14. Pharmacology: Other

14.001 N-acylhydrazone derivative (LASSBio-785) antagonizes *Apis mellifera* venom activity in mice. Tavares-Henriques MS[1], Teixeira-Cruz J M[1], Monassa de Souza P[1], Monteiro-Machado M[1], Cons BL[1], Barreiro EJ[2], Fraga CAM[2], Melo PA[2] [1]UFRJ – Farmacologia, [2]UFRJ – Farmacologia e Química Medicinal

Introduction: Accidents caused by *Apis mellifera* bee stings are a public health problem in the Americas, and there are reports of many cases of envenomation in humans and animals. The bee venom consists of a complex mixture of substances that induce a local and systemic inflammatory response affecting the heart, skeletal muscle, kidney, in blood volume and concentration, which can lead to death. Although the patients receive emergence care, there is no specific treatment in this type of poisoning. OBJECTIVE: Our goal is to evaluate the effect of the LASSBio 785, a synthetic substance on the in vivo and in vitro effects of A. mellifera venom. **Methods**: In vivo we performed experiment in Swiss adult mice (20-25 g) which housed, handled and experimental procedures were in compliance with the recommendations of the Animal Care and Use Committee of Universidade Federal do Rio de Janeiro (protocol #DFBCICB0026). For the plantar edema activity, we inject 1 µg/paw bee venom at different doses (1-10 µg/paw). We evaluated the effect of the treatment by i.p. injections of LASSBio 785 at different doses (10-30 µg/g) on the venom injection effect. We inject the same dose of bee venom in the skin to increase the permeability and performed the same treatment with LASSBio 785 (30 µg/g) by i.p. route. The hematocrit was measured from the blood collected of anesthetized animals who received DL i.p. injection of 10 µg/g of venom and also in animals that received LASSBio 785 (30 µg/g) after 2 h. Myotoxicity was evaluated by the plasma creatine kinase (CK) activity measurement in blood collected from mice after the perimuscular injection in the hind paw and in the treatment with LASSBio 785. Phospholipase and hyaluronidase activities were evaluated in vitro by decreasing the turbidity method of a hen's egg yolk and the hyaluronic acid solutions, respectively. Data are expressed by the mean ± standard error (n=6) and we considered statistically significant at $p < 0.05$. **Results**: All bee venom doses (1-10 µg/paw) were able to cause a peak of edema in 15 minutes; (*1 = 7.0 ± 0.9 mm^2, * 3 = 6.0 ± 0.6 mm^2; * 10 = 5.8 ± 1.0 mm^2 vs control = 0.9 ± 0.1 mm^2), that antagonized by LASSBio 785 (30 µg/g). The increase of skin permeability and the hematocrit values induced bee venom, was partially neutralized by LASSBio 785. The compound LASSBio 785 did not inhibit phospholipase or hyaluronidasic bee venom activities. **Conclusion**: These data are indicating that LASSBio 785 decrease the inflammatory effect induced by A. mellifera bee venom without affect the enzymatic tested activities. **Financial support**: CAPES; CNPq; FAPERJ, INCT DE FÁRMACOS E MEDICAMENTOS (CNPq/ FAPERJ) and PRONEX

14.002 Antimicrobial activity of Selin-11-en-4α-ol isolated from *Nectandra grandiflora* **essential oil.** Rodrigues P[1], Garlet QI[2], Pires LC[1], Spall S[1], Gressler LT[3], Bandeira Júnior G[3], Vargas APC[3], Heinzmann BM[1] [1]UFSM – Farmácia e Farmacologia, [2]UFSM – Farmacologia, [3]UFSM – Medicina Veterinária

Introduction: Microbiological control in aquaculture proceedings is a relevant concern, since bacterial contamination of fish and fish products goes to humans through feeding. *Plesiomonas shigelloides, Citrobacter freundii, Acinetobacter calcoaceticus* and *Aeromonas hydrophila* are Gram-negative bacteria linked with fish infection (JOH, S.J.Vet Microbiol, 163: 190, 2013). These microorganisms can also lead to infections and debilitating conditions in humans, such as gastroenteritis, peritonitis, pneumonia, skin and soft tissue infections (NEMEC, A. Int J Syst Evolut Microbiol, 65: 934, 2015). Nowadays, natural products, mainly essential oils (EO) and its components, are targets for studies of new drugs with antibiotic properties that can bypass the microbial resistance observed to classical antibiotics (YAP et al. The Open Microbiol J, 8:6, 2014). This work describes the antimicrobial potential of Selin-11-en-4α-ol (SS), a sesquiterpene alcohol found in *Nectandra grandiflora* (Lauraceae) EO against fish pathogenic bacteria. **Methods:** *N. grandiflora* leaves were collected in Jaguari, RS, Brazil. EO extraction was performed by hydrodistillation in Clevenger apparatus for 3h (BRAZILIAN PHARMACOPOEIA, 5th. ed., 2010). SS was isolated by column chromatography procedure. Isolated SS was characterized by GC-MS and GC-FID. The antimicrobial assay were performed by microdilution method according to *Clinical Laboratory Standards Institute* guidelines (2008), using strains of *P. shigelloides*, *A. calcoaceticus*, *C. freundii, A. hydrophila* obtained from naturally infected silver catfish (*Rhamdia quelen)* and a standard strain of *A. hydrophila* ATCC7966. The applied concentrations ranged from 6400 to 3.12 µg/mL for determination of minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC). **Results:** SS amounted 5.09% of the EO and was isolated with 98.28% purity. The yield of the isolation process was 78%. MIC and MBC values observed, respectively, were as following: *P. shigelloides* (800 and >3200 µg/mL), *A. calcoaceticus* (800 and >3200 µg/mL), *C. freundii* (3200 and >3200 µg/mL)*, A. hydrophila* (200 and 3200 µg/mL) and *A. hydrophila* ATCC7966 (3200 and >3200 µg/mL). There are no reports concerning the antimicrobial properties of SS, however EO containing this compound (24.6%) showed bactericide activity against *Streptococcus* sp. (RASOANAIVO, P Chem Biodivers, 1876: 1886, 2013). Natural compounds presenting MIC values between 600 and 1500 µg/mL are classified as moderate inhibitors, while those with MIC values below 600 µg/mL are considered strong inhibitors. **Conclusion**: Following this thought, SS inhibited moderately the growth of *A. calcoaceticus* and *P. shigelloides* strains, and showed strong antimicrobial activity against *A. hydrophila*. Therefore, SS enclosures antimicrobial potential that could be applied as preventive or in treatment interventions for microbial control. **Financial Support:** FAPERGS/PRONEX; FINEP; INCT ADAPTA; CNPq and FAPEAM

