animal Research with the protocol number 9354/16. **Results:** The EeSD 500mg/kg also reduced the castor oil-induced diarrhea, decreasing the defecation frequency (0.400 ± 0,400), which was 8,200 ± 0,800 in the group that received the vehicle and castor oil. **Conclusion:** Therefore, it is verified that *Scoparia dulcis* promotes an inhibitory process over the intestinal transit and antidiarrheal activity, making possible the use as a medicament for diarrheal disease, with a better cost-benefit in the future. **Financial Support:** UNIFSA. **Key words:** *Scoparia dulcis*; Intestinal Constipation; Diarrhea. **References:** BARBURI, R.C. **Diarreias agudas. Aspectos clínicos, etiológicos e terapêuticos.** Revista Brasileira de Medicina. SãoPaulo - P. 3-12, 2010. MURTI, R.; PANCHAL, M.; TAYA, P.; SI. R. **Pharmacological Properties of ScopariaDulcis: A Review.** Pharmacologia, Vol.3, p.344-347, 2012. OFORI-AMOAH, KOFFUOR. G.; A. Bronchodilatory and Anti-inflammatory Effects of a Hydro-Ethanolic Extract of *Scopariadulcis* Linn.Pharmacologia, Vol.6, p.337-346, 2015. **License number of ethics committee**: 9354/16 **Financial support**: UNIFSA

08.010 *Spirulina platensis* **prevents alterations of intestinal contractile reactivity in Wistar rats fed with hypercaloric diet**. Carvalho MLT[1], Souza ILL[2], Ferreira ES[2], Diniz AFA[2], Cavalcante FA[3], Silva BA[4] [1]UFPB, [2]UFPB, [3]DFP-UFPB, [4]DCF-UFPB

Introduction: The excess of adiposity is directly related to the degree of macrophages infiltration, favoring the development of several diseases, which implicate in arterial hypertension, type 2 diabetes mellitus, metabolic syndrome, gastrointestinal dysfunctions, among others (Nam, Gut Liver, v. 11, p. 323, 2017). Recently, we have shown that the consumption of a hypercaloric diet decreases the intestinal contractile reactivity of Wistar rat and that food supplementation with *Spirulina platensis*, a blue-green algae, restored the intestinal alterations (Ferreira, dissertation, UFPB, 2017). Thus, we aimed to elucidate a possible beneficial effect of this algae in the prevention of intestinal changes induced by the consumption of a hypercaloric diet. **Methods:** Wistar rats (8 weeks of age) were divided into groups fed with a standard diet and supplemented orally with either saline solution (DP) or *S. platensis* powder at doses of 25, 50 and 100 mg/kg (DP25, DP50 and DP100, respectively), groups fed with a hypercaloric diet and supplemented orally with either saline solution (DHC) or doses of 25, 50 and 100 mg/kg of powder *S. platensis* (DHC25, DHC50 and DHC100, respectively). All groups were fed and supplemented for 8 weeks. The results were expressed as mean and standard error of the mean and analyzed by one-way ANOVA followed by Tukey's post-test (p <0.05, n = 5). **Results:** Cumulative concentration-response curves to carbachol (CCh), pharmacomechanical agonist, in groups fed with a standard diet and supplemented with *S. platensis* showed a reduction in contractile efficacy at doses of 25 (E_{max} = 65.1 ± 5.7%), 50 (E_{max} = 54.4 ± 6.2%) or 100 mg/kg (E_{max} = 60.5 ± 5.2%) in relation to in relation to DP group (E_{max} = 100%), as well as an increase in the contractile potency of DP100 group (pCE_{50} = 6.8 ± 0.2) compared to DP50 group (pCE_{50} = 6.3 ± 0.1). On the other hand, the groups fed with a hypercaloric diet, DHC (E_{max} = 32.7 ± 7.5%) or those supplemented with *S. platensis* at doses of 25, 50 and 100 mg/kg (E_{max} = 45.4 ± 2.3, 60.9 ± 1.7, 79.2 ± 4.9%, respectively), presented a decreased contractile efficacy in relation to DP group (E_{max} = 100%), but did not alter the CCh potency at any dose. In addition, cumulative concentration-response curves to KCl, an electromechanical agent, also showed a decrease in contractile efficacy in DP groups that were supplemented with the alga at doses of 25 (E_{max} = 58.7 ± 3.3%) and 50 mg/kg (E_{max} = 52.5 ± 4.9%), with no change in KCl potency at any dose. Additionally, in DHC group cumulative concentration-response curve to KCl showed a decrease in contractile efficacy (E_{max} = 42.7 ± 3.1%) compared to DP group (E_{max} = 100%). Moreover, supplementation with *S. platensis* at doses of 25 (E_{max} = 72.7 ± 5.3%) and 50 mg/kg (E_{max} = 73.4 ± 3.0%) increased the effectiveness of the contractile agent. **Conclusion:** Food supplementation with *S. platensis* prevented a decrease in the contractile reactivity of the ileum isolated from Wistar rats in response to different contractile agents, caused by the hypercaloric diet consumption. **License number of ethics committee**: Ethical Committee on Animal Use/UFPB (017/2016) **Financial support**: CNPq, CAPES, PPgPNSB/UFPB

