09 Natural Products and Toxinology

09.001 Antiatherosclerotic Properties of *Echinodorus grandiflorus* (**Cham. & Schltdl.**) **Micheli. - from antioxidant and lipid-lowering effects to anti-inflammatory role**. Palozi RAC[1], Gasparotto FM[1], Lívero FAR[2], Lourenço ELB[2], Gasparotto Junior A[1] [1]UFGD – Ciências da Saúde, [2]Unipar – Ciências da Saúde

Introduction: *Echinodorus grandiflorus*, popularly known as “chapéu de couro” is an important medicinal species native to South America. Over the past century it is been used as a popular hypolipemiant agent in Brazil. In fact, due to its wide use, in 2010 the genus was included in the 5th edition of the Brazilian Pharmacopoeia. So, despite its extensive popular usage, the hypolipidemic and antiatherosclerotic effects remain unknown. So, we proposed to evaluate the role of the purified aqueous extract obtained from E. grandiflorus (ESEG) against dyslipidemia and the development of atherosclerosis in rabbits. In addition, the pharmacological mechanisms involved in this cardioprotective activity were also investigated. **Methods:** Throughout 60 days, male New Zealand rabbits received diet supplemented with 1% cholesterol (CRD). After 30 days of CRD, animals were divided randomly into five groups (n = 6) and treated (p.o.) with ESEG (10, 30 and 100 mg/kg), SMV (simvastatin 2.5 mg/kg), or vehicle (filtered water, 1 ml/kg) once daily for 30 days. At the end of 60 days, serum lipids, oxidized low-density lipoprotein (ox-LDL), thiobarbituric acid reactive substances, nitrotyrosine and serum IL-1β, IL-6, sICAM-1, sVCAM-1 levels were measured. Finally, samples from aortic arch and thoracic segment were collected for investigation of the tissue antioxidant defense system, and histopathological analysis. **Results:** The positive control rabbits showed an expressive increase in serum lipids, with estimated values in 1739 ± 51.35 ± 1.6, 1651 ± 58, and 211 ± 7.7 mg/dl for TC, HDL-C, LDL-C, and TG, respectively. The 30-day-ESEG-treatment was able to reduce TC, LDL-C, and TG levels in a dose-dependent manner, reaching a reduction of approximately 65% at ESEG 100 mg/kg. In fact, at the highest dose, ESEG was able to induce a lipid-lowering effect similar to that obtained with SMV administration. In addition, ESEG-treatment was able to modulate the arterial antioxidant defense system, reducing lipid and protein oxidation, with significant reduction of ox-LDL levels at ESEG 30 and 100 mg/kg doses. Similarly, serum IL-1β, IL-6, sICAM-1, levels were significantly reduced by the highest dose of ESEG and the sVCAM-1 had their levels reduced by the intermediate and the highest dose as well, was also observed a expressive reduction of atherosclerotic lesions in the intima layer of all arterial branches evaluated and a significantly reduction in macroscopic lesions in aorta segments from rabbits submitted to CRD. **Conclusion:** Our results suggest that ESEG has secondary metabolites responsible for significant hypolipidemic, antioxidant and antinitrosant properties, which can modulate the local inflammatory process by reducing the evolution of the atherosclerotic disease. This study presents ESEG as probable new herbal medicines with possible direct application in the treatment and prevention of the atherosclerotic disease. **License number of ethics committee**: UFGD - protocolo nº 08/2015 **Financial support**: Capes e CNPq

09.002 7-hydroxycoumarin induces hypotension, **vasodilation and reduction of cardiac contractility**: **A promising molecule for treatment of cardiovascular diseases**. Alves QL[1], Simões LO[1], Menezes JE[2], Cruz JS[3], Silva DF[4] - [1]CPqGM-Fiocruz-BA – Biotecnologia e Medicina Investigativa, [2]UFS – Fisiologia, [3]ICB-UFMG – Bioquímica, [4]UFBA – Biorregulação

Introduction: Coumarins exhibit a wide variety of biological effects, among them are activities on the cardiovascular system and the 7-hydroxycoumarin (7-HC) may be a source of new anti-hypertensive agents. The aim of this study was to investigate the vascular and cardiac effects of 7-HC *in vivo* and *in vitro* approaches. **Methods:** Male wistar rats (300-350g) were euthanized and the superior mesenteric artery, cardiomyocytes and atria were isolated to subsequent studies of contractility. In another set of experiments, rats were fitted with polyethylene catheters inserted into the lower abdominal aorta and inferior vena cava through the left femoral artery and vein, respectively, in order to record blood pressure, heart rate or electrical parameters. 7-HC was intravenously administered at 2.5; 5; 10 and 20mg/kg. **Results:** In cardiomyocytes of H9c2 rats, 7-HC was non-toxic at the concentrations tested. In ventricular cardiomyocytes isolated, 7-HC was able to reduce contractility at concentrations of 10 and 100µM as well as the peak time of contraction with 1, 10 and 100µM without altering the cellular morphology. In atria 7-HC (10^{-9}M-10^{-4}M), induced negative inotropic effect without significant change in cardiac rhythmicity. In other set of experiments, studies performed with superior mesenteric artery rings isolated from normotensive rats, 7-HC induced an endothelium-independent vasodilator effect. Furthermore, 7-HC (10^{-9}-3x10^{-4}M) induced vascular vasodilation, which was significantly attenuated by both preincubation of the artery rings with depolarizing tyrode solution with KCl 60mM or 20mM. This attenuation suggests the participation of potassium channels. To test this hypothesis, a blocker of inward rectifier K^+ channels (K_{ir}), $BaCl_2$ (30µM) was pre-incubated and did not significantly alter 7-HC-induced vasodilatation, however, the blocking of delayed rectifier K^+ channels, with 4-amynopiridine (1mM) and the large-conductance Ca^{2+}- activated K^+ channels (BK_{Ca}) with TEA (1mM), significantly attenuated the 7-HC effect. In addition, to verify the influence of 7-HC on the calcium influx, 7-HC (100□M) in the presence of depolarizing solution without calcium, was able to significantly reduce the $CaCl_2$-induced contraction. *In vivo* assays, 7-HC reduced blood pressure and induced tachycardia in non-anesthetized rats, while in the electrocardiographic test in anesthetized animals, 7-HC did not appear to change cardiac electrical parameters such as heart rate, PR interval, and QRS interval. **Conclusion:** Our results suggest that 7-HC has direct cardiac activity, both at the cellular and tissue level, besides induces vasorelaxation artery, endothelium-independent way, probably involving potassium channels (K_{ir} and BK_{Ca}) and calcium influx attenuation. In addition, 7-HC reduced blood pressure, without altering electrical parameters, becoming a promising molecule with cardiovascular activity. **License number of ethics committee**: ICS/UFBA - 130/2017 **Financial support**: FAPESB and CNPq

09.003 Lupeol stearate promote gastroprotective activity in rodents. Somensi LB[1], Costa P[1], Boeing T[1], Mariano LNB[1], Magalhães CG[2], Da Silva LM[1], Andrade SF[1] [1]Univali – Pharmaceutical Sciences, [2]UEPG – Química

Introduction: Lupeol is a triterpene isolated from several plants with a diversified pharmacological potential and previous studies have shown that lupeol has a gastroprotective action at a dose of 3 mg/kg (LIRA, S.R.S, Inflammopharmacol, v.17, p.221, 2009). The chemistry of natural products is a widely used tool for the modification of chemical structures, aiming at potentiating biological effects and/or reducing toxic effects. Thus, this study evaluated: (*a*) the consequences of structural modifications on the Lupeol in its antiulcer effect, and (*b*) the mode of action of the most potent derivative. **Methods:** Lupeol (**1**) was isolated from hexane branch extract of *Maytenus salicifolia* and the Lupeol stearate (***2***), Lupeol palmitate (***3***), Lupeol miristate (***4***), Lupeol laurate (***5***) and Lupeol caprilate (***6***) were obtained reacting ***1*** with an adequate carboxylic acid (SILVA, A.T.M, BJPS, v.53, p.1, 2017). Female *Swiss* mice were treated with vehicle (10% DMSO, 10 mL/kg, p.o), carbenoxolone (positive control, 200 mg/kg, p.o) or Lupeol esters (0.1 - 3 mg/kg, p.o or i.p) before administration of acidified ethanol (10 ml/kg, p.o) or indomethacin (100 mg/kg, p.o). After, oxidative and inflammatory parameters were measured in ulcerated tissue. The antisecretory effect of the most potent derivative was evaluated in pylorus ligated rats. Further, its antiulcer effects against acidified ethanol were evaluated in mice pretreated with N-ω-nitro-L-arginine methyl ester (L-NAME, 70 mg / kg, ip), N-Ethylmaleimide (NEM, 10 mg / kg, ip), yohimbine (1 mg/kg, ip) or indomethacin (10 mg/kg, p.o) (CEUA: 056 / 17p). **Results:** Acidified ethanol ulcerated the gastric mucosa by 64.45 ± 6.58 mm^2. In contrast to ***1***, the oral administration of esters ***3***, ***4***, ***5*** and ***6*** at 3 mg/kg (p.o) not reduced the ethanol/HCl-induced ulcer. Interestingly, the ester ***2*** decreased significantly the ethanol/HCl-induced ulcer at a minimum effective dose of 0.3 mg/kg (DE_{50}= 0.40 mg/kg – 95% confidence interval: 0.18 to 0.89 mg/kg), indicating that this structural modification potentiates the antiulcer potential of ***1***. As expected, carbenoloxone also reduced the ulcer area. The antiulcer effects of ***2*** (0.3 mg/kg) was accompanied by the reduction in myeloperoxidase activity and the normalization of the superoxide dismutase and catalase to basal levels. Moreover, intraperitoneal administration of ***2*** at 0.1 mg/kg also was able to prevent ethanol/HCl-induced ulcer by 55%. The indomethacin-induced ulcer was reduced by 67% after the oral administration of ***2*** (0.3 mg/kg), vs. vehicle-ulcerated group (2.4 ± 0.4 cm^2). Regarding antisecretory activity, intraduodenal administration of ***2*** (1 mg/kg) increased the gastric pH (p<0.05) and decreased the total acidity (p<0.05) of the gastric juice, vs. the vehicle group. Furthermore, was observed that the pretreatment with NEM, yohimbine and indomethacin, but not L-NAME, abolished the gastroprotective effect of the compound ***2***, confirming the participation of non-protein sulfhydryl compounds, α_2 receptors and prostaglandins on the its effects. Taken together, these findings indicate that the esterification with a higher aliphatic chain carboxylic acid to obtain the compound ***2*** potentiated the antiulcer activity of ***1*** and that this compound can elicit gastroprotective action due a diversified mode of action, including reduction of gastric acidity. **License number of ethics committee**: CEUA: 056 / 17p **Financial support**: CNPQ, CAPES.

09.004 Anti-inflamatory and antinociceptive activity of enamarine isolated from *Cantinoa stricta*.
Barbosa FL[1], Ehrenfried CA[1], Oliveira CS[2], Stefanello MEA[2], Zampronio AR[1] [1]UFPR – Farmacologia e Toxicologia de Produtos Naturais, [2]UFPR – Química

Introduction: Studies from our group and others have shown that several plant species with complex secondary metabolites, even if they do not present a use in folk medicine, are promising for the discovery of bioactive molecules. The Lameaceae family occupies the third place in the ranking of importance among families with bioactive molecules. For some plants of this family such as *Cantinoa stricta*is there are no studies indicating any possible pharmacological effect. The aim of the present study is to evaluate the anti-nociceptive effect of the ethanolic extract of *Cantinoa stricta* (EECS) and from the isolated pyrone enamarine (ENM). **Methods:** Male Swiss mice (± 25 g, n= 6-8) received EECS (10-100 mg/kg), dichloromethane fraction (DCM, 30 mg/kg), ENM (1-3 mg/kg), or indomethacin (IND,5 mg/kg) by oral route 1 h before the injection of formalin (2.5%, 20 µl) or lipopolysaccharide (LPS, 100 ng, 20 µl) into the right hind paw. LPS-induced mechanical hyperalgesia was evaluated using dynamic plantar anesthesiometer. Additionally, animals received intraplantar (i.pl.) injections of ENM (30-300 ng), IND (150 ng) or dipyrone (DIP, 320 µg) 15 minutes before the injection of LPS (100ng), interleukin (IL)-1β (IL-1β, 100pg), prostaglandin E_2 (PGE_2, 100ng), dopamine (DOP, 3µg), epinephrine (EPN, 100ng), forskolin (FOR, 1µg), or dybutiryl cAMP (dbcAMP, 5 µg) injected into the hind paw. **Results:** The oral treatment with EECS 10, 30 and 100 mg/kg dose-dependently reduced the second phase of formalin-induced nociception by 65%, 60% and 53% respectively. Similarly, the DCM fraction and the positive control IND reduced the 2nd phase of formalin-induced nociception by 68% and 62%. The oral treatment with EECS 18 and 30 mg/kg also reduced the LPS-induced mechanical hyperalgesia by 42% and 94%, respectively. Both, IND and DCM fraction abolished this response. The oral treatment with ENM 1.8 and 3.0 mg/kg or IND 5 mg/kg reduced the LPS-induced mechanical hyperalgesia by 45%, 100% and 100%, respectively. The local treatment with ENM 30, 90 and 300 ng also reduced LPS-induced mechanical hyperalgesia induced by LPS in 22%, 42% and 86%, respectively, while IND reduced it by 87%. Furthermore, the i.pl. treatment with ENM (300 ng) reduced the mechanical hyperalgesia induced by DOPA (92%) and EPN (95%) but not the IL-1β, PGE_2, FOR or dbcAMP-induced mechanical hyperalgesia. Whilst DIP (positive control) abolished this response. **Conclusion:** These results suggest that the EECS has an important antinociceptive effect in the inflammatory pain**,** since it reduced the second phase of formalin and mechanical hyperalgesia induced by LPS. Its antinociceptive effect seems to be in part related to the presence of ENM, whereas this pyrone also had an antinociceptive effect on mechanical hyperalgesia induced by LPS. These data also suggest that ENM has a different mechanism of action comparing with non-steroidal anti-inflammatory drugs, since it did not reduce IL-1β-induced hyperalgesia and its action seems to be particularly important in the reversal of the sympathetic component of pain. **License number of ethics committee**: 937 **Financial support**: CAPES, CNPq

09.005 Investigation of the antiofidic activity of *Mikania glomerata*. Cesar MO[1], Strauch MA[1], Machado MM[1], Tavares-henriques MS[1], Souza PDN[2], Melo PA[1] [1]UFRJ – Farmacologia e Química Medicinal, [2]UFRJ – Bioquímica e Biologia Celular

Introduction: Snake accidents represent a public health problem in many countries with around 2.5 million accidents per year in the world (Chippaux, 1998). The recommended treatment is serum therapy with polyvalent serum or specific serum, if the genus of the snake is identified. Serotherapy is ineffective in neutralizing the inflammatory process, local tissue injury and hemorrhage, which leads to disabling sequelae and lesions (Fletcher and Rosenberg, 1997; Del Brutto and Del Brutto, 2012). It is of great importance to research different inhibitors of synthetic or natural venom venoms to add them to the current therapy (Da silva et al., 2007). In this way, vegetal extracts that have an active chemical profile and recognized pharmacological activity can be used as plant derivatives with potential for the development of herbal medicine as a complementary treatment to serum therapy (Mazzari AND Prieto, 2014). The literature shows *Mikania glomerata Spreng*. as a native plant of the Brazilian flora with recognized antiofidic activity (Mourão et al., 2014). The present project aims at the development of a phytotherapic topical application capable of antagonizing the effects of the ophidian accident not neutralized by the Antiophytic Serum, especially the inflammatory activity and the local effects of venom of snakes. **Methods:** In order to carry out the experiments of evaluation of the inhibition of snake venom activity, the venom of *Bothrops Jararacussu* provided by the Vital Brazil Institute and the *Mikania* extract supplied by the Laboratory of Galenic Development (LADEG – UFRJ). *In vitro* experiments were carried out to evaluate the inhibition of phospholipase and proteolytic activity of *Jararacussu* venom. **Results:** In the evaluation of the phospholipase activity the Jararacussu venom was used in the concentration of 10 µg/mL and the extract was tested in 10, 30 e 100 µg/mL where only the highest concentration inhibited about 50 % of the poison effect. In the evaluation of the proteolytic activity of *B Jararacussu* concentrations of 30, 100 and 300 µg/mL for inhibition of 10 µg/mL of the poison and the extract of *M. glomerata* inhibited about 20 - 30 % in the concentration of 100 µg/mL. **Conclusion:** The extract showed that it has activity of inhibition of the effect of *B. Jararacussu*. However, some experiments still need to be performed. Subsequently, it is intended to carry out the *in vitro* tests as: evaluation of the effects of the extract on the hyaluronidase and collagenase activity of the venom of snakes and are necessary to be performed *in vivo* experiments as the evaluation on hemorrhagic activity. **Financial support**: FAPERJ

09.006 *Cochlospermum regium* (**Mart. ex Schrank**) **Pilg**.: **Antiulcer activity and mode of action of hydroethanolic extract of xylopodium against acute and chronic gastric ulcers in experimental animals**. Arunachalam K, Amilcar SD, Eduarda P, Martins DTO UFMT – Ciências Básicas em Saúde

Aim: *Cochlospermum regium*, popularly known as "algodãozinho-do-campo", is a native non-endemic shrub found in the Cerrado, Pantanal, Amazon and Caatinga forests, Brazil. The infusion and decoction of the rhizome of *C. regium* are used for the treatment of gastritis, ulcers, arthritis, intestinal infections, gynecological infections, skin diseases, among others. This study investigates the gastroprotective activity and mode of action of the hydroethanolic extract of *C. regium* xylopodium (HECr) using acute and chronic ulcer models on mice. In addition, phytochemical analysis of HECr was also performed. ***Methods:*** *C. regium* xylopodium was collected prior approval to access the traditional knowledge (no. 247/2013) associated with genetic resources for research purposes (no. 199/2014) by CGEN/MMA. All the experimental animals were used after approval by the Committee for Ethics in the Use of Animals (CEUA-UFMT) under no. 23108.224227/2017-01. HECr was obtained from xylopodium powder by maceration with 70% hydroethanolic solution. Phytochemical characterization was carried out by high-performance liquid chromatography (HPLC). Antiulcerogenic activity and mode of action of the HECr (25, 100 and 400 mg/kg p.o.) were assessed in acidified ethanol (70% EtOH/0.3 M HCl) -induced acute gastric ulcers (0.3 mL/mice) by evaluation of mucus production, PGs (indomethacin10 mg/kg p.o.), NO (L-NAME 10 mg/kg ip.), K^+_{ATP} channels (glibenclamide 10 mg/kg p.o.) and α_2-adrenoreceptor (yohimbine 2 mg/kg ip.) action on mice. Chronic gastric ulcer healing activity of HECr at the same doses was evaluated on acetic acid (50 µL, 99.8%)-induced ulcer on mice by quantification of gastric lesions (mm^2), histopathological analysis and antioxidant (GSH, CAT and MPO) effects. ***Results:*** The HPLC analysis of HECr revealed the presence of gallic acid, rutin, myricetin, morin and kaempferol. HECr (25, 100 and 400 mg/kg) increased the gastric wall mucus production by 243.56%, 470.54%, 585.00% ($p < 0.001$) respectively. HECr at most active dose (100 mg/kg) reversed completely the reduction of PGs by indomethacin (398.74%, $p < 0.01$), NO production by L-NAME (370.75%, $p < 0.01$), closure K^+_{ATP}- channels by glibenclamide (344.54%, $p < 0.01$) and yohimbine α_2-adrenoreceptor blockage (380.53%, $p < 0.01$). In the chronic ulcer, HECr (25, 100 and 400 mg/kg) decreased ($p <0.001$) the ulcerated area duting 7 days of treatment by 58.80%, 77.87% or 71.10% respectively. HECr at all doses or cimetidine (50 mgkg) promoted healing of gastric lesions by regenerating mucosa and reduced inflammatory cells influx in histopathological analysis as by increasing the level of GSH at doses of 100 mg/kg (90.59%, $p < 0.001$) and 400 mg/kg (73.24%, $p < 0.001$) and activity of CAT at all doses by 226.07% ($p < 0.05$), 365.83% ($p < 0.01$), 441.20% ($p < 0.001$) and reducing MPO activity at all doses by 44.05% ($p < 0.01$), 58.38%, ($p < 0.01$) and 49.05% ($p < 0.01$), respectively. ***Conclusion:*** HECr exerts preventive and curative effects against acute and chronic gastric ulceration in mice by multitarget action, probably due to the presence of gallic acid and flavonoids. *Keywords*: *Cochlospermum regium*, gastroprotective, phenolics, mice. **License number of ethics committee**: Institutional Committee for Ethics in the Use of Animals (no. 23108.224227/2017-01) **Financial support**: CAPES/Pró-Amazônia (no. 23038.000731/2013-56); CAPES/PNPD (no. 23108.180072/2016-02); CNPq (no. 132286/2015-7); FAPEMAT (no. 205978/2011).

09.008 Heart-protective effects of *Echinodorus grandiflorus* (**Cham. & Schltdl.**) **Micheli in rabbits that are fed a high-cholesterol diet**. Silva AO[1], Gasparotto FM[2], Lívero FAR[3], Lourenço ELB[3], Gasparotto Junior A[2] [1]UFGD – Farmacologia e Toxicologia de Produtos Naturais, [2]UFGD – Farmacologia e Toxicologia, [3]Unipar – Farmacologia

Introduction: Excess weight and dyslipidemia are among the most serious health problems in Western societies. These conditions enhance the risk of cardiac disease and have been linked with a higher prevalence of cardiac arrhythmias and sudden death. The present study investigated the cardioprotective effects of *Echinodorus grandiflorus* on ventricular remodeling in rabbits that were fed a 1 % cholesterol-rich diet (CRD). **Methods:** We first obtained an ethanol soluble fraction of *E. grandiflorus* (ESEG) and performed a detailed phytochemical study by liquid chromatography-diode array detection/electrospray ionization mass spectrometry. For 60 days, male rabbits were fed the CRD or a diet without the addition of cholesterol. After 30 days, different groups of rabbits were treated with ESEG (10, 30, and 100 mg/kg, p.o.), simvastatin (2.5 mg/kg), or vehicle once daily for 30 days. At the end of 60 days, the serum lipoprotein ratio, electrocardiographic profile, histopathological alterations, and the cardiac antioxidant defense system were investigated. **Results:** Electrocardiographic analysis showed morphological and functional alterations in CRD-fed animals, indicating left ventricle hypertrophy. The total cholesterol/high-density lipoprotein ratio and low-density lipoprotein/high-density lipoprotein ratio were significantly higher in CRD-fed rabbits. Myocardial flaccidity, fatty degeneration, and concentric left ventricular hypertrophy were observed. An increase in lipid peroxidation levels, decrease in superoxide dismutase activity, and decrease in reduced glutathione levels were observed in the myocardium in all CRD-fed rabbits. **Conclusion:** Treatment with ESEG, especially the highest dose, significantly reduced all of these alterations, thus demonstrating the cardioprotective effect of ESEG on cardiac changes that are induced by a CRD.