14.003 Cationic liposomes containing antioxidants reduces pulmonary injury in experimental model of sepsis. Araujo MP, Pereira CFC, Araújo RB, Galvão AM, Maia MBS
UFPE – Farmacologia de Produtos Bioativos

The intracellular redox state of alveolar cells is a determining factor for tolerance to oxidative and pro-inflammatory stresses. This study investigated the effects of intratracheal co-administration of antioxidants encapsulated in liposomes on the lungs of rats subjected to sepsis. For this, male rats subjected to sepsis induced by lipopolysaccharide from Escherichia coli or placebo operation were treated (intratracheally) with antibiotic, 0.9% saline and antioxidants encapsulated or non-encapsulated in liposomes. Experimental model of sepsis by cecal ligation and puncture (CLP) was performed in order to expose the cecum. The cecum was then gently squeezed to extrude a small amount of feces from the perforation site. As an index of oxidative damage, superoxide anions, lipid peroxidation, protein carbonyls, catalase activity, nitrates/nitrites, cell viability and mortality rate were measured. All experimental procedures involving animals were performed in accordance with the Brazilian College of Standards for Ethics in Animal Experimentation (COBEA) and approved by the Ethics Committee on Animal Experiments (CEUA) UFPE under letter 215/09, process n°. 23076.018913/2009-41. Infected animals treated with antibiotic plus antioxidants encapsulated in liposomes showed reduced levels of superoxide anion (54% or 7.650 ± 1.263 nmol/min/mg protein), lipid peroxidation (33% or 0.117 ± 0.041 nmol/mg protein), protein carbonyl (57% or 0.039 ± 0.022 nmol/mg protein) and mortality rate (3.3%), p value <0.001. This treatment also reduced the level of nitrite/nitrate and increased cell viability (90.7%) of alveolar macrophages. Taken together, theses results support that cationic liposomes containing antioxidants should be explored as coadjuvants in the treatment of pulmonary oxidative damage.

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14.004 Evaluation of the influence of CYP2C19*17 polymorphism on the major depression disorder remission in patients receiving escitalopram treatment. Nascimento LRS[1], Vianello RP[2], Ghedini PC[1], de Brito RB[1] [1]UFG – Farmacologia, [2]Embrapa

Introduction: Escitalopram (ESC) is a selective serotonin reuptake inhibitor, indicated for the treatment of depression and anxiety disorders. The CYP2C19 gene presents variation sites that may affect the pharmacokinetics of antidepressant medications. The CYP2C19*17 variant allele is associated with *increased enzyme activity,* which might imply an increased risk of therapeutic failure. On the basis of these informations, this study was performed aiming to evaluate if CYP2C19*17 polymorphism influences the remission of depressive symptoms in a group of patients receiving ESC. **Methods:** 21 patients of both sexes, who met the criteria for the remission of a major depression disorder (MDD) for at least twelve months and received ESC long-term, were genotyped for CYP2C19*17. The DNA was extracted from the venous blood. The amplification of gene region of CYP2C19*17 polymorphism was performed using polymerase chain reaction (PCR) followed by sequencing technique. The phenotype was estimated based on the combination of alleles detected. **Results** were analyzed using X^2 and Fisher's exact test with SPSS software package (version 21.0; SPSS Inc., IL, US). A p-value <0.05 was considered statistically significant. **Results:** Based on the genotype frequencies observed, 7 (22.6%) subjects were designated as heterozygous ultra-rapid metabolizers (UMs, *1/*17) and 14 were *CYP2C19* extensive metabolizers (EMs*, *1/*1*). The UMs homozygous *17/*17 was not found in this group. No significant difference was found in the ESC doses used between the groups; however, all patients using an ESC combination (ESC plus mirtazapine or bupropion) were UMs (*1/*17) (P= 0.001). **Conclusion:** The results indicate that the *17 ultra-rapid allele seems to be the factor responsible, through the ESC combination, for MDD remission in these patients. Future studies with larger sample size should be necessary with the aim to confirm the influence of CYP2C19*17 polymorphism on this issue. **Financial support:** Capes, CNPq and Fapeg Research approved by the Human Research Ethical Committee from Federal University of Goiás (protocol number 204/2009).