08.011 Evaluation of the antidiarrheal and antimicrobial activity of (-)-fenchone isomer in experimental models. Pessôa MLS[1], Serafim CAL[1], Alves Junior EB[1], Pessoa MMB[1], Formiga RO[2], Diniz Neto H[1], Lima EO[1], Batista LM[1] [1]UFPB – Ciências Farmacêuticas, [2]UFSC – Ciências Farmacêuticas

Introduction: Fenchone is a bicyclic monoterpene, which is present in essential oils of many plant species and it is cited in ethnopharmacological studies for the treatment of gastrointestinal disorders. Therefore, the present study aimed to evaluate the antidiarrheal and antimicrobial activity of fenchone in experimental models. **Methods:** For the evaluation of antidiarrheal activity, Swiss male mice (Mus musculus) (n = 7) were used, weighing between 25 - 35 g. They were submitted to a 12-hour fast and treated with 5% tween 80 - 10 mL/kg (negative control), loperamide (5 mg/kg) and different doses of fenchone 37.5, 75, 150 and 300 mg/kg, respectively. After 1h, diarrhea was induced by oral administration of castor oil (10 mL/kg), in boxes covered with paper to account total number of stools (solid stools, semisolid and liquid), percentage of liquid feces and percentage of diarrheal inhibition in a period of 4 hours (AWOUTERS, F., J. Pharm Pharmacol, v. 30, pp. 41-45, 1978). In order to evaluate the antimicrobial activity, Minimum Inhibitory Concentration (MIC) on bacterial and fungal strains: Staphylococcus aureus ATCC-25923 and LM-177, Pseudomonas aeruginosa ATCC-25853 and LM-297, Escherichia coli ATCC-18739 and LM-39, Candida tropicalis ATCC-13803 and LM-20, Candida krusei ATCC-6258 and LM-13, were emitted by the plate microdilution technique using a 96-well cell culture. For that, RPMI/BHI broth was used and 100 µL of the solution preparation were withdrawn by serial dilution at concentrations parting from 1024 µg/mL to 16 µg/mL. Besides, 10 µl of bacterial and fungal strains suspensions were added and incubated (35 ± 2 °C for 24-48 hours) for later reading. Subsequently, the determination of Minimum Fungicidal Concentration (CFM) and Minimum Bactericidal Concentration (CBM) were performed. (CLSI, 2008; CLELAND, R., Antibiotics in Laboratory Medicine, P. 739, 1991; ELOFF, JN; Med., Vol. 64, page 711, 1998). **Results:** In the evaluation of antidiarrheal activity the animals treated with vehicle (5% tween 80) showed a 23 (20-24) and 81% of faecal evacuation rate. The treatment with fenchone at 150 and 300 mg/kg doses reduced the evacuation index (EI) to 4 (3-6) with 81% of diarrheal inhibition ($p < 0.01$) and 3 (1-4), 88% ($p < 0.001$), respectively, when compared to negative control group. The standard drug loperamide (5 mg/kg, v.o.) produced 87% inhibition of diarrhea. In the antimicrobial activity essay, fenchone inhibited the growth of 4 (66%) of the 6 fungal strains studied in the concentration of 32 µg/mL, with only 2 strains being inhibited up to the concentration of 64 µg/mL, therefore MIC was 32 µg/mL. However, this tested natural compound showed no inhibitory activity against any of the bacterial strains. The Minimum Fungicidal concentration (CFM) was 32 µg/mL for 3 (50%) of the tested strains. **Conclusion:** Thus, it is possible to suggest that fenchone presents both antidiarrheal and antifungal activity in the experimental models evaluated. **Acknowledgments:** CNPq / UFPB / PgPNSB / IperFarm. Ethics Committee on Animal Use (CEUA/UFPB): Nº 035/2017.

08.012 Effects of calcium channel blockers in non-adrenergic non-cholinergic gaba-induced relaxation in rat duodenum. Petri C[1], Sousa IA[1], Almendra JSL[1], Alves Filho FC[1], Cavalcanti SMG[2], Cavalcanti PMS[3] [1]UFPI – Biofísica e Fisiologia, [2]FACIME-UESPI, [3]UFPB - Ciências Farmacêuticas