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09.009 *Byrsonima intermedia* **A**. **Juss recovers intestinal mucosa after ulcerative colitis**: **Role of anti-inflammatory and anti-oxidant pathways**. Fagundes FL[1], Romano KSF[1], Périco LL[2], Rodrigues VP[2], Gambero A[3], Vilegas W[4], Lima CAH[2], Santos RC[1] [1]USF – Compostos Bioativos, [2]IBB-Unesp – Fisiologia, [3]USF – Imunofarmacologia, [4]Unesp-Litoral Paulista

Introduction: The inflammatory bowel disease (IBD)has chronic and relapsing character and unknown etiology. However, immunologic, genetic and food aspects are involved in the initiation. The treatment is based in corticosteroids, aminosalicylates and biologic therapy. However, all classes of drugs present side effects and limitations. In this sense, the natural products highlight alternatives in the treatment of IBD. Byrsonima Intermedia A. Juss is a plant of Brazilian Cerrado with popular indication for treatment of gastrointestinal disturbs, that has analgesic and anti-inflammatory activity. The aim of this work is to evaluate the mechanisms of action of methanolic extract of Byrsonima Intermedia leaves (MEB)in the model of IBD with recurrences **Methods.** Male Wistar rats were divided in group vehicle, MEB(doses of 62.5, 125 e 250 mg/kg) and SHAM.All animals received the intracolonic administration of TNBS (acid 2,4,6 trinitrobenzenosulfonic-3 mg solubilized in 50% ethanol) in days 1, 14, 21 and 28. In the 28th day until 34th, the animals received the treatments by gavage, with exception of SHAM group. In the 35th day has occurred the euthanasia and samples of colon were collected for macroscopic classification of lesions, quantifications of cytokines IL-1β, IL-6, IL-10 e TNF-α and biochemical determinations of enzymes Mieloperoxidase (MPO),Super oxide dismutase(SOD),Catalase(CAT),Reduced Glutathione(GSH)and the verification of lipid peroxidation by the Malondialdehyde assay.The results were expressed as mean and s.e.m and the statistical significance was determined by one-way analyses of variance(ANOVA)followed by Dunnett's test and/or Kruskal-Wallis. **Results:** MEB reduced the macroscopic lesions in the dose of 125 mg/kg compared with the vehicle(1.83± 0.3 vs 4.0±0.6)and the activity of MPO in the dose of 125 and 250 mg/kg(4578±208.3 and 3958±148.4 U/g)compared to the vehicle group (8419±1824 U/g).However, was not able to significant reduce the levels of CAT and lower the levels of MDA at any dose. In the dose of 125 mg/kg there was more than 100% rise in the SOD activity when compared with vehicle group (8.374 ± 0.813 vs 3.998 ± 0.667)and in the doses of 125 and 250 mg/kg there were a rise of 45% and 56%, respectively in the activity of GSH(9,45 ± 0,79 and 9,66 ± 0,97)if compared with the vehicle's group (6,34 ± 0,36).In what concerns about the cytokines, MEB was not able to reduce the levels of TNF-α and IL-1β. In the other side, the extract increase the levels of IL-10 in the dose of 125 mg/kg(41.655 ± 5.242) if compared to the vehicle(22.227 ± 3.020). **Conclusion:** Together, these results demonstrate that MEB was effective in the reduction of macroscopic lesions and the inflammatory picture of animals submitted to TNBS model, as well as, increase the activity of enzymes of endogenous anti-oxidant system, confirming the popular indication to treatment of gastrointestinal diseases. **License number of ethics committee**: 001.04.2015 **Financial support**: Biota/Fapesp (process number 09/52237-9)

09.010 Initial trial to development of new use drug aiming the skin wound treatment for clinical application in horses. Hussni MF[1], Gushiken LFS[1], Beserra FP[1], Takahira RK[2], Hussni CA[3], Pellizzon CH[1] [1]IBB-Unesp – Morphology, [2]FMVZ-Unesp – Veterinary Clinic, [3]FMVZ-Unesp – Veterinary Surgery

Introduction: Skin wounds starts a mechanisms cascade to restore its integrity and, in horses, results in excessive granulation and exsudate- implying in healing delays, leading to animal incapacitation or death. New therapeutic strategies that accelerates skin wound healing by topical administration appears as the best option, showing greater effectiveness with lower dose and lower systemic effects. Caffeic Acid(CA) is a natural medicine that has being widely studied by oral administration, since it has antioxidant action due to its second hydroxyl in the ortho/para position, resulting in protective damage tissue activity, hepatoprotective and anti-inflammatory actions, such as gene expression block for some pro-inflammatory cytokines.This study analyzes a new CA topical formulation, that absorbs exudate from the wound and does not melt, for a potential use in the veterinary field. The first experiments were carried out on rats. **Methods:** We developed a cream with CA as active principle, and zinc oxide, calcium hydroxide, starch and glycerin as vehicle. Male *Wistar* rats were divided in groups (n=6): sham (no wound or treatment), control (wound without treatment), control treated with base(without CA), 0,25%, 0,5% and 1% CA. After anesthesia, a 3cm wound was performed on the back of each animal, treated and measured once a day during 14 days. Clinical signals as border edema and exudates were analyzed. After euthanasia, blood samples were submitted to biochemical toxicity analysis for kidney and liver enzymes: AST (aspartate aminotransferase), ALT (alanine aminotransferase), γGGT (gamma glutamyltransferase), urea and creatinine (enzymatic values of sham group were established as standard). Skin samples were destined to determine the levels of the reduced glutathione antioxidant protein (GSH) to evaluate the antioxidant potential of CA. All data were analyzed by ANOVA followed by Newman-Keuls, $p<0.05$. **Results:** After 14 days of treatment, CA-treated groups and base did not show important wound retraction when compared with no treatment wounded group for days 3(7,7±1cm²), 7(4.6 ±1.1cm²) and 14(1.9±0.6cm²). However, there were positives macroscopic aspects in CA-treated groups, such as adhered scar, low (0,5% and 1%) or non (0,25%) exudates and border edema,compared to controls groups. Analysis for kidney and liver enzymes did not show toxicity for ALP(120±10UL), AST(150±10UL), Creatinine(0,38±0,05mg/dL), GGT(0,9±0,02UL) and Urea(0,50±0,025mg/dL). GSH quantification has not shown different levels in all treatments (90±5nmol/mg of protein), but all wounded groups has shown significant difference when compared to sham group (35nmol/mg of protein). **Conclusion:** The experiment reached our main goal, which was the development of CA-cream, whose treatment did not melt and had an adhered scar, without exudates and any damages on liver or kidney, which rarely occurs in skin wound healing horses. In our study, all CA-treated groups were only able to reduce the GSH level when compared to sham group, without differences among them. Therefore, is possible that GSH may not be one of the antioxidant routes which CA acts. Further analysis will be carried out to evaluate other possible antioxidant routes. **License number of ethics committee**: (Bioscience Institute/UNESP/Ethical Committee for Animal Research-987/2017) **Financial support**: 2017/18197-6 São Paulo Research Foundation(FAPESP)

09.011 *In vitro* **antioxidant and photoprotective activities of several rosemary extracts**. Monteiro MC[1], Takayama KS[1], Baracat MM[1], Casagrande R[1], Couto RO[2], Georgetti SR[1] [1]UEL – Pharmaceutical Sciences, [2]UFSJ – Pharmacy

Introduction: The solar UV radiation is the main environmental inducer factor of skin cancer. Typically, sunscreens are used aiming at to prevent skin cancer caused by sun exposure. However, the currently used sunscreens may be overwhelmed by excessive sun exposure or present several deleterious effects on the skin (e.g., allergy, inflammation, etc.). Hence, novel materials for chemoprevention of UV-induced skin cancer are required for overcome such limitations. In this pursuit, one of the safest approaches is the use of antioxidant phytochemicals (Georgetti et al. 2006). Rosemary (*Rosmarinus officinalis* L.) presents several phytochemicals that can be valuable in the prevention and/or treatment of these photooxidative disorders, including phenolic acids, flavonoids, tannins, terpenes and volatile compounds. Herein, we report on the *in vitro* antioxidant and photoprotective activities of several extracts obtained from rosemary leaf. **Methods:** Rosemary leaves were dried and powdered. The extracts were obtained by dynamic maceration by using solvents of different polarities (acetone, ethanol and methanol) mixed with water at several proportions (20, 50 and 80% v/v). Thereafter, the extracts were filtered and the solvents were removed using a rotatory evaporator under vacuum. Further, the products were freeze-dried. Total polyphenol content (TP) was determined by the Folin–Ciocalteau colorimetric method; the antioxidant activity (AA) was evaluated by using the stable DPPH radical (Campanini et al. 2014); and the *in vitro* sun protection factor (SPF) was assessed by the spectrophotometric method developed by Mansur (1986). The results were compared by ANOVA followed by Tukey's t test. Significant statistical differences were considered if $p < 0.05$. **Results:** TP ranged from 24.15 to 159.75mg/g; the AA ranged from 0.44 to 3.77mM and the SPF from 1.13 to 11.16. Tukey's test indicated that for TP the best solvent was 20% ethanol; for AA the 80% ethanol and for SPF the 80% acetone. There were weak correlations between TP and AA ($R^2 = 0.14$) and TP and SPF ($R^2 = 0.14$), indicating that beside the polyphenols, there are several others phytochemicals affecting the photochemioprotective effects in rosemary extracts. Moreover, a moderate correlation between AA and SPF ($R^2 = 0.43$) was observed, which suggests that the *in vitro* AA may be a predictor for SPF. **Conclusion:** The synergism between the whole antioxidant phytochemicals of rosemary extracts may display a key role on their antioxidant activity, sun protection factor and, therefore, on their capacity for skin cancer prevention. These findings challenge us for further investigations concerning the phytochemical characterization of such extracts and their chemoprotection mechanisms. **References:** Georgetti et al. Eur J Pharm Biopharm., vol. 64, p.99, 2006. Campanini et al. AAPS PharmSciTech, vol.15, p.86, 2014. Mansur et al. An. Bras. Dermatol., vol.61, p.1210, 1986. **Financial support**: Fundação Araucária and CNPq, Brazil

09.012 Plurality in the antioxidant mechanisms of hydroalcoholic Rosemary extract as assessed by several *in vitro* methods. Sibioni DF, Casagrande R, Bacarat MM, Georgetti SR, Couto RO, Takayama K [1]UEL – Ciências Farmacêuticas

Introduction: Over the last few decades, both the academic and industrial communities are increasing their research interest on antioxidants, mainly those from natural sources and able of preventing the deleterious effects of free radicals in acute and chronic illness. Among the herbal medicines with therapeutical benefits for human health, rosemary (*Rosmarinus officinalis* L.) is widely known as powerful source of natural antioxidants, including di-and triterpenoids, phenolic acids, flavonoids and volatile compounds (KONTOGIANNI, 2013). The aim of this study was to evaluate the antioxidant mechanisms of a hydroalcoholic rosemary extract by using several *in vitro* methods. **Methods:** The hydroalcoholic extract was obtained by dynamic maceration of the dried and powdered rosemary leaves (1: 10 w/v) using 80% ethanol (v/v). Thereafter, it was filtered and the solvent was removed using a rotatory evaporator under vacuum. Further, such product was freeze-dried in order to obtain the dried extract (DRE). The DPPH and ABTS scavenging ability of DRE were determined by the decrease in absorbance at 517 and 730 nm, respectively. The FRAP assay was used to determine the ferric reducing antioxidant power of DER at 595 nm (CAMPANINI et al., 2014). The reduction of luminescence emission was evaluated by the sequestration of free radicals generated in the HRP system and superoxide anion sequestration generated by the system xanthine/XOD (MARQUELE et al., 2005). The IC_{50} (concentration that inhibits 50%) of the DRE was determined using GraphPad Prism software package. **Results and discussion:** The antioxidant activity of DRE for all *in vitro* methodologies showed dose-dependent response (0.156-15µg/mL DPPH, 0.389-8.99µg/mL ABTS , 0.00625-0.2µg/mL HRP system and 0.000488-0.625µg/mL XOD system).The maximum activity of the extract in the DPPH and ABTS assay were obtained at the concentration of 15 µg/mL (79.73%) and 8.99 µg/mL (100%) with an IC_{50} of 5.21 and 1.88µg/mL, respectively. In the FRAP assay, DRE reducing power was 1.28 µmol/L trolox equivalent/µg/mL. The IC_{50} observed were 0.031 µg/mL (HRP system) and 0.025 µg/mL (XOD system). The various IC_{50} values observed for the DRE display the plurality of mechanisms and the extension that each radical can be scavenged. **Conclusion:** Altogether, such findings demonstrate that rosemary extract may bring a broad range of acting mechanisms and therapeutical approaches aiming at the oxidative stress management. **References:** Campanini et al. AAPS PharmSciTech, vol. 15, p.86, 2014. Kontogianni et al. Food Chemistry, vol.136, p.120, 2013. Marquele et al. Journal of Pharmaceutical and Biomedical Analysis; vol.39, p.4550, 2013. **Financial support**: Fundação Araucária and CNPq, Brazil.

09.013 Analgesic, **anti-inflammatory and antioxidant properties of an arabinan-rich pectin obtained from acerola** (*Malpighia emarginata*) **in mice**. Ciapparini PG[1], Dallazen JL[1], Ferreira DM[1], Da Luz BB[1], Klosterhoff RR[2], Cordeiro LMC[2], Werner MPF[1] [1]UFPR – Farmacologia, [2]UFPR – Bioquímica e Biologia Celular

Introduction: *Malpighia emarginata* (Malpighiaceae), popularly known as “acerola”, is a tropical and subtropical fruit native from American lands. In addition to vitamin C, acerola is an important source of phytochemicals and the fruit intake is recommended due its high antioxidant propriety against several diseases. Interestingly, soluble dietary fibers, such polysaccharides are also abundant constituents of acerola (10% of dry fruit). It was previously demonstrated that an arabinan-rich pectin (named ACWS) extracted from acerola present anti-fatigue activity in the weight load swim test in rats (Klosterhoff et al, Int J Biol Macromol; v.106, p.473, 2018). In order to access other systemic effects of ACWS, this study aimed investigate the antinociceptive, anti-inflammatory and antioxidant effects of ACWS in animal models of pain. **Methods:** Male Swiss mice (~30 g, CEUA/BIO-UFPR 1104) were pretreated by intraperitoneal route (i.p.) with ACWS (0.1, 1 and 10 mg/kg), diclofenac (50 mg/kg) or vehicle (V: 0.9 % saline), 30 min before the intraplantar injection of 2.5% formalin (20 µL, i.pl.). In the acetic acid-induced writhing response, mice were pretreated (i.p.) with ACWS (1, 10 and 30 mg/kg), dexamethasone (1 mg/kg) or vehicle, 30 min before 0.6% acid acetic injection (0.45 mL/mice, i.p.) and the total leukocytes infiltration was counted by using a Neubauer chamber. Mechanical allodynia and paw edema were assessed by von Frey monofilaments and digital micrometer, respectively, in mice pretreated (i.p.) with ACWS (10 mg/kg), dexamethasone (1 mg/kg) or vehicle 30 min prior i.pl. carrageenan injection (300 µg/20 µL). After, the injected paw surface was excised to analysis antioxidant (lipid peroxidation (LPO), glutathione (GSH) levels, superoxide dismutase (SOD) and catalase (CAT) activity) and inflammatory parameters (myeloperoxidase (MPO) and TNF-α and IL-1β levels). The antioxidant potential of ACWS was also evaluates by DPPH radical-scavenging assay. **Results:** In the formalin-induced nociception, both ACWS (0.1, 1 and 10 mg/kg) and diclofenac reduced only the inflammatory phase in 44.2, 63.3, 88.1 and 69.2%, respectively (V: 266.0 ± 34.7 s). ACWS (10 and 30 mg/kg) and DEXA diminished acetic acid-induced writhing in 56.5, 78.2 and 55.0%, respectively (V: 45.1 ± 1.6 s), and leukocyte migration in 64.3, 60.9 and 44% (V: 87.0 ± 8.2 cells). Mechanical allodynia and paw edema were greatly reduced by ACWS (10 mg/kg) and DEXA 3 to 6 h following carrageenan injection. At 4 h, ACWS and DEXA significantly altered LPO (32.0 and 75.0%), GSH (8280.8 and 7081.4 µg/g of tissue), SOD (19.0 and 20.0%), CAT (both at 100.0%), MPO (26.1 and 11.6%) and TNF-α (70.0 and 62.0%), when compared to the respective controls. ACWS also reduced DPPH levels (ID50 53.4 ± 1.0 µg/mL). **Conclusion:** The remarkable antinociceptive and anti-inflammatory effects of ACWS in different mouse models of pain were achieved mainly through the reduction of leukocyte infiltration, TNF-α releasing and antioxidant effects. Collectively, these results support the antinociceptive effectiveness and reveal additional beneficial effects of acerola and its polysaccharides. **Support**: CNPq **License number of ethics committee**: CEUA/BIO-UFPR: 1104 **Financial support**: CNPq

09.014 Coagulant activity of an endophytic fungus extract from piper *Aduncum plant*. Souza LMMA, Furtado KMS, Espíndola KMM, Amorim RP, Cardoso MV, Ferreira RG, Monteiro MC UFPA – Farmácia

Introduction: Endophytic fungi are microorganisms that live in symbiotic association with plants. Therefore, they are considered producers of bioactive molecules of great therapeutic importance. In recent years, the increase in the incidence of cardiovascular diseases and the adverse effects of anticoagulant drugs stimulate the search for new anticoagulant compounds. Thus, the objective of this work was to evaluate the coagulant activity of the PAC 123 endophytic fungus extract from *Piper aduncum*. **Methods:** The PAC 123 fungal extract was selected and, then its anticoagulant activity was evaluated *in vitro.* The evaluation of the coagulant activity was performed *in vitro* through the plasma recalcification time. In this assay, 100µl fungal extract from different days of culture (1, 2, 3, 5 and 7 days) were incubated with 200µL of the citrated plasma at 37 °C plus 100 µL of a calcium chloride solution, thus the plasma coagulation time was evaluated. **Results:** The PAC 123 fungal extract at the different culture times showed coagulant action *in vitro*, mainly in the 5th day of culture that this extract shortened the clotting time by over 60% as compared to untreated whole blood (2min24s). The maximum clotting time of untreated whole blood was 3min58s (100% of clot retraction time). In this regards, the clot retraction times of the fungus extract at the different culture times showed the following values: Control: 3min58s (100% - maximum clotting time), 1º day of culture - 3min10s (86.6%), 2º day of culture - 2min53s (70.7%), 3º day of culture - 2min45s (68.4%), 5º day of culture - 2min24s (62.6%) and 7º day of culture - 2min54s (70.9 %). **Conclusion:** Thus, PAC 123 fungal extract shortened the clotting time for native whole blood, indicating an important role for the platelet in the amplification of the coagulation process. Thus, it can have a great potential both in intensive care or surgery and as a screening test in patients with suspected coagulation abnormalities.

Keywords: Endophytic fungi, fermentation broth, coagulant activity, *Piper aduncum*. **License number of ethics committee**: PARECER 1090857 **Financial support**: CAPES, CNPQ, UFPA, FAPESPA

09.015 Antinociceptive and anti-inflammatory effect of a polyphenolic-rich fraction of *Annona crassiflora* **Mart. fruit peel in mice**. Araújo PHS[1], Justino AB[2], Costa MS[1], Saraiva ALL[2], Cunha TM[3], Espíndola FS[2], Silva CR[1] [1]UFU – Bioquímica e Toxinas Animais, [2]UFU – Bioquímica e Biologia Molecular, [3]FMRP-USP – Inflammatory Diseases

Introduction: Inflammatory diseases like arthritis are between the most common chronic situations affecting the worldwide population. Arthritis is characterized by pain and inflammation, and some of the markers of the inflammatory process includes TNF-α, IL-6 and nitric oxide (NO). Currently, options for treatment have various undesirable side effects and many patients end up opting for treatments based on folk medicine. In this scenario, *Annona crassiflora* Mart., a Brazilian savanna derived plant, is empirically used in traditional medicine to treat arthritis. Recently, a study showed that the fruit peel of Annona is rich in polyphenols with antioxidant properties and anti-inflammatory potential. Thus, the aim of this study is to assess the possible antinociceptive and anti-inflammatory effect of a polyphenol-rich fraction obtained from the fruit peel of *Annona crassiflora* Mart. (PRFA). **Methods:** Adult male Wild type C57BL/6 mice (20-25 g) were used and all procedures were approved by Institutional Ethics Committee (process number 105/17). Firstly, macrophage culture was stimulated with LPS (100 ng/ml) for 24 hours in the presence of 0.1-1.0 µg/mL of PRFA. The supernatant was collected 6 h after for the analysis of IL-6, nitric oxide, and TNFα. Another group of animals was orally treated with PRFA (10, 30 and 100 mg/kg) 30 min before the intraplantar injection (ipl) of 20 ul of glutamate (10 uM/paw). Immediately after, the time spent licking the injected paw was observed for 30 min. Also, a group received ipl injection of 20 uL/paw of Freund's Adjuvant Complete (CFA, 1mg/ml) 30 min after orally pre-treatment with the PRFA (30 mg/kg), and the acute response to mechanical nociception, edema and spontaneous nociception was evaluated at 1-24 h after injection. Furthermore, the later inflammatory response was evaluated 48h after CFA administration, and the animals received treatment with PRFA immediately after, then the same parameters were analyzed from 1-24h after its administration. **Results:** LPS was able to increase IL-6, TNFα and NO release from stimulated macrophages by more than 500%, being that the PRFA prevented the release of IL-6 and NO, in 40,5% and 76,6%, respectively, but was not effective in reducing TNFα. Also, 30 mg/kg of PRFA was able to prevent the nociception induced by ipl glutamate injections in 75%. Additionally, 30 mg/kg of PRFA prevented acute (from 1 up to 4 h) and chronic (4 h) mechanical nociception induced by CFA. Acute spontaneous nociception was also prevented 1 and 2 h after CFA injections, and edema was prevented at 24 h after acute, and from 2 - 4 h after chronic inflammation induction. **Conclusion:** Our findings indicate that PRFA is a promising tool for the treatment of pain, partially confirming the popular use, and more studies need to be done to clarify these effects and the safety of the fraction. **License number of ethics committee**: 105/17 **Financial support**: Conselho Nacional de Desenvolvimento Científico-CNPq, Fundação de Amparo à Pesquisa do Estado de Minas Gerais-FAPEMIG.