14.005 Preliminary data about the influence of CYP2C19*2 polymorphism on the response to escitalopram treatment. Alves GLD[1], Vianello RP[2], Ghedini PC[1], de Brito RB[1]
[1]UFG – Farmacologia, [2]Embrapa – Agricultura

Introduction: The CYP2C19 gene presents variation sites that may affect the pharmacokinetics of several drugs of clinical importance, including antidepressant medications as escitalopram (ESC). CYP2C19*2 variant allele is associated with decreased enzyme activity rates, which might imply an increased risk of drug side effects. This study investigated if CYP2C19*2 polymorphism has influence on ESC treatment in patients with remission of depressive symptoms taking ESC at oral doses of 10, 15 or 20 mg/day and with an average use of 2.5 years. **Methods:** DNA was extracted from blood samples obtained from 22 patients (6 males and 16 females, aged 22-66 years) and CYP2C19*2 mutation was evaluated by PCR-RFLP. Data were analyzed using X^2 and Fisher's exact test. A p-value of less than 0.05 was considered statistically significant. Statistical analysis were performed using the SPSS software package (version 21.0; SPSS Inc., IL, US). **Results:** Two genotypes were found in the present samples, including 16 subjects (72.7%) with no mutated alleles (*1/*1) and 6 (27.3 %) with one mutated allele (*1/*2). No sample carrying two CYP2C19 mutated alleles (*2/*2) was found in the present series. The dose of 15 mg/day ESC was the most frequent in patients carriers of loss-of- function *2 allele (4; 66.8%), where as the doses of 10 and 20 mg/day had the same distribution (1; 16.6%). These results were not different when compared to noncarriers of *2 allele: 62.6% (10), 18.7% (3) and 18.7% (3) for doses of 15, 10 and 20 mg/day, respectively (P= 0.492). **Conclusion:** These preliminary data suggest no influence of the CYP2C19*2 polymorphism on dose-response to chronic treatment with ESC. Further studies with a larger sample size should be performed to confirm the data. **Financial support:** Capes, CNPq and Fapeg Research approved by the Human Research Ethical Committee from Federal University of Goiás (protocol number 204/2009).

14.006 Electromyographic evaluation of Thiocolchicoside and ethanol drug interaction
Cordeiro PGA[1], Sousa PHS[1], Souza DS[1], Lobato AMV[1], Martins MFC[1], Pereira EHS[1], Machado JLP[1], Nascimento LNS[1], Lopes MSP[1], Farias RAF[1], Jóia-Mello V[1], Hamoy M[1] [1]UFPA – Farmacologia e toxicologia de produtos naturais

Introduction: Thiocolchicoside is a very often used clinical drug due to its myorelaxing, anti-inflammatory and analgesic activities. However its molecular target and path mechanism are still in prospecting, but seems to be associated with GABAergic activities (Biziere, 1981). The development of studies focused on thiocolchicoside and ethanol interaction could describe meaningful clinical manifestations. **Objectives**: Evaluate the electromyography and behavioural profile of the animals treated with the tiocolchicosídeo and its interaction with ethanol and compared with the interaction between benzodiazepines and alcohol. **Methodology:** 54 Wistar rats adult males were used, weighing 250 - 300g, from the vivarium of the Federal University of Pará (CEUA 101-2015) and maintained in the Laboratory of Pharmacology and Toxicology of Natural Products. The animals were divided into nine groups (n = 9) and received by said treatments VO.G1 control - saline G2 - 5 mg / kg thiocolchicoside; G3 - 5 ml / kg of 40% ethanol; G4 5 mg / kg thiocolchicoside and 5 ml / kg of 40% ethanol; G5 2mg / kg Diazepam; G6- 2mg / kg Diazepam and 5ml / kg of 40% ethanol. Steel implants and electrodes were built and used in the eighth intercostal muscle space. **Results:** Regarding the energy intensity captured by the electrode in the electromyogram of the intercostal muscles, the normal animal group had a mean of 7.545 ± 0.4760 mv^2 / Hz x 10^{-3} showing significant difference in relation to the application of alcohol 2.619 ± 0.5294 mv^2 / Hz x 10^{-3} and diazepam 2.596 ± 0.2952 mv^2 / Hz x 10^{-3} which separately accounted decrease in contractile force in the intercostal. After applying thiocolchicoside respiratory depression was very close to the normal pattern and the level of energy captured at the electrode was (6.007 ± 0.6 23 mv^2 / Hz x 10^{-3}). The lower electrical activity in the contraction of the intercostal was observed using diazepam combination with alcohol which represented an average of 0.3698 ± 0.09011 mv^2 / Hz x 10^{-3} demonstrating abdominal breathing with severe decrease in frequency. The association of thiocolchicoside with ethanol showed depression in respiratory rate in a lower intensity than the benzodiazepine, but statistically significant difference when compared with the group that received alcohol only, indicating drug interactions and possible potentiation (1.286 ± 0.1129 mv^2 / x 10^{-3} Hz).**Conclusion**: The results indicate a strong interaction between thiocolchicoside and ethanol, which can compromise the patient's breathing similar to what happens with benzodiazepines.
Acknowledgments: Laboratório de Farmacologia e Toxicologia de Produtos Naturais
Approval Animal Research Ethical Committee: CEUA/UFPA 101-2015

14.007 Assessment to drug therapy in patients with chronic diseases users of SUS in Novo Hamburgo, RS Bigolin C[1], Vieira I[1], Betti AH[1], Perassolo MS[1], Raach JR[1], Vargas TG[1], Schimidt A[1], Vanzzela S[1], Seibel LM[1 1]Universidade Feevale – Instituto de Ciências da Saúde