Introduction: Gamma-aminobutyric acid (GABA) is an inhibitory neurotransmitter in central nervous system. However, in enteric nervous system GABA exhibits excitatory actions. In the rat duodenum, there are evidences of non-adrenergic non-cholinergic (NANC) relaxations promoted by GABA are mediated by neuronal nitric oxide synthases (nNOS) activation. As Ca^{2+} is required for nNOS activation, the hypothesis is that the depolarization of enteric neurons induced by GABA is a key event to the influx of Ca^{2+} required for nNOS activation. The main aims of this study were to determine whether Gadolinium (Gd^{3+}), Nickel (Ni^{2+}) and verapamil -Ca^{2+} channels blockers- are able to inhibit GABA-induced NANC relaxations in rat duodenum. **Methods:** All experimental procedures were approved by the Committee on Animal Research and Ethics/UFPI (374/2017). Wistar rats (about 0.3 kg) were keep fasted (48 hours) and then were euthanized by decapitation after injection of pentobarbital (50 mg/Kg, intraperitoneally). The abdominal cavity was opened and longitudinal segments of the duodenum measuring 3.0 cm were removed and placed in 15 ml organ baths containing Ca^{2+}-free Tyrode´s solution [(g/L): NaCl 8; KCl 0.2; $MgCl_2$ 0.1; NaH_2PO_4 0.1; $NaHCO_3$ 1 and glucose 1.0] or Jalon´s solution [(g/L): NaCl 9; KCl 0.46; $CaCl_2$ 0.2; $NaHCO_3$ 0.5 and glucose 0.5] containing also guanethidine (3 µM) and atropine (0.3 µM) at 30ºC, continuously bubbled with air and placed under 2 g of resting tension to recordings of the isometric contractions. Then the preparation was washed through stabilization period of 2 hrs, thereafter the GABA-induced relaxation was determined in Ca^{2+}(1 mM)-induced (Ca^{2+}-free Tyrode´s solution) or basal tone (Jalon´s solution). There was left a 30 min interval between additions of GABA (100 µM) and the effect of Gd^{3+} (100 µM), Ni^{2+} (100 µM) or verapamil (300 nM) was observed after its preincubation (5 min) before the second addition of Ca^{2+} or GABA. **Results:** During the plateau of Ca^{2+}-induced contractions in calcium-free Tyrode preparations, GABA addition promoted transient relaxations of 73.80 ± 8.83% (n=6) over contraction maintained by Ca^{2+}. While the second GABA addition promoted transient relaxations that were not significantly different from the initial relaxations, 84.47 ± 16.74% (n=6). Neither Ni^{2+} or Gd^{3+} preincubation affected Ca^{2+}-induced contraction. In Ni^{2+} presence, GABA-induced relaxations were reduced from 79.32 ± 3.62% to 66.43 ± 3.26% (t-test, $p < 0.038$; $n = 4$). The Gd^{3+} preincubation did not significantly changed the GABA-induced relaxations [69.51 ± 2.94% (control) to 64.51 ± 2.94% (plus Gd^{3+}); unpaired t-test, $p < 0.666$; $n = 3$]. On the other hand, in the Jalon´s solution the GABA addition in basal tonus promoted transient relaxations, which were not altered in the three consecutive additions of GABA. The verapamil addition significantly reduced baseline tone, while subsequent relaxations promoted by GABA addition were reduced to 20.3 ± 2.9% (n=3) over the temporal control (85.99%, n=2). **Conclusion:** These results indicate that neuronal channels sensitive to Ni^{2+} and verapamil mediates Ca^{2+} influx in the GABA-induced NANC relaxations of the rat duodenum. **License number of ethics committee**: 374/2017

08.013 Pharmacological evaluation of *Lippia alnifolia* **essential oil**: **Anticough**, **expectorant and antiasthmatic activities**. Vilela DAD[1], Macêdo CAF[1], Brito MC[1], Menezes PMN[1], Ribeiro TF[1], Lucchese AM[2], Ribeiro LAA[1], Silva FS[1] [1]UNIVASF – Ciências Farmacêuticas, [2]UESF – Ciências Exatas

