ABSTRACTS

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09. Natural Products and Toxinology

09.001 Diuretic effect of *Mimosa bimucronata* (DC.) Kuntze leaves extracts and its main constituent methyl gallate in rats. Mariano LNB[1], Schlickmann F, Boeing T, Silva LM, Steimbach VMB, Krueger CMA, Andrade SF, Cechinel-Filho V, Souza P Univali – Ciências Farmacêuticas

Introduction: Some species of the genus *Mimosa* showed promising results in previous investigations focusing the cardiovascular and renal system, which include diuretic effect; however, no chemical analyses or animal model has been conducted so far to evaluate the biological properties of *Mimosa bimucronata* (DC.) Kuntze, a specie popularly known in Brazil as "maricá" and of natural occurrence on the Brazilian coast. Therefore, this study aimed to explore the chemical composition and the diuretic actions of extracts, fractions and of the majority constituent obtained from *M. bimucronata* leaves in rats. **Methods:** Male Wistar rats received the oral treatment with vehicle (1 ml/kg), hydrochlorothiazide (10 mg/kg), methanolic extract from *M. bimucronata* (MEMB; 10 – 100 mg/kg), dichloromethane (DCM; 3 – 30 mg/kg) and ethyl acetate (EA; 3 – 30 mg/kg) fractions or the isolated compound methyl gallate (MG; 0.3 – 3 mg/kg). The cumulative urine volume, electrolytes excretion (Na^+ and K^+), pH and osmolality were determined at the end of the experiment (after 8 hours). Cell cytotoxicity of MG, at concentrations of 0.3 – 30 µg/ml, were verified on A7r5 and L929 cell lines. Additionally, the capacity of MG to stimulate the generation of nitrite, a marker of nitric oxide generation, in A7r5 cells has also been accessed. **Results:** The chemical studies using HPLC-fingerprint analysis demonstrated that the phenolic compounds are the majorities in the plant, with the MG being the main substance identified. We showed that MEMB (30 and 100 mg/kg) and EA fraction (30 mg/kg), but not DCM, revealed a significantly increase in the urinary volume when compared with control rats (vehicle-treated only). This effect was associated with increased levels of urinary Na^+ and K^+, as well as enlarged osmolality values. None of the treatments modified urinary pH values. Similarly, the majority constituent of this plant the MG, at dose of 1 and 3 mg/kg, also displayed diuretic, natriuretic and kaliuretic properties when given to both normotensive and spontaneously hypertensive rats. Atropine, a muscarinic receptor antagonist, fully prevented MG-induced diuresis, natriuresis and kaliuresis. In contrast, the previous treatment with indomethacin (a cyclooxygenase inhibitor) or with L-NAME (a non-selective nitric oxide synthase inhibitor) did not exert any influence in the diuretic effect of MG. In addition, after 24 h exposure, MG did not alter the viability of thoracic aorta smooth muscle (A7r5) and fibroblast (L929) cell lines and neither stimulated a directly nitrite generation in the supernatant of A7r5 cell. **Conclusion:** Taken together, our findings show, for the first time, that *M. bimucronata* extracts and its majority compound methyl gallate present diuretic, natriuretic and kaliuretic properties when orally given to rats, an effect that showed to be dependent on the activation of muscarinic acetylcholine receptor. Research support: CNPq, CAPES, FAPESC and UNIVALI. Authorization from CEUA/UNIVALI: 045/16.

09.002 Chlorella improves health-related quality of life in impaired glucose tolerance and type-2 diabetic patients Martins F[1], Castro TCL[1], Torello CO[1], Fernandes EC[2], Toledo JH[2], Queiroz MLS[1] [1]FCM-Unicamp – Farmacologia, [2]FCM-Unicamp – Ciências Farmacêuticas

Type-2 diabetes (T2D) is related to low overall health, loss of quality of life, high mortality and morbidity [1-5]. Impaired glucose tolerance (IGT) is an intermediate state between normal glucose tolerance and overt diabetes, and subjects with this condition have an increased risk to develop T2D[6-7]. Despite advances in scientific research and development of new drugs, in many cases there is lack of efficacy and undesirable adverse effects[8], which stimulates the search for alternative therapies[9]. For this reason, the Chlorella (CV) alga arises as a natural food supplement that assists health. Thus, our objective was to evaluate the impact of CV on health-related quality of life (HRQoL), stress levels and glycosylated hemoglobin (HbA1c) of individuals with IGT and T2D. Volunteers with T2D (n=25) and IGT (n=20) from Diabetes Group of the Centro de Saúde da Comunidade (CECOM), University of Campinas, Brazil, received oral doses of 3 g CV daily. HRQoL was assessed by Short Form-36 Health Survey instrument (SF-36)[10-11]. Stress levels were evaluated using the Perceived Stress Scale (PSS)[12-13] and morning salivary cortisol levels. HbA1c was analyzed by high-performance liquid chromatography method. Analyzes were performed before use of CV (T0), after 6 (T6) and 12 (T12) months of intake. In the T2D group, significant ($P<0.05$) improvement was observed in six of the eight SF-36 domains at T6 and T12: physical limitation (59 ± 44 at T0, 77 ± 36 at T6 and 84 ± 30at T12), body pain (59 ± 32 at T0, 76 ± 21 at T6 and 69 ± 25 at T12), general health (59 ± 24 at T0, 72 ± 16 at T6 and 70 ± 17 at T12), vitality (51 ± 24 at T0, 72 ± 19 at T6 and 69 ± 21 at T12), social functioning (58 ± 30 at T0, 84 ± 19 at T6 and 78 ± 23 at T12), mental health (65 ± 27 at T0, 81 ± 15 at T6 and 76 ± 19 at T12) . In the IGT group, significant ($P<0.05$) improvement was reported on mental health at T6/T12 (67 ± 20 at T0, 80 ± 16 in T6 and 83 ± 14 in T12), and more domains was affect by CV at T12: body pain (64 ± 23 at T0 and 84 ± 19 at T12), general health (70 ± 17 at T0 and 78 ± 90,03 at T12) and vitality (67 ± 21 at T0 and 81 ± 14 at T12). In both T2D and IGT groups, CV ingestion led to a progressive reduction of stress levels at T6 and T12. No changes were found in morning salivary cortisol and HbA1c levels after CV use. Our results demonstrated that CV intake improved the quality of life and decreased stress levels of T2D and IGT patients. **References:** (1) Slagter et al., *PLoS One*. 10(10):e0140599; 2015. (2) Risstad et al., *Obes Surg*. 25:2408; 2015. (3) Al Hayek et al., *Diabetes Metab J*; 38:220; 2014. (4) Marrero et al., *Qual Life Res.* 23:75; 2014. (5) Aguiar et al., *Arq Bras Endocrinol Metab.*52:931; 2008. (6) Neumann et al., *Health Qual Life Outcomes.* 24:12; 2014. (7) Tuomilehto et al., *N Engl J Med*.344:1343; 2001. (8) Chang et al., *Evid Based Compl Altern Med.* 2013:378657; 2013. (9) Kibiti & Afolayan, *Pharmacogn Mag*. 11:S258-74; 2015. (10) Ware & Sherbourne, *Med Care*. 30:473;1992. (11) Ciconelli et al., *Rev Bras Reumatol.*39:143; 1999. (12) Cohen et al., *J Health Soc Behav.* 24:385; 1983. (13) Luft et al., *Rev Saude Publica*. 41:606; 2007. **Sources of Research Support:** FAPESP, CAPES and CNPq. We thank collaborators from CECOM/UNICAMP. Human Research Ethical Committee (CAAE: 30981114.4.0000.5404)