Introduction: Adherence to the medical regimen is an essential step in the management of chronic diseases and continues to rank as a major clinical problem in these disorders. Adherence has been defined in different ways; the World Health Organization defines it as “the extent to which a person’s behavior, taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider”. Therefore, the aim of this study was to assess adherence to drug therapy in patients’ users of SUS in Novo Hamburgo, RS. **Methods:** A non-experimental cross-sectional design was conducted to measure adherence to drug therapy in 65 patients with chronic diseases. Demographic and medical profiles of patients and the factors associated with adherence were evaluated. Medication adherence was assessed using the Morisky-Green Test (MGT) and Brief Medication Questionnaire (BMQ). The Human Research Ethical Committee approved this research (n° 1.056.949). **Results:** The profile of the patients studied was 81.5% females, 61 ± 14 years old, and 55.9% with incomplete primary education. It was identified the use of 67 different drugs: fluoxetine (32.3%), omeprazole (27.7%), simvastatin (23.1%), losartan (21.5%), calcium carbonate (18.5%) and atenolol (18.5%). Each patient used on average 4 ± 2 drugs (minimum 1 and maxim 9 drugs). According to the MTG adherence evaluation, 5.2% of patients demonstrated non-adherence, 29.3% low adherence, 15.5% moderate adherence and 50% high adherence. According to BMQ, 57.6% of patients have potential non-adherence, 25.4% positive screening for belief barriers and 78% memory barriers in relation to theirs drugs. The MTG and BMQ presented a poor correlation ($r=0.49$, $P<0.01$). **Conclusion:** These results suggest a low adherence to drug therapy of the population studied. Considering the negative consequences to patients with poor adherence to drug therapy, such as memory difficulties, new strategies will be traced with them to improve their health condition. **Financial support:** Feevale and CNPq.

14.008 Human thioredoxin influences Staphylococcus aureus virulence in vitro Silva BLR[1], Mendes SJF[1], Pereira DMS[1], Ferro TAF[1], Monteiro-Neto V[1], Fernandes ES[1,2] [1]Ceuma – Programa de Pós-Graduação, [2]King's College London – Cardiovascular Division

Introduction: *Staphylococcus aureus* (*S. aureus*) is one of the leading causes of skin and soft tissue infections. An increase of incidence of community-acquired methicillin resistant *S. aureus* (CA-MRSA) skin infections in healthy individuals (David et al., 2010), has raised concerns on disease management. In this context, host´s immune response to infection plays a detrimental role. Thioredoxin (TRX) is a protein produced by all species, from bacteria to humans (Lee et al., 2012). Produced by the host during oxidative stress, TRX is a potent antioxidant, acting to downregulate an existing inflammatory response. Although microrganism-derived TRX is associated with evasion from the host's immune system, host-derived TRX may be linked to increased microorganism virulence (Collet et al., 2010; Korge et al., 2015). However, little is known on how human TRX affects bacterial virulence. Here, we investigated the effects of human recombinant TRX on *S. aureus* virulence *in vitro.* **Methods:** For this, 10 µl of *S. aureus* (ATCC 25923) (10^8 CFU/ml) were incubated with different concentrations of human TRX (1.0-4.0 µg/ml) for 18h at 37^oC. Vehicle-treated *S.aureus* were used as controls. Growth, cell viability, metabolism capacity and ability to form biofilm were analysed. Growth was evaluated by the microdilution method (Sader et al. 2009). For quantification of cell viability and metabolic capacity *S. aureus* was incubated with of PrestoBlue® (20µl/well; Life Technologies), and results were calculated according to manufacturer´s instructions. Finally, biofilm formation was performed according method described by Stepanovic et al. (2004). **Results:** Human TRX (0.25 µg/ml) increased *S. aureus* growth (1.2 fold-increase) and reduced biofilm formation by 52% when incubated at 4 µg/ml. Human TRX had no effects on *S. aureus* viability and metabolism at any of the tested concentrations. **Conclusion:** Depending on its concentration, human TRX can regulate different aspects of *S. aureus* virulence. This is of importance as different patients may produce different amounts of thioredoxin when infected with this microorganism, and this would probably impact patient's ability to respond to infection. However, the real impact human TRX effects may have *in vivo* with host´s immune system fighting *S. aureus* infection, remains unclear. **Financial support:** This research was funded by FAPEMA, CNPq and CAPES. Collet and Messens. Antioxid Redox Signal, 13:1205, 2010. David and Daum. Clin Microbiol Rev. 23:616, 2010. Korge et al. Biochim et Biophys Acta, 1847:514, 2015. Lee, S, Kim. Antioxid Redox Signal. Vol 1: 4322; 2012. Sader et al. Antimicrob Agents Chemother. 53: 3162-3165; 2009. Stepanovic et al. Appl Microbiol 38: 428-432; 2004.

14.009 Evaluation of chromones as inhibitors of acetylcholinesterease through molecular docking and molecular dynamics. Orduz-Diaz LL, Rincón S, Coy-Barrera E Facultad de Ciencias Básicas y Aplicadas, Universidad Militar Nueva Granada – Laboratorio de Química Bioorgánica

Introduction: One of the most promising approaches within the treatment of the early stages of Alzheimer disease (and other cases of dementia) is the acetylcholinesterase (AChE) inhibitors-based therapy [1]. However, the efficacy of approved drugs has several limitations, being necessary the searching and evaluating additional biologically active compounds having increased effectiveness in inhibiting the AChE enzyme. Currently, there is evidence that some naturally-occurring chromone-related compounds exhibited inhibition of AChE at different levels [2]. **Methods:** A group of 75 naturally-occurring chromone-related compounds were assessed at *in silico*-level through molecular docking and molecular dynamics to identify those molecules that have higher affinity for the target enzyme (i.e., ACE) using Autodock/Vina and Gromacs, respectively. Additionally, test compounds were also structurally optimized at DFT level in order to calculate quantum properties. Docking calculations per ligand were performed ten times and the resulting data (affinity in kcal/mol and RMSD in Å) were analyzed by multivariate analysis in order to examine at molecular level the better interactions as selecting criteria. The ligands possessing the best docking results were studied by molecular dynamics simulations within the active site of AChE. Thus, for the most-stable chromone-enzyme complexes, a detailed structural interactions analysis and their relevance were also documented. **Results and Conclusions:** Affinity and RMSD values were correlated through multivariate statistical analysis, demonstrating good classification of chromones and the relationship between affinity, quantum properties and chromone-type was therefore achieved. Each chromone-type compounds exhibited particular interactions with the residues into the AChE active site. Thus, within the purpose of contributing to the discovery and development of potential agents for Alzheimer disease therapy, this approach let us to propose four hit chromone-related structures as promising AChE inhibitors. *The present work is a product derived by the Project INV-CIAS-2050 financed by Vicerrectoría de Investigaciones at UMNG - Validity 2016.* **References:** [1] Forero DA, et al. 2006. *Neurosci Res,* 55, 334. [2] Benamar H, et al. 2010. *J Biol Sci*, 10, 1. [3] Huang, Ling, et.al. 2013. Curr Top Med Chem, 13(15), 1864.