The species *Lippia alnifolia* is used in popular medicine to treat asthma, the essential oil of *Lippia alnifolia* (EOLA) has been using in this work to investigate its pharmacological effects. All experimental procedures were approved by the UNIVASF Ethics Committee on Animal Use, under protocol number 0006/021014. Mice were placed in a glass chamber and individually aerated by nebulization with 0.4 M citric acid for 3 minutes for cough observation and then separated into groups (n=5). After 24 hours, the animals were submitted to a new nebulization of citric acid solution, but with pretreatment (30 minutes) with morphine 5 mg/kg (CP), EOLA 30, 100 and 300 mg/kg or 0,9% NaCl (CN). The parameters latency and frequency of cough were observed. Expectorant activity was determined by measuring the concentration of phenol red in the bronchooveolar lavage (BAL). For this, the animals were separated into groups (n=5) and fasted for four hours. They were then treated according to the corresponding groups: Ambroxol 120 mg/kg (CP), EOLA 30, 100 and 300 mg/kg or 0,9% NaCl (CN). 30 minutes later, phenol red solution (500 mg/kg) was administered. After a further 30 minutes, the animals were euthanized and the LBA was obtained. Subsequently, the concentration of phenol red was measured in a UV-VIS spectrophotometer by optical density at 565 nm wavelength and the results expressed in µg/mL. Initially the animals were immunized with the i.p. of a 500 µg/mL OVA solution. This procedure was performed on days 0 and 14. On day 21, the feed was removed for 1 hour and the animals treated with dexamethasone 2 mg/kg (CP), EOLA 30, 100 and 300 mg/kg or 0,9% NaCl (CN). One hour later the animals were challenged by inhalation of 10% aerosolized ovalbumin for 30 minutes, the procedure described above was repeated for 5 consecutive days. In addition, a control group of animals "immunized" with only 0.9% NaCl solution was also challenged by inhalation with 0.9% NaCl, for comparison of baseline parameters. On the 26th day of the experiment, blood and BAL samples were collected for global and differential cell counts. Treatment with EOLA at doses of 30, 100 and 300 mg/kg significantly decreased the frequency of coughing in mice by 41.5%, 62.5% and 92.9%, respectively. In addition, after treatment, an increase in red phenol secretion was observed in 147%, 329.54% and 218.69%. Antiasthmatic activity was also observed for EOLA, comparing the animals in the control group with those treated with the doses of 30, 100 and 300 mg/kg, where they were able to decrease eosinophilia by 78.41%, 56.9% and 65.04%, respectively. L. Alnifolia essential Oil presented significant effects of Anticough, expectorant and antiasthmatic activity, supporting the use of this plant in the alternative treatment of asthma. **License number of ethics committee**: 0006/021014 **Financial support**: Fundação de Amparo à Ciência e Tecnologia do Estado de Pernambuco

08.014 Evaluation of gastroprotective activity of estragole in animal models. Alves Jr EB, Serafim CAL, Pessoa MLS, Formiga RO, Barros MEFX, Batista LM UFPB – Ciências Farmacêuticas

Introduction: Estragole is a monoterpene present in essential oils of various plant species and presents pharmacological activity of great relevance for the treatment of diseases of the gastrointestinal tract. Therefore, the present study aimed to evaluate the acute toxicity, gastroprotective activity and mechanisms of action of stragole using *in vivo* experimental approaches. **Methods:** For the experimental proceedings with animals, it was used male Swiss mice (Mus musculus) weighing 25-35 and male Wistar rats (Rattus norvegicus) weighing 180-250g. In the acute toxicity assessment, mice (n= 3) were treated with tween 80 5% (control group) or stragole (300 and 2000 mg/kg). After the treatment, behavioral evaluation of the animals during the first 4 hours and after 24 hours during 14 days and the water and feed consumption were evaluated. Then, animals were euthanized and their organs were examined macroscopically and weighed to obtain the index of organs. The number of animal deaths during the experimental period was used to measure the lethal dose 50% (LD50) (OECD 423, 2001; ALMEIDA, R. N.; Rev. Bras. Cien. Farm., v. 80, p.72, 1999). For the evaluation of gastroprotective activity, animals (n= 7) were submitted to ethanol- (MORIMOTO; J. pharmacol, 57, 495, 1991), stress- (by immobilization and cold) (LEVINE, R. J.; ulcers, p 92-97, 1991) and non-steroidal anti-inflammatory drugs- (NSAIDs) (PUSCAS, I.; Arzneim. Forsch., v. 47, p. 568, 1997) induced gastric ulcer models. For the evaluation of the antiulcer mechanisms promoted by stragole, the participation of nitric oxide (NO) (SIKIRIC, P.; European Journal of Pharmacology, v. 332, p. 23-33, 1997), sulfhydryl groups (-SH) (MATSUDA, H.; LI, Y., YOSHIKAWA, M. Life Sciences, v. 65, p.27-32, 1999) and ATP-dependent potassium channels (K_{ATP}) (OLINDA, T. M.; Phytomedicine, v.15, n. 5, p.327 333, 2008) was assessed. Ulcers were determined by the area of ulcerative lesion (ULA) in mm^2 for rats and ulcerative lesion index (ULI) for mice. **Results:** In the acute toxicity evaluation, estragole (2000 mg/kg) showed a decrease in water and feed consumption, compared to the control group. Besides, there was no difference in organ index or behavioral alterations in this experiment. Then, LD50 was estimated to be higher than 2000 mg/kg with one death at the highest dose. The results obtained in the ethanol-induced gastric ulcer protocol demonstrated that carbenoxolone (100 mg/kg) or estragole (62.5, 125 and 250 mg/kg) administered orally reduced ULA to 60, 69, 74 and 95%, respectively, when compared to negative control group. In the stress-induced gastric ulcer model, cimetidine (100 mg/kg) or estragole (31.25, 62.5, 125 and 250 mg/kg) reduced ULI to 41.9, 44.9, 53.4, 59.0 and 64.9%, respectively. In the model of gastric ulcer induced by NSAIDs, cimetidine (100 mg/kg) or estragole (31.25, 62.5, 125 and 250 mg/kg) reduced ULI to 59.4, 46.0, 47.4, 55.8 and 63.9%, respectively. Those effects were related to the participation of NO and –SH compounds, but not to the K_{ATP} pathway. **Conclusions:** Thus, it was possible to conclude that the estragole presents low toxicity and also gastroprotective activity, which is related to cytoprotective mechanisms. **Acknowledgment:** CAPES/UFPB/PgPNSB/IPeFarM. **Ethics Committee on Animal Use (UFPB)**: Protocol number 134/2017.