09.016 *In vitro* **antitumoral and antimicrobial activity of plants from Mimosoideae subfamily**. Silva SANM[1], Barros AB[1], Nobre ARA[1], Moraes MO[2], Moura AF[2], Daboit TC[3], Mendes MGA[3], Nolêto RP[3], Araújo AJ[1], Marinho-Filho JDB[1] [1]UFPI – Biodiversidade e Biotecnologia), [2]UFC – Fisiologia e Farmacologia, [3]UFPI – Micologia

Introduction: The search for bioactive compounds from plants proves to be an effective alternative, of lower cost and low collateral effects, thus being able to be accessible to all social classes. In Brazil, some plants are popularly used for the treatment of several diseases, among them, *Mimosa tenuiflora, Mimosa verrucosa, Mimosa pteridifolia and Piptadenia stipulacea*, popularly known by "Jurema". These plants are belonging to the family Fabaceae, subfamily Mimosoideae, mainly having effect against inflammations and wounds. The objective of this study was to determine classes of secondary metabolites presents and to evaluate the biological activity of crude ethanolic extracts from bark of four Jurema species. **Methods:** Qualitative phytochemical evaluation was performed through colorimetric reactions. The antimicrobial activity was assayed by microdilution in a 96-well plate against strains of *Staphylococcus aureus* (ATCC29213), *Escherichia coli* (ATCC25922), *Candida albicans* (ATCC18804) and *Trichophyton interdigitale* (ATCC75896). The antitumor activity was performed by MTT assay in a 96-well plate against four cancer cell lines, HCT-116 (colon), PC-3 (prostate), SF-295 (glioblastoma) and HL-60 (acute promyelocitic leukemia). Hemolytic activity was determined by serial dilution using O^+ human erythrocytes. **Results:** In the phytochemical prospection was observed that each species have variation of secondary metabolites, such as tannins, flavonoids and saponins. All samples have antibacterial activity against *E. coli* and *S. aureus*, with MIC between 15.6 µg/mL and 2000 µg/mL, and demonstrated antifungal action against *C. albicans* and *T. interdigitale*, with MIC between 78.13 µg/mL and 1250 µg/mL. It was found that *P. stipulacea* presented antitumor action against some of the cancer cell lines evaluated, with IC_{50} below 50 µg/mL. Regarding hemolytic activity, *M. tenuiflora* obtained only at the highest tested concentration of 1000 µg/mL, *M. verrucosa* and *P. stipulacea* at 500 µg/mL, and *M. pteridifolia* did not obtain activity at any of the concentrations evaluated. **Conclusion:** The ethanolic extracts of Jurema peels have considerable biological activities that are probably related to the presence of secondary metabolites, such as tannins and some classes of flavonoids. Therefore, new studies must be carried out to verify which molecules are present in these extracts, responsible for the observed biological effects. **Financial support**: CNPq, INCT, BioNat and FAPEPI

09.017 Antimicrobial and immunomodulatory activity of oneendophytic fungi extract from *Piper aduncum*. Rodrigues DVS[1], Souza LMMA[1], Oliveira ALB[1], Ferreira RG[2], Furtado KMS[2], Espíndola KMM[2], Monteiro MC[1] [1]UFPA – Farmacologia e Inflamação, [2]UFPA – Farmácia Industrial

Introduction: Endophytic microorganisms, especially fungi, stand out as important sources of biomolecules for medicine, agriculture and industry. These fungi are a source of new bioactive molecules with great pharmacological potential in nature. The objective of this work was to evaluate the antimicrobial and immunomodulatory activity of an endophytic fungi extract isolated from the plant species *Piper aduncum*. **Methods:** The evaluation of the antimicrobial activity was performed using the microdilution method using the PAC 119 fungal extract (patent) at the concentrations of 2.5; 1.5; 1; 0.5 and 0.25 mg/mL, against bacteria: *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa,* as well as the yeast *Candida albicans*, for determination of MIC, MBC and MFC. The evaluation of immunomodulatory activity was performed after obtaining peripheral blood mononuclear cells (PBMC's) and through cell proliferation, phagocytosis and nitric oxide dosage assays at concentrations of 0.25; 0.5; 1 mg/mL and cytotoxicity at concentrations of 0.06 mg/mL to 30 mg/mL. **Results:** The fungal extract showed a better antibacterial activity against gram-positive bacteria *S.aureus*(MIC of 1 mg/mL) compared to gram-negative bacteria *E. coli* and *P. aeruginosa* (MIC > 2.5 mg/mL). However, the extract showed moderate antifungal activity against *C. albicans* (MIC of 1.5 mg/mL). The fungal extract did not show cytotoxic activity against PBMC's, since the cells remained viable at all concentrations tested. In this regard, the fungal extract was more effective against bacteria compared to eukaryotic cells, showing greater selectivity for prokaryotes. All concentrations of the fungal extract were able to stimulate proliferation of PBMCs at 24 hours. In addition, when the extract was incubated with the ConA mitogen at different concentrations, there was no change in the proliferative effect induced by ConA, showing a similar effect to the mitogen. The fungal extract at different concentrations showed an immunostimulating effect, since they were able to stimulate the phagocytic capacity of PBMCs similar or greater than LPS. On the other hand, when incubated with LPS, the extract did not alter the phagocytic capacity induced by LPS, presenting values similar to LPS alone. All tested concentrations of fungal extract were able to induce increase in NO production in PBMC for 24 hours. However, only the higher concentration of the extract (1 mg/mL) was able to stimulate NO production in a manner similar to LPS, showing that the stimulatory effect of the extract on NO production may be dependent dose. **Conclusion:** These data indicated that the fungal extract showed good antimicrobial and immunomodulatory activities *in vitro*, constituting a promising source of potentially active substances that might have applications in medicine, agriculture and the pharmaceutical industry

09.018 A polysaccharide fraction from ipê roxo leaves with gastroprotective activity. Maria-Ferreira D[1], Ferreira-Silva L[1], Carlotto J[2], da Luz BB[1], Dallazen JL[1], de Souza LM[2], Werner MFP[1], Cipriani TR[2] [1]UFPR – Farmacologia, [2]UFPR – Bioquímica

Introduction: Peptic ulcer disease is a common disorder and the treatment commonly involve the long-term inhibition of acid secretion, mainly by proton pump inhibitors. However, recent studies showed adverse effects, justifying the search for new therapies. *Handroanthus heptaphyllus*, commonly known as "ipê-roxo", has been traditionally used to treat digestive disorders. Although beneficial effects are generally attributed to lapachol and β-lapachone, other compounds, such as polysaccharides are found. The gastroprotective and antioxidant potential of polysaccharides was previously demonstrated (Maria-Ferreira D et al., Natural Products Coordinated Session, 45º SBFTE, 2013 and Plos One, 2014) and accordingly, it could provide an alternative to improve ulcer healing and prevent recurrence. Thus, our aim was to investigate the protective and healing effects of a polysaccharide fraction from *H. heptaphyllus* in acute and chronic models of gastric ulcer in rats. **Methods:** Rats (*Rattus norvegicus*) were orally (p.o.) treated with vehicle (C: water, 1 ml/kg) or crude precipitate of polysaccharides (RFAP: 1, 3, 10 and 30 mg/kg), 1h before 1 mL of absolute-ethanol ulcer induction. RFAP was frozen and thawed, resulting in a soluble fraction (RFAP-S), analyzed by methylation and NMR. Theoretical ED50 was calculated (10 mg/kg) and employed (v.o. or i.p.) in further experiments. Acute ulcers were induced by 1 mL of absolute ethanol or indomethacin (100 mg/kg) and 1 hour or 4 hours after stomachs were collected to measure lesions, GSH and mucus levels. Chronic gastric ulcer was induced by 80% acetic acid, and 7 days after, stomachs were removed to measure ulcer area and GSH levels. Hypersecretion was induced by pylorus ligation and secreted volume, pH and acidity were measured (CEUA/BIO-UFPR 1093). *In vitro* antioxidant and metabolic analysis was carried out in Caco-2 cells. **Results:** RFAP (1, 3, 10 and 30 mg/kg, v.o.) reduced the gastric lesions in 28, 72, 63 and 72%, respectively, when compared to control group (C: 172.0 ± 18.3 mm^2). RFAP-S (type II arabinogalactan, with side chains of arabinans) v.o. and i.p., reduced ulcer lesions in 37 and 60%, preserved the mucus layer in 20 and 34% and GSH levels (i.p.) in 55% when compared to the control group (C: 2211.4 ± 120.7 and 1485.7 ± 90.3 µg of Alcian blue/g of tissue; 1400.6 ± 132.3 µg of GSH/g of tissue). In the indomethacin model, RFAP-S (v.o.) reduced lesioned area in 54% (C: 8.0 ± 1.6 mm^2), and inhibited mucus and GSH depletion in 70 and 57%, comparing to control (C: 2660.5 ± 69.7 µg of Alcian blue/g of tissue; 1007.4 ± 87.1 µg of GSH/g of tissue). Furthermore, RFAP-S (v.o.) reduced chronic ulcer area in 36% (C: 183.90 ± 15.81 mm^2) with the maintenance of GSH levels (RFAP-S: 702.8 ± 53.7 µg of GSH/g of tissue). The gastric healing property was confirmed by H&E histological stain. RFAP-S did not alter gastric hypersecretion. Moreover, when Caco-2 cells were treated with H_2O_2, RFAP-S (10 µg/mL) preserved the GSH levels in 24% when compared to the vehicle group. Importantly, RFAP-S (10 µg/mL) is not toxic to cells. **Conclusion:** Collectively, we demonstrated that the RFAP-S has an interesting antiulcerogenic activity in rats. These effects could be associated to maintenance of gastric mucus and modulation of antioxidant mechanisms. However, additional studies are required to investigate complementary mechanisms involved in the effects produced by RFAP-S. **License number of ethics committee**: 1093 **Financial support**: PNPD-CAPES

09.019 Evaluation of free radical scavenging properties of *Trichilia catigua* **crude extract**. Semeao LO, Oliveira BM, Michelin AP, Matsumoto AK, Bonifacio KL, Higachi L, Barbosa DS, Corazza AC, Casagrande R, Lonni AASG UEL – Análises Clínicas e Toxicológicas

Introduction: The exposure to ultraviolet radiations (UVR) is the key source of skin sunburn. It may produce harmful entities, reactive oxygen species (ROS) and and reactive nitrogen species (RNS) leading to aging. The skin can be treated and protected from the injurious effects of ROS by using various pharmaceutical formulations, such as cosmetic formulation. Thus, the topical antioxidants are an interesting strategy for skin protection against oxidative stress caused by different agents. Some of the biological activities of *Trichilia catigua* can derive from their ability to protect or inhibit against free radicals. Topical application of a cosmetic formulation with *Trichilia catigua* extract (TCE) is aimed at strengthening the antioxidant defenses of the skin and thus attenuate the wrinkles that appear with the ageing. **Methods:** *In vitro,* the antioxidant capacity of TCE was assessed by their ability to donate hydrogen and stabilize the free radical 2,2-diphenyl-1-picryl-hydrazyl ($DPPH^{\bullet}$); and scavenge 2,2'-azino-di-(3-ethylbenzthiazoline-6-sulphonic acid ($ABTS^{+}$). The *in vitro* that inhibits oxidative process concentration by 50% of $DPPH^{\bullet}$ and $ABTS^{+}$ was IC_{50}. The IC_{50} was determined by GraphPadPrism® software, version 4.00 April 2003 using a hyperbolic curve (one site binding hyperbola). The results were expressed as mean ± standard error (SEM). Results were considered statistically significant $p<0.05$. **Results:** In $ABTS^{+}$ assay, the results demonstrated that TCE scavenged the positively charged $ABTS^{+}$ radical in concentration-dependent manner. The maximum activity was found to be 99.04% at the concentration of 8.25 µg/mL and IC_{50} of 3.96 µg/mL. The extract showed a linearity of 0.98 between 1.38 to 8.25 µg/mL. In determination of $DPPH^{\bullet}$ radical scavenging activity, the results showed that TCE scavenged the negatively charged radical ($DPPH^{\bullet}$), in concentration-dependent manner. The maximum activity was found to be 89.98% at the concentration of 10 µg/mL and IC_{50} of 3.54 µg/mL. The extract showed a linearity of 0.98 between 1.32 to 6.63 µg/mL. **Conclusion:** Our results demonstrate that TCE presented antioxidant activity in the colorimetric methodologies performed, having the capacity to stabilize the radical $ABTS^{+}$ as well as to donate hydrogen to the radical $DPPH^{\bullet}$. However, further studies should be carried out.

09.020 Endothelium-dependent effects of *Echinodorus grandiflorus* (**Cham. & Schltdl.**) **Micheli mediated by M_3-muscarinic and B_2-bradykininergic receptors on peripheral vascular resistance and its modulatory effects on calcium-activated potassium channels in mesenteric vascular beds**. Guarnier LP, Carvalho ES, Palozi RAC, Schaedler MI, Romão PVM, Silva AO, Tirloni CAS, Barros ME, Gasparotto AJ UFGD – Ciências da Saúde

Introduction: *Echinodorus grandiflorus* (Cham. & Schltdl.) Micheli (Aquifoliaceae) has been used as a diuretic agent by several Brazilian native populations. It has been shown that the several extracts obtained from leaves of this species have important diuretic and hipotensive effects. Nevertheless, the secondary metabolites responsible for this activity, as well as the molecular mechanisms responsible for its effects on peripheral vascular resistance (PVR) remain unknown. The aim of this work was to carry out a biomonitoring study with *E. grandiflorus* extracts and evaluates the mechanisms responsible for the vasodilatory effects (VE) on isolated perfused mesenteric vascular beds (MVBs). **Materials and Methods:** First, an ethanolic extract (92.8% ethanol; 1: 4 w/v) was obtained from *E. grandiflorus* leaves (EEEG) and a liquid-liquid fractionation was performed. EEEG and its butanolic fraction (ButFr) were analyzed by liquid chromatography–mass spectrometry. Then, the possible VE of EEEG's and ButFr on MVBs were evaluated. Finally, the molecular mechanisms involved in the vasodilator responses of ButFr on the mesenteric arteriolar tone were also investigated. All experimental procedures were approved by Institutional Ethics Committee/UFGD (protocol 35/2017). **Results:** EEEG and ButFr presented high levels of total flavonoids with an estimated amount of 198.9 and 265.7 mg/g, respectively. In preparations with functional endothelium ButFr dose-dependently reduced the perfusion pressure (PP) in MVBs, in doses of 0.1 and 0.3 mg. The peak effect of doses was decreased by 80 ± 7 and 99 ± 4%, respectively, in preparations without endothelium. Similarly, the effects were reduced by 40 ± 5% and 50 ± 8% in MVBs perfused with L-NAME, and 70 ± 3% and 51 ± 6% when perfused with indomethacin. The VE was completely inhibited in preparations perfused with L-NAME plus indomethacin. Reductions in PP generated by doses in control preparations were reduced by ~ 40 ± 4% and ~ 52 ± 7% when perfused with atropine and by ~ 39 ± 3% and ~ 58 ± 5% after perfusion with HOE-140. Simultaneous treatment with atropine and HOE-140 vanished the VE induced by ButFr. The perfusion of MVBs with physiological solution (PSS) added of 40 mM KCl completely blocked the effects of ButFr. Interestingly, PSS perfusion with tetraethylammonium fully inhibited vasorelaxation induced by all ButFr-doses. **Conclusion:** This study showed that EEEG's fraction has important VE on MVBs. Apparently, these effects are dependent on endothelial M_3-muscarinic and B_2-bradykininergic receptors inducing nitric oxide and prostaglandins release followed by K+ channels activation in the vascular smooth muscle. **License number of ethics committee**: Comitê de ética em pesquisa animal UFGD: protocolo 35/2017 **Financial support**: Fundação de Apoio ao Desenvolvimento do Ensino, Ciência e Tecnologia do Estado de Mato Grosso do Sul (FUNDECT, Brazil), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq, Brazil) e Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES, Brazil).

09.021 Evaluation of acute oral toxicity and pharmacological properties of Phy01. Câmara FMS[1], Silva MN[2], Ribeiro CHMA[3], Monteiro MC[4], Silva JPB[4], Pereira WLA[5], de Oliveira DMC[6], Freitas BR[1], Souza-Júnior FJC[1], Santos AN[1], Souza PHFS[1], Queiroz LY[1], Andrade DM[1], Maia CSF[1], Fontes-Júnior EA[1] [1]LAFICO-UFPA, [2]LABCROL-UFPA, [3]LABHEM-UFPA, [4]LABEIM-UFPA, [5]LABOPAT-UFRA, [6]LAFAV-UFRA

Introduction: Margaritaria sp. (Phyllanthaceae), is a shrub, terrestrial and aquatic species, with up to 15 m height found in tropical forests (Cazetta et al., 2008). Photochemical study carried out on its leaves has shown to contain substances that promote various biological activities. In this perspective, the present study proposes to investigate the acute oral toxicity and the activities on the nociception and vascular permeability of the ethanolic extract of Margaritaria sp. identified as Phy01. **Methods:** Animals used were kept in a controlled environment (T=22 ± 1 ºC, light/dark cycle of 12h), with water and feed ad libitum. Oral toxicity study was conducted according to OECD 425 directive and Anvisa Resolution nº 90. Female wistar rats (n=10, 150-200 g) were divided into two groups: control (vehicle, v.o., 0.1 mL/100 g) and Phy01 (2000 mg/kg, v.o). Behavioral (open field, hippocratic evaluation, water and feed intake), systemic (weight gain, macroscopy and relative weight of vital organs), histological and biochemical (ALT, AST, urea and creatinine) parameters of toxicity were evaluated after tratment, being also verified the occurrence of deaths. The antinociceptive properties were investigated through murine models (n=56, swiss males, 25-30 g), including writhing test (WT), evaluating nociception and plasma extravasation to the peritoneal fluid, and formalin test (FT), performed to investigate neural and inflammatory mechanisms of the activity. Nociceptive tests were preceded by spontaneous locomotor evaluation, in order to verify alterations in wakefulness or motor impairment. Statistical analysis was performed using Student "t" tests, ANOVA (post-test of Holm-Sidak) or Kruskal-Wallis (Dunn's post-test). **Results:** Oral administration of 2.000 mg/kg of Phy01 did not promote significant changes in toxicity parameters evaluated, and there were no deaths as well. Although there was a significant reduction of locomotion in animals treated with Phy01 200 mg/kg (10±4,2; $p<0,05$) *versus* Control (32±2,4), the same did not occur with other tested doses 400 and 800 mg/kg (28±3,2; 23±2,9). The effects on writhing was erratic, promoting reductions of 19%, 42% and 28% with 200, 400 and 800 mg/kg (50±6,9; 36±4,9; 44±3,6) tratment, respectively, in relation to control group (62±7,5). On the other hand, no changes were observed in plasma proteins extravasation to peritoneal fluid. FT was conducted with 400 mg/kg of Phy01, since it promoted an effect equivalent to the indomethacin standard (25 ± 3.6) activity in WT. It did not promote changes in formalin-induced biphasic nociception. **Conclusion:** Results demonstrate, for the first time, that Phy01 is a low toxicity xenobiotic, evidencing its relative safety for oral administration. They also demonstrate that Phy01 has low influence on nociception process. **References:** Cazetta, E. Braz. J. of Botany, v.31, p.303, 2008. **License number of ethics committee**: CEUA-UFPA 9568260617. **Financial support**: Acknowledgments and **Financial support**: Federal University of Pará; Evandro Chagas Institute.

09.022 Influence of *Luehea divaricata* **Mart. extracts on peripheral vascular resistance and the role of nitric oxide and both Ca^{+2}-sensitive and Kir6.1 ATP-sensitive K+ channels in the vasodilatory effects of isovitexin on isolated perfused mesenteric beds**. Schaedler MI, Tirloni CAS, Palozi RAC, Guarnier LP, Silva AO, Gasparotto Junior A, Romão PVM UFGD – Eletrofisiologia e Farmacologia Cardiovascular

Introduction: *Luehea divaricata* Mart. (Malvaceae) is widely used by different ethnic groups of the Pantanal region for the treatment of cardiovascular diseases. Recent studies have shown that extract obtained from *L. divaricata* leaves have an important diuretic, hypotensive and antioxidative effects. Moreover, phytochemical analyzes of *L. divaricata* exhibit a high concentration of phenolic compound and flavonoids, highlighting the isovitexin. Despite the effects on the cardiovascular system it is not known by what mechanisms *L. divaricata* acts. In this way this study intends to evaluate the vasodilator effect of the semi-purified fractions obtained from the leaves of *L. divaricata* and isovitexin on isolated perfused mesenteric vascular beds (MVBs), as well as the mechanisms involved in the vascular effects. **Materials and Methods:** First, leaves from *L. divaricata* were dried for 5 days in an air circulation oven and then ground. The infusion was prepared by adding 1 liter of boiling water to each 100 g of powder. The infusion was treated with 3 volumes of EtOH, which gave rise to a precipitate and an ethanol soluble fraction (ESLD). ESLD was submitted to liquid-liquid fractionation. The resulting the aqueous fraction (AqueFr) was analyzed by liquid chromatography-mass spectrometry. Then, the possible vasodilatory effects of AqueFr on MVBs were evaluated. Finally, the molecular mechanisms involved in vasodilator responses of the AqueFr and its main metabolite – isovitexin - on the MVBs were also investigated. All experimental procedures were approved by Institutional Ethics Committee of UFGD (protocol number 16/2015) and conducted in accordance with the Brazilian Legal Standards on Scientific Use of Animals. **Results:** A detailed phytochemical study was performed with the AqueFr. So, these main compounds were identified: dirhamnosyl-hexosyl-quercetin, rhamnosyl-hexosyl-quercetin, vitexin, rutin, isovitexin, rhamnosyl-hexosyl-kaempferol, and rhamnosyl-hexosyl-kaempferol. In preparations with functional endothelium ESLD and AqueFr reduced the perfusion pressure (PP) in MVBs about ~ 18, 46 and 53 mm Hg at doses of 0.01, 0.03, and 0.1 mg. Isovitexin reduced the PP in MVBs about ~ 26, 56 and 66 mm Hg at doses 100, 300 and 1000 nmol respectively. Endothelium removal or inhibition of nitric oxide synthase by L-NAME significantly reduced the vasodilatory effects induced by AqueFr (72 ± 7%) and isovitexin (80 ± 9%). Perfusion with nutritive solution containing 40 mM KCl abolished the vasodilatory effect of all AqueFr and Isovitexin doses. Treatment with glibenclamide, or tetraethylammonium, reduced by around ~ 78 ± 8% vasodilation induced by all AqueFr and ~ 70 ± 7% by all isovitexin doses. In addition, association of tetraethylammonium and glibenclamide, or L-NAME and glibenclamide, fully inhibited AqueFr and Isovitexin induced vasodilation. **Conclusion:** This study showed that AqueFr obtained from *Luehea divaricata* and its metabolite - isovitexin - has important vasodilatory effects on MVBs. Apparently, these effects are dependent on endothelium-NO release and both K_{Ca} K+ channels and Kir6.1 ATP-sensitive K+ channels activation in the vascular smooth muscle. **License number of ethics committee**: 16/2015-UFGD **Financial support**: FUNDECT and CNPq.