14.010 Metabolic evaluation of obese mice treated with lipid nanoparticle of sclareol. Cerri GC[1], Lima LCF[2], Ferreira LAM[3], Santos SHS[1] [1]ICB-UFMG – Farmacologia e Fisiologia, [2]UFES – Morfologia, [3]UFMG – Pharmaceutical Products

Introduction: Metabolic syndrome is one of the consequences of obesity and has several components that predispose an individual to increased risk of cardiovascular disease and insulin resistance (1 and 2). Sclareol is a diterpene isolated from Salvia sclarea. Sclareol has been used as ingredient in cosmetics (3). Furthermore, this diterpene has been shown (i) to activate cytotoxic and cytostatic pathways against leukemia cell lines, (ii) anti-inflammatory and (iii) antioxidant properties (4, 5 and 6). However, Sclareol has low bioavailability due to its high lipophilicity, therefore the use of Sclareol *in vivo* is hampered (4, 6 and 7). This study aim is to evaluate the metabolic effects of Sclareol in different formulations (lipid nanoparticle and free) of mice with high fat diet induced metabolic syndrome. **Methods**: Swiss male mice were initially divided into two groups throughout 4 weeks: standard diet (ST) and high fat diet (HF). Subsequently, insulin sensitivity test and glucose tolerance test were performed. Each group was divided into 3 treatments subgroups: free sclareol (Sc), lipid nanoparticle of sclareol (L-Sc) and empty lipid nanoparticle (L). The sclareol (free and lipid nanoparticle) were administered intraperitoneally in 300ul and 1mg/kg dose. Treatments were performed for 30 days. Afterward, the glucose tolerance test and insulin sensitivity test were performed. The animals were euthanized by decapitation, blood and target organs were collected and stored. **Results**: During treatment body weight reduced approximately 20%. Significant improvement of glycemic profile in HF L-Sc mice was shown (area under the curve: ST L 8100 ± 401.8 *vs* HF L 25950 ± 5965** *vs* HF L-SC 10460 ± 1506**;** P<0.001). It was also observed approximately 22% adiposity reduction in HF L-Sc mice compared with HF L mice. Furthermore, histological liver analysis showed a significant decrease of liver fat in HFL-Sc mice compared with HFL mice. Conclusion: The lipid nanoparticle of sclareol improved metabolic parameters in obese mice (decreased body weight, body fat, hepatic fat and improved insulin resistance). Sclareol when associated with lipid nanoparticle may be a new therapeutic strategy to assist in the treatment of diseases associated with metabolic disorders. References: 1) Grundy. Circulation.109.433.2004. 2) Santos. Diabetes.57.340.2008. 3) Bhatia. Food and Chem.Toxic.46.270.2008. 4) Hatziantoniou. Pharma. Research.380.2006. 5) Huang. Nat. Prod. 75.54.2012. 6) Mahaira. Euro.Jour.of Pharm.666.173.2011. 7) Dimas. Apoptosis.12.685.2007. Submission protocol CEUA: 289/2014. **Financial support:** FAPEMIG, CNPq, Capes.

14.011 Evaluation of influence of CYP2C19*2 and CYP2C19*17 polymorphisms on response to clozapine treatment. Semedo AT[1], DeBrito RB[1], Vianello R[2], Ghedini PC[1] [1]UFG – Farmacologia, [2]Embrapa – UFG

Introduction: The CYP2C19 gene presents variation sites that may affect the pharmacokinetics of several drugs of clinical importance, including antipsychotics medications as clozapine (CLZ). CLZ is a drug used for the treatment refractory schizophrenia (TRS), however, 30-40% of the patients do not respond completely to CLZ treatment, constituting the individuals with super-refractory schizophrenia (SRS). Considering the CYP2C19 polymorphisms are associated with alterations in the CLZ metabolism, this study evaluated if CYP2C19*2 and CYP2C19*17 polymorphisms influence the response to CLZ treatment. **Methods**: 34 patients who met the criteria for TRS and 35 individuals for SRS receiving CLZ at least for 12 months were included for genotype testing. DNA of patients was extracted from venous blood and CYP2C19*2 and CYP2C19*17 polymorphisms were analyzed by polymerase chain reaction (PCR) followed by sequencing technique. The phenotype was estimated based on the combination of alleles detected. Group comparisons were performed, using X^2 and Fisher´s exact test. A p-value < 0.05 was considered statistically significant. Statistical analyses were performed, using the SPSS software package (version 21.0; SPSS Inc., IL, US). All procedures of this study were approved by the Human Research Ethical Committee from Federal University of Goiás (protocol number 1.483.734). **Results**: Among 34 patients with TRS, 13 (38.2%) were *1/*1, 7 (20.6%) were *1/*2, 11 (32.4%) were *1/*17 and 3 (8.8%) were *2/*17. Patients with SRS showed the following genotypes frequencies: 11 (31.4%) for wild type *1/*1, 1 (2.9%) were *1/*2, 20 (57.1%) heterozygous for *1/*17 and 3 (8.6%) were heterozygous for *2/*17. The predicted phenotypes for TRS were: 47.1% extensive metabolizers (EMs) (*1/*1 and *2/*17), 20.5% intermediate metabolizers (IMs) (*1/*2) and 32.4% ultra-rapid metabolizers (UMs) (*1/*17). The phenotypes in SRS patients were: 40% EMs, 2.9% IMs and 57.1% UMs. No homozygous mutant was observed. The results showed there are no differences in the distribution of genotypes and phenotypes frequencies between TRS and SRS patients (P=0.06). **Conclusion**: The present study showed CYP2C19*2 and CYP2C19*17 not influence the response to CLZ treatment. **Financial support**: Fapeg, Capes, CNPq