08.015 Selective adrenergic beta-blocker reduced oxidative stress in myocardial muscle after intestinal ischemia-reperfusion in rats. Andrade-Leite A, Camargo CR, Teixeira LC, Coelho KASO, Lelis IO, Marques-Sanchez C, Oliveira-Junior IS Unifesp-EPM – Cirurgia

Introduction: Intestinal ischemia-reperfusion (IR) is a frequently occurring phenomenon during abdominal and thoracic vascular surgery, small bowel transplantation, hemorrhagic shock, and surgery using cardiopulmonary bypass, carrying high morbidity and mortality. Intestinal IR is associated with intestinal barrier function loss, which facilitates bacterial translocation into the circulation, thereby triggering systemic inflammation. Gut IR-induced inflammation has been studied extensively in animal models, human intestinal IR induced inflammatory responses remain to be characterized including ours effects at distance. The selective adrenergic beta-blockers were used for hypertension treatment. The alpha-1 adrenergic receptor are found predominantly on smooth muscle membranes of arteries, veins and sphincters of the urinary and GI tract [1,2,3,4]. **Purpose**: To investigate the effects of atenolol in oxidative stress in a myocardial injury by intestinal ischemia/reperfusion in rat model. **Methods:** This study was approved by the Animal Experimentation Ethics Committee (CEUA - 5980160514), Federal University of São Paulo (UNIFESP). Adult Wistar male rats (± 250 g body weight) were randomly (n=5), anesthetized and divided in: Sham: submitted to operation only; group SS+IR: intravenous saline solution (SS) infusion following superior mesenteric artery occlusion during 60 minutes (ischemia) and open for 120 minutes (reperfusion); group AT+IR: intravenous atenolol infusion (2 mg/kg) following superior mesenteric artery occlusion during 60 minutes (ischemia) and open for 120 minutes (reperfusion), all animals were submitted to muscular relaxation for mechanical ventilation using ambient air with tidal volume: 5 mL/kg; positive end-expiratory pressure, 2 cmH_2O, respiratory rate: 60-70 incursions per minute. In the end of experiment the animals were euthanized and the heart's tissue were analyzed for malondialdehyde by ELISA. **Results:** The group SS+IR (16.7±1.364 nmol/mg) demonstrated the higher malondialdehyde levels when compared with the atenolol treated-groups (10.76±1.569 nmol/mg) (p=0.001) in the heart tissue. **Conclusion:** Our findings indicate a significantly oxidative stress reduction in rat hearts after intestinal ischemia-reperfusion. **References:** 1. Shepherd G. Treatment of poisoning caused by beta-adrenergic and calcium-channel blockers. Am J Health Syst Pharm. 2006;63(19): 1828-35. 2. Khalid MM, Hamilton RJ. Stat Pearls [Internet]. Stat Pearls Publishing; Treasure Island (FL): Oct 9, 2017. Toxicity, Beta-Blocker. 3. Ladage D, Schwinger RH, Brixius K. Cardio-selective beta-blocker: pharmacological evidence and their influence on exercise capacity. Cardiovasc Ther. 2013;31(2): 76-83. 4. Grootjans J et al. Human Intestinal Ischemia-Reperfusion–Induced Inflammation Characterized: Experiences from a New Translational Model. Am J Pathol. 2010; 176(5): 2283–2291. **License number of ethics committee**: CEUA - 5980160514 - Federal University of São Paulo (UNIFESP).

08.016 Promising anti-diarrheal effects of preparation from leaves of *Campomanesia reitziana* **D. Legrand, a Brazilian medicinal plant**. Mariott M, Mariano LNB, Boeing T, Zanchett C, Da Silva RCMVAF, De Souza P, Andrade SF, Cechinel-Filho V, Da Silva LM Univali – Pharmaceutical Sciences