09.023 Effect of *Tityus bahiensis* ***and*** *Tityus serrulatus* **crude venom on rats platelet reactivity**. Morau MV, Bonfitto PHL, Naime ACA, Antunes E, Marcondes S FCM-Unicamp – Farmacologia

Introduction: Scorpion accident is considered a serious public health problem in Brazil. *Tityus bahiensis (Tb) and Tityus serrulatus (Ts),* frequently found in São Paulo state, are the scorpion species responsible for the majority of scorpion sting accidents in Brazil. Symptoms of envenomation by *Ts* and *Tb* range from local pain to severe systemic reactions such assystemic inflammatory response syndrome (SIRS). There are practically no studies about *Ts or Tb* venom in the hemostasis. Although it has already been reported that the *Ts* venom decreases the coagulation time, there is no study about their effects on platelets. The aim of the present work was to study the effects of the *Tityus bahiensis* and *Tityus serrulatus* crude venom on rat platelet activity. **Methods:** The present study was approved by the Committee for Ethics in Animal Research (State University of Campinas – UNICAMP, protocol number 4314-1). The lyophilized venom of *T. serrulatus* and *T. bahiensis* were provided by Institute Butantan, SP, Brazil. Arterial blood was collected in ACD-C (9: 1 v/v) from abdominal aorta of male Wistar rats. Platelet-rich plasma was obtained after centrifugation of whole blood at 200g for 20 min and the platelets were washed using citrated buffer. Washed platelets were suspended in Krebs's solution and the number adjusted to $2x10^8$platelets/ml. Platelet aggregation was evaluated using a two-channel aggregometer. Platelets were incubated with crescent concentrations of the venom of *Ts* and *Tb* (1μg/ml - 300μg/ml) for different period of time (5, 15 or 30 min) before ADP addition. The levels of TXA^2, cGMP and cAMP were determined by the ELISA method. In addition, flow cytometry was also performed to measure reactive oxygen species (ROS) production. The statistical significance between groups was determined by using ANOVA followed by the Tukey test. **Results:** Incubation for 5 min of platelets with *Ts* venom inhibited ADP-induced aggregation (1μM) in a dose-dependent manner (inhibition of 10, 28 and 85% using concentrations of 1, 10 and 100 μg / ml, respectively). ADP-induced aggregation was abolished by the incubation of platelets with *Ts* venom (300 μg/ml) for 30 min. *Tb* venom inhibited 42% aggregation only at the concentration of 300 μg/ml (30 min of incubation). Inhibition of ADP-induced aggregation by venoms of *Tb* (300 μg / ml) and *Ts* (100 μg / ml) was accompanied by a reduction in TXA2 synthesis (reduction of 24 and 65% in the presence of *Tb* and *Ts*, respectively). The venoms of *Tb* and *Ts* increased about 2.0 fold the intraplatelet levels of cGMP compared to the saline group, while cAMP levels were not altered.The production of reactive oxygen species has also not been altered by toxins. **Conclusion:** The inhibition of ADP-induced platelet aggregation is markedly greater with the equimolar concentration of *Tityus serrulatus* venom than *Tityus bahiensis*. The inhibitory effect of *Tityus serrulatus and bahiensis* venom on ADP-induced platelet aggregation is independent of cAMP levels or ROS production, however, cGMP and TXA2 probably take part on this effect.

Financial Support: CNPq **Animal Research Ethical Committee:** CEUA - Unicamp 2016- 4314-1

09.024 Neutralization of Crotoxin from *Crotalus durissus terrificus* **by crotoxin neutralizing factor**. Pinto EKR[1], Natalia MVS[1], Paula LO[2], Patricia CC[2], Consuelo LFD[2], WalterLGC[1] [1]ICB-UFMG – Farmacologia e Fisiologia, [2]FUNED – Pesquisa e Desenvolvimento

Introduction: Among the snakes of major medical importance in Brazil, poisoning by *Crotalus durissus* stands out due to its high lethality. The toxicity of the crotalic venom is related to the presence of Crotoxin (CTX), a protein that corresponds to 50-70% of the total venom. It is a potent neurotoxin that induces peripheral respiratory paralysis due to the blockade of neuromuscular transmission. Despite the great effort dedicated to the issue, the molecular mechanism underlying the neurotoxicity of CTX remains to be fully elucidated. Previously studies reveled that Crotoxin Neutralizing Factor (CNF), a protein present in the plasma of *C.d. terrificus* snakes, is capable to inhibit the CTX toxic effects in *in vivo* experiments[1]. However, there are no *in vitro* studies in neuromuscular preparations showing the inhibitory action of CNF. Therefore, the objective of this study was to evaluate the ability of CNF to inhibit the neuromuscular blockade induced by CTX. The experimental procedures were approved to the Ethics Committee, Protocol CEUA: 17/2017. **Methods:** Paralyzing activity was evaluated through the recording of isolated contractions evoked indirectly in phrenic-diaphragm preparations. During the experiments, the preparations were exposed for 120 minutes to CTX (5 µg/mL) or CNF (50 µg/mL) or to the preincubation mixture of CTX (5 µg/mL) with CNF (5 or 20 or 50 µg/mL). CTX and CNF samples were preincubated for 15 minutes at 35 °C. **Results:** Control and CNF groups did not present alterations in the amplitude of indirectly evoked twitches over the time. CTX (5 µg/mL) alone induced the total blocked of muscle contractions in 60 minutes. The preincubation of CTX 5 µg/mL with CNF 5 µg/mL was not able to neutralize the effect of this toxin. However, when the CTX 5 µg/mL was preincubated with CNF 20 µg/mL, a decrease in the toxic activity of CTX was observed, with partial blockage of muscle contractions. Pre-incubation of CTX 5 µg/mL with CNF 50 µg/mL was able to fully inhibit the CTX paralyzing activity in 120 minutes. **Conclusion:** The functional studies performed in the present study confirm that CNF is able to inhibit the toxic activity of CTX at neuromuscular junction. **Acknowledgments:** *Coordenação de Aperfeiçoamento de Pessoal de Nível Superior* (CAPES), *Fundação Ezequiel Dias* (FUNED) and *Pró-Reitoria de Pesquisa da UFMG* (PRPQ). **Referências:** FORTES-DIAS et al. **T Jour Biol Chemi.** v. 269, p.15646, 1994. **License number of ethics committee**: CEUA: 17/2017 **Financial support**: CAPES

09.025 Antibacterial activity of cordiaquinones B, E, L, N and O obtained from *Cordia polycephala*. Oliveira MA[1], Barros AB[1], de Araujo GS[1], de Araujo AR[2], Soares MJS[3], de Freitas HPS[4], Pessoa ODL[4], Marinho-Filho JDB[1], Araújo AJ[1] [1]UFPI – Ciências Biomédicas, [2]UFPI – Biotecnologia, [3]UFPI – Farmacologia, [4]UFC – Química Orgânica

Introduction: Bacterial infections are a leading cause of death, especially in developing countries, and resistance to antibiotics contributes to make those infections a major public health problem. Cordiaquinones (CQs) are naphthoquinones obtained from species of genus *Cordia.* This class of substances is characterized by the presence of two carbonil groups bounded to an aromatic ring and had shown antifungal, larvicidal and antitumor activities in previous studies. Thus, the aim of this work was to evaluate antibacterial activity of CQs B, E, L, N and O against different strains of bacteria. **Methods:** The CQs were assayed for their antibacterial activity by determination of minimum inhibitory concentration (MIC) by microdilution in 96-well plates following CLSI recommendations. For this, Gram positive (*Staphylococcus epidermidis* ATCC 12228; *Staphylococcus saprophyticus*; *Enterococcus faecalis* ATCC 29212; *Staphylococcus aureus* ATCC 29213; *Staphylococcus aureus* Med 55 (Clinical Specimen Methicillin Resistant); *Staphylococcus epidermidis* 70D (Clinical Specimen) and Gram negative (*Salmonella choleraesuis* ATCC 14028 and *Klebsiella pneumoniae* ATCC 700603 – ESBL producing) strains were used. Later, 10 µL of each well where no growth had been observed were placed onto a Mueller Hinton agar plate, in order to determine the Minimum Bactericidal Concentration (MBC). Atomic Force Microscopy was performed to identify alterations in cells morphology. **Results:** Most Gram-positive tested strains were susceptible to CQs B, E, L and N. The best result was a MIC value of 7.8 µM of CQ L against *S. saprophyticus.* Their best MBC value was 62.5 µM of CQs B and E against *S. saprophyticus.* CQ O have not shown activity against any tested strain. None of these cordiaquinones have shown activities against the Gram-negative tested strains. Morphological changes have been observed in *S. saprophyticus* cells treated with CQ L, when analyzed by AFM. The presence of methoxyl groups in CQ B and E could interfere in their antibacterial activity, as well as terminal hydroxyl group in CQ L. Weaker and absent activity of CQ N and O, respectively, could be related to their absence of those groups. **Conclusion:** There is an urgent need for new antibacterial agents, due to the increasing bacterial resistance. The results showed in this work suggests that cordiaquinones have an antibacterial potential, once they can inhibit growth of several strains of bacteria, both sensible and resistant, however, they did not have effect on growth of Gram-negative strains, which may be associated with the structural differences between those two groups of bacteria. Further studies will be performed to investigate the mechanism involved in cordiaquinones antibacterial action. **Financial support**: Supported by: CNPq, FAPEPI and INCT BioNat.

09.026 Pharmacological potential of alkylamides from *Acmella oleracea* **to treat inflammatory pain**. Dallazen JL[1], Maria-Ferreira D[1], da Luz BB[1], Nascimento AM[2], Cipriani TR[3], de Souza LM[4], Werner MFP[1] [1]UFPR – Farmacologia,[2]UFAC – Bioquímica, [3]UFPR – Bioquímica e Biologia Celular, [4]Pesquisa Pelé Pequeno Príncipe – Bioquímica

Introduction: *Acmella oleracea* (L.) R.K. Jansen (*Compositae*) is an Amazonian plant popularly known as "jambu" and widely used in folk medicine to relief toothache. Jambu edible flowers are rich in alkylamides, manly in spilanthol, which is responsible to evoke tingling, numbness and local anesthesia in the mouth. This study evaluated the anesthetic and antinociceptive effects of local treatment with the hexanic fraction (HF) rich in alkylamides from jambu. **Methods:** HF was obtained from jambu flowers and alkylamides were identified by GC-MS analysis. The HF and IBA (synthetic isobutylalkenyl amide used as control) dose (0.1 µg/20 µL, intraplantarly) was selected based in previous results obtained in acute pain models (Dallazen et al., Oral Communication at 49th SBFTE, 2017). First, male Swiss mice (~30 g, CEUA/BIO-UFPR 1107) received HF or IBA (i.pl.) to evaluate the effect *per se* on mechanical (von Frey filaments) and thermal (hot plate at 52 ± 0.2 °C) paw withdrawal thresholds, using 1% lidocaine (20 µL, i.pl.) as positive control. Mice were pretreated with HF or IBA, dexamethasone (1 mg/kg, i.p.) and vehicle (V: 0.002% tween 80 or 0.02% DMSO, 20 µL, i.pl.), 30 min before carrageenan-induced inflammatory pain (300 µg/20µL, i.pl.). The mechanical allodynia (von Frey test) and paw edema (measured with digital micrometer) were evaluated for 6h. At peak effects of HF and IBA, the plantar surface of hindpaw was excised and homogenized to measure the following parameters: myeloperoxidase (MPO), lipid hydroperoxides (LPO), glutathione (GSH), catalase (CAT) and TNF-α. **Results:** Phytochemical analysis of HF confirmed the presence of spilanthol. Intraplantar injection of HF increased the mechanical threshold from 1.1 ± 0.1 g to 2.6 ± 0.4 g and 2.8 ± 0.4 g, after 30 and 60 min, respectively. Thermal latency was increased at 15, 30 and 60 min in 22.3, 34.5 and 28.8%, respectively, when compared to vehicle group (13.9 ± 0.6 s). IBA unchanged the mechanical sensitivity but reduced the thermal latency at 15 and 30 min in 36.8 and 28.8%, respectively (V: 14.0 ± 0.6 s). The control lidocaine significantly enhanced both mechanical threshold (at 30 min from 1.3 ± 0.1 g to 2.8 ± 0.3 g) and the paw heat latency (at 30 and 60 min in 27.0 and 74.1%, respectively, V: 13.2 ± 0.5 s). On carrageenan model, a time-course analysis revealed that mechanical allodynia and paw edema were completely abolished by HF and IBA for 3 and 5h, respectively, and DEXA reduced both parameters for up 5h. HF, IBA and DEXA reduced MPO activity in 68.2, 47.3 and 52.3% (V: 10.7 ± 0.9 O.D./mg of protein); LPO levels in 66.7, 41.6 and 75.1% (V: 28.5 ± 1.0 mmol/mg of tissue); prevented the depletion of GSH in 65.7, 64.9 and 64.7% (2502 ± 344 µg/mg of protein); restored CAT activity in 55.2, 50.7 and 56.3% (V: 0.3 ± 0.1 O.D./min/mg of protein) and reduced TNF- α levels in 69.6, 70.7 and 60.0% (V: 1102 ± 230 pg/mg of protein). **Conclusion:** These new data add evidences that alkylamides promote anti-inflammatory, antioxidant and analgesic effects. The analgesic and anesthetic properties resulting from local injection of HF reinforce the therapeutic potential of alkylamides from jambu flowers for inflammatory pain treatment.
License number of ethics committee: CEUA/BIO-UFPR: 1107 **Financial support**: CAPES

09.027 Antibacterial activity of Cordiaquinone J isolated from *Cordia leucocephala*. Araújo GS[1], Araújo AR[1], Barros AB[1], Oliveira MA[1], Freitas HPS[2], Pessoa ODL[2], Marinho Filho JDB[1], Araújo AJ[1], Araújo-Nobre AR[1] [1]UFPI – Biodiversidade e Biotecnologia, [2]UFC – Química Orgânica e Inorgânica

Introduction: Cordiaquinone J is a 1,4-naphthoquinone isolated from the roots of *Cordia leucocephala* with antifungal, larvicidal and cytotoxic activities previously described. However, its antibacterial activity has not yet been evaluated. Thus, the aim of this work was to evaluate antibacterial activity of Cordiaquinone J against two strains of bacteria. **Methods:** The cordiaquinone J were assayed for their antibacterial activity by determination of minimum inhibitory concentration (MIC) by microdilution in 96-well plates following CLSI recommendations. The strains of *Staphylococcus aureus* (ATCC 29213) and *Staphylococcus epidermidis* (ATCC 12228) were used as test microorganisms. Cordiaquinone J was added to microtiter wells containing Mueller-Hinton broth followed by serial dilutions with final concentrations ranging from 3.9 - 500 µM. Then standardized inoculum was added to a final concentration of 5×10^5 CFU/mL. Oxacillin was used as positive control. MIC was defined as the lowest concentration of cordiaquinone J at which no bacterial growth could be detected. To determine the minimum bactericidal concentration (MBC), an aliquot was removed from the wells concentrations in which there wasn't visible bacterial growth, which was inoculated on the surface of Mueller-Hinton agar. After 24 h of incubation at 37°C, the MBC was considered the lowest concentration that inhibited visible bacterial growth on the agar. All tests were performed in triplicate. **Results and Discussion:** The results showed that cordiaquinone J inhibited the growth of strains evaluated. The MIC values were equal to 62.5 µM for both strains tested. The cordiaquinone J exhibited bactericidal activity with MBC values of 250 µM for both strains tested. In many cases, the biological activity of quinone is attributed to the ability to accept electrons to form the corresponding radical anion or dianion species. The variable capacity of quinones to accept electrons is due to the electron-attraction or donation substituents at the quinone moiety which modulate the redox properties responsible for the resulting oxidative stress. It has previously been described the antibacterial activity of naphthoquinones isolated from other genus of plants suggesting that they react with oxidoreductases in the cytoplasm and in the cell wall, it may also bind to bacterial adhesins, interfering with the availability of receptors on the cell surface. However, the mechanism by which cordiaquinone J acts has not yet been elucidated. **Conclusion:** The results presented here indicate that the cordiaquinone J seem to be a good choice for the development of new strategies to treat bacterial infection. **Financial support**: CNPq, FAPEPI and INCT BioNat

09.028 Antibacterial activity from diterpenoids extracted of Brazilian alga *Dictyota menstrualis*.

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Introduction: The marine algae have been intensively investigated for different purposes, in particular for cosmeceutical and pharmaceutical applications. The Dictyotaceae is the most representative family from the Brown algaes. In fact, previous reports on the chemical studies from members of Dictyotaceae family showed the isolation and characterization of more than 400 structurally diversified diterpenes, which were described from 35 species around the world. In the present study, the chemical investigation of the *n*-hexane and EtOAc extracts of the Brazilian *D. menstrualis* alga is described and antibacterial assay were performed to evaluate the potential of the isolated compounds. **Methods:** The marine material was dried at room temperature and grounded. The extraction process was carried out with n-hexane, followed by EtOAc, for the obtainment the respective crude extracts, after the solvents evaporation under reduced pressure. The *n*-hexane extract was exposed to chromatographic column (CC) over silica gel and an increasing mixture of *n*-hexane/EtOAc was used as solvent, which resulted in 6 sub-extracts, named from A to F. Subsequently, the sub-extract B was rechromatographed under the same conditions, to obtain 10 other sub-extracts. The HPLC with a Gemini-phenomenex semi-preparative C-18 column and H_2O (0.1% TFA)/methanol, was used in sub-extracts BC and BH to obtain 8 compounds. Antibacterial tests were used to evaluate the activity of these compounds against Gram-positive (*Staphylococcus aureus* ATCC 29213) and Gram-negative bacteria (*Escherichia coli* ATCC 25922), based on CLSI (2015). **Results:** Chromatographic procedures over silica gel and HPLC of the n-hexane and EtOAc extracts of *D. menstrualis* resulted in the isolation and characterization of new guaiane diterpenes, along with previously reported diterpenoids. The structures of the isolated compounds were established by the interpretation of their spectroscopic data (1D and 2D NMR, IR and HRESIMS) and the by comparison with published data of analogous compounds previously reported. None of the compounds tested demonstrated activity against *E. coli* at the concentration tested. Only compound 6 demonstrated activity against *S. aureus*, with MIC of 320 µM. All other compounds did not demonstrate activity at the highest concentration tested being considered MIC >500 µM. **Conclusion:** These results corroborate the data in the literature, which demonstrate that diterpenes only have activity against Gram-positive bacteria. Molecules extracted from marine organisms have shown MIC concentrations that are similar to that found in this research. **Supported by:** CNPq, CAPES, FAPEPI and INCT BioNat. **Financial support**: CNPq, CAPES, FAPEPI and INCT BioNat.