09.003 Central antinociception induced by resveratrol is mediated by endogenous opioids, μ-and Δ-opioid receptors. Oliveira CC, Almeida AFS, Teixeira LRM, Noronha TM, Duarte IDG, Santos SHS, Romero TRL, Perez AC UFMG – Fisiologia e Farmacologia

Introduction: The resveratrol is a naturally occurring phytoalexin present in grapes and derivatives, with therapeutic activities widely reported, including analgesic effects. However, the mechanisms of resveratrol antinociceptive action has not been completely elucidated, which can promote limitations in therapeutic utilization. In this manner, the aim of this work was to assess the mechanisms of the resveratrol-induced central antinociceptive effect, analyzing the opioid system involvement in this biological action. **Methods:** The paw pressure test was used and hyperalgesia was induced by intraplantar injection of carrageenan (200 μg). Resveratrol and opioid system drugs were administered via the intracerebroventricular route in Swiss male mice (n=4). Statistical analyses: One-Way ANOVA followed by Bonferroni's post-test. **Results:** Our results demonstrated that the unspecific opioid receptor antagonist, the μ- and δ-opioid receptor antagonists, respectively, naloxone (2.5 and 5 μg), clocinnamox (2 and 4 μg) and naltrindole (6 and 12 μg), antagonized resveratrol (9 μg)-induced central antinociception in a dose-dependent manner. On the other hand, the κ-opioid receptor antagonist nor-binaltorphimine (10 and 20 μg) was not able to inhibit the central antinociceptive effect induced by the resveratrol (9 μg). Additionally, the administration of the aminopeptidase inhibitor bestatin (20 μg) significantly enhanced low-dose resveratrol (3 μg)-induced central antinociception. **Conclusion:** These data provide evidence for the involvement of endogenous opioids, μ- and δ-opioid receptors in resveratrol-induced central antinociception. **Financial Support:** CNPq, CAPES and FAPEMIG. **CEUA Protocol Number:** 278/2016.

09.004 Chromomycin A2 is a putative modulator of transcription factor TBX2. Sahm BDB, Jimenez PC, Kimani S, Bauermeister A, Lopes NP, Prince S, Costa-Lotufo LV ICB-USP

Introduction: The TBX2 transcriptional factor has been shown to play an important role in carcinogenesis, and figures as a potential target for new anticancer therapies. Recent searches have been looking for molecules that modulate its action but no substance was found so far. Natural products are historically known to offer a wide variety of bioactive compounds. Among them, marine natural products are a prolific source with many unique and complex substances. In this scenario, the aim of the present work was to identify new compounds that modulate TBX2 in tumor cell lines within extracts produced by marine bacteria from the Brazilian coast. **Methods**: Functional chromatography (FC), a specialized target-directed screening protocol, was used to identify small molecules that specifically bind TBX2. Recombinant protein, obtained by heterologous expression in *E. coli* transfected with vector pET28b, were linked to a resin, which was then incubated with crude natural extracts or pure compounds. Unbound materials were washed and the resin was extracted with ethanol to recover the retained materials. The ethanolic extracts were analyzed by LC-MS/MS to identify molecular masses. Microscale thermophoresis was applied to access the molecular interaction between target protein and ligand. For bioactivity validation, we performed biological assays such as MTT, clonogenic and western bloting using melanoma cell lines with different TBX2 expression. **Results**: Around 50 samples were evaluated on the TBX2 FC. Extracts derived from actinobacterias BRB-081 and BRB-256 showed *m/z* hits related to compounds such as surugamide and staurosporines. Among pure compounds, chromomycins were also retained by the TBX2 resin, however LC-MS and MS/MS analyses found considerable amounts of chromomycin A2 (CA2) in the elution fraction, indicating a stronger ligation of this molecule. Thermophoresis preliminary analysis suggested a K_d (dissociation constant) for CA2-TBX2 binding affinity as low as 703nM, denoting a high specificity. Bioactivity validation by MTT and clonogenic assays demonstrated that cells with TBX2 knockdown are more sensitive to CA2 then the wild type. **Conclusions**: Herein, we validated the FC technique using TBX2 protein as a target. Moreover, we found that CA2 is a putative ligand of TBX2, having been identified through a target-oriented screening protocol. This is further supported by data from thermophoresis preliminary analyses. Biological assays suggest that TBX2 partakes in CA2 cytotoxicity against melanoma cells, still additional experiments are in progress to better understand CA2 modulation of TBX2 and its pathway. Acknowledgments: FAPESP (2015/17177-6), CNPQ/PRO-AFRICA (440232/2015-5), CNPQ and CAPES.

09.005 Anti-diarrheal therapeutic potential and safety assessment of sulphated polysaccharide from Gracilaria intermedia seaweed in mice. Sousa NA[1], Leodido ACM[1], Araújo TSL[1], Souza LKM[1], Sousa FBM[1], Filho MDS[1], Nogueira KM[1], Freitas ALP[2], Medeiros JVR[1] [1]UFPI, [2]UFC