Introduction: The diarrhea is characterized by the enhancement of intestinal motility promoting the evacuation of semi-solid or aqueous stools three or more times per day. This condition is typically self-limiting; however can lead to profound dehydration and chronically to shock or organ damage. In Brazilian folk medicine, the leaves of *Campomanesia reitziana* D.Legrand (Myrtaceae), popularly named as *gabiroba*, have been used to treat diarrhea and dysentery. However, there are no pharmacological investigations on the antidiarrheal potential of decoction, extracts or fractions from leaves of *C. reitziana*. **Methods:** 340 g of fresh leaves was macerated with methanol during ten days, obtaining 19.58 g of the methanolic extract from leaves of *C. reitziana* (MECR). Further, MECR was bipartioned to obtain the ethyl acetate fraction (EAF, 15.2% yield) and the dichloromethane fraction (DMF, 17.62% yield). Decoction (DEC) of leaves from *C. reitziana* was elaborated in the ratio of 10 g of dry leaves to 100 ml of water. The effects of MECR (30-300 mg/kg), EAF (30-300 mg/kg), DMF (30-300 mg/kg) and DEC on the gastric emptying, intestinal transit and on the diarrhea induced by castor oil were verified in mice. Functional studies were performed to assess the effects of EAF on jejune contractile responses. The effects of EAF on the viability of intestinal epithelial murine cells (IEC6 cells) were measured. **Results:** The DEC (100 mL/kg, p.o) reduced the gastric emptying and intestinal transit by 52% and 45%, compared to the vehicle group (72% of gastric emptying and 40% of intestinal transit rate). The MECR (300 mg/kg, p.o), but not DMF, also reduced the gastrointestinal motility of healthy mice. Interestingly, the FAE (100 mg/kg, p.o) reduced the intestinal transit by 41%, but not changes the gastric emptying. Corroborating with the popular use of *C. reitziana*, the castor oil-induced diarrhea was completed inhibited by the oral intake of the DEC (100 ml/kg) or FAE (100 mg/kg) and partially abolished by MECR (300 mg/kg, p.o). As expected, loperamide (10 mg/kg, the positive control) reduced the gastric emptying, the intestinal transit and the diarrhea in mice. Given the results achieved by FAE *in vivo*, experiments *ex vivo* and *in vitro* were performed. The contraction induced by the cumulative addition of Ach (1 nM - 10 mM) was reduced by ≅ 65% in the presence of the FAE (300 µg/mL). In addition, the FAE fraction promoted a concentration-dependent CE_{50} = 0.31 (0.16 - 0.57 µM) to 1.75 (0.77- 3.97 µM, vehicle and FAE 300 µg/mL, respectively) reduction in the 5-HT (1µM)-induced contraction. According to the MTT test, FAE not change the viability of the murine IEC-6 cells. Phytochemicals trials revealed the myricitrin as the major compound found in the FAE. **Conclusion:** In view of the obtained data, it is possible to infer the presence of phytochemicals, mainly flavonoids, in leaves of *C. reitziana* capable of reducing gastrointestinal motility, justifying the antidiarrheal use in Brazilian popular medicine. In addition, FAE were able to concentrate such phytochemicals without affecting the cellular viability of epithelial intestinal cells. **License number of ethics committee**: CEUA/UNIVALI: 032/17p **Financial support**: **Financial support**: CNPq, CAPES, FAPESC and UNIVALI

08.017 Ferulic acid ethyl ester prevents intestinal inflammatory response and gastrointestinal delay in a model of postoperative ileus in mice Lacerda JVM[1], Lima IBC[1], Pereira LCA[1], Sousa MC[1], Nogueira KM[1], Souza LKM[1], Medeiros JVR[2], Oliveira RCM[3], Sousa DP[4], Santos RF[5] - [1]UFPI, [2]UFPI – Biologia, [3]UFPI – Biofísica e Fisiologia, [4]UFPB – Ciências Farmacêuticas, [5]UFPI – Bioquímica e Farmacologia

Introduction: Postoperative ileus (POI) is an abnormal pattern of gastrointestinal motility that frequently occurs after abdominal surgery and intestinal inflammatory response plays a critical role in the pathogenesis of POI. The ferulic acid ethyl ester (ethyl-3-hydroxy-4-methoxycinnamate -C12H14O4, FAEE), is a phenolic compound belonging to the class of phenylpropanoids, esterified derivative of ferulic acid, widely present in plants and grains such as rice and corn. Esterified FA derivatives are more lipophilic compounds, and have more potent antioxidant and anti-inflammatory properties. The present study investigated whether FAEE can ameliorate intestinal inflammation and impaired gastrointestinal transit seen in the mouse model of POI. **Methods:** The animals were divided into three groups (Sham, FAEE and vehicle). Experimental POI was induced in adult male Swiss mice by standardized intestinal manipulation (IM). Twenty-four hours later, gastrointestinal transit was assessed by charcoal propulsion test. FAEE was administered orally 30 minutes before the measurement of Gastrointestinal Transit (GIT). To evaluate the inflammatory and antioxidant response, the myeloperoxidase (MPO), nitrite (NOx), Superoxide dismutase (SOD), reduced glutathione (GSH) and malondialdehyde (MDA) levels of ileum were determined in mices.. Experimental POI in mice was characterized by decreased gastrointestinal transit and intestinal inflammatory response. **Results:** FAEE treatment led to recovery of the delayed intestinal transit induced by IM. FAEE significantly inhibited the MPO activity, a marker of neutrophil infiltration, and NOx, increased significantly SOD and GSH levels, markers antioxidants, and significantly inhibited MDA levels, a product of lipid peroxidation. **Conclusion:** FAEE treatment ameliorates the intestinal inflammatory response and the impaired gastrointestinal motility in the mouse model of POI. **Financial Support:** CAPES. The procedures were approved by the Ethics Committee on Animal Experimentation. (ECAE/UFPI nº 297/2017)