14.012 Evaluation physicochemical and potential antifungal of *Camellia sinensis* Infused (L.) Kuntze isolated against clinical dermatophytes Silva SL[1], Carmo ES[2], Souza JBP[2] [1]UFPB – Farmácia, [2]UFCG

Introduction: Dermatophytoses are infections caused by fungi, which are limited to keratinized portions of the skin, hair or nails. Knowing the limited therapeutic tools and increased fungal resistance, it is perceived in the natural products important alternatives to be investigated. The aim of this study was to determine the physical and chemical parameters of infusions of Camellia sinensis (L.) Kuntze and their potential antifungal against dermatophytes. **Methods**: The determination of moisture content, content of total ash and acid-insoluble ash, as well as the dry residue were carried out according to protocols described by the organization standardizes quality control of plant drugs in Brazil (National Health Surveillance Agency. 1, 546, 2000) and antifungal susceptibility of the strains Trichophyton rubrum front of different drug infusions obtained from vegetable and agranel sachet were performed according to protocols described by (clinical and laboratory standards institute. 18, 22, 2002). **Results**: The data of moisture content were 11.33% and 11.19%, for the drug, bulk and sachet respectively. The content of total ash and acid insoluble ash, also fulfilled the parameters of literature, except for the content of acid insoluble ash for bulk drug with value greater than 1.5%. The soluble solids content in liquid extractor (dry) demonstrated that infused when subjected to extraction processes with agitation provided higher yields. In the evaluation of the antifungal susceptibility by microdilution technique, there was no inhibition of growth of the strains Trichophyton rubrum, when exposed to infusions from C. sinensis. **Conclusions**: Therefore realized with the physical and chemical tests, except for the insoluble ash content in acid for bulk vegetable drug, both ways of obtaining (bulk and sachet) are within the limits specified in the literature and that the tested infusions were not able to inhibit the strains *Trichophyton rubrum*. Acknowledgments: At the Center of Education and Health the Federal University of Campina Grande.

14.013 Evaluation of antinociceptive activity of oleoresin of Copaifera reticulata Almeida Junior JS[1], Silva EBS[1], Araujo JA[1], Sartoratto A[2], Moraes TMP[1], Oliveira ECP[3], Moraes WP[1] [1]ISCO-Ufopa – Saúde Coletiva, [2]UNICAMP – CPQBA, [3]IBEF-Ufopa – Biodiversidade e Florestas

Introduction: *Copaifera reticulata* popularly known as 'copaíba' is a type of medicinal plant widely spread throughout the Amazon region, where the indigenous, first inhabitants in the region, found that when the tree trunk is tapped an oleoresin with medicinal properties is exuded. This oleoresin is used in traditional medicine, especially as anti-inflammatory and antinociceptive, and therefore it is necessary to carry out studies that show its effects reported in ethnopharmacological work. In this context, this study proposed to evaluate the antinociceptive effect of oleoresin of *C. reticulata* through hot-plate, writhing and formalin tests, aiming to corroborate the search for evidences to justify its use in traditional healing and, further on, obtaining phytotherapics made of natural products native from the Amazon. Additionally, this study aimed to determine the chemical composition of the oleoresin of *C. reticulata*, determining its acute toxicity. **Methods:** The oleoresin used for the experiments was collected in the Tapajós National Forest (FLONA), in the municipality of Belterra-PA, in a dry period, and characterized chemically by a Gas Chromatograph coupled with Mass Spectrometry (GC-MS). The acute toxicity testing was conducted according to the guidelines of The Organisation for Economic Co-operation and Development (OECD) OCDE-423/2001 (OECD, 2001) to stablish the dose and biological safety level of the oleoresin, followed by the chemical characterization and afterwards the hot-plate, writhing and formalin tests. **Results:** The acute toxicity test of the oleoresin determined that the toxic dose is above 2000 mg/Kg. The oleoresin of *Copaifera reticulata* presented as major constituents six sesquiterpene compounds which together correspond to 74.74% of the total chemical composition, which are: beta-elemene (6,96%), trans-alfa-bergamotene (12,76%), cis-eudesma-6,11-dieno (14,20%), beta-selinene (8,7%), alfa-selinene (7,03%), and beta-bisabolene (25,15%). In the hot-plate test, copaíba promoted significant changes in the latency time. In the formalin test it was observed a reduction of time spent licking in the first and second phase of the test. The evaluation by writhing test showed activity in the three tested doses, which reduced the number of stereotypical reactions significantly. **Conclusion:** The results here presented demonstrate that the oleoresin of *Copaifera reticulata* showed central and peripheral antinociceptive activity. However, it is necessary to continue the studies to determine the mechanism of molecular interaction of oleoresin components with nociceptive pathways. **Key words:** Antinociceptive, Hot-plate, Formalin, Writhing, Oleoresin of *Copaifera reticulata*. **Financial Support:** Universidade Federal do Oeste do Pará (Federal University of West of Pará) **Number of approval by the Ethics Committee of Universidade Federal do Oeste do Pará for use of animals:** Certificate number 07004/2013.