09.029 New rifampicins isolated from marine actinomycetes with activity against multi-drug resistant bacteria. Araújo AJ[1], Barros AB[1], Araújo-Nobre AR[1], Silva A B[2], Pinto FCL[2], Torres MCM[3], Costa-Lotufo LV[4], Silveira ER[2], Pessoa ODL[2], Marinho-Filho JDB[1] [1]UFPI – Biodiversidade e Biotecnologia, [2]UFC – Química Orgânica e Inorgânica, [3]UEPB – Química, [4]ICB-USP – Farmacologia

Introduction: Substances with pharmacological potential derived from biological sources has been one of the main ways of searching for new drugs. In this context, *Salinispora arenicola*, an actinomycete isolated from seawater, has demonstrated in previous studies the presence of metabolites with activity against tumor cells, which demonstrates the importance of the study of these components compared to other activities. In the last 40 years the discovery of several antimicrobial agents, among them Rifamycins, considered today one of the main drugs of choice for the treatment of some antibacterial infections like Tuberculosis. Thus, the aim of this work was to evaluate antibacterial activity of new rifampicins isolated from marine actinomycetes against different strains of bacteria. **Methods:** Antimicrobial bioguided fractionation from the EtOAc extract (9 x 1.0 g) of *S. arenicola* was performed on SPE C18 cartridge to give two fractions (A and B). From fraction A was purified two compounds, **1** and **2**. While the fraction B provided compound **3**. The structures of **1-3** were elucidated by 1D and 2D NMR and HRESIMS spectroscopic data. The antibacterial assay used methods based in CLSI (2015), against five bacterial strains, *Staphylococcus aureus* (ATCC 29213), Methicillin-resistant *Staphylococcus aureus* (MRSA ATCC 43300), *Enterococcus faecalis* (ATCC 29219), *Enterococcus faecalis* (ATCC 51299 Vancomycin Resistant) and *Escherichia coli* (ATCC 25922). 96-well plate microdilution was used to determine the minimum inhibitory concentration (MIC). **Results:** All compounds showed better activity against Gram-positive bacteria. Compound **1** showed MIC ranging from 20 to 80 µM for susceptible strains and 40 µM for MRSA, showing no activity against resistant strain of *E. faecalis*. Compound **2** presented MIC values between 4.9 and 19.8 µM for susceptible strains and 2.49 and 39.7 µM for resistant strains. This difference in activity between these compounds occurs only by the presence or absence of an OH group on carbon 32. Both compounds did not demonstrate activity against *E. coli*. The best activity was observed for compound **3,** with MIC of 0.028 µM for sensitive and resistant *S. aureus*, 0.24 µM for *E. faecalis* sensitive and 4 µM for *E. faecalis* resistant to Vancomycin. In addition, this compound was the only one that showed activity against *E. coli*, with MIC of 128 µM. This substance presents a structural difference, which relies on the presence of a nitrogen aromatic compound, absent in substances **1** and **2**. **Conclusion:** This result is in agreement with data reported for rifamycins, since this class of drug generally demonstrates activity against Gram-positive bacteria. The isolated rifamycins from marine actinomycetes, mainly compound **3**, might be novel therapeutic alternatives for the treatment of bacterial infections, including those caused by multidrug-resistant microorganisms. **Financial support**: Supported by: CNPq, CAPES, FAPEPI and INCT BioNat

09.030 *Sedum dendroideum* **tea infusion as a useful source of bioactive compounds for the healing of gastric ulcers**. Da Luz BB[1], Oliveira AF[2], Maria-Ferreira D[1], Dallazen JL[1], De Souza LM[3], Cipriani TR[2], Werner MFP[1] [1]UFPR – Farmacologia, [2]UFPR – Bioquímica e Biologia Celular, [3]Pesquisa Pelé Pequeno Príncipe - Bioquímica

Introduction: *Sedum dendroideum* (Crassulaceae) popularly known as “bálsamo” is an edible plant employed in Brazilian folk medicine as salad, juice or infusion for the treatment of gastric ulcers. Previously, we showed that *Sedum dendroideum* infusion (SDI) shows gastroprotective effects against acute ulcer models, without changes in gastric acid secretion (Da Luz *et al*., 49th SBFTE, 2017). Thus, the present study investigates the phytochemical composition, healing effects and toxicological parameters of SDI in a chronic gastric ulcer model, and further mechanisms of action underlying this effect. **Methods:** Phytochemical analysis was carried out in a high-performance liquid chromatography. The healing property was analyzed in the 80% acetic acid-induced chronic gastric ulcers. Rats were orally treated with vehicle (water, 1 mL/kg), SDI (191 mg/kg), omeprazole (40 mg/kg) or sucralfate (100 mg/kg), twice daily for 5 days after ulcer induction. Following treatments, toxicological effects, macroscopic ulcer appearance, microscopic histological (HE, mucin PAS-staining) and immunohistochemical (PCNA) analysis, inflammatory (MPO and NAG activity, cytokine levels measurements) and antioxidant (SOD and CAT) parameters were investigated in ulcerated tissues. All experiments were conducted in agreement with the “Guide for the Care and Use of Laboratory Animals” (8thed, National Research Council, 2011) and approved by the Committee of Animal Experimentation of the Federal University of Paraná (CEUA/BIO − UFPR; approval number 1010). **Results:** Phytochemical analysis revealed the presence of different flavonol glycosides, containing myricetin and quercetin, along with the kaempferol as aglycones. The chronic treatment with SDI accelerated the healing of chronic gastric ulcer in 36.64% when compared to vehicle group (194 ± 12.50 mm^2). In addition, SDI significantly increased the number of epithelial proliferating cells and mucin staining in 52.95 and 52.96 % respectively, when compared to the untreated group (PCNA: 109.66 ± 3.44 cells stained; Mucin: 6.35 ± 5.40 pixels/field × 10^4). The positive controls, omeprazole and sucralfate, also increased the number of epithelial proliferating cells and mucin staining when compared to vehicle (Omeprazole: PCNA: 57.89 %; Mucin: 44.02 %; Sucralfate: PCNA: 61.15 %; Mucin: 53.74 %) Moreover, SDI reduced neutrophil and mononuclear leukocyte infiltration (MPO and NAG) in 93.02 and 29.79 %, respectively, TNF-α and IL-1β levels in 62.43 and 57.75 % respectively, as well as the oxidative stress, restoring SOD and CAT activities in 25.13 and 56.78 %, respectively. All these data were found to be comparable with omeprazole and sucralfate treatments. **Conclusion:** Collectively, our results reinforce and justifies the effectiveness of *Sedum dendroideum* infusion for the treatment of gastric ulcer. The gastroprotective mechanisms underlying this effect are attributed to the increasing of gastric cell proliferation, reinforcement of mucus protective barrier and improvement of the inflammatory and oxidative stress response. Finally, we conclude that SDI offering therapeutic alternatives for the treatment of gastric ulcers. **License number of ethics committee**: CEUA/BIO − UFPR; approval number 1010 **Financial support**: CAPES, Fundação Araucária (call 311/2014).

09.031 Antioxidant and anti-inflammatory mechanisms involved in the gastroprotective effect of the boldine alkaloid. Mariott M, Santos AC, Vargas AC, Somensi LB, Boeing T, Mariano LNB, Da Silva RCMVAF, De Souza P, Andrade SF, Da Silva LM Univali – Ciências Farmacêuticas

Introduction: The medicinal plant *Peumus boldus* Molina (Monimiaceae), popularly known as Boldo-do-Chile, presents the alkaloid boldine as the majority constituent in extract obtained from leaves, which demonstrated gastroprotective effect in our previous study (results submitted for publication). Therefore, the present study aimed to evaluate the antioxidant and inflammatory parameters involved in the gastroprotective effect of boldine in the acute model of gastric ulcer induced by acidified ethanol. **Methods:** Female Swiss mice were divided into groups to receive by oral route: vehicle (water plus 1% tween 80), carbenoxolone (200 mg/kg, the positive control) and boldine (100 mg/kg). Naïve group did not receive any treatment during the whole experiment. One hour later, the acidified ethanol (60% HCl 0.3 M, ml/kg) was orally given to the animals. After another one hour, the stomachs were removed and processed for histological, histochemical and biochemical analyzes. **Results:** The exposure of the stomachs to the ethanol/HCl caused damage to the gastric mucosa evidenced by the loss of the architecture of the gastric pits and by submucosa edema. The treatment with boldine was able to preserve the gastric tissue changes, but did not reduce the edema in the submucosal layer, similar to the positive control group carbenoxolone. In addition, the treatments with boldine or carbenoxolone augmented the labeling of mucin levels by 245.32% and 223.62%, respectively, in relation to the vehicle-treated ulcerated group. Regarding the analysis of the oxidative stress markers, it was possible to verify that pretreatment with boldine partially prevented the depletion of reduced glutathione levels, one of the main non-protein endogenous antioxidants, besides avoiding the increase in lipoperoxides levels, an indicator of peroxidation of lipid membranes and consequently of the oxidative stress. Boldine was also effective in preventing the increase in the activity of the enzymes superoxide dismutase, catalase and glutathione *S*-transferase, when compared with vehicle-treated ulcerated group, showing values comparable to those obtained with the analysis of gastric tissue from naïve animals. Finally, in relation to the inflammatory parameters, boldine also prevented the increase on neutrophil migration to the injured tissue, a parameter accessed indirectly by the measurement of myeloperoxidase activity, and the levels of tumor necrosis factor, a pro-inflammatory cytokine, were also decreased on stomachs from boldine-treated group. **Conclusion:** Taking together, the results described herein indicate that the favoring of protective factors of the gastric mucosa, that is the antioxidant system and the mucus barrier, as well as avoiding the inflammatory process, is the main mode of gastroprotection promoted by boldine. **Research support:** CNPq, CAPES, FAPESC and UNIVALI. **Authorization from CEUA/UNIVALI:** 004/17p. **License number of ethics committee**: 004/17p. **Financial support**: CNPq, CAPES, FAPESC and UNIVALI

09.032 Anti-inflammatory and antinociceptive properties of *Piper hispidum* **in mice**. Soares LAP[1], Cabral PFA[1], Silva GF[2], Bastos-Pereira AL[1] [1]UDESC – Medicina Veterinária, [2]UDESC – Produção Animal

Introduction "Piper hispidum" (PH) is an amazonic plant, empirically used and known by its medicinal properties. This study aimed to evaluate the effects of PH, orally administered in mice submitted to inflammatory and nociceptive models. **Methods** Experiments were conducted with Swiss mice, housed at standard controlled conditions. All experiments were approved by the UDESC Ethical Committee in Animal Use (#9212100817). The plant material was consisted of micropowdered leaves, kindly given by Luis Lopez, from Amazonia Peruana National University. To perform the experiments, an oral infusion was prepared from this material, using boiled distilled water as solvent, followed by centrifugation (20 minutes at 10000 r.p.m). The animals were submitted to a 1-hour fasting period before treatments (Vehicle, PH or Positive Control Groups, these depending on the test). Paw edema (KASSUYA et al., 2009), acetic acid abdominal writhings (MORI et al., 2011), formalin (HUNSKAAR and HOLE, 1987), hot plate (EDDY and LEIMBACH, 1953) and open field (TADAIESKY et al., 2006) tests were performed. After the paw edema experiment, paws were collected and frozen (-80ºC) to be afterwards subjected to myeloperoxidasis assay (DE YOUNG et al., 1989). **Results** Acetic acid induced abdominal writhes (33.7 ± 7.3 for Vehicle group) which were attenuated by prior treatment with Ketoprofen 20 mg.kg-1 (11.7 ± 2.1) or PH, in 30 (14.8 ± 8.16), 100 (8.5 ± 4.3) and 300 (15 ± 4.2) mg.kg-1 dosis. Based on this result, 100 mg.kg-1 was the chosen dose for subsequent experiments. During the formalin test, PH administration decreased licking time during central (Vehicle 249.6 ± 16.4, PH 117.8 ± 15.8, Morphine 7,5 mg.kg-1 30.8 ± 5.5 seconds) and inflammatory phases (Vehicle 188.4 ± 17.2, PH 27.5 ± 14.6, Morphine 0 seconds; in the 20-minutes measures). In the hot plate test, PH treatment did not alter the withdrawal paw latency, as compared to vehicle group (Vehicle 19.6 ± 8.7, PH 21.5.8 ± 12.5, Morphine 7,5 mg.kg-1 52.2 ± 8 seconds). The open field test revelated that PH does not seem to alter mice locomotion (Inertia time: Vehicle 4.5 ± 0.8, Diazepam 5 mg.kg-1 6.1 ± 0.9, PH 3.5 ± 0.8 seconds; Immobility time: Vehicle 55 ± 4.9, PH 53.17± 9, Diazepam 119.6 ± 24seconds) and exploratory behavior (Stand up time: Vehicle 49.1 ± 3.7, PH 55.8 ± 3.4, Diazepam 25.6 ± 7.7 seconds) significantly. Paw edema was slightly decreased in the PH group but not so evident as in the positive control group (Δ paw thickness, in µm: Vehicle 952.8 ± 135.3; PH 661.3 ± 90.2 seconds, Dexamethasone 2 mg.kg-1 217.5 ± 56). This same tendency was observed in the myeloperoxidase assay, when the plant treatment was not able to alter this enzyme values, compared to vehicle group (Vehicle 47.8 ± 7; PH 37.3 ± 3, Dexamethasone 18.1 ± 1.4 mOD/mg of paw). **Conclusion** PH seems to present anti-inflammatory and mainly antinociceptive effects, confirming its popular use. More investigations ought to be performed to confirm these results, as well as the analyzes of its chemical components, to understand its action mechanism. **References:** DE YOUNG, L.M. Agents Actions, v. 26, p. 335, 1989. EDDY, N. J. Pharmacol Exp Ther, v. 107, n. 3, p. 385, 1953. HUNSKAAR, S. Pain, v. 30, p. 103, 1987. KASSUYA, C. A. J Ethnopharmacol, v. 124, p. 369, 2009. MORI, L. S. Ann Phytomed, v. 18, p. 143, 2011. TADAIESKY, M.T. Eur J Pharmacol, v. 535, p. 199, 2006. **License number of ethics committee**: 9212100817

09.033 Anti-inflammatory activity of crude extract, **fractions and alkaloid from** *Psychotria minutiflora* (**Rubiaceae**). González BL[1], Souza JG[2], Ames FQ[3], Peixoto MA[2], Pomini AM[2], Bersani-Amado CA[3], Moura VM[1], Oliveira SM[2] [1]Uningá – Farmácia, [2]UEM – Química, [3]UEM – Farmacologia e Terapêutica

Introduction: *Psychotria* species belonging to the important family Rubiaceae has been used in folk and traditional medicine in the treatment of some diseases and in religious rituals. Several experimental studies from *Psychotria* species related different biological activities as cytotoxic, anti-inflammatory, analgesic and antimicrobial [1]. The presence of mostly alkaloids, are directly involved in the pharmacological activities of this species [2]. **Method:** This study investigated the *in vivo* topical anti-inflammatory activity of the crude methanolic extract (EB), non-alkaloidal chloroform (FCA), alkaloidal chloroform (FCB), alkaloidal chloroform-methanol (FCM), aqueous (FAQ) fractions and two major alkaloids isolated from *P. minutiflora* by croton oil-induced mice ear edema model and myeloperoxidase (MPO) inhibition. The male Swiss mice (30?40 g) were kept under controlled temperature (22ºC) and a light/dark cycle (12 h), with free access to water and food. Experimental protocols were approved by the Ethics Committee on Animal Experimentation of the State University of Maringá (CEUA/UEM 9804/2016). **Results:** The indole alkaloids strictosidinic acid **(1)** and vincosamide **(2)** were isolated from *P. minutiflora* and structural identification of known compounds was performed by spectroscopic techniques (1D NMR and 2D NMR). Indomethacin (1 mg/ear) used as control anti-inflammatory drug reduced ear edema and MPO activity at 68.4% ($p < 0.05$) and 91.3% ($p < 0.05$), respectively. The EB showed anti-edematogenic activity at the highest dose of 5.0 mg/ear, inhibiting edema at 70.7% ($p < 0.05$) and MPO activity at 100% ($p < 0.05$). The FCA inhibited the edema at doses 5.0 and 2.5 mg/ear (73%, $p < 0.05$ and 77.5%, $p < 0.05$, respectively), and showed inhibition of MPO activity at dose 5.0 mg/ear (89.3 %, $p < 0.05$). The fractions FCB and FCM also exhibited a significantly anti-edematogenic activity at dose 5; 2.5 and 1.25 mg/ear (72.9%, $p < 0.05$; 70.7%, $p < 0.05$; 62.7%, $p < 0.05$ and 66.1%, $p < 0.05$; 66.1%, $p < 0.05$; 66.6%, $p < 0.05$, respectively). Both fractions demonstrated a decrease in the MPO activity in 100% % ($p < 0.05$). The alkaloids **1** and **2** didn?t inhibit the formation of edema in the concentrations tested, nonetheless, FAQ (5.0 mg/ear) and **1** (1.25 mg/ear) promoted a reduction of 81.0% and 81.9% % ($p < 0.05$) in the MPO activity, respectively. **Conclusion:** This work showed that crude extract EB, fractions and major alkaloid isolated from aerial parts of *P. minutiflora* exhibited robust antiinflammatory activity, as observed by its inhibition of edema and cellular recruitment. Therefore, it has been suggested that this plant may be useful as a natural alternative source in the prevention and treatment of infectious skin diseases. However, further research should be conducted to verify these possibilities. **Reference:** [1] Calixto, N. O. J. *Braz. Chem. Soc.*, vol. 27, 1355, 2016 [2] Yang, H. *Chem. Biodivers*., vol. 13, 807, 2016 **License number of ethics committee**: CEUA/UEM nº 9804220716 **Financial support**: CAPES

09.034 Evaluation of acute toxicity and antimicrobial activity of α-Asarone in experimental models. Serafim CAL[1], Pessôa MLS[1], Alves Júnior EB[1], Formiga RO[2], Diniz Neto H[1], Lima EO[1], Batista LM[1] [1]UFPB – Pharmaceutical Sciences, [2]UFSC – Pharmaceutical Sciences

Introduction: α-Asarone is a monoterpene present in essential oils of plant species of *Acorus* genus with many pharmacological activities described in the literature. Therefore, the present study aimed to evaluate the acute toxicity and antimicrobial activity of α-asarone in experimental models. **Methods:** For the acute toxicity, it was used male Swiss mice (*Mus musculus*) (n=3), weighing 25-35 g. They were treated with tween 80 12% (control group) or α-asarone (300 and 2000 mg/kg). After treatment, a behavioral evaluation was carried out during the first 4 hours and after 24 hours for 14 days. Futhermore, water and feed consumption were evaluated. Then, animals were euthanized and their organs were examined macroscopically and weighed to obtain organ index. The number of deaths during the experimental period were used to estimate lethal dose 50% (LD_{50}) (OCDE 423, 2001; ALMEIDA, R. N.; Rev. Bras. Cien.Farm., v. 80, p. 72, 1999). 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 acute toxicity test, the group treated with 300 mg/kg of α-asarone presented central nervous system depressant effects, such as sedation, during the first hour of evaluation. In addition, feed intake and weight decreased in the control group. For the group treated with 2000 mg/kg, all animals died and the liver and spleen increased in comparison to the control. Thus, LD_{50} was approximately 500 mg/kg (category 4 of the OECD 423). The antimicrobial activity of α-asarone inhibited the growth of 4 (66%) of the 6 fungal strains tested from the concentration of 32 µg/mL, with only 2 strains being inhibited from the concentration of 128 µg/mL. Therefore, MIC was 32 µg/mL. However, α-asarone did not present antibacterial activity. The CFM was 32 µg/mL for 4 (66%) of the tested strains and 128 µg/mL for the remaining strains. **Conclusion:** Thus, it was possible conclude to α-asarone presents moderate toxicity and strong antimicrobial activity that is related to its antifungal effect. **Financial support**: CNPq / UFPB / PgPNSB / IperFarm. Ethics Committee on Animal Use (CEUA/UFPB): Protocol number 035/2017.

09.035 *Spirulina platensis* **modulates the uterine reactivity of wistar rats**. Lacerda-Júnior FF[1], Ferreira PB[2], Melo TAR[1], Diniz AFA[2], Silva MCC[2], Silva BA[3] [1]UFPB, [2]UFPB, [3]DCF-UFPB

Introduction: *Spirulina platensis* (SP), also known as *Arthrospira platensis* (Oscillatoriaceae), considered as a valuable antioxidant source is a blue-green alga helical shape, with a length of 0,2 to 0,5 mm, being cultivated on a large scale in many countries for commercial purposes and is currently receiving more attention as a potential food supplement (1, 2). Recently, was demonstrated that food supplementation with SP altered contractile vascular reactivity in rat, by modulation on nitric oxide (3), and reversed the damage the contractile reactivity the ileum rat (4) and prevents damage to erectile function (5). The aim was to evaluate the possible effects of supplementation with SP on the contractile and relaxing machinery of the uterus. **Methods:** Wistar virgins' female rat were divided into control groups (GS) and orally supplemented with SP lyophilized powder dissolved in saline NaCl 0.9% at doses of 50 (GSP50) and 100 mg/kg (GSP100) were supplemented for 8 weeks and 24 h prior to euthanasia received diethylstilbestrol (1 mg/kg, s.c.) for induction of estrus. Uterus was removed and monitored the muscle reactivity. Results were expressed as mean and S.E.M. and analyzed by one-way ANOVA followed by Tukey's post-test ($p < 0.05$; n = 5). **Results:** In the pharmacomechanical mecanism, supplementation with SP at doses of 50 (E_{max} = 98.6 ± 7.4%; pCE_{50} = 3.3 ± 0.06) and 100 mg/kg (E_{max} = 88 ± 1%; pCE_{50} = 3.5 ± 0.2) did not alter the contractile efficacy and potency of oxytocin, when compared to the control (E_{max} = 100%; pCE_{50} = 3.3 ± 0.1). The same was observed for relaxant efficacy and potency of isoprenaline in GSP50 (E_{max} = 100%; pCE_{50} = 12.0 ± 0.2) and GSP100 mg/kg (E_{max} = 100%; pCE_{50} = 11.8 ± 0.9) compared to GS (E_{max} = 100%; pCE_{50} = 12.4 ± 0.1). In the evaluation of component electromechanical, the supplementation with SP in GSP50 (pCE_{50} = 1.4 ± 0.01) and GSP100 (pCE_{50} = 1.6 ± 0.08) did not change contractile potency of KCl when compared to GS (pCE_{50} = 1.5 ± 0.01). However, the uterine contractile efficacy was reduced in GSP50 (E_{max} = 73.5 ± 4.9) and GSP100 (E_{max} = 84.8 ± 3.2) in relation to GS (E_{max} = 100%). In the relaxant efficacy for nifedipine, did not change for any of the doses tested (E_{max} = 100%). Already for the potency, the control curve (pCE_{50} = 10.0 ± 0.1) was shifted to the right, in both GSP50 (pCE_{50} = 9.0 ± 0.2) and GSP100 (pCE_{50} = 8.3 ± 0.2), with a decrease in the relaxant potency. **Conclusion:** Supplementation with *S. platensis* at doses of 50 and 100 mg/kg modulates negatively the electromechanical component of myometrium and may be useful in pathological conditions involving uterine hypercontractility, such as dysmenorrhea, premature birth and abortion. 1. KHAN, Current Pharm. Biotec., v. 6, p. 373, 2005. 2. BRASIL, 2017a. 3. Brito, Thesis, UFPB, 2014. 4. Ferreira, Dissertation, UFPB, 2017. 5. Souza, Front Physiol, v.8, p.1, 2017. **License number of ethics committee**: Ethical Committee on Animal Use/UFPB (0211/14) **Financial support**: **Financial support**: CNPq, CAPES, PPgPNSB/UFPB

09.036 Effect of chrysin in peptic ulcer: **gastroprotection against ethanol and repair of intestinal mucosa after polypharmacy**. Piffer GM[1], Fagundes FL[1], Périco LL[2], Rodrigues VP[2], Hiruma-Lima CA[2], dos Santos RC[1] [1]USF – Compostos Bioativos, [2]IBB-Unesp – Fisiologia

Introduction: Peptic ulcers are a gastrointestinal disorder caused by an imbalance between protective factors (mucus secretion) and aggressors (hydrochloric acid excess) on gastric or duodenal mucosa. The aggressive factor can be aggravated by smoking, stress, NSAIDs, aging, presence of *H. pylori* bacteria, including chronic alcohol consumption, which is considered a major cause of gastric ulcer, prompting to a vascular damage and necrosis of the tissue. The practice of polypharmacy (concomitant drugs) with de frequency use of non-steroidal anti-inflammatory drugs (NSAIDs), such as aspirin, associated with drugs as a gastroprotection's is one of the causes of intestinal ulcers that need to be investigated. The treatment for this disease has limited efficacy, taking to side effects and recurrence. With this, we search for therapeutics alternatives in natural compounds, such as chrysin, a flavonoid found mainly in plants, honey and propolis with anti-inflammatory and antioxidant activities already known. The aim of this work was to evaluate the pharmacological potential of chrysin in prevention and repair of gastric and duodenal ulcers. **Methods:** For this, Swiss male mice (n= 5-6, 30g) were used. In gastric lesion induced by absolute ethanol, the animals received vehicle (0.9%), carbenoxolone (100mg/kg) and chrysin (10, 50 and 100mg/kg). After 60 minutes of pre-treatment administration, the animals received absolute ethanol (0.2mL/animal) and one hour after, euthanasia was performed. The analysis of the macroscopic lesion was made through software AVSoftBioView and were expressed as mean area in mm2. In polypharmacy induced duodenal ulcer the animals received omeprazole daily (20 mg/kg) for 14 days. On the second day, the animals additionally received aspirin (10mg/kg) and on the 5th day administration of celecoxib (10 mg/kg twice daily) was added. On the 9th day, chrysin was added at a dose of 10mg/kg. On the 14th day, 3 hours after the final administration of celecoxib, the animals were euthanized and samples of duodenum were collected for analysis of myeloperoxidase (MPO) enzyme activity. The results were expressed as mean and standard error mean and the statistical significance was determined by one-way analyses of variance (ANOVA) followed by Dunnett's test. **Results:** Chrysin reduce the macroscopic lesions at all dose levels (33.71±18.26, 56.06±25.87, 110±55.72) when compared to the vehicle (329.9±114.2) in the gastric ulcer model induced by ethanol. In the polypharmacy induced duodenal ulcer model, chrysin was able to reduce MPO activity, which is a marker of tissue neutrophil infiltration, at a dose of 10 mg/kg (122.9±19.84 U/g) when compared to the vehicle (254.6±43.78 U/g). **Conclusions:** The results confirmed the protective and anti-inflammatory activity of chrysin in the gastric mucosa and intestinal tissue, respectively. Although the results obtained from these experimental models are of great importance, it is still necessary to implementation new analyzes to elucidate the mechanism of the pharmacological activity of chrysin in gastrointestinal disorders. **License number of ethics committee**: 01.0226.2014 **Financial support**: FAPESP 2016/21102-4