08.018 Gastroprotective and antioxidant activities of phytol in rats. Araújo RPN[1], Sousa SS[1], Nunes DB[1], Sousa MC[1], Sousa DP[2], Silva FV[3], Oliveira RCM[1], Santos RF[1] [1]UFPI – Plantas Medicinais, [2]UFPB – Ciências Farmacêuticas, [3]UEMA – Química e Biologia

Introduction: Gastric ulcer is one of the most prevalent diseases in adults in the world, having, in most cases, a benign nature, but may eventually cause complications such as bleeding and perforations, which are significant for morbidity and mortality. Given the high demand for drugs for the treatment of diseases of the gastrointestinal tract and the search for new substances, it is necessary to study natural products. Phythol, (3,7,11,15-tetramethylhexadec-2-en-1-ol) is a diterpene belonging to the group of long chain branched unsaturated acyclic alcohols and precursor of phythanic acid. It can be found in the marine environment or in essential oils. In other studies, it demonstrates antimycobacterial and anti-inflammatory activity. Up to the present date, there have been no studies on the possible gastroprotective and antioxidante effects of Phythol on experimental models of acute ulcers in rats. This study aimed to evaluate the potential antioxidante of this monoterpene in ethanol induced gastric lesion model in rats. **Methods:** Acute gastric lesions were induced in Wistar rats (n=5 animals/group) by oral route (1.0 mL/animal) of absolute etanol. Vehicle (NaCl 0.9 %, 10 mL/kg), Phythol (6.25, 12.5, 25 and 50 mg/kg) or carbenoxolone (100 mg/kg) were administered orally 1 h before application of the ulcerogenic agent. Animals were euthanized 30 min after ethanol administration and stomachs were removed. The area of gastric lesions was measured using Image J software-NIH® and was calculated as follows: lesion area (%) = lesion area (in square millimeters) × 100/total area (in square millimeters). We attempted to investigate the possible mechanisms that are involved in this protective action, so protocols for antioxidant activity were performed using the lowest dose of phythol with significant gastroprotective activity. Stomachs withdrawn from the Sham group and groups treated orally with vehicle, phythol (12.5 mg/kg) or carbenoxolone, were used to quantify following parameters: determination of non-protein sulfhydryl groups (NP-SH), myeloperoxidase activity (MPO) and analysis of malondialdehyde (MPO), dismutase superoxide (SOD) and catalase (CAT) in the homogenates from each group. The results are expressed as mean ± SEM. The statistical significance (*$p<0.05$) for differences between groups was calculated through the analysis of variance (ANOVA) and Tukey's post-hoc test using the GraphPad Prism™ 5.0 software (San Diego, CA, USA). **Results:** In this ulcer model, phythol showed a significant gastroprotective effect at doses of 12.5, 25 and 50 mg/kg, promoting a gastroprotective effect of 96%*, 90%*, 95%*, respectively, in relation to vehicle group. Treatment with phythol at 12.5 mg/kg restored gastric mucosa, reduced MPO (74%*) and MDA (59%*), increased NP-SH (88%*) and restored CAT activity and SOD compared to the vehicle group. **Conclusion:** These data show the gastroprotective activity of phythol and suggests that it may be associated with its antioxidant action. **Reference:** SALAMA, SM Scientific Reports, v.6, p. 1-14, 2016. MEWALAL, R. Trends in Biotechnology, v.35, n.3 , p.227-240, 2017 **License number of ethics committee**: CEEA/UFPI nº299/2017 **Financial support**: CNPq

08.019 Açaí (*Euterpe oleracea* **Mart**.) **extract improves biomarkers for inflammation and oxidative stress in ethanol-induced ulcer in rats**. Breviglieri E[1], Benhur JC[2], Somensi LB[2], Boeing T[2], Mariano LNB[2], de Souza P[2], da Silva RCMVAF[2], de Andrade SF[2], da Silva LM[2] [1]Estácio – Medicina, [2]Univali – Ciências Farmacêuticas