14.014 Involvement of TRPV1 in the wound healing of skin lesion after irradiation with a Blue-LED Hemostatic Device. De Siena G[1,2], Alfieri D[3], Magni G[2], Tripodi C[3], Tatini F[2], Geppetti P[1], Rossi F[2] [1]University of Florence – Department of Health Sciences, [2]National Research Council – Institute of Applied Physics, [3]Light4tech Firenze S.r.l.

Introduction: The activation of the TRPV1 receptor induces neurogenic inflammation, as arteriolar vasodilation (flares) and edema due to extravasation of plasma from post-capillary venules, and it is triggered by the release of substances as the pro-inflammatory neuropeptides substance P (SP) and or calcitonin gene-related peptide (CGRP) from sensory nerve terminals. The TRPV1 is involved in pain modulation and perception in several mechanisms such as in chronic wounds (Mitchell et. al Pain. 155:733, 2014; Lee et al J Dermatol Sci. 65:81, 2012), and it is able to detect chemically different products of cell and tissue injury and promote pain and inflammation. Proalgesic and pro-inflammatory agents, collectively referred to as 'the inflammatory soup', are produced following tissue injury, ischaemia or cell stress. In this study, we investigate on the activation of TRPV1 receptor after a blue-light treatment of the mechanically induced injuries. It seems that the EmoLED device, through a photo-thermal effect, induces the opening of the ion channels at temperatures 38-45°C and consequent activation of the platelets and the vascular endothelium.Thus, EmoLED device increases the wound healing and also reduces the pain at the wound region. **Methods:** 12 C57BL\6 wild type and 6 TRPV1 receptor Knockout (KO) mice, with superficial skin wounds, were treated with the EmoLED for 30s. In the wild type mice group, half were treated with NaCl 0.9% and identified as control, half were treated with capsazepine (CPZ) 4mg / kg i.p.. **Results:** In C57BL\6 wild type, treated with NaCl, the effect of EmoLED is the exudate reduction right after the treatment, the total fall of the crust and the wound healing in 45% of the animals after 5 days from the treatment. In KO mice we saw similar effects starting at 6th p.o. day. In wild type mice with CPZ, it was observed partial or total fall of the crust at 5 p.o. days, i.e. earlier than in controls. **Conclusions:** The EmoLED device inducing a photothermal stimulation promotes the premature recovery of mechanically induced injuries, which seems to be related to TRPV1, and could be used to induce a fast recovery of wound healing. **Acknowledgements:** The research leading to these results has received funding from Tuscany Region and EU FP7 BiophotonicsPlus projects “LighTPatcH” (Led Technology in Photo Haemostasis). All the experimental procedures are in accordance with EU Directive 2010/63/EU for animal experiments and approved by Italian Council of Health with process number 959/2015-PR.

14.015 Long-term non-steroidal anti-inflammatory therapy in Colombia. Portilla A[1], Pérez JJ[2], Montealegre AC[3], Lozano Y[3] [1]Audifarma S.A – Gerencia de Investigación Farmacoepidemiológica, [2]Audifarma S.A. – Gerencia de Investigación Farmacoepidemiológica, [3]Fundación Universitaria de Ciencias de la Salud – Dirección de Posgrados – Especialización en Enfermería Nefrológica

Introduction: Nonsteroidal anti-inflammatory (NSAID) is a set of drugs, which is indicated in the treatment of fever, pain and swelling and it is a pharmacological group widely used worldwide (1). Despite their clear indications, it should not forget its wide range of risks associated with their use, especially in chronic therapy (2). Several publications have recommended their use at low doses and shorter-term therapy as possible (3). In this context, the prevalence of NSAIDs long-term therapy in Colombia was determined and the impact of a sanitary intervention over patients chronically exposed to these drugs is presented in this paper. **Methods**: Descriptive and retrospective cross-sectional study, which includes all prescriptions of NSAIDs in three of the largest Health Insurance Providers in Colombia; the data were collected from the database records of Audifarma S.A, a distributor, from January 2006 to March 2016. Regarding this information, the prevalence of NSAID prescription and the number of patients chronically exposed were estimated. In one of these Health Insurance Providers, a cohort of patients with chronic therapy (>36 months) was selected. Some health education activities about rational use and risk of this kind of treatment were developed and they were addressed to the patients and their prescribers. **Results**: The population of the three Health Insurance Providers during 2015 was 3,2 million, and 17,6% of them received drugs by medical prescription. The prevalence of NSAID prescription was 3,0% (95% CI 2,98% -3,02%), which is equivalent to 17,0% of patients with medical prescription in 2015 (96850 patients/month). The most commonly used NSAIDs were: Naproxen (48,9%), Diclofenac (35,7%) and Ibuprofen (15,1%). Long-term NSAID therapy (>12 months) was evidenced in 33,4% of patients (32360), 1019 of them received treatment >36 months (1,1%), 180 patients (0,2%) >60 months and 15 patients >100 months. The patient cohort started in January 2014 with 201 patients without renal disease (RD) and 386 patients with RD; in the first quarter of 2016, 100 patients without RD had withdrawn the NSAID therapy and 347 patients with RD had also suspended it. Conclusion: Long-term NSAID therapy may be necessary in some conditions; however, sanitary interventions can be directed to rationalize their use. References: 1. Abramson SB. Nat Rev Rheumatol. 2011;7(3):133-4. 2. Schnitzer TJ. Clin Rheumatol. 2006;25 Suppl 1:S22-9. 3. Risser A. 2009;80(12):1371-8. The authors thank Audifarma S.A. for the Financial Support: This protocol was evaluated and approved by the Bioethics Committee in the category of “research without risk,” according to Resolution No. 008430 of 1993 of the Ministry of Health of Colombia, which establishes the scientific, technical, and administrative standards for health research, respecting the bioethical principles endorsed by the Declaration of Helsinki.