Introduction: Seaweeds are a source of sulphated polysaccharides, which are recognized as having biological activities. Thus, the objective of the study was to evaluate the antidiarrheal efficacy, the possible mechanisms involved in this effect and acute toxicity of the sulphated polysaccharide extracted from *Gracilaria intermedia* (SP-Gi) in rodents. **Methods:** Committee Research n° 11/2013. The antidiarrheal activity of SP-Gi (3, 10, and 30 mg/kg, *p.o*.) was evaluated for castor oil (10 ml/kg, *p.o*.) induced diarrhea and *enteropooling.* Sample of the small intestine was collected for Na^+/K^+-ATPase activity. Intestinal motility test was performed using 0.2 ml of charcoal (*p. o*.) as a marker of the distance traveled in the intestine. Gastric emptying was measured using the solution glycolic containing phenol red (300 µl, *p.o*.). To evaluate the secretory diarrhea, it was used method of isolation of intestinal loops inoculated with cholera toxin (CT) evaluating the parameters: fluid levels, chloride ions (Cl^-) and absorption. To evaluate the interaction between SP-Gi, CT and GM1 receptor was performed sandwich ELISA test. The action of SP-Gi was also evaluated on diarrhea induced by enterotoxigenic *Escherichia coli* (ETEC). The antibacterial activity of SP-Gi was tested against *E. coli* bacteria (ATCC 25922) by agar diffusion method. In addition, an acute toxicity study of SP-Gi was performed with clinical observation of the animals, analysis of biochemical parameters in blood, weight and histological analysis of organs (liver, kidney, heart, spleen). **Results**: SP-Gi (3, 10, 30 mg/kg) ($p<0.05$) reduced total faecal mass (mg) (9.65, 3.32, 1.3) and also ($p<0.05$) decrease total diarrheal feces (g) (9.31, 3.07, 1.0). SP-Gi (30 mg/kg) reduces intestinal fluid volume (34.04%). The activity of Na+/K+-ATPase in the small intestines ($p<0.05$) increased following the administration of the SP-Gi (30 mg/kg) (923.0 µmol $mg^{-1}h^{-1}$). The results suggest that, SP-Gi ($p<0.05$) reduces intestinal motility by inhibiting cholinergic receptors. The percentage of gastric retention of marker showed that the administration of SP-Gi not affect gastric emptying. SP-Gi decreased ($p<0.05$) CT-induced intestinal fluid secretion (0.03 g/cm), inhibited ($p<0.05$) CT-induced Cl^- secretion (100.60 mEq/L) and did not alter the intestinal fluid absorption. Incubation of GM1 with SP-Gi before incubation with CT ($p<0.001$) decreased the detection of CT by ELISA. SP-Gi treatment ($p<0.05$) inhibited (46.08%) the diarrhea ETEC induced and do not exert antibacterial activity against strains of *E. coli*. The maximal dose of 2000 mg/kg did not cause death or any toxic signs in treated female mice. The plasma levels of the enzymes AST, ALT and urea were not significantly different from respective controls. The assessment of organs did not reveal any abnormalities or difference in their mean weights. Likewise, the histological analysis of the organs also revealed no pathological changes between groups **Conclusion**: The low acute oral toxicity provide scientific support for the use of SP-Gi in the prevention and/or treatment of diarrhoeal diseases. **Financial support**: CNPq.

09.006 Effects of *Loxosceles intermedia* venom in rats skin Teixeira RGS[1], Ribeiro MF[1], Garcia TA[1], Gama LF[1], Bravo TP[1], Oliveira KC[1], Abreu VS[1], Souza CMV[2], Calil-Elias S[1] [1]UFF – Farmacologia, [2]IVB – Artrópodes

Introduction: Accidents caused by spiders of the genus Loxosceles represent an important public health problem in Brazil, being the major species of medical importance *L. intermedia*, *L. laeta* and *L. gaucho*. The venom of these spiders induces an intense dermonecrosis at the bite site, and less commonly, systemic disease that can be fatal. The mechanism of action of this venom is not fully elucidated, it is a multifactorial process, which involves the direct action of the venom on the tissues and the body's response to aggression caused by it. The rodents are an experimental model less susceptible to development the local effects of poisoning by Loxosceles spiders. Thus, their use is great clinical interest, whose goal is to unravel the mechanism of this protection in these animals. This study aimed to characterize the effect of *Loxosceles intermedia* venom in rat of different ages. ***Methods:*** The cutaneous lesions were induced on the backs of rats by intradermal injection of the *L. intermedia* venom. To describe the actions of the venom of *L. intermedia* in rat, it was proposed to use three different ages old: 1, 4 and 8 months. On days 3 and 30 after the spider venom inoculation the skin samples were obtained from the lesioned sites and processed for histopathological analysis. Manipulation and procedures with animals obeyed the principles of CEUA / UFF (Ethics Committee on Animal Use Universidade Federal Fluminense). **Results:** The results showed that lesion area at the site of venom inoculation was directly proportional to age old. For the group with 1 month old (n=4) was observed small lesion in 50 % of animals. In relation to 4 months group (n=4) was observed bigger lesion than the first group in 75% of animals. The group with 8 months old (n=4) showed lesion with large area after 3 days at 100% of the animals. Histopathological analysis of the site of venom intradermal inoculation showed significant differences, as intense vascular congestion in animals with 1 month and inflammatory infiltration at the site of inoculation in the rats skin with 4 and 8 months. At this last group was observed formation of thicker crust, without the presence of scarring in the skin after 30 days of venom inoculation. Histopathological analysis demonstrated regeneration of derme/epiderme without deposition of collagen in all groups after 30 days. **Conclusion:** This study demonstrated that rats with different ages may have different responses to inoculation of *Loxosceles intermedia* venom, being this result relevant for future investigations that relate the age and the protection of skin to the formation of injury due to poisoning. Financial support: CAPES, FAPERJ, CNPq *Process number (CEUA-UFF):* 417/2013

09.007 Evaluation of the renal profile of rats submitted to the subchronic treatment with the essential oil of *zingiber zerumbet*. Batista NY[1], Graça ACS[1], Candido K[1], Pessoa EV[1], Lima ES[2], Correa JWN[3] [1]UFAM, [2]UFAM – Ciências Farmacêuticas, [3]UFAM – Ciências Fisiológicas

Introduction: The essential oil of *Zingiber zemrubet* (OEZZ) has been widely used in the Amazon region for therapeutic purposes. However, there are no reports in the literature whether the use of this product induces hydroelectrolytic imbalances and renal changes. Thus, the objective of this study was to evaluate the renal profile of rats submitted to subchronic treatment with OEZZ. **Method:** Animals, Wistar rats, were divided into three groups (n = 6) who received orally the following treatments for 21 days: 50 mg / kg OEZZ; 100 mg / kg OEZZ; and distilled water for the control group. At the end of the treatment, 16-hour urine samples were collected from animals in a metabolic cage for 3 consecutive days for analysis of the biochemical parameters related to altered renal function. Control of urinary volume, feed intake and water was performed. **Results:** Animals submitted to subchronic treatment with OEZZ showed a decrease in creatinine (Control: 2.27 ± 0.8mg / dL, OEZZ50: 1.21 ± 0.7g / dL); urea(Control: 46.5 ± 5.17mg / dL, OEZZ50: 35.8 ± 2.2mg / dL, OEZZ100: 32.4 ± 6.2mg / dL) and calcium clearance (Control: 16.6 ± 1.3mg / DL; OEZZ50: 14.8 ± 3.6mg / dL, OEZZ100: 11.6 ± 3.7mg / dL), clearance. During treatment there were also no significant differences in feed and water intake. In the highest dose group, 100 mg / kg, two animals died with visible lesions in the liver on a macroscopic analysis. **Conclusions:** The essential oil of Z. zerumbet when used in a subchronic treatment promoted a decrease in the excretion of urea and creatinine levels at the doses tested, suggesting a possible impairment of renal function. Its effects may be indicative of possible hepatic overload that should be investigated in more detail as well as lethal toxicity at the highest dose tested. **References:** [1]RODRIGUES, K. et al. Antifungal Activity Of Brazilian Amazon Plants Extracts Against Some Species Of Candida Spp. Intern J Phytopharmacology, v. 5, n. 6, p. 445-53, 2014. **Financial support:** This research was funded by the Fundação de Amparo à Pesquisa do Estado do Amazonas and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior. The project was approved by the Animal Use Ethics Committee of the Federal University of Amazonas (CEUA-UFAM 001/2015). **Acknowledgments:** As units of development and the collaborators.