09.037 Antinociceptive activity of EPI-10-olguine isolated from *Cantinoa stricta*. Barbosa FL[1], Ehrenfried CA[1], Oliveira CS[2], Stefanello MEA[2], Zampronio AR[1] [1]UFPR – Farmacologia, [2]UFPR – Química

Introduction: Previous results of our group have shown that the ethanolic extract of *Cantinoa stricta*, a plant from the Lamiaceae family possess an important anti-nociceptive activity, by reducing the second phase of formalin-induced nociception and the mechanical hyperalgesia induced by intraplantar (i.pl.) injection of lipopolysaccharide (LPS). We were able to isolate from *C. stricta* two pyrones identified as enamarine and epi-10-olguine (EPI). Neither of them present scientific evidence of the actions cited. The aim of the present study is to evaluate the anti-nociceptive activity of EPI isolated from *C. stricta* and its possible pharmacological targets. **Methods:** Male Swiss mice (± 25 g, n= 6-8) received i.pl. injections of EPI (100-1000 ng), IND (150 ng) or dipyrone (DIP, 320 µg) 15 min before the injection of LPS (100 ng), interleukin -1β (IL-1 β, 100 pg), prostaglandin E_2 (PGE_2, 100 ng), dopamine (DOP, 3µg), epinephrine (EPI, 100 ng), forskolin (FOR, 1 µg) or dybutiryl cAMP (dbcAMP, 5 µg) injected into the right hind paw. Mechanical hyperalgesia was evaluated using dynamic plantar anesthesiometer. **Results:** The i.pl. treatment with EPI 300 and 1000 ng reduced the mechanical hyperalgesia induced by LPS by 35% and 93%, respectively while IND (positive control) reduced it by 90%. Additionally, the i.pl. treatment with EPI (1000 ng) reduced the mechanical hyperalgesia induced by DOP and EPI by 92% and 94%, respectively, whilst DIP (positive control) abolished this response. However, EPI, at the same dose, was unable to change the mechanical hyperalgesia induced by IL-1β, PGE_2, FOR, or dbcAMP. **Conclusion:** These results suggest that the EPI has an important antinociceptive effect in the inflammatory pain**,** since it reduced the mechanical hyperalgesia induced by LPS and may contribute to the antinocieptive effect identified for the ethanolic extract of *C. stricta*.These data also suggests that EPI has a mechanism of action different from non-steroidal anti-inflammatory drugs, since it did not reduce IL-1β-induced hyperalgesia and this nociceptive action seems to play an important role in the reversal of the sympathetic component of pain. **License number of ethics committee**: CEUA protocol Nbr. 937. **Financial support**: CNPq and CAPES.

09.038 Acute administration of linalool complexed with β-cyclodextrin produced a higher hypotensive effect compared with uncomplexed form. Medeiros CFA[1], Camargo SB[1], Siqueira JS[2], Quintans LJ[2], Vasconcelos DFSA[1] [1]UFBA – Biorregulação, [2]UFS – Fisiologia

Introduction: Hypertension is a multifactorial clinical condition. Despite the large number of medications used to control blood pressure, currently resistant hypertension makes it difficult to control this disease. An alcoholic monoterpene, (-) - linalool (LIN) has a promising biological action in the treatment of hypertension, as described in previews studies conducted by our group. In addition, the complexation of linalool with β-cyclodextrin (β-CD) appears to improve its solubility, volatility and increase stability of the host molecule. Despite the beneficial effects of linalool, studies assessing the therapeutic potential of this compound, using drug delivery system, through assays analyzing different routes of administration has not yet been demonstrated. The aim of the study was to evaluate whether acute administration (oral and i.v. way) of linalool complexed with β-cyclodextrin produced a higher hypotensive effect compared to uncomplexed form. **Methods:** Direct measurement of blood pressure and heart rate were performed in the spontaneously hypertensive rats (SHR - 12 weeks). The animals were divided into 3 distinct groups, which they received oral or i.v. treatment with vehicle, LIN (50mg/kg) or linalool complexed with β-cyclodextrin (LIN/β-CD, 50mg/kg). **Results:** LIN/β-CD induced hypotensive effect at i.v. administration compared to the control (0,16 ± 0,20; mmHg, n=5) and this effect was associated with a tachycardia (%PAM: -41.56 ± 3.23; mmHg); (%HR: 17.64 ± 5.61; bpm, n=5). On the other group, LIN induced hypotension compared to the control (0,16 ± 0,31; mmHg, n=5) and bradycardia (%PAM: -47.28 ± 5.36; mmHg); (%HR: -68.27 ± 3.87; bpm, n=5). In addition, LIN/β-CD was observed to exhibit hypotensive effects in non-anesthetized SHR after 15 min., as well as, at 4, 5 and 6 hours after oral administration (%PAM: -0,51 ± 2,50; 1,26 ± 2,10; -19,99 ± 6,08; -13,18 ± 4,79; mmHg, n=6), when compared to LIN (%PAM: -8,98 ± 2,74; -15,19 ± 5,85; -1,87 ± 0,58; 2,60 ± 1,84; mmHg, n = 6) and was observed that LIN/β-CD has a bradycardic effect, specially at 4 e 6 hours (%HR: -6,71 ± 1,41; -9,64 ± 2,96; bpm, n=6) compared to LIN (%HR: 0,69 ± 1,93; -0,04 ± 1,79; bpm, n=6). **Conclusion:** LIN/β-CD induced hypotension intravenously similarly to the LIN, however curiously the LIN/β-CD induced hypotensive effects at 15 min., 4, 5 and 6 hours after oral administration temporarily better than to free linalool. It seems that the complexation of linalool improved hypotensive activity and beneficial effects at cardiovascular system. Keywords: Linalool, cyclodextrins, inclusion complex, antihypertensive, hypertension. **License number of ethics committee**: CEUA - ICS/UFBA n° 085/2015 **Financial support**: Fundação de Amparo à Pesquisa do Estado da Bahia - FAPESB

09.039 Tocolytic action induced by synthetic derivative of the isoquinoline alkaloids in rat uterus is mediated BY K_{ATP} AND SK_{Ca}. Sarmento DM[1], Dourado TMH[1], Oliveira S[1], Borges FVP[2], Silva LAA[2], Rodrigues LC[2], Braga VA[3], Vasconcelos U[4], Travassos RA[5] [1]UFPB – Farmacologia, [2]UFPB – Química Orgaânica, [3]UFPB – Biofísica e Fisiologia, [4]UFPB – Microbiologia, [5]UFPB – Biofísica e Farmacologia

Introduction: Natural products are a rich source of compounds for the discovery of new drugs as well as inspiration for the synthesis of new molecules (Cragg, Biochim. Biophys. Acta., v. 1830, p. 3670, 2014). Isoquinoline is one of the most widely distributed alkaloids with proven therapeutic potential (Bhadra, Med Res Rev., v.31, p.821, 2010). Uterine contractile activity plays an important role in many and varied reproductive functions (Aguilar, Hum. Reprod. Update., v. 16, p. 725, 2010). This study aimed to investigate a possible tocolytic effect of these two dihydroquinazolinones obtained by organic synthesis, 2- (4-hydroxy-3,5-dimethoxyphenyl) -3-phenyl-2,3-dihydroquinazolin-4 (1H) -one (C100) and (2-(4-hydroxy-3-methoxyphenyl)-3-phenyl-2,3-dihydroquinazolin4(1H)-one) (C300) in the rat uterus, indicating a possible participation of the potassium channels in this effect. **Methods:** Female Wistar rats (Rattus norvegicus) were obtained from Bioterium Prof. Thomas George of IPeFarM/UFPB. All rats were euthanized by decapitation with guillotine. After dissection, the two uterine horns were separated by an incision and longitudinally opened. To obtain isometric responses the horns were individually suspended in organ baths (10 mL) containing Tyrode solution (pH = 7,4) at 37 ºC, bubbled with 95% O_2 and 5% CO_2 mixture and resting tension of 1 g. The relaxation produced was expressed as the reverse percentage of the initial contraction produced by oxytocin and the relaxing potency of the substance was evaluated by comparing the EC 50 values. All procedures were approved by the UFPB Ethics Committee on Animal Use (Protocol/CEUA nº 070/2016) **Results:** Only C300 relaxed significantly and concentration-dependent (EC_{50} = 2.4 ± 0.6 x 10^{-5} M, n = 5) when the uterus was pre-contracted by oxytocin. However, when pre-contracted by 60 mM KCl, it had its attenuated potency (EC_{50} = 1.1 ± 0.1 x 10^{-4} M, n = 5). In the presence of TEA^+ 10 mM, non-selective K^+ channel blocker, the tocolytic effect promoted by C300 was attenuated (EC_{50} = 1.5 ± 0.6 x 10^{-4} M, n = 5). In the presence of selective blockers such as TEA^+ 1 mM (BK_{Ca} blocker), $BaCl_2$ (K_{ir} blocker) and 4-AP (K_V blocker), the relaxing potency of C300 was not altered. On the other hand, in the presence of glibenclamide (K_{ATP} blocker) the relaxing potency was attenuated (EC_{50} = 1.6 ± 0.2 x 10^{-4} M) and in the presence of apamine (SK_{Ca} blocker) had its relaxation practically abolished (E_{max} = 18.4% ± 4%, n = 3). **Conclusion:** Given the data presented, we can suggest that, at least in part and at the functional level, the mechanism of action by which C300 exerts its tocolytic effect in rat uterus involves the positive modulation of K_{ATP} and SK_{Ca}. **Keywords:** dihydroquinazolinones, uterus, tocolytic effect, potassium channels.

License number of ethics committee: CEUA nº 070/2016 **Financial support**: CNPq CAPES UFPB

09.040 Pharmacological screening of synthetics alkaloids against gram-negative rods. Albuquerque JSS[1], Oliveira BTM[2], Dourado TMH[1], Borges FVP[3], Silva LAA[3], Rodrigues LC[3], Vasconcelos U[2], Travassos RA[1] [1]UFPB – Farmacologia, [2]UFPB – Microbiologia, [3]UFPB – Química Orgânica

Introduction: A wide number of pathogens associated with human infections exhibit multidrug-resistance (Davies, Microbiol. Mol. Biol. Ver., v. 74, p. 417, 2010) and it is mandatory to develop new antimicrobials in order to minimize this emerging concern (Enoch, J. Infect., v. 55, p. 205, 2007). Among several promising molecules, alkaloids correspond to a natural widespread class of substances with important pharmacological activities (Bhadra, Med. Res. Rev., v. 31, p. 821, 2011). In this context, this study aimed to investigate the antimicrobial activity of two synthetic alkaloids against seven Gram-negative rods and to study their action in the cell wall. **Methods:** The two molecules, 1-(3-methoxy-4-hydroxyphenyl)-7-methoxy-1,2,3,4 tetrahydroisoquinoline (MTHP) and (2-(4-hydroxy-3-methoxyphenyl)-3-phenyl-2,3-dihydroquinazolin4(1H)-one) (C300) were obtained by organic synthesis. The bacterial suspensions turbidity was made in sterile 0.9% NaCl solution, from a fresh culture, standardized by tube #1 on the MacFarland scale. The minimum inhibitory concentration (MIC) was determined using serial dilutions from 10^{-3} to 10^{-10} in presence and absence of sorbitol 0.8 M. **Results:** MTHP inhibited *Pseudomonas aeruginosa* RX01 and *Escherichia coli* AV12 in the highest concentration tested. C300 inhibited also *Burkholderia cepacia* RX02 in the highest concentration tested, however showed to be more effective against *Escherichia coli* AV12 and *Enterobacter aerogenes* AV14. In addition, both isolates were able to grow in the presence of sorbitol. **Conclusion:** C300 was effective against fermenting-rods by acting on the cell walls of these organisms. **Keywords:** multidrug-resistance; synthetic alkaloids; antimicrobial; enterobacteriacea
Financial support: CNPq CAPES UFPB

09.041 Pharmacological screening of synthetic molecules against multidrug-resistant gram-negative bacilli. Albuquerque JSS[1], Gaspar VD[1], Dourado TMH[1], Borges FVP[2], Silva LAA[2], Rodrigues LC[2], Vasconcelos U[3], Travassos RA[1] [1]UFPB – Farmacologia, [2]UFPB – Química Orgânica, [3]UFPB – Microbiologia

Introduction: Antimicrobial resistance in bacterial pathogens is a challenge that is associated with high morbidity and mortality. Multidrug resistance patterns in Gram- negative bacteria are difficult to treat and may even be untreatable with conventional antibiotics (Frieri, J. Infect. Public. Health., v. 10, p. 369, 2017). Based on this premise, the search of new potential molecules with antimicrobial activity has been increasing in order to overcome the occurrence of severe infections caused by Gram-negative rods (Enoch, J. Infect., v. 55, p. 205, 2007). This study aimed to investigate the antimicrobial effect of two synthetic molecules against seven Gram-negative bacilli: the alkaloid C100, 2- (4-hydroxy-3,5-dimethoxyphenyl) -3-phenyl-2,3-dihydroquinazolin-4 (1H) -one and licarine (2,3-dihydrobenzofuran). **Methods:** The susceptibility of the isolates to the two molecules was tested by the microdilution test. The NFGNB suspensions were made in a sterile 0.85% NaCl solution, from a recent culture, standardized by tube #1 on the MacFarland scale. The minimum inhibitory concentration (MIC) was determined using serial dilutions from 10^{-3} to 10^{-10} in presence and absence of sorbitol 0.8M. **Results:** Licarine was active on *Burkholderia cepacia* RX02 and *Escherichia coli* AV12, in the highest concentration tested. C100 also showed activity against *Pseudomonas aeruginosa* RX01 in the higher concentration tested, however was more effective against *Escherichia coli* AV12 and *Enterobacter aerogenes* AV14. Additionally, in the presence of sorbitol, the MIC increased. **Conclusion:** Both molecules showed activity, however C100 were more effective to the fermenting-Gram-negative strains due to act on the cell wall. The target protein needs to be known. **Keywords:** multidrug-resistance; synthetic molecules; antimicrobial activity **Financial support**: CNPq CAPES UFPB

09.042 Evaluation of the antiproliferative activity of *Dugetia furfuracea* and *Psidium guineense* leaves in human tumor cells. Santos RC[1], Nascimento KF[1], Volobuff CRF[1], Pederiva MMC[2], Santos SM[2], Oliveira PC[2], Carvalho JE[3], Foglio MA[3], Sousa IMO[3], Formagio ASN[1] [1]UFGD – Ciências da Saúde, [2]UFGD – Biologia Geral, [3]Unicamp – Farmacologia e Ciências Biológicas

Introduction: Plant species, as well as application in folk medicine, also represent a rich source of bioactive molecules that can contribute to the development of new drugs, representing a strategy for pharmaceutical innovation. Brazil is considered rich in biodiversity and it has a great abundance of native plants, and the Cerrado biome represents about 23% of the country's land surface. Among the species widely used in folk medicine is *Psidium guineense* Swartz (Myrtaceae), popularly known as "field araca", its leaves are used in the treatment of colds and inflammations, such as bronchitis.. A previous study by our research group reported anti-inflammatory, antiproliferative, antioxidant and antimycobacterial activity in a sample of essential oil extracted from the leaves of this species Another common species of the region and also studied by our group is the Duguetia furfuracea (A. St.-Hil.) Benth. & Hook, popularly known as "araticum". The infusion of its leaves and branches is used in the treatment of rheumatism and renal colic. A study recently conducted by our research group showed the anti-inflammatory and antioxidant activity of methanolic extract from leaves of this species. Considering the previously found results, the present work had the objective of evaluating the antiproliferative activity of extracts of leaves of *P. guineense* and *D. furfuraceae* in different human cell lines. **Methods:** The antiproliferative activity of MEPG (methanolic extract of *Psidium guineense*) and TFDF (tween fraction of *Duguetia furfuracea*) were evaluated "*in vitro*" according to the sulforhodamine B method (Monks et al., 1991). The human cell lines glioma (U251), breast (MCF-7), resistant ovary (NCI / ADR-RES), renal (786-0), lung (NCI-H460), prostate (PC-3), ovarian (OVCAR-3), colon (HT-29), leukemia (K-562) and keratinocytes (HaCaT) were obtained from the National Cancer Institute (Frederick, MD). Doxorubicin (0.025 to 25 µg / mL) was used a positive control. **Results:** TFDF showed GI_{50} values (which refers to the drug concentrations that resulted in a 50% reduction in cellular growth) for six of ten cell lines tested in a range from 35.38 ug/mL in U251 to 167.43 ug/mL NCI/ADR-RES. On the other hand, for TGI (cytostatic activity) TFDF was effective only for one cell line U251 in a concentration of 82.69 ug/mL and showed efficacy for LC_{50} (cytotoxic activity) for the same cell line (U251) at 180.90 ug/mL. MEPG showed GI_{50} for all of ten tested cell lines in a range from 7.63 ug/mL in K-562 to 104.11 ug/mL in NCI/ADR-RES. However, MEPG did not showed effective results for cytostatic and cytotoxic activities. **Conclusion:** These results have shown that the biome cerrado has a great potential to discover natural products with pharmacological activity. TFDF showed promissory results mainly for glioma cell lines and MEPG showed reduction in cellular growth for all tested cell lines. Further studies are required to provide more information about this two species *Psidium guineense* and *Duguetia furfuracea* and its respective compounds activity. **Financial support**: CAPES FUNDECT

09.043 Quaternization of angico gum: **Rating parameters and biological activity reaction**. Ribeiro FOS[1], Sousa AKA[1], Araújo AR[2], Silva DA[1] [1]UFPI – Biotecnologia, [2]UFPI – Biomedicina

Introduction: Research into the biological properties of polysaccharides, for biotechnology purposes, has become increasingly prominent. Chemical modifications are important tools for obtaining new agents with specific properties. **Objective:** In this approach, the objective of the work was to modify the gum of the red angico (*Anadenanthera colubrina var. Cebil* (Griseb.) Altschul) – GAN, using quaternary ammonium (CHPTAC) and the evaluation of the best conditions for the polysaccharide modification reaction, such as time and temperature, as well as the antibacterial activity and its biocompatibility. **Methods:** For the quaternization of the gum, the ratio used was 1: 4: 4 (M) for GAN/CHPTAC/NaOH. The modification was conducted at different temperatures (40, 60 and 80°C) and time period (12, 24 and 36 h). The characterization of the chemical structure of the modified polysaccharide was carried out using Infrared Spectroscopy (FTIR/ATR). For the determination of the surface charge of the polysaccharide, measurements of potential Zeta (mV) were performed. The antimicrobial evaluation was carried out by determining the minimum inhibitory and bactericidal concentration (MIC and MBC, respectively) for Gram-positive bacteria: *Staphylococcus aureus* ATCC 29213, *Staphylococcus aureus* (MRSA) 43300 and *Staphylococcus epidermidis* ATCC 12228. Finally, a hemolytic assay was performed to evaluate the cytotoxicity. **Results:** Five modified derivatives (GAQ 1, GAQ 2, GAQ 3, GAQ 4 and GAQ 5) were obtained. In the FTIR spectra obtained from GAN and quaternized derivatives, it is possible to observe the appearance of a small band around 1480 cm^{-1}, which may be related to C-H bonds of the quaternary ammonium methyl group, and in the region of 1407 cm^{-1} related to the vibrational stretching mode of C-N bonds, which can be attributed to a discrete structural modification of the gum arising from CHPTAC pools. The best result of the quaternized derivatives was observed for the samples GAQ 3, regarding Zeta potential (GAQ 3: 26.8 mV) and bactericidal effect (GAQ 3: MIC-MBC = 125-125 µg/ml for *S. epidermidis*). For GAQ biocompatibility assessment, GAQ 3, at concentrations equivalent to those used in antimicrobial assays, did not show hemolytic activity. According to the parameters tested, GAQ 3 (with a time of 24 hours at a temperature of 60ºC) was the best derivative in relation to the surface charge obtained, which may be related to the anti-staphylococcal activity presented, concomitant with the excellent biocompatibility with erythrocytes. These results indicate that GAQ 3 is one of the most promising derivatives as an antibacterial agent for biomedical applications. **Financial support**: CNPq

09.044 Efficiency of the α-Terpineol monoterpene on antidiarreica activity in rodents. Negreiros PS, Lopes JSL, Costa DS, Silva VG, Araújo LEPF, Santos TMA, Nunes DB, Santos RF, Oliveira RCM
UFPI – Plantas Medicinais