14.016 Use of Thiamine during epidemic Chikungunya and Zika in Colombia, Torres DR[1], Laverde LA[2], Cortés CD[2] [1]Audifarma S.A – Gerencia de Investigación Farmacoepidemiológica, [2]Audifarma S.A. – Gerencia de Investigación Farmacoepidemiológica

Introduction: The increase in cases of Chikungunya virus (CHIKV) and Zika virus (ZIKV) in Latin America alerted health agencies and medical community about the possible risks of these diseases, and recommendations for mitigation were generated[1]. These two infections share similarities, including the mode of transmission and symptomatology; therefore, the main recommendations focus on vector control and symptomatic treatment with acetaminophen and hydration. Nevertheless, in Colombia some nonscientific media reported the utility of thiamine to prevent mosquito bites and the transmission of these diseases, despite the fact that there is no scientific evidence to support it[2] and the health institutions do not encourage its use[3]. Therefore, it is appropriate to evaluate the use of thiamine in Colombia during the epidemiological peaks of CHIKV and ZIKV. **Methods**: Retrospective cross-sectional study with retrospective collection of information, which includes all prescriptions of acetaminophen and thiamine in two health insurance providers with 2,5 million people from January 2014 to March 2016. The data was collected from Audifarma S.A., one of the most important distributors in Colombia.
We obtained the prevalence of acetaminophen and thiamine prescriptions in different regions of Colombia, and it was compared with the registers of Instituto Nacional de Salud (INS) about CHIKV and ZIKV. **Results**: The use of acetaminophen increased in the cities of Colombian Atlantic coast with a first peak in October, November and December 2014 and January 2015, from 31,200 patients in the first three quarters of 2014 to 47,200 patients in the fourth quarter of 2014 and a second peak of 38100 patients in the fourth quarter of 2015. The use of Thiamine also increased; however, it was more gradual, from 5250 patients in the first three quarters of 2014 to 7020 patients in the first quarter of 2015 and 6100 patients in the third quarter of 2015, which is a peak of smaller proportion. The CHIKV and ZIKV outbreak began in Colombia in August 2014 and October 2015, respectively[4,5]. **Conclusion**: In 2014, prescriptions of acetaminophen and thiamine increased in the cities of Colombian Atlantic coast, simultaneously with the epidemiological peaks of CHIKV and ZIKV. Sanitary agencies should strengthen recommendations to discourage the prescription of thiamine to prevent mosquito bites, because of the lack of evidence in scientific literature. Unnecessary expenses for the health system and a false idea of safety in patients must be avoided. **References**: 1. Didier Musso et al. Lancet. 386 (9990): 243. 2015 2. Ministerio de Salud. Available in: https://www.minsalud.gov.co/paginas/Los-mitos-urbanos-sobre-el-virus-del-chikungu%C3%B1a-.aspx 3. Anthony R. Ives et al. J Am Mosq Control Assoc. 21(2):213. 2005 4. Oscar Pacheco et al. N Engl J Med. In press. 2016 5. Instituto Nacional de Salud. Available in: http://www.ins.gov.co/Noticias/Paginas/Lo-que-debes-saber-sobre-la-fiebre-Chikungunya.aspx The authors thank Audifarma S.A. for the Financial Support: This protocol was evaluated and approved by the Bioethics Committee in the category of “research without risk,” according to Resolution No. 008430 of 1993 of the Ministry of Health of Colombia.

14.017 CTK 01512-2, a recombinant isoform of the n-type calcium channel blocker phα1β induce antinociception in different chronic pain model in mice .Rigo FK[1], Rossato MF[2], Trevisan G[3], Dal Toe S[3], Ferreira J[4], Gomez MV[5] [1]UNESC – Farmácia e Farmacologia, [2]EERP-USP – Farmácia e Farmacologia, [3]UNESC – Farmacologia Bioquímica e Molecular, [4]UFSC – Farmacologia, [5]Instituto de Ensino e Pesquisa da Santa Casa de Belo Horizonte – Farmacologia Bioquímica e Molecular

Chronic pain is a debilitating feature of different condition, limiting life quality. Thus the adequate management of pain is imperative. Today it is knowing that voltage gated calcium channels (VGCC) can modulate pain transmission and be used as analgesic to treat different chronic pain conditions, as Phα1β, a peptide isolated from *Phoneutria nigriventer* venom. It blocks selectively N-type VGCC and induce antinociception in different chronic pain model. Recently we developed the peptide CTK 01512-2, the recombinant isoform of Phα1β. Thus, wee intent to investigate the analgesic profile of CTK 01512-2 in different animal models of chronic pain. To induce chronic pain, we submitted Balb C female mice (20 – 30g) inoculated with 10^5 4TI cells (breast cancer associated chronic nociception) and Swiss male mice (20 - 30g) to 4 four consecutive injections of paclitaxel 1 mg/kg (chemotherapy-associated chronic nociception) or to sciatic nerve chronic constriction injury (neuropathic chronic pain – CCI). After intravenous (e.v) treatment with different doses of CTK 01512-2, we observed that it presented antinociception (anti-allodynic) effect in breast cancer, chemotherapy and neuropathy associated chronic pain, with effective dose (ED_{50}) of 0.08 (0.02 - 0.18), mg/Kg and 0,03 (0,008-0,16) mg/Kg , e.v (respectively); and maximal effect (E_{max}) of 100 % (respectively). Therefore, we demonstrated that, similarly to Phα1β, CTK 01512-2 presents antinociceptive (anti-allodynic) effect when administered systemically in different types of chronic pain, in mice.

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