09.008 Effects of copaiba oil in dermonecrosis induced by *Loxosceles intermedia* venom. Ribeiro MF[1], Teixeira RGS[1], Garcia TA[1], Oliveira FL[2], Souza AM[1], Machado TB[1], Cardoso PF[3], Júnior SNS[3], Sobrinho AP[3], Nascimento AS[1], Souza CMV[3], Calil-Elias S[1] [1]UFF, [2]UFRJ, [3]IVB

Introduction*:* Envenomation caused by spiders *Loxosceles* represent an important public health problem in Brazil. This venom induces dermonecrosis at the bite site and systemic disease. Disagreement about the effectiveness of the antivenom serum in neutralization of local effects shows different therapeutic approaches. The use of plants from folk medicine can contribute to improve the local effects of envenomation. Therefore, this study verified the healing effect of copaiba oil in treatment of lesions induced by the venom of *Loxoceles intermedia* spider. ***Methods:*** Male albino rabbits (Oryctolagus cuniculus) were divided in control, venom and treated groups (n = 12 each one) and observed in three different times: 3, 10 and 30 days (n = 4 each group / each time). The cutaneous lesions were induced on the backs of rabbits by intradermal injection of 100 µL of the *L. intermedia* venom (4.8 µg/kg). To determine the dose of venom to be applied, three different doses of venom were tested intradermally on the back of rabbits (1.2, 2.4 and 12 µg of venom protein / kg of body weight). The lowest dose of venom capable of inducing a necrotic area of at least 1 cm^2 in 72 hours in 100% of the animals (n=4) is defined as Minimum Necrotic Dose (MND). The lesion analysis was performed by comparing the wound area in each experimental group. For this analysis the lesions were photographed by the Nikon COOLPIX L810 digital camera, 16.1 megapixels, maintained on a tripod at constant distance from the base. These images were analyzed through the program Image Pro Plus. Topical treatment with 1 mL of crude oil from *cobaifera* was performed 6 hours after injection of the venom and repeated for 30 days. On days 3, 10 and 30 after the spider venom inoculation and their respective treatments the skin samples were obtained from the lesioned sites and processed for histopathological analysis. All animals had blood collected, 0 and 24 hours after venom inoculation, for measurement hematological parameters. All animal procedures were performed in accordance with protocols approved by the Ethics Committee for the Use of Animals of the Vital Brazil Institute (CEUA-IVB). ***Results:*** The MND was defined as 2,4 µg/kg. Reduction in platelet counts occurred in all groups inoculated with venom, being significantly different from control group, with no significant difference between them. Decrease of heterophiles in the blood was observed just to venom without treatment. The topical treatment with copaiba oil demonstrated differentiated healing profile, lesion with large area was observed after 3 days and formation of thicker crust, without the presence of scarring in the skin after 30 days of venom inoculation. Histopathological analysis demonstrated a better regeneration of dermis/epidermis without deposition of collagen in the group treated with copaiba oil. ***Conclusion:*** Thus, we propose that copaiba oil could be a possible topical treatment of cutaneous lesions induced by *Loxosceles intermedia* venom, which may improve the healing process. *Financial suport:* CAPES, FAPERJ, CNPq *Process number (CEUA-IVB):* 01/2013

09.009 Evaluation of cardiorenal properties and acute toxicity of the *Luehea divaricata* an indigenous species from Brazilian pantanal. Tirloni CAS, Palozi RAC, Silva AO, Tomazetto TA, Schadler MI, Marques AAM, Gasparotto Junior A UFGD – Ciências da Saúde

Introduction: Although *Luehea divaricata*is is popularly used in the Brazilian pantanal for the treatment of different types of kidney diseases no study was carried out to prove this ethnobotanical indication. Our objective was to investigate the possible cardiorenal effects and acute toxicity of an herbal preparation popularly used in the Brazilian Pantanal. **Materials and Methods:** To prepare a purified aqueous extract from *L. divaricata* the dry leaves of were extracted by infusion (1:10 w/v). The infusion was treated with 3 volumes of EtOH, which gave rise to a precipitate and an ethanol soluble fraction (ESLD). Acute oral toxicity was performed after single administration of different doses (5, 50, 300, 2000 mg/kg) of ESLD in male and female Wistar rats. Then, we evaluated the diuretic and hypotensive properties of ESLD (30, 100, 300 mg/kg) after acute and prolonged treatment (seven days), and investigated the role of serum angiotensin converting enzyme (ACE), aldosterone, vasopressin, and redox state in these effects. All experimental procedures were approved by Institutional Ethics Committee of UFGD (protocol number 16/2015).Serum ACE activity was determined by indirect fluorimetry, aldosterone and vasopressin levels were measured by Enzyme Linked Immunosorbent Assay (ELISA, Immuno-Biological Laboratories, Inc), TBARS levels were measured using TBARS assay kits (Cayman Chemical, Ann Arbor, Michigan, USA) according to manufacturer's instruction. Finally, the plasma nitrite concentration was determined by enzymatically reducing nitrate according to technique described by Schmidt et al. (1989). **Results:** We did not observe any signs of toxicity in treated animals. Acute treatment with a single dose of ESLD significantly increased diuresis after 8 h (Control: 0.22 ± 0.06 ml/100g; ESLD 30, 100 and 300 mg/kg: 0.40 ± 0.03**;** 0.38 ± 0.05 and 0.41 ± 0.03 ml/100g, respectively; $p < 0.05$). After prolonged treatment ESLD (30 mg/kg) also showed a significant increase in urinary volume after 3, 5 and 7 days (third day = control: 22 ± 0.7; ESLD 30 mg/kg: 29 ± 0.2 ml/100g; fifth day = control: 31 ± 1.3; ESLD 30 mg/kg: 39 ± 1.7 ml/100; seventh day = control: 42 ± 1.1; ESLD 30 mg/kg: 54 ± 3.1 ml/100g; $p < 0.05$). Similarly, renal excretion of sodium and chloride were significantly increased in ELSD groups after acute and prolonged treatment. On the other hand, mean arterial pressure (control: 94 ± 2.9; ESLD 30 mg/kg: 71 ± 8.1; ESLD 100 mg/kg: 69 ± 4.2 mm Hg; $p < 0.05$) and systolic blood pressure (control: 110 ± 3.5; ESLD 30 mg/kg: 87 ± 7.3; ESLD 100 mg/kg: 81 ± 4.1 mm Hg; $p < 0.05$) were significantly reduced only after acute treatment. In animals treated with vehicle alone, TBARS levels were 6.2 ± 0.8 mmol/L. Treatment with ESLD at dose of 30 mg/kg was able to reduce TBARS levels to 3.7 ± 0.6 mmol/L. In addition, prolonged ESLD administration (30 mg/kg) was able to increase nitrite levels by ~ 45%. On the other hand, none of the ESLD doses were able to affect aldosterone and vasopressin concentrations or serum ACE activity. **Conclusion:** The data obtained showed that ESLD has an important diuretic and hypotensive effect, which is probably dependent on the reduction of oxidative stress and increased bioavailability of nitric oxide. **References:** Schmidt, H.H.H.W.,et al.;Enzymatic formation of nitrogen oxides from L-arginine in bovine brain cytosol. Biochem. Biophys. Res. Commun, vol.165, pag.278, 1989.