Introduction: Açaí (*Euterpe oleracea* Mart.) berries, characterized by high polyphenol concentrations (predominantly anthocyanins), have demonstrated numerous biological activities, including anti-inflammatory and antioxidant action. Because oxidative stress and inflammatory damage are intimately linked to gastric mucosal injury, this study investigated the potential gastroprotective of the dried açaí extract (DAE). **Methods:** The antiulcer activity of DAE was evaluated against gastric lesion model induced by absolute ethanol (1mL/kg, p.o) in rats. Following this, its ability to regulate antioxidant defenses and reduce inflammatory parameters was evaluated in the ulcerated tissues. The scavenger capability of DAE was assessed by DPPH assay. **Results:** The extract showed antioxidant activity *in vitro* (CI_{50}=210 µg/mL, 95% confidence interval equal: 131.9 to 334.7). The oral administration of DAE (30 and 100 mg/kg) reduced the area of ulcerative lesions induced by ethanol in 83 and 67%, respectively, compared to vehicle-ulcerated group (96.9 ± 12.8 mm²). As expected, carbenoxolone (200 mg/kg, p.o, used as positive control) also reduced the ulcer area. Besides, the DAE (100 mg/kg, p.o) induced increase on the reduced glutathione content and on the glutathione-*S*-transferase activity by 68% and 31%, respectively, vs vehicle-ulcerated group. Furthermore, animals treated with DAE showed levels of SOD activity in similar values to found in non-ulcerated groups ($p>0.05$) and elevated CAT activity compared to non-ulcerated group ($p<0.01$). Besides, the administration of DAE (100 mg/kg, p.o) was able to decrease by 67% the mieloperoxidase activity (an indirect marker of neutrophil migration MPO), as well as, reduced by 34% the TNF levels, related to vehicle ulcerated group. **Conclusion:** Taken together, our findings suggest that DAE reduces the inflammation and maintains oxidant/antioxidant homeostasis, resulting in a gastro-protective effect against ethanol-induced gastric damage. Therefore, DAE might be a promising natural resource or useful neutraceutical for treatment of gastritis and gastric ulcer. **License number of ethics committee**: CEUA/UNIVALI: 034/16p **Financial support**: **Financial support**: CNPQ, CAPES and UNIVALI.

08.020 Extracellular cyclic AMP is a novel source of adenosine in airways and regulates airway smooth muscle contractility. Pacini ES[1], Sanders-Silveira S[1], Jackson EK[2], Godinho RO[1] [1]Unifesp-EPM – Farmacologia, [2]University of Pittsburgh – Pharmacology and Chemical Biology

Introduction: cAMP is a universal intracellular second messenger involved in the bronchodilator effects of β_2-adrenoceptor (β_2-AR) agonists. In other tissues, cAMP also works as an extracellular messenger, after its efflux and interstitial conversion into 5'-AMP and adenosine by ecto-enzymes. Considering the central role of the β_2-AR/AC/cAMP signaling cascade in airway smooth muscle relaxation, the elevated levels of bronchoconstrictor adenosine in the lung of asthma patients, and the tolerance to the bronchoprotective effect of β_2-AR after its regular use, in the present study we evaluated the possible efflux of cAMP from tracheal tissue in response to β_2-AR agonists and the role of extracellular cAMP in airway smooth muscle relaxation. **Methods:** Tracheal rings obtained from adult male Wistar rats were mounted in a tissue bath system containing Krebs-bicarbonate buffer at 37°C and subjected to the following protocols: A) Carbachol (CCh) precontracted tracheas were incubated with increasing concentrations of cAMP, adenosine or fenoterol ± CGS-15943, and the isometric contraction forces were recorded and expressed as a percentage of the CCh EC_{30}. B) Tracheal rings were incubated for 0-60 min with 1 mM IBMX ± 1 µM fenoterol, and the extracellular cAMP collected from medium was measured using the Lance Ultra cAMP Kit (Perkin Elmer, USA). C) Tracheas were incubated with 300 µM of cAMP or vehicle for 1-60 min, and purines from the incubation medium were quantified using liquid chromatography–tandem mass spectrometry. Values are expressed as mean ± S.E.M. **Results:** Exogenous cAMP or adenosine induced contraction of tracheal smooth muscle in a concentration-dependent manner with distinct potencies (pEC_{50}; cAMP = 4 ± 0.5; adenosine = 5 ± 0.1) and maximum responses (cAMP = 19 ± 6%; adenosine = 60 ± 1%) (n=5-20). Pretreatment of tracheas with 20 µM CGS-15943 (a nonselective adenosine receptor antagonist) shifted the concentration-relaxation curve to fenoterol 11-fold to the left (n=3-5). Fenoterol increased by up to 550% the extracellular cAMP levels (basal = 1.52 ± 0.24 pmol/mg tissue, n=5-6). Incubation of rat trachea with cAMP induced a time-dependent generation of extracellular 5'-AMP, adenosine and inosine in the medium that reached 54 ± 3, 110 ± 18, 52 ± 8 and 43 ± 5 ng/mL, respectively (n=6), after 30-60 min. Conversely, in the absence of cAMP, the basal levels of purines were constant throughout the experiment. **Conclusion:** These results show that activation of β_2-AR induces the efflux of cAMP from tracheal cells and that extracellular cAMP is a relevant source of adenosine and other purines in airways. The expression of the extracellular cAMP-adenosine pathway with contracting effects on tracheal muscle and the ability of CGS-15943 to potentiate the relaxing effect of fenoterol indicate that the combination of β_2-AR agonists with adenosine receptor antagonists could have potential clinical use in the treatment of asthma and chronic obstructive pulmonary diseases. **License number of ethics committee**: CEUA #9987150714. **Financial support**: CAPES, CNPq and Fapesp.