Introduction: The diarrhea is a common gastrointestinal disorder characterized by changes in stool consistency with increased water content, making them liquid or pasty, and changes in the frequency of bowel movements. According to UNICEF, diarrhea is one of the leading causes of child deaths, accounting for approximately 9% of all deaths in children under 5 years of age in 2015. The treatment of diarrheal diseases is usually centralized in the replacement of fluids and electrolytes using oral rehydration solutions, 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. Thus, the aim of the present study was to investigate the effect of monoterpene α-Terpineol (α-TPN) on antidiarrheal activity and possible mechanisms involved in the evidenced activity. **Methods:** Initially, the antidiarrheal activity of α-TPN was evaluated in acute diarrhea model and enteropooling induced castor oil, where Swiss mice were pretreated with α-TPN (6,25; 12,5; 25 and 50 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. To evaluate the gastrointestinal transit, the mice received castor oil and 1 h later were treated with α-TPN (12.5 mg/kg, p.o.). After 1 h, all animals received 0.2 mL of activated charcoal orally, and after 20 min the animals were euthanized and the distance covered by the charcoal in the intestine from the pylorus to the cecum was measured. Opioid and / or antimuscarinic participation in gastrointestinal transit was also investigated using naloxone (2 mg/kg, s.c., opioid antagonist) and bethanechol (3 mg/kg, i.p., muscarinic agonist), respectively. **Results:** α-TPN (6,25; 12,5; 25; 50 mg/kg, v.o.) significantly reduced (*p<0,05) total fecal mass (54,90; 48,03; 44,36 and 23,52%, respectively) and especially the diarrheal stools (47,11; 65,95; 55,62 and 10,33%, respectively), when compared with the control group (saline 10 mL/kg, p.o.). Loperamide-treated group also reduced (*p<0,05) fecal mass (94,36%) and diarrheal stools (96,65%), compared to the control group. α-TPN, in all tested doses, was effective in reducing (*p<0,05) the intestinal content (45,76; 77,96; 66,10 and 40,67%, respectively), when compared to control (0,0%). Loperamide also reduced the intestinal content in the loperamide-treated group (70,64%), when compared with the saline-treated group. α-TPN reduced gastrointestinal transit (29,96%), when compared to control (49,87%), this reduction was through the anticholinergic mechanisms. **Conclusion:** Given the presented results, the antidiarrheal activity of α-TPN is demonstrated by reduction of gastrointestinal motility in acute diarrhea through anticholinergic action **License number of ethics committee**: CEEA/UFPI nº 303/2017 **Financial support**: UFPI/CAPES

09.045 Suramin antagonizes Phospholipase A_2 and Myotoxic effects of *Crotalus durissus terrificus* **crude venom and crotoxin**. Rocha-Junior JRS, Strauch MA, Monteiro-Machado M, Nogueira-Souza PD, Melo PA UFRJ – Farmacologia e Química Medicinal

Introduction: Crotalid snakebites are a serious health problem in the South America and these accidents induce edema hemorrhage and myonecrosis. One frequent envenomation with neurologic and myotoxic effect manifestations is the one induced by the rattlesnake *Crotalus durissus terrificus* (Cdt) crude venom. **Methods:** Our experiments investigated under different approaches either *in vitro* or *in vivo*, the antagonism of Cdt venom myotoxicity and phospholipase A_2 (PLA_2) by suramin. We also tested suramin against the main Cdt isolated toxin, crotoxin. The PLA_2 activity of the Cdt venom or the crotoxin were tested alone or in the presence of suramin. The *in vivo* tests were performed in adult Swiss mice under the license protocol (DFBCICB022). The venom lethality and the myotoxicity were tested by intraperitoneal (i.p.) or by intramuscular (i.m.) injections, respectively. Myotoxic effect was evaluated by the increase of plasma creatine kinase (CK) activity expressed in U/L. **Results:** Venom i.p. of injections (0.05 to 0.20 mg/kg) of Cdt crude venom induce lethality of 20 to 100 % respectively. The i.m. injection of 0.5 mg/kg of Cdt crude venom induces an increase of plasma CK activity from the basal level (200 U/L) to range of 3000 U/L. The preincubation or the post treatment with suramin (1.0 mg/kg) decreases circa of 30 and 50% this effect, respectively. The PLA_2 activity of Cdt crude venom or crotoxin (10 µg/mL) increase in a concentration dependent way. Both activities were inhibited until 100% by suramin in concentration dependent way (0.3-10 µM). **Conclusion:** Our data are showing that suramin is able to antagonize some Cdt myotoxicity *in vivo*, and PLA_2 activity, as well as the crotoxin PLA_2 activity. **License number of ethics committee**: CEUA UFRJ (DFBCICB022) **Financial support**: Support by FAPERJ; CNPq and CAPES

09.046 Pharmacological effects and systemic alterations caused by *Leptodeira annulata* (**Banded Cat-Eyed Snake**; **Dipsadidae**) **venom**. Torres-Bonilla KA, Justo AF, Dias L, Hyslop S
Unicamp – Farmacologia

Introduction: The venom composition and properties of the majority of rear-fanged snakes is largely unknown, although interest in these secretions has increased considerably in recent years. The toxic effects of *Leptodeira annulata* (banded cat-eyed snake) venom have been poorly investigated, perhaps because of this species´ non-aggressive behavior, the low number of notified bites and the low venom yield. In this work, we investigated some pharmacological properties *in vitro* and the systemic alterations *in vivo* caused by the venom of *L. annulata*. **Methods:** Rat aortic rings were mounted in organ baths containing aerated (95% O_2 + 5% CO_2) Krebs solution. After stabilization, the rings were contracted with KCl (40 mM) to test the tissue integrity, then, the preparations were pre-contracted with phenylephrine (PE; 1 µM) and afterwards, acethylcholine (Ach; 1 µM) was added to test the endothelial function. The rings were pre-contracted once again with PE and the venom (different concentrations) was added to assess the relaxing capacity. To investigate the mechanism of action, protocols with and without endothelium, EDTA, indomethacin, L-NAME and ODQ were done. At the end of the experiments, the rings were collected for histological analysis. The effects of *L. annulata* venom on the hemodynamic responses were studied on anesthetized rats. Carotid artery (pressure measure) and femoral vein (drugs injection) were cannulated. The monitored parameters were: arterial pressure, cardiac frequency, electrocardiogram and respiratory frequency. At the end of the hemodynamic experiments, the rats were euthanized and different organs (lung, liver, kidney and heart) were collected for histopathological analysis. The results were expressed as the mean ± SD and statistical comparisons were done using one-way and two-way ANOVA followed by the Tukey-Kramer *post hoc* test. A value of $p<0.05$ indicated significance. **Results:** *Leptodeira annulata* venom caused dose-dependent relaxation of aortic rings. The relaxing effect was partially inhibited by the endothelium removal, the treatment of venom with EDTA and by the pre-incubation of the rings with indomethacin, ODQ and L-NAME indicating at least two different vasodilation pathways including NO/GC/GMPc and arachidonic acid methabolites involving the action of SVMPs and PLA_2 and without the affectation of the tissue integrity. *L. annulata* venom did not cause alterations in the hemodynamic response of rats, even with a dose of 6 mg/kg. However, the venom (1, 3 and 6 mg/kg) caused histopathological changes in rat lungs (hemorrhage, thrombus formation and inflammation) without visible alterations in liver, kidney and heart. **Conclusions:** *Leptodeira annulata* venom was able to produce marked relaxation of aortic rings *in vitro*. The relaxing effect was endothelium-dependent and involves the NO/GC/GMPc and arachidonic acid methabolites pathways. The venom did not change the hemodynamic parameters and produced inflammation, hemorrhage and thrombus in lungs *in vivo.* The observed effects seem to be mediated mainly by SVMPs followed by PLA_2. **License number of ethics committee**: Institutional Committee for Ethics in Animal Use (CEUA/UNICAMP, protocol no. 4479-1(A)/2017). **Financial support**: CAPES, CNPq

09.047 Therapeutic potencial of *Mimosa caesalpiniifolia* **in liver of rats exposed to cadmium chloride**. Lima EC[1], Cláudio SR[1], Silva MJD[2], Vilegas W[2], Moura CFG[1] [1]Unifesp – Biosciences, [2]Unesp – Prospecção de Produtos Naturais

Introduction: Cadmium is an environmental pollutant of great relevance to public health since it is a non-essential metal toxic to the human body, being the underlying mechanisms of toxicity based on oxidative stress. Exposure to cadmium occurs primarily through smoking and intake of contaminated food. *Mimosa caesalpiniifolia* (Mimosa) is a plant rich in polyphenols with antioxidant and antigenotoxic properties. The aim of this study was to evaluate the therapeutic potential of Mimosa in liver of rats exposed to cadmium chloride. **Methods:** A total of 40 Wistar rats (90 days, ~ 250 g) were distributed into eight groups (n = 5), as follows: i) control: submitted to 0.9% saline injection (0.5 mL) and treated with tap water ; (ii) cadmium: cadmium chloride injection at 1.2 mg/kg and tap water; iii) Mimosa extract: submitted to 0.9% saline solution (0.5 mL) injection and treatment with Mimosa extract at 250 mg/kg; iv) Mimosa fraction: submitted to 0.9% saline injection and treatment with Mimosa acetate fraction at 62.5 mg/kg; v) cadmium and Mimosa extract 62.5: submitted to cadmium chloride at 1.2 mg/kg injection and treatment with Mimosa extract at 62.5 mg/kg; vi) cadmium and Mimosa extract 125: subjected to cadmium chloride at 1.2 mg/kg injection and treatment with Mimosa extract at 125 mg/kg; (vii) cadmium and Mimosa 250 extract: submitted to cadmium chloride 1.2 mg/kg injection and treatment with Mimosa extract at 250 mg/kg; (viii) cadmium treated with fraction of Mimosa acetate: submitted to cadmium chloride 1.2 mg/kg injection and treatment with acetate fraction of Mimosa extract at 62.5 mg /kg. Saline solution and cadmium were given as a single intraperitoneal dose on day zero and, after 15 days, the rats received the treatments described above every day via gavage for 15 days. At the end of the experimental period (30 days), the liver from all animals was collected for histopathological analysis by means of H.E stain and antioxidant gene expression of Copper-Zinc Superoxide Dismutase (CuZn-SOD), Manganese Superoxide Dismutase (Mn-SOD) and Catalase (CAT) by Real Time Polymerase Chain Reaction (qPCR). The study was approved by the Animal Ethics Committee of Federal University of São Paulo with number nº 1230060217. **Results:** Animals exposed to cadmium presented severe histopathological changes, such as areas of coagulation necrosis, followed by cytoplasmic vacuoles and some inflammatory cells. Among the experimental groups, only the animals treated with extract at 62.5 mg/kg and 125 mg/kg showed tissue regeneration when compared to cadmium group. Analysis of qPCR showed that Mimosa was able to reduce the expression of the enzyme SOD-CuZn in all groups exposed to fraction and different extracts. Expression of the SOD-Mn was increased in all groups treated with the different concentrations of the Mimosa extract while the Catalase remained slightly constant in all groups without statistical significance ($p<0,05$). **Conclusion:** Taken together, the results of this study suggest that Mimosa, at concentrations of 62.5 and 125 mg/kg, was able to protect liver against the harmful effects induced by cadmium, and that the polyphenols present in the extracts and in the fraction were able to modulate SOD-CuZn and SOD-Mn expression exposure in rats. Support: CAPES. **License number of ethics committee**: 1230060217 **Financial support**: CAPES

09.048 ACWS, **A chemically-defined polysaccharide from acerola ameliorates dextran sulfate sodium-induced colitis in mice**. Maria-Ferreira D[1], da Luz BB[1], Dallazen JL[1], Klosterhoff RR[2], Cordeiro LMC[2], Werner MFP[1] [1]UFPR – Farmacologia, [2]UFPR – Bioquímica

Introduction: Ulcerative colitis (UC) is a chronic relapsing inflammatory disorder of colonic mucosa. Conventional immunomodulators have side effects and high cost, leading the search for new therapeutic strategies. Additionally, UC is characterized by a disbalance between intestinal microbiota and mucosal immune responses, which in turn affect the production of short chain fatty acids (SCFAs) and impairs intestinal health. Remarkable, dietary carbohydrates can be converted in SCFAs and therefore exhibit beneficial effects on colonic epithelial homeostasis. In this regard, we already showed that the polysaccharide RGal improves intestinal barrier function in dextran sulfate sodium (DSS) colitis in mice (Maria-Ferreira, D. et al., JRV Award 1st place, 47º SBFTE, 2015; Maria-Ferreira, D. et al., Honorable mention, 49º SBFTE, 2017), providing substrates for bacterial fermentation and supporting the production of SCFAs, since the RGal structure remains intact in colon. Therefore, here we hypothesized that ACWS, an arabinan-rich pectin polysaccharide isolated from *Malpighia emarginata* fruits (acerola) could promote anti-colitis effects. **Methods:** Colitis was induced by 5% of DSS. Mice were orally treated once daily with vehicle (water, 1 mL/kg) Entocort® (budesonide, 0.3 mg/kg) or ACWS (30, 100 or 300 mg/kg), and disease activity index (DAI) was monitored. After 7 days, colons were collected and measured, homogenized for quantification of myeloperoxidase (MPO), N-Acetylglucosamine (NAG), IL-1β and TNF-α levels. Colonic tissues were also processed for histological and immunohistochemistry analysis. **Results:** ACWS prevented colon length reduction (30 mg/kg: 9.5 ± 0.6 cm; 100 mg/kg: 8.7 ± 0.3 cm; 300 mg/kg: 9.0 ± 0.2 cm) when compared to DSS group (6.9 ± 0.1 cm). In the following experiments, only 30 mg/kg of ACWS was investigated. ACWS reduced DAI and weight loss in 79 and 75%, the presence of occult blood in feces and preserved the spleen weight. It also reduced the MPO and NAG activity in 62 and 22%, and decreased IL-1β and TNF-α levels in 26 and 38%, when compared to DSS group (MPO: 6.5 ± 0.5 and NAG 2.7 ± 0.0 D.O./mg of protein; IL-1β: 2715 ± 164.9 and TNF-α: 1446 ± 73.8 pg/mg of protein). Furthermore, the histological H&E stain revealed a pronounced destruction of colonic tissue in the DSS group, whereas ACWS treatment markedly improved the histologic appearance of colon. In sharp contrast to the decreased mucin-PAS staining and immunohistochemical PCNA proliferating cells in DSS colitis mice, ACWS treatment significantly restored these parameters (320.3 ± 11.6 nº of proliferating cells). Unlike ACWS, weight loss and shortening of the colon length following corticosteroid budesonide treatment was not different from DSS diseased mice. However, the budesonide reduced DAI, MPO, NAG, IL-1β and TNF-α levels in 63, 45, 29, 48 and 54% when compared to DSS group. **Conclusion:** Collectively, our results reveal that oral administration of ACWS ameliorate clinical symptoms, histological aspect, colonic regeneration and mucus production, as well as the underlying colonic inflammation in the DSS colitis model. Further studies should be carried out to elucidate and compare the mechanism underlying the budesonide and ACWS effects. In summary, our findings may shed light on the use of validated polysaccharides in the treatment of UC. **Support:** PNPD-CAPES, CNPq (425721/2016-7) **License number of ethics committee**: 1174 **Financial support**: PNPD-CAPES, CNPq (425721/2016-7)

09.049 Methanolic crude extract, **fractions and phenolic compounds from** *Eugenia mattosii* **D. Legrand leaves induced relaxation on aorta rings of normotensive and spontaneous hypertensive rats**. Da Silva RCMVAF, Vechi G, De Souza P, Silva LM, Andrade SF, Cechinel-Filho V Univali – Ciências Farmacêuticas

Introduction: The *Eugenia* genus has been described as a promising source of phytochemicals with pharmacological potential to treat several diseases. The aim of the present study was to verify the effect of methanolic crude extract, fractions and phenolic compounds, cryptostrobin and (-)-catechin of *E. mattosii* leaves on vascular reactivity. **Methods:** Isometric tensions were measured on aorta rings of normotensive (NTR) and spontaneous hypertensive rats (SHR). **Results:** The results showed that methanolic crude extracts of -leaves (MCE-leaves) and stems (0.1-1000 µg/mL) as well as, fractions obtained from leaves were able to induce a concentration-dependent relaxation in both endothelium-intact and -denuded aortas pre-contracted with phenylephrine (1 µM). The MCE-leaves were the most effective, since the maximal relaxation obtained was with the concentration of 300 µg/mL (≈ 83%), in both aortas from NTR and SHR. After the pretreatment with L-NAME and methylene blue, the MCE-leaves -induced relaxation was significantly decreased, in aorta rings from NTR. However, in aorta from SHR only L-NAME treatment reduced the relaxation induced by MCE-leaves. In addition, the contraction induced with KCl (60 mM) was also considerably inhibited by MCE-leaves (300 µg/mL) in both NTR and SHR. On the other hand, pretreatment with MCE-leaves decreased phenylephrine-induced contraction in Ca^{2+} -free preparation only in aortic rings from NTR. This study also reveals that both compounds cryptostrobin isolated from chloroform fraction and (-)-catechin from the ethyl acetate fraction (0.1-300 µg/mL), induced a marked relaxation in endothelium-intact aortic rings from NTR and endothelium-dependent and-independent vessels of SHR. Moreover, aorta rings pre-incubated with both compounds reduced significantly the PE-induced contraction (1 nM to 10 mM). Besides that, pretreatment of aortic rings from SHR, with L-NAME or ODQ, resulted in significant changed of relaxant effect induced by (-)-catechin, and little effect in cryptostrobin-induced relaxation. In addition, atropine, TEA and glibenclamide blunted the relaxation induced by (-)-catechin, but not from cryptostrobin. On the other hand, cryptostrobin, but not (-)-catechin, reduced the contraction induced by cumulative addition of phenylephrine. Besides that, cryptostrobin attenuate the contraction of rat aorta rings induced by internal Ca^{2+} release and external Ca^{2+} influx. **Conclusion:** The MCE-leaves induces relaxation in rat aorta, which involves the modulation of NO/cGMP dependent signaling pathway. Furthermore, cryptostrobin and (-)-catechin have activity on vascular smooth responsiveness, and these effects may involve, at least in part, by enhancing endothelium nitric oxide activity and blocking of calcium entry or changes on intracellular calcium utilization or mobilization. **License number of ethics committee**: The Ethical Committee of UNIVALI approved the studies and all methodologies used (authorization nº 055/17p). **Financial support**: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, CAPES, Brazil; Conselho Nacional de Desenvolvimento Científico e Tecnológico, CNPq, Brazil. Universidade do Vale do Itajaí (UNIVALI).

09.050 Acetylcholine release and ion channel modulation by PLA_2 ß-neurotoxins from *Micrurus lemniscatus lemniscatus* (**Amazonian Coral-Snake**) **Venom**. Floriano RS[1,2], Panunto PC[1], da Silva Jr NJ[3], Rowan EG[2], Hyslop S[1] [1]Unicamp – Farmacologia, [2]University of Strathclyde – Strathclyde Institute of Pharmacy and Biomedical Sciences, [3]PUC-Goiás – Biologia

Introduction: Envenomation by coral snakes (*Micrurus* spp.) is characterized by neurotoxicity mediated by Þ-neurotoxins that block post-synaptic nicotinic (cholinergic) receptors and phospholipase A_2 (PLA_2) ß-neurotoxins that cause potent presynaptic blockade. *Micrurus l. lemniscatus* occurs in the Brazilian Amazon and occasionally causes human envenomation. We have investigated the pharmacology of two presynaptic PLA_2 toxins from this venom. **Methods:** The pharmacological profile of toxins P^{30} and P^{37} (obtained by RP-HPLC of venom) was investigated using intra- and extracellular electrophysiological recordings [miniature endplate potentials - MEPPs and Ca^{2+} perineural currents] in mouse neuromuscular preparations, and by ion current recordings in whole cell patch-clamp mode in rat dorsal root ganglion (DRG). Intracellular Ca^{2+} mobilization was assessed by fluorescence in SK-N-SH neuroblastoma cells. **Results:** In diaphragm muscle, P^{30} and P^{37} (1 □g/ml) stimulated peripheral neurotransmitter release: P^{30} exhibited a triphasic change in MEPP frequency [from 42±5.5 (t_0) to 17±1.3* (t_2), 51±8 (t_{15}) and 12±2.9* ($t_{60\ min}$) MEPPs/min, *p<0.05, n=5; mean±SEM] while P^{37} produced only a progressive decrease in ACh release [from 57±8.5 (t_0) to 6±1.3* ($t_{60\ min}$) MEPPs/min, *p<0.05, n=5]. P^{30} (1 □g/ml) caused an initial increase in the perineural current associated with Ca^{2+} influx in mouse triangularis sterni nerve-muscle preparations followed by partial blockade of the Ca^{2+} current [from 1.09±0.21 (t_0) to 1.34±0.24 (t_5) and 0.33±0.07* ($t_{60\ min}$) mV, *p<0.05, n=5]; P^{37} (1 □g/ml) was less active, causing only a minor non-significant decrease in current. In SK-N-SH cells loaded with Fluo-4 AM, P^{30} (1 □g/ml) caused large, transient changes in intracellular Ca^{2+} [□F/F0 ratio, in AU: 1.05±0.09 (normal Ca^{2+}) *vs*. 0.15±0.04 (zero Ca^{2+}), p<0.05, n=5], as also seen with ß-bungarotoxin [□F/F0 (AU): 1.25±0.17 (normal Ca^{2+}) *vs*. 0.41±0.05 (zero Ca^{2+}), p<0.05, n=5], while the effects caused by P^{37} were less pronounced [□F/F0 (AU): 0.61±0.06 (normal Ca^{2+}) *vs*. 0.15±0.04 (zero Ca^{2+}), p<0.05, n=5]; neither toxin altered intracellular Ca^{2+} in cells maintained in zero Ca^{2+} conditions. P^{30} and P^{37} did not affect currents flowing through native Na^+ and K^+ channels expressed in DRG cells; P^{30} caused a significant decrease in the Ca^{2+} current measured in whole cell patch-clamp recordings [from -1204±52 (t_0) to -629±28* ($t_{8\ min}$) pA, *p<0.05, n=6], while P^{37} caused an initial increase in the current associated with Ca^{2+} influx followed by a significant decrease [from -891±75 (t_0) to -988±53 (t_1) and -499±89* ($t_{8\ min}$) pA, *p<0.05, n=6]. **Conclusion:** These findings indicate that P^{30} and P^{37} act presynaptically to affect motor neurotransmission, most likely by modulating Ca^{2+} channel activity. **License number of ethics committee**: Committee for Ethics in Animal Use (CEUA/UNICAMP, protocol no. 3477-1) **Financial support**: CAPES, CNPq, FAPESP (R.S. Floriano, grant nos. 2014/24409-8 and 2016/23432-1)

09.051 Assessment of respiratory failure induced by rattlesnake crotoxin: **Role of PGE_2 and peripheral neurotoxicity**. Sartim MA[1], Sorgi CA[1], Souza COS[1], Petti AP[1], Fonseca VMB[2], Borges MC[2], Faccioli LH[1], Sampaio SV[1] [1]FCFRP-USP – Análises Clínicas e Toxicológicas, [2]FMRP-USP – Clínica Médica