09.010 Pharmacological characterization of adenosine action in neuromuscular preparations *in vitro*. Schezaro-Ramos R, Hyslop S FCM-Unicamp – Farmacologia

Introduction: Adenosine 5´-triphosphate (ATP) is co-released with acetylcholine (ACh) from motor terminal nerves. In addition, skeletal muscle expresses a specific transport system for cyclic AMP (cAMP) efflux and an extracellular pathway for cAMP-adenosine metabolism that allows the sequential conversion of cAMP to adenosine (ADO). At mammalian neuromuscular junctions (NMJs), ADO can interact with adenosine receptors in the nerve terminal and skeletal muscle (inhibitory A_1 receptors and excitatory A_{2A} receptors), thereby modulating ACh release and muscle twitch tension. Although the role of ADO receptors in isolated nerve terminals and directly-stimulated skeletal muscle have been investigated, the precise physiological mechanisms involved in such interactions in the NMJ are still unclear. In this study, we investigated the effect of ADO on neuromuscular function mouse phrenic nerve-diaphragm (PND) preparations *in vitro***. Methods:** PND preparations removed from male Balb/c mice (~20 g) killed with an overdose of isofluorane were suspended in Tyrode solution that was aerated continuously at 37 ^{o}C. The preparations were stimulated indirectly (5 V, 0.2 ms) or directly (50 V, 2 ms, in the presence of 8.16 µM d-tubocurarine). ADO receptor agonists and antagonists were added to the bath and the PND twitch responses were recorded. The results were expressed as the mean ± SEM and statistical comparisons were done with Student´s *t*-test or one-way ANOVA followed by the Tukey-Kramer post-test; a value of $p<0.05$ indicated significance. **Results:** At low concentration (1 µM), ADO produced partial blockade (12.7 ± 3.7% blockade; n=6; $p<0.05$) in indirectly-stimulated PND, whereas higher concentrations caused concentration-dependent facilitation (4.9 ± 5.2% and 14.0 ± 2.7% facilitation by 10 and 100 µM, respectively; n=6; $p<0.05$). In directly-stimulated PND, ADO induced only neuromuscular blockade (25.4 ± 7.2%, 16.2 ± 9.1% and 13.3 ± 5.9% of blockade produced by 1, 10 and 100 µM, respectively; n=6; $p<0.05$); the decrease in blockade with increasing concentration probably reflected attenuation of this inhibition by the facilitatory action of ADO at higher concentrations. In contrast, 5′-(N-ethylcarboxamido)adenosine (NECA, 1-100 µM), an A_1 and A_{2A} receptor agonist, produced concentration-dependent blockade of both directly- and indirectly-stimulated PND, but without the twitch facilitation observed with ADO in indirectly-stimulated preparations. 8-Cyclopentyl-1,3-dipropylxanthine (DPCPX, 5 µM), an A_1 receptor antagonist, effectively prevented the blockade produced by ADO (100 µM) and NECA (100 µM) in directly- and indirectly-stimulated preparations. N6-Cyclopentyladenosine (CPA), an A_1 receptor agonist, produced concentration-dependent blockade of directly- and indirectly-stimulated preparations. **Conclusion:** These results indicate that ADO blocks neurotransmission in PND preparations probably through its action on inhibitory A_1 receptors, but the twitch tension facilitation seen with higher concentrations of ADO may be unrelated to an action on excitatory A_{2A} receptors. **Financial support:** CAPES, CNPq, FAPESP. **Ethical approval:** Committee for Ethics in Animal Use (CEUA/UNICAMP, protocol no. 4480-1/2017).

09.011 Evaluation of anti-inflammatory, antinociceptive, anxiolytic, antidepressant and anticonvulsant potential of hydroalcoholic extract of *Piper aduncum* L. (Piperaceae) in Swiss mice. Oliveira ACT[1], Aguiar MFR[1,2], Feitosa IB[1,3], Neves AB[1,2], Facundo AV[2], Dias QM[1,2] [1]Fiocruz-RO – Neuro e Imunofarmacologia, [2]UNIR, [3]IBCCF-UFRJ

Introduction: The *Piper aduncum* L. is an Amazonian plant of the Piperaceae family of type multi-trunk bush with approximately five meters of height and popularly known as mático. In traditional medicine this plant is used as analgesic, anti-inflammatory, antiseptic, anti-hemorrhagic, insecticide, molluscicidal and antitumor. However, there are few controlled experimental studies that confirm such pharmacological properties. In this sense, the present study evaluated whether the hydroalcoholic extract of *Piper aduncum* L. (HEPA) has antinociceptive, anti-inflammatory, anxiolytic, antidepressant and anticonvulsant properties in murine experimental models. **Methods**: The study used male Swiss mice (30 - 35g) provided by FIOCRUZ RO facility. Initially, the animals were pretreated by gavage with one of the HEPA doses (100, 500 and 1000 mg / kg) and, after one hour, subjected to one of the following tests: The formalin 1% test (nociception model), carrageenan 1% test (inflammation model), elevated plus maze test (anxiety model and locomotor activity), and pentylenetetrazol (PTZ)-induced seizure test. In the forced swim test (depression model), the animals were pretreated with HEPA gavage in regime of subchronic administration, this is, 3 successive injections of each dose (100, 500 and 1000 mg / kg) in the times 23.5h, 5h And 1h before the test. **Results:** The pretreatment with HEPA significantly reduced the number of nociceptive behaviors in the two phases of the formalin test of dose-dependent manner. In the second phase of the test, the HEPA completely abolished the nociceptive behaviors in the doses of 500 and 1000 mg / kg and significantly attenuated the behaviors at the dose of 100 mg / kg. The HEPA also significantly retarded the development of carrageenan-induced paw edema at the dose of 1000 mg / kg, but not the other doses. In the elevated plus maze test, the HEPA did not change significantly the number of entry into the open arms, at any of the doses tested, and significantly reduced the number of entry into the closed arms, total number of arms entrance and number of rearing behavior at the dose of 1000 mg / kg, but not the other doses. Lastly, the HEPA did not alter significantly the PTZ-induced clonic-tonic convulsion threshold and did not change swim and immobility time in the forced swim test at the doses tested. **Conclusion**: The study demonstrated that the HEPA has an intense antinociceptive effect in the nociceptive and inflammatory phases of the formalin test. In the doses of 100 and 500 mg / kg, but not at the dose of 1000 mg / kg, HEPA-induced antinociception probably does not result from motor impairment. The HEPA also had a discrete anti-inflammatory effect in the highest dose tested. Lastly, the results indicate that the HEPA does not present significant anxiolytic, anticonvulsant and antidepressant activity at the doses tested. Key words: Hydroalcoholic extract of *Piper aduncum*; antinociception; anti-inflammatory effect; anxiety effect; antidepressant effect; anticonvulsant effect. **Financial Support**: CNPq Research approval by Animal Research Ethical Committee (Protocol 2016-03)

09.012 Effects of bergenin tratament on the activation of inflammatory mediators on TNBS-induced acute colitis. Oliveira GAL[1], Chaves LS[2], Sousa FBM[1], Pacheco G, Rosillo MAR[3], Martinez MLC[3], Hidalgo MS[3], Villegas I[3], Medeiros JVR[2], Lastra CA[3]
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Introduction: The bergenin (BG) is one of the main active constituents of plants of the genus *Peltophorum*, is classified as C-glycoside derived from 4-O-methyl gallic acid. This compound presents pharmacological properties such as antibacterial activity, antitumor and antidiabetic. The colitis are intestinal inflammatory diseases (IBD) characterized by the presence of ulcers in the colon. This disease not have specific treatment, because the most commonly drugs used to treat of colitis are associated with low therapeutic efficacy and adverse effects, hence this study investigate the anti-inflammatory effect of BG an TNBS-induced acute colitis in rats. **Methods:** Male Wistar rats were randomized into groups for evaluating the effect of bergenin on colitis induced by TNBS: Control (saline), TNBS control, TNBS+BG 25 (25mg/kg) and TNBS+BG 50 (50mg/kg). Was assessed different inflammatory parameters: Macroscopic and histopathological evaluation, assessment of leukocyte involvement and inflammation mediators quantification. **Results:** The groups of animals treated with TNBS+BG at doses of 25 and 50 mg/kg showed lower weight loss (-14.98 ± 3.2 and -17.63 ± 3.8) compared to the TNBS control (-24.18 ± 1.9). The BG also reduced significant the macroscopic damage score (TNBS+BG25 = 5.62 ± 0.18; TNBS+BG50 = 4.62 ± 0.18 and TNBS control = 9.75 ± 0.16), adhesions score (TNBS+BG25 = 1.12 ± 0.1; TNBS+BG50 = 0.37 ± 0.1 and TNBS control = 2) and diarrhea score (TNBS+BG25 = 0.87 ± 0.1; TNBS+BG50 = 0.75 ± 0.1 and TNBS control = 1), suggesting lower inflammation. In the histological sections obtained from the groups treated with BG at doses of 25 and 50 mg/kg it was possible to observe a reduction of the inflammation, the preservation of the glandular structure, presence of mucus and little inflammatory infiltrate. With regard to inflammatory mediators, the groups treated with BG had significantly lower expression levels of STAT3, iNOS, COX-2, IL10, IL-1β and IFN-γ compared to the TNBS. The BG also increases the levels of the Ikb-α in relation to the TNBS group. TNBS produced a significant increase of NALP3 and ASC proteins expression; however, BG treatment was capable to revert the changes. We observed that pro-caspase 1 expression and cleaved caspase-1 was increased significantly in TNBS group while the two forms was significantly decreased after BG tratament. TNBS is capable to up-regulate caspase-11 (pro-caspase, partially cleaved and cleaved forms), and the BG tratament in both doses studied was capable to downregulate of this procaspase. Our results also demonstrated that the BG treatment significantly reduced IL-18 protein expression. **Conclusion:** Our study has provided evidence that the bergenin reduced the damage caused by TNBS in an experimental model of acute colitis in rats, reduced levels of pro-inflammatory proteins and cytokines probably by blocking canonical and non-canonical inflammation pathways. **Support:** CAPES, CNPq, FAPEPI. CEP: European Council Directive 2010/630 / EU

09.013 Antinociceptive and anti-inflammatory evaluation of ethanolic crude extract of P1 (EEP1) in rodents Freitas BR[1], Lopes KS[1], Queiroz LY[1], Souza PHFS[1], Santos RR[1], Oliveira JP[2], Silva CYY[2], Silva MN[2], Fontes-Júnior EA[1] [1]UFPA – Pharmaceutical Sciences, [2]UFPA – Organic Chemistry

Introduction: P1 is a medicinal plant native of the tropical and subtropical zones, such as the Amazon area. In traditional medicine, this plant is used to treatment of inflammatory disorders. **Objective:** To investigate the effects of the ethanolic crude extract of P1 leaves (EEP1) in reliable animal models of nociception and inflammation. **Material and methods:** Dried leaves were macerated with absolute ethanol. Then, the extract was filtered and concentrated by rotary evaporation to obtain EEP1. After the acute toxicity test (AT), antinociceptive effect was evaluated by acetic acid-induced writhing teste (WT) and formalin test (FT) in mice. The anti-inflammatory activity was evaluated by carrageenan (CPE)- and dextran (DPE)-induced paw edema tests in rats. Additionally, sedative effect of the EEP1 was investigated in the open field test (OF). EEP1 and vehicle were administered orally by gavage, while morphine, indomethacin and cyproheptadine were given subcutaneously. The groups and its doses for each test are described below: AT (n=5/group) test EEP1 (2000 mg/kg) and control group (CG) with vehicle. WT (n=6/group) EEP1 test groups (25, 75, 200 e 400 mg/kg), CG and indomethacin (10 mg/kg). FT (n=6-8/group): EEP1 (242.661 mg/kg), CG and morphine (4 mg/kg, s.c.). OF (n=8/group): EEP1 (242.661 mg/kg) and CG. CPE (n=6/group): EEP1 (242.661 mg/kg), CG and indomethacin (10 mg/kg). DPE (n=6/group): EEP1 (242.661 mg/kg), CG and cyproheptadine (10 mg/kg). Ethical committee (CEPAE 62-2015) approved all procedures. Statistical analysis was performed using Student's t-test, and one-way ANOVA with Tukey's post hoc test. $P < 0.05$ were considered as statistically significant. **Results:** Acute oral administration of EEP1 (2000 mg/kg) showed low toxicity profile. In WT, the EEP1 exhibited concentration-dependent inhibition for the noxious stimulus, respectively 27.36, 38.05, 46.54 and 55.98% of inhibition, achieving similar results compared with indomethacin 10 mg/kg (69.81%), and its half maximal inhibitory concentration value (IC50) was 242.661 mg/kg. EEP1 promoted antinociceptive activity in both phases of FT, with 24.23% and 35.97% decrease of of the time that the animals spend licking their paw, respectively. EEP1 did not interfere on spontaneous locomotor activity in OF. In CPE, EEP1 weakly inhibited the edema formation, presenting difference with the control group (44,39%) and equivalent to indomethacin (61,2%) only in the fifth hour of evaluation. Additionally, it not interfered in the development of edema in DPE. **Conclusion:** These data indicate for the first time that EEP1 has a weak peripheral antinociceptive and anti-inflammatory activity in animal models, corroborating with the traditional use of P1. These results suggest that EEP1 contains substances that are involved in the inhibition of several inflammatory mediators, however, probably in low concentrations. **Financial support:** UFPA, CNPq and CAPES. **P.S.:** The references for this work are not listed due to patent process of this study.