Introduction: Crotoxin (CTX), the main component of *Crotalus durissus terrificus* rattlesnake venom, is a phospholipase A_2 with neurotoxic properties responsible for peripheral neuromuscular paralysis. In the present work we evaluated the mechanism of respiratory failure induced by CTX in mice as concerning the involvement of leukocytes, eicosanoids and peripheric nerve system. **Methods:** Male Swiss mice (7-8 weeks old) were administrated with CTX (300µg/Kg) or saline subcutaneously and lung collected after 2, 6 and 12 hours (hrs). From lung homogenate were analyzed: vascular permeability assessed by lung Evans Blue extraction by spectrofotometry; eicosanoids lipid mediators were quantified by mass spectrometry, and mieloperoxidase (MPO) by colorimetric assay; leukocytes from lung digestion were assessed for total and differential counting in panoptic-stained cytospin preparations and neutrophil phenotyping by flow cytometry. Lung function was evaluated using FlexVent system from animals injected with CTX or saline 12 hrs previously and histological analysis was performed in hematoxylin/eosin stained lung preparations. In order to evaluate the involvement of lipid mediators and peripheral nervous system, pharmacological antagonists/inhibitors were i.p. administrated previously to CTX: indomethacin (4mg/Kg), MK-591 (40mg/Kg), metyl-atropine (10mg/Kg), hexametonium (10mg/Kg), propranolol (5mg/Kg) and neostigmine (0.1mg/Kg). Animal care procedures and experimental protocols were approved by The Committee for Ethics on Animal Use from the Pharmaceutical Sciences School of Ribeirão Preto. **Results:** Mice presented an increase in vascular permeability and PGE_2 concentration in lungs 2 hrs after administration of CTX. The toxin also induced a gradual increase in lung MPO quantification from 6 to 12hrs, accompanied by a conservative increase in neutrophils ($Ly6G^+$ $CD62L^+$ $CD45^+$ cells) present in lung parenchyma but not in bronchoalveolar cavity. As for the lung function, CTX induced majorly a decrease in quasi-static compliance parameter, which reflects the reduced capacity of intrinsic elastic properties of the respiratory system (lung+chest wall). The histology analysis showed a modest leukocyte infiltrate (most neutrophil) followed by edema, hemorrhage, hyperemia and increase in septal wall thickness. Among drugs, the prostaglandin biosynthesis inhibitor indomethacin and the ganglionic blocker nicotinic receptor antagonist hexamethonium were capable to increase survival rate of CTX-treated mice. As concerning lung parameters alterations induced by CTX, indomethacin was capable to reduce PGE_2 and vascular permeability while hexamethonium was capable to reduce MPO quantification. **Conclusion:** We conclude that CTX is responsible to induce a direct effect on lungs by inducing PGE_2 production responsible for vascular permeability. Also, CTX induces an indirect effect on lungs by inducing diaphragm neuromuscular failure via cholinergic blockade, resulting in increase in MPO and consequently neutrophil infiltration. The results show that CTX is capable to modulate a complex system involving PGE_2 formation and peripheric nervous system modulation in order to induce its biological activity. **License number of ethics committee**: 15.1.807.60.1 **Financial support**: Fundação de Amparo à Pesquisa do Estado de São Paulo

09.052 Antinociceptive and anti-inflammatory activities of *Philodendron bipinnatifidum* **Schott ex Endl** (**Araceae**) **are mediated by opioid receptors and oxidative stress inhibition**. Scapinello J[1], Schindler M[2], Anzollin GS[2], Siebel AM[1], Boligon AA[3], Saraiva TES[4], Maus NP[4], Betti AH[4], Oliveira JV[1], Dal Magro J[1], Oliveira D[5], Müller LG[2] - [1]Unochapecó - Ciências Exatas e Ambientais, [2]Unochapecó - Ciências da Saúde, [3]UFSM – Ciências da Saúde, [4]Feevale - Ciências da Saúde, [5]UFSC – Engenharia Química e de Alimentos

Introduction: Leaves and stems of the *Philodendron bipinnatifidum* Schott ex Endl (Araceae) are used in popular medicine at inflammation cases, such as erysipela, as well as orchitis and in the reumatism treatment. The present study was conducted to investigate the antinociceptive and anti-inflammatory activities of *P. bipinnatifidum* Schott ex Endl stems ethyl acetate extract (EPB). **Methods:** The EPB was used at 250, 375 and 500 mg/kg (oral route, p.o.) in male Swiss mice. Antinociceptive activity of the plant extract was evaluated by acetic acid induced writhing and formalin tests. To investigate the possible participation of opioid system in EPB-mediated effects, naloxone was previously administered to mice. Anti-inflammatory activity was evaluated by using carrageenan-induced paw oedema. The open-field test was performed to investigate the possible EPB effects on the locomotor and exploratory activities. To assess the protective role of EPB on carrageenan-induced oxidative stress, the levels of NPSH, TBARS, as well as SOD and CAT activities were evaluated in blood and paw tissue. The acute toxicity of the EPB was investigated by using OECD 423 guideline. **Results:** *Th*e EPB chemical analysis by GC and HPLC revealed the presence of flavonoids (luteolin and quercetin) and phytosterols (β-sitosterol and stigmasterol). The oral treatment with the EPB inhibited mice abdominal writhings ($P<0.01$) at 375 and 500 mg/kg, and reduced the formalin effect at the first-phase (500 mg/kg, $P<0.05$) and also at the second-phase (500 mg/kg, $P<0.001$) of the test. EPB (375 and 500 mg/kg) did not alter spontaneous locomotion in the open field test, but the number of fecal bolus was significantly lower for the EPB group at 500 mg/kg when compared to the vehicle-treated group ($P<0.05$). The pretreatment with naloxone significantly inhibited the antinociceptive activity induced by EPB in the formalin test, revealing the possible involvement of the opioid receptors. The EPB administered at 500 mg/kg (p.o.) prevented carrageenan-induced paw oedema ($P<0.05$ and 0.01) up to 6 h after carragenan injection. Evaluation of TBARS and NPSH levels, SOD and CAT activities in the blood and paw tissue of animals submitted to the carrageenan assay suggest that the anti-inflammatory effect of EPB may be related to oxidative stress inhibition. The acute administration of the EPB (2000 mg/kg, p.o.) caused no mice mortality, demonstrating low toxicity. **Conclusions:** The extract of *P. bipinnatifidum* Schott ex Endl displays antinociceptive and anti-inflammatory activities, without causing toxicological effects. The pharmacological activity of this vegetal species may be related to the presence of flavonoids and phytosterols and is mediated by opioid receptors and oxidative stress inhibition. **License number of ethics committee**: 017-17 **Financial support**: PIBIC/FAPE - Unochapecó

09.053 *Maytenus robusta* **Reissek**, **a medicinal plant useful to treat digestive diseases**, **promotes ameliorative effects in colon and liver of mice exposed to dextran sulfate sodium**. Mees M[1], Mariott M[2], Meurer M[2], Mariano LNB[2], Boeing T[2], Somensi LB[2], Da Silva R[2], Souza P[2], Santos AC[2], Niero R[2], Cechinel-Filho V[2], Andrade SF[3], Da Silva L[2] [1]Univali – Ciências Farmacêuticas, [2]Univali – Ciências Farmacêuticas, [3]Univali – Farmácia

Introduction: The ulcerative colitis (UC) is an inflammatory bowel disease related to genetic, environmental an immunological mechanism. The available drugs for the treatment of UC are limited, expensive and highly associated with side effects. Moreover, a close relationship between UC and hepatic disorders has been described. Given that additional preventive/adjuvant strategies to UC or the liver damage associated to it are required, the present study evaluated the effects of the hydroalcoholic extract do *Maytenus robusta* Reissek (Celastraceae) on colon and liver of mice with colitis induced by dextran sodium sulfate (DSS). **Methods:** The effects of the hydroalcoholic extract of *M. robusta* (HEMR) on intestinal epithelial cells (IEC-6 line) and on inflammatory and oxidative damage in the colon and liver caused by intake of dextran sulfate (DSS) 3% in drinking water in Swiss mice were evaluated. For this, cell culture techniques and the effects of HEMR (1-100 mg/kg, p.o) on pre-clinical (weight loss, diarrhea, presence of blood in the faeces), macroscopic (colon length and colon weight), histological, histochemical and biochemistry parameters (GSH, LOOH, SOD, CAT, GPx, GST, MPO, TGO, TGP, IL-6, IL-10 and TNF) were assessed. **Results:** The incubation of HEMR (1-100 µg/mL) did not alter the viability, but reduce nitrite production of IEC-6 stimulated by bacterial lipopolysaccharide. *In vivo*, was possible to observe attenuations in the macro and microscopic alterations in the colonic tissue from mice treated with HEMR (100 mg/kg, which in turn reduced the disease activity index. In addition, in the colonic tissue, the treatment with HEMR(100 mg/kg) increased GSH levels by 202% and reduced LOOH levels by 58%, compared to the vehicle group. The level of CAT activity in the colon of HEMR-treated mice was normalized to values similar to the non-colitic group. Interestingly, the group treated with HEMR showed increased colonic GST activity reaching 171% compared to the non-colitic group. Besides, HEMR reduced the activity of MPO (a neutrophil infiltration marker) and inflammatory cytokines secretion (TNF and IL-6) on the colon. However, administration of HEMR was not able to reverse reduced levels of IL-10 in the colony of mice exposed to DSS. Regarding hepatic parameters, HEMR was not able to reverse changes in GSH and LOOH levels and neither increase in the activities of SOD, CAT or MPO in mice exposed to DSS. But, HEMR increased hepatic GST levels, decreased the GPx activity in relation to the non-colitic group. In addition, HEMR reduced hepatic IL-6 levels by 37%. Furthermore, the HEMR treatment reduced AST and ALT serum levels, markers of liver damage, in mice exposed to DSS. Finally, the HEMR was able to reduce intestinal transit by 12% compared to the vehicle group. **Conclusion:** In this set, our findings suggest that HEMR minimizes inflammation of the colonic mucosa and maintains the antioxidant activity of the colon. In addition, HEMR may be a potential tool to prevent hepatic injury secondary to ulcerative colitis (CEUA/UNIVALI: 035/15). **Financial support**: CNPq, CAPES, FAPESC, UNIVALI. **License number of ethics committee**: 035/15 **Financial support**: CNPq, CAPES, FAPESC, UNIVALI

09.054 Eucalyptol reduces airway hyperresponsiveness induced by cigarette smoke in rats. Feitosa EK[1], Oliveira-Melo P[2], Lima CC[2] [1]UFERSA – Ciências da Saúde, [2]ISCB-UECE

Introduction: Cigarette smoke is a pollutant able to cause primarily disease in the respiratory tract and can change the contractile mechanism of smooth muscle resulting in airway hyperresponsiveness. Eucalyptol (EUC) is a monoterpene oxide anti-inflammatory and muscle relaxant in airway which that already has shown activity in several types of excitable tissues including in several smooth muscle types. This compound is a promising to be a pharmacological treatment to airway hyperresponsiveness. **Aim:** To investigate the effect of EUC on airway hyperresponsiveness in rats exposed to cigarette smoke. **Methods:** This project was approved by CEUA/UECE (10462460-4/66). Wistar rats (250 – 300 g) were divided into the following groups: control (sham-exposed); EUC (mice treated with EUC for 30 days), cigarette smoke (CS) (mice exposed to 12 cigarettes a day for 30 days); CS+EUC (mice exposed to 12 cigarettes a day for 30 days and treated with 1 mg/mL eucalyptol for 30 days). Mice in the CS and control groups received vehicle for 30 days. Eucalyptol (or the vehicle) was administered by inhalation (15 min/daily). Mice were sacrificed 24 hr after the completion of the 30-day experimental procedure and the tracheal rings were placed under tension balance of 1g in isolated organ bath containing Krebs-Henseleit (KH) buffer (pH 7.4, 37 ° C) with gasification constant. Changes in tension were measured by a force transducer connected to a computerized data system. The viability of the tissue was tested by the contractile response to 60 mM of potassium chloride (K60). We evaluated the EUC response in the electromechanical and pharmacological coupling and voltage-operated calcium channels. Results were expressed in grams force (gF) and were considered statistically significant when $p<0.05$. **Results:** The EUC reduced the hyperresponsiveness in the electromechanical coupling in the CS+EUC group (1.52 ± 0.31 gF) when compared to CS group (3.77 ± 0.77 gF; $p<0,05$). The hyperresponsiveness in the pharmacomecanic coupling was reduced (2,92 ± 0,43 gF) in the CS+EUC group when compared to CS group (3,07 ± 0,12 gF; $p<0,05$). The contraction Ba^{2+} induced was lower in the CS+EUC group (1,84 ± 0,18 gF) when compared to CS group (0,97 ± 0,15 g/F).This results didn't show difference when compared to nifedipine effect. Suggesting a voltage-operated calcium channels blocked by EUC. **Conclusion:** The treatment with eucalyptol reduces airway hyperresponsiveness in rats exposed to cigarette smoke, probability by voltage-operated calcium channels block **License number of ethics committee**: 10462460-4/66 **Financial support**: CNPq, FUNCAP, UFERSA

09.055 Evaluation of the anti-ulcerogenic activity of the metanolic extract from Pentaclethra macroloba (**Willd**.) **Kuntze in animal models**. Nobrega PA, Sales PF, Correa FRFB, Cabral GNV, Nascimento AA Unifap – Ciências Biológicas e da Saúde

Introduction: Pentaclethra macroloba, popularly known as "Pracaxi" is a medicinal plant abundant in the Amazon region, has current use in folk medicine of the communities of this region, as anti-inflammatory, healing and for treatment of gastric problems. The aim of this study was to evaluate the gastroprotective activity of the metanolic extract of the stem bark from Pentaclethra macroloba (EMPM), as well as to identify possible mechanisms involved in this activity in experimental animals. **Methods:** The evidence of EMPM activity was based on experimental models that mimic the etiological factors of gastric lesions in man. Were induced ulcers using the Acidified Ethanol model (Mizui, Jpn J Pharmacol, v. 33, p. 939, 1983.) and the nonsteroidal anti-inflammatory model (Rainsford, J Pharm Pharmacol. v.39, p. 669, 1987). Was also evaluated the involvement of the sufidryl groups in the gastroprotective action of the EMPM (MATSUDA, Life Sci, v.65, p. 27,1999). In this experiment a group of animals (n = 5) were used for each of the three dose levels of the extract (100, 250 and 625 mg / kg), as well as for the control group (vehicle). After each experiment, the stomachs were evaluated for: (a) total area of the lesion, (b) percentage of ulcer, (c) index of ulcerative lesions; (d) inhibition or cure percentage. Numerical results were expressed as mean ± standard error of mean. Differences between groups were determined using analysis of variance (ANOVA) and method of Dunnett. For comparisons between two groups used the t-Student test. We used $p<0.05$ and the GraphPad Prism program version 5.01. The Animal Ethics Committee of the Universidade Federal do Amapá approved all experiments (CEUA-UNIFAP 006/2015). **Results:** EMPM (100, 250 and 625 mg/kg) showed a gastroprotective effect against lesions induced by acidified ethanol, reaching a cure rate of 96.08%, 98.51% and 100%, respectively. This demonstrates an expressive gastroprotective activity against local aggressors. In the model of induction of gastric lesion by NSAIDs, EMPM (625 mg/kg) was able to reduce all the parameters evaluated demonstrating a cure rate of up to 84.33%. Suggesting antiulcerogenic effect via cytoprotective mechanisms. When the extract was administered in the presence of a sulfhydryl groups inhibitor (NEM), the antiulcerogenic response was attenuated. This demonstrates that the sulfhydryl groups participate in the gastroprotective mechanism evoked by the extract. **Conclusion:** In the light of all the results we conclude that the extract of Pentaclethra macroloba presents a remarkable antiulcerogenic activity for different etiological agents and this effect is related to the participation of the sulfhydryl groups. **License number of ethics committee**: CEUA-UNIFAP 006/2015 **Financial support**: CNPq/PIBIC/CAPES

09.056 Tartrolon D cytostatic and cytotoxic effects on tumor cells. Brito TL[1], Miller BW[2], Florêncio KGD[1], Silva AET[1], Haygood MG[2], Wilke DV[1] [1]UFC – Fisiologia e Farmacologia, [2]The University of Utah – Pharmacy

A established model of symbiosis occurs between the bivalve mollusks of Teredinidae family, known as shipworms, and an abundant population of γ-proteobacteria, including members of the *Teredinibacter* genus, inhabiting the host's gill bacteriocytes. These bacteria can synthesize enzymes and natural products that have many different possible roles, including aiding in lignocellulose digestion, predation, chemical defense or antibiosis. The production of tartrolon D (TLD) was reported from shipworm symbiont bacteria previously. The tartrolons are a class of symmetric macrodiolides with interesting biological activities such as insecticide, antibiotic and cytotoxic. In this work, we aimed to evaluate the antiproliferative effects of TLD on tumor cells. TLD was obtained from the acetate extracts of *Teredinibacter turner* T7901 cells pellet at the Symbiont Basal Medium with cellulose as the only C source. Initially the antiproliferative effect was investigated against four human tumor cell lines (HCT 116, B16-F10, PC-3M and MCF-7) and two non-tumor cells (L929 and HEK293A) by the sulforhodamine B (SRB) assay after 48 h incubation. The antiproliferative effect was further evaluated after 24 and 72 h on HCT 116 by the SRB assay. Then morphological changes, through panoptic staining, along with several flow cytometry assays were carried out to glimpse at cytotoxic effects on HCT 116 cells incubated with TLD at 6, 12 and 24 μM for 24 or 48 h. Noteworthy TLD induced strong cytostatic effects on all cell lines evaluated (excepting PC-3M) with inhibition concentration mean (IC50) values in the nanomolar range. HCT 116 was the most sensitive cell line depicting IC50 = 40 nM after 48 h. This cell also depicted a strong time dependent effect. The TLD IC50 values on HCT 116 were until three hundred times lower after 72 h (IC50 = 2 nM) when compared with 24 h incubation (IC50 = 600 nM). Besides the cytostaticity, cells treated with TLD, in the micromolar range, depicted pyknosis, DNA fragmentation and membrane instability under optical microscope. Furthermore, quantitative morphological analysis, along with membrane integrity, cell cycle profile and DNA fragmentation assays, conducted by flow cytometry, indicated severe stress and cell death along with cell cycle arrest. G2/M arrest was observed on HCT 116 treated with 24 μM of TLD after 24 and 48 h. HCT 116 TLD-treated cells depicted two distinct morphological changes, increased granularity and shrinkage after 48 h. Finally, membrane integrity loss and DNA fragmentation were observed on cells incubated for 48 h with 24 μM TLD. This is a pioneer study on the cytotoxic properties of TLD on tumor cells and it pictures a promising scenario for further anticancer investigation. **Financial support**: CNPq

09.057 Anti-inflammatory effect of the fixed oil from seeds of *Hancornia specisosa*. Gomes Abreu FF[1], Oliveira JP[1], Palmeira DN[1], Fiorotto P[1], Oliveira AS[1], Santos EJ[2], Camargo E[1] [1]UFS – Physiology, [2]UFS – Chemical Engineering

Introduction: *Hancornia speciosa* Gomes is known as “mangabeira” and is used in folk medicine to treat cancer and inflammatory diseases. Leaves and fruits have been extensively studied but there is no investigation on the biological effects of the oil extracted from its seeds. This study evaluated the anti-inflammatory activity of the fixed oil from mangaba seeds (OSM) in mice. **Methods:** Adult male Swiss mice (25-30 g) were used and the protocols were approved by the Ethics Committee for Animal Research (n°28/2018). The topical anti-inflammatory activity was evaluated in the ear edema induced by 12-O-tetradecanoylphorbol-13-acetate (TPA). Treatment with OSM (0.3, 1 and 3 mg/ear) or dexamethasone (0.05 mg/ear, control) was concomitantly administrated with TPA (1 µg/ear) in the ipsilateral ear. After 6 hours, edema (weight of ipsilateral subtracted from contralateral ear), myeloperoxidase (MPO) activity, cytokine levels (IL-6 and IL-1β) and vascular permeability were measured. For evaluation of the systemic anti-inflammatory activity, mice were treated with vehicle (Tween 0,5% in saline, 10 mL/kg), OSM (100 or 200 mg/kg, i.p.) or dexamethasone (5 mg/kg, s.c.) administered 30 min before the intrapleural injection of carrageenan (1 mg/cavity). The fluid leakage from the pleural cavity was collected 4 h after induction for assessment of total leukocyte counts, MPO activity and cytokine levels (TNF-α and IL-1β). Results were expressed as mean±S.E.M. and were evaluated by one-way ANOVA followed by Tukey's test, with $p < 0.05$ considered as significant. **Results:** Administration of TPA induced ear edema and elevated MPO activity (19.1±2.5 mg and 119.8±11.0 UMPO/site). The topical administration of OSM reduced both edema (5.6±1.1 mg for 3 mg/ear, $p<0.001$) and the MPO activity (78.1±11.9 and 46.5±6.3 UMPO/site for 1 and 3 mg/ear; $p<0.05$ and $0<0.001$; respectively) induced by TPA. OSM also reduced the levels of IL-1β at 3 mg/ear (70.1±4.7 pg/site; $p<0.001$) and IL-6 at 1 and 3 mg/ear (119.2±18.5 and 50.2±6.9 pg/site respectively; $p<0.001$ for both) when compared to vehicle group (180.8±12.5 and 308.0±31.1 pg/site for IL-6 and IL-1 β respectively). The vascular permeability assessed by Evan´s blue dye extravasation in ear tissue was reduced by OSM at 3 mg/ear (85.0±13.4 ng/mg of tissue; $p<0.01$) when compared to vehicle-treated group (140.9±13.1 ng/mg of tissue; $p<0.01$). In the carrageenan-induced pleurisy, OSM (100 and 200 mg/kg) reduced total leukocyte counts in the pleural lavage (1.9±0.1 and 1.9±0.2 cells/cavity; $p<0.001$ for both) when compared to vehicle group (3.9±0.2 cells/cavity). The myeloperoxidase activity in pleural lavage was also reduced by 100 and 200 mg/kg of OSM (1.8±0.1 and 1.7±0.3 UMPO/cavity respectively; $p<0.05$ for both doses) when compared to vehicle-treated group (3.5±0.6 UMPO/cavity). These doses of 100 and 200 mg/kg of OSM also reduced TNF-α levels by 36 ($p<0.05$) and 52% ($p<0.01$) and IL-1β levels by 81 and 65% and ($p<0.001$ for both doses) in the pleural lavage fluid. Treatmente with dexamethasone significantly reduced all parameters evaluated in both models. **Conclusion:** We demonstrated for the first time that OSM possesses anti-inflammatory activity, which highlights the potential of this preparation from *H. speciosa*. **License number of ethics committee**: 28/2018 **Financial support**: CNPq and CAPES