09.014 *Dilodendron bipinnatum* Radlk. extract inhibits TNF-α independently of IL-8 in LPS-activated Caco-2 cells. Ferreira LA[1,2], Martins DTO[3], Miyajima F[4], Oliveira RG[2,1 1]UFMT – Basic Sciences in Health, [2]UNIC – Pharmacy, [3]UFMT – Basic Sciences in Health, Faculty of Medicine., [4]UFC – Neuropharmacology, Drug Research and Development Center

Introduction: *Dilodendron bipinnatum* (Db), Sapindaceae, popularly known as "mulher-pobre", whose inner stem bark is used by Pantanal riparian in the forms of infusion and maceration to treat inflammatory conditions. We have recently shown that the hydroethanolic extract from the inner stem bark of Db (HEDb) inhibits the production of pro-inflammatory cytokines IL-1β and TNF-α, as well as MAPK p38 and JNK, NF-κB and COX-2 in RAW 264.7 cells exposed to LPS. IL-8 and TNF-α are both strong pro-inflammatory mediators in both acute and chronic stages of intestinal and systemic inflammatory disease states and Caco-2 cell lines from human epithelial colorectal adenocarcinoma cells have been largely used as in vitro models for the mechanistic investigation of intestinal inflammation. To investigate the anti-inflammatory activity of HEDb mediated by TNF-α and IL-8 in LPS-stimulated Caco-2 cells. **Methods:** Confluent Caco-2 with density of $3x10^5$ cells were plated onto a 12-well microplate overnight. The cells were pre-treated with either HEDb (1, 5 or 20 µg/mL), or dexamethasone (10 µg/mL) for 1 h and stressed with LPS for 24 h. The cells were harvested and washed twice with cold PBS and incubated with Annexin V and 7-amino-actinomycin D (7-AAD). Both cell viability and fluorescence intensity were evaluated by flow cytometry. The quantitation of both TNF-α and IL-8 was performed by ELISA (pg/mL) using the cell supernatant. Results and **Conclusion:** HEDb, LPS and dexamethasone all demonstrated to be non-cytotoxic with viability to Caco-2 cells above 80%. The concentration of TNF-α in response to LPS was significantly higher when compared to basal conditions (17.3 ± 1.68 pg/mL versus 1.83 ± 0.39 pg/mL; $p<0.001$). Pre-treatment with HEDb (1, 5 or 20 µg/mL) reduced TNF-α levels by 21.8% ($p<0.01$), 60.5 and 82.1% ($p<0.001$), respectively, in relation to the LPS treated group only. Dexamethasone, the standard drug used for the assay, inhibited TNF-α concentration by 81.0% ($p<0.001$). As expected, treatment with LPS for 24 h accounted for over two-fold increase in the levels of IL-8 (292.6 ± 11.90 pg/mL) compared to non-stimulated cells (124.5 ± 2.34 pg/mL, $p<0.001$). The pre-treatment with all three concentrations of HEDb did not reduce the levels of IL-8 ($p>0.05$), whilst dexamethasone inhibited in 34% ($p<0.001$). The HEDb exerts its anti-inflammatory in vitro activity at least, in part, by inhibiting TNF-α but not IL-8. INAU-INCT/CNPq, FAPEMAT, CAPES/Pró-Amazônia and UFMT. Reference: de Oiveira RG. Dilodendron bipinnatum Radlk. inhibits pro-inflammatory mediators through the induction of MKP-1 and the down-regulation of MAPKp38/JNK/NF-κB pathways and COX-2 in LPS-activated RAW 264.7 cells. J Ethnopharmacol. 202:127-137, 2017.

09.015 Endothelium-independent vasorelaxant effect of MTHP is mediate by potassium channels opening in rat thoracic aorta. Oliveira S[1], Souza Neta OAC[1], Sarmento DV[1], Rodrigues LC[2], Braga VA[2], Vasconcelos U[2], Travassos RA[3] [1]UFPB, [2]UFPB – Biotecnologia, [3]UFPB – Biologia Celular e Molecular

Introduction: The natural products are a rich source of compounds for the discovery of new drugs. The importance of these natural products in the discovery and inspiration drug is proven and their synthesis is of significant interest (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). A new synthetic derivative of the isoquinoline alkaloids, 1-(3-methoxy-4-hydroxyphenyl)-7-methoxy-1,2,3,4,tetrahydroisoquinoline (MTHP), was obtained by the Pictet-Spengler reaction. We aim to verify the vasorelaxant activity of MTHP in rat aorta without functional endothelium, investigating a possible participation of the potassium channels in this effect. **Methods:** Male Wistar rats (*Rattus norvegicus*) were obtained from Bioterium Prof. Thomas George of IPeFarM/UFPB. All rats were euthanized by decapitation with guillotine. The aortic rings about 3-5 mm wide were obtained from the thoracic aorta. To obtain isometric responses, the rings were individually suspended on stainless steel rods in organ baths (10 mL) containing Krebs 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 was expressed as the reversal percentage of the initial contraction elicited by contractile agent and EC50 values were obtained by nonlinear regression. All procedures were approved by the UFPB Ethics Committee on Animal Use (Protocol/CEUA nº 0605/13). **Results:** The vasorelaxant activity of MTHP in rat aorta with intact endothelium (EC50 = 5.7 ± 1.1 x 10^{-5} M, n = 5) was attenuated around 3.3 fold in the presence of TEA+ 5 mM (EC50 = 3.8 ± 0.8 x 10^{-5} M, n = 5), a non-selective blocker of K+ channels. Interestingly, the relaxant curve of MTHP was not altered in presence of glibenclamide, K_{ATP} blocker (EC50 = 8.2 ± 1.7 x 10^{-5} M, n = 5) and $BaCl_2$, K_{ir} blocker (EC50 = 7.9 ± 2.2 x 10^{-5} M, n = 5). However, in the presence of TEA^+ 1 mM, BK_{Ca} blocker (EC50 = 2,3 ± 0,5 x 10^{-4} M, n = 5), apamin, SK_{Ca} blocker (EC50 = 1.9 ± 0.3 x 10^{-4} M, n = 5) and 4-AP, K_V blocker (EC50 = 1.5 ± 0.3 x 10^{-4} M, n = 5) the relaxation action was decreased on 4, 3,3 and 2,6 fold, respectively. **Conclusion:** In conclusion, the relaxant effect of MTHP appears to be due to activation of K+ channels and the subtype BK_{Ca}, SK_{Ca} and K_V can be involved in spasmolytic effect of this alkaloid in rat aorta without functional endothelium. Complementary studies in functional and molecular levels are needed to fully elucidate the mechanism of relaxation produced by MTHP in rat aorta. **Key-words:** isoquinoline alkaloid, endothelium-independent, aorta, potassium channels. **Financial support:** UFPB/CNPq/CAPES **Animal Research Ethical Committee:** 0605/13

09.016 Cytotoxic potential of Pradimicin T in Cancer Cells Almeida LC[1], Bauermeister A[2], Santos EA[3], Moraes LAB[2], Costa-Lotufo LV[1] [1]ICB-USP – Farmacologia, [2]FFCLRP-USP – Química, [3]ICB-USP – Biologia Celular e Desenvolvimento

Introduction: Cancer is one of the diseases with the highest mortality rate. Natural products are an important source of new compounds and have great participation in drug discovery programs. In this context, study aims to evaluate the cytotoxic effects of a pradimicin analogue. Pradimicins are produced by actinobacteria and have their molecular structure based on an aglycone of naphthacenequinone with an aminoglycoside moiety. The analyzed pradimicin analogue (Pradimicin T), produced by actinobacteria *Amycolatopsis* sp. IRD-009, has mainly the D-amino acid replaced by a methoxyl besides other structural modifications. Previous works on this class of substances demonstrated its antifungal and antiviral properties; however, its antitumor activity has not yet been evaluated. **Methods:** Cytotoxicity evaluation of Pradimicin T (0.0032 to 50 µM) was performed by MTT assay against four cell lines: HCT-116 (colorectal carcinoma), MM 200 (melanoma), MCF-7 (breast carcinoma) and RPE (normal retinal cells), using doxorubicin as positive control. IC50 values along with 95% confidence intervals were calculated by nonlinear regression using GraphPad Prism 5. To analyze the mechanism underlying cytotoxic action, assays were performed in HCT 116 cell lines, after 48 hours of treatment with 1.25 µM, 2.5 µM, and 5 µM concentrations. Exclusion tripan blue assay was applied, as well as panotic stain to investigate the cell membrane integrity and cell morphology, respectively. Optic and confocal microscopy were used. Flow cytometry was used to assess the cell cycle; the results were analyzed with FlowJo software. Statistics were performed by analysis of variance (ANOVA), followed by the Tukey's test, performed by the software "Graphpad Prism 5". **Results:** The IC_{50} values of Pradimicin T ranged from in 0.8 µM in HCT 116 to 2.7 µM in MM 200 cells. Furthermore, Pradicimin T showed a concentration and time dependent cytotoxicity in HCT-116 with IC_{50} values of 15.2 µM and 4.5 µM, after 24 and 48 hours, respectively. Regarding the cell cycle, the evaluated molecule did not demonstrate any significant difference in the cell cycle phases (G1: 42.8 ± 2.8%; S: 25.0 ± 1.4; G2: 15.6 ± 0.9) in comparison to the control (G1: 46.8 ± 2.4%; S: 27,2 ± 1.8%; G2: 17,9 ± 1.3%). There was a reduction in the cell density (1.25 µM – 28.9 %; 2.5 µM – 47.2%; 5 µM – 53.3%) and in the number of viable cells (1.25µM - 33.3%; 2.5 µM – 47.2%; 5µM - 50.6%) in a concentration-dependent manner, but with no increase of non-viable cells. Morphologic analysis showed cell body reduction in all Pradimicin T treatments. **Conclusion:** Pradimicin T has a potential antitumor activity, especially against colorectal carcinoma cell line. Preliminary results on the mechanism of cytotoxic action indicated a cytostatic rather than cytotoxic effect of the compound. Further studies will be performed in order to characterize the molecular target of Pradimicin T. **Financial support:** CAPES, CNPQ (pro-arquipélago and INCTBioNat) and FAPESP (2015/17177-6)

09.017 *Zingiber zerumbet* promotes arterial vasodilation by blockade of calcium influx. Graça ACS[1], Batista NY[1], Pessoa EV[1], Pinheiro CCS[2], Correa JWN[3] [1]UFAM, [2]Inpa, [3]UFAM – Ciências Fisiológicas

Introduction: The essential oil of the rhizomes of Zingiber zemrubet (OEZz), together with Zerumbone (Zer), its main constituent, has revealed anti-inflammatory and antioxidant activities[1]. However, its effect on vascular function remains to be investigated. Thus, the objective of this work was to evaluate the biological effect of OEZz and Zer on the vascular responses observed in aortic rings of normotensive rats. **Methods** The essential oil was extracted from Zingiber zerumbet rhizomes by hydro distillation. The presence of Zer in OEZz was identified by gas chromatography coupled to mass spectrometry (GC-MS). The chromatographic isolation of Zer was achieved using ultra high-performance liquid chromatography. To evaluate vascular function, experiments were performed on isolated aortic rings of Wistar rats using different concentrations of OEZz and Zer (0,001-1000µg/ml). **Results** It was observed that Zer was the major constituent (83.52%) of OEZz. The concentration-effect curves showed a vasodilatory effect dependent on OEZz concentration and independent of the presence of endothelium, with similar potency and efficacy of OEZz in rings with (EC_{50}=622,72 µg/mL, Emax=102,45; N=7) and without vascular endothelium (EC_{50}=771,21 µg/mL; Emax=104,15; N=7). Zer demonstrated a vasodilator effect dependent on its concentration. However, its potency and efficacy (EC_{50}=90,80µg/mL; Emax=86.79; N=6) were significantly lower than those observed for OEZz ($p<0,05$). Preincubation of aortas with OEZz or Zer (1000µg/mL) completely blocked phenylephrine-induced vasoconstriction ($p <0.0001$ vs. control). In another protocol, after intracellular calcium depletion, OEZz reduced in 20% the potency and 75% the efficacy of calcium-mediated vasoconstriction in rings pre-incubated with phenylephrine (10^{-7}M) or KCl (60 mM). In this protocol, Zer reduced in 15% the potency of calcium-mediated vasoconstriction without modifying its efficacy. **Conclusion** The essential oil of Z. zerumbet and its main compound Zerumbone has demonstrated a concentration dependent vasodilator response in aortic rings of Wistar rats that were independent of the integrity of the vascular endothelium. The vasodilatory effects may be justified by the ability of Zerumbone to promote calcium channel blockade in vascular smooth muscle cells. In view of the potential vasodilatory, anti-inflammatory and antioxidant activities described, further studies of OEZz and Zer should be conducted to elucidate its potential for the treatment of cardiovascular disorders such as arterial hypertension and vascular dysfunction. **References** 1- SIDAHMED, H. Antisecretor, gastroprotective, antioxidante e anti-helicobcter pylori atividade de zerumbone de Zingiber Zerumbet (L.) Smith. PloS one, v. 10, p. E0121060, 2015. **Financial support** Fundação de Amparo à Pesquisa do Estado do Amazonas and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior. The project was approved by the Animal Use Ethics Committee of the Federal University of Amazonas (CEUA-UFAM 001/2015). **Acknowledgments** We would like to acknowledge the Pharmacology Laboratory- FCFRP, in the person of Dr. Lusiane Maria Bendhack, which allowed us to perform part of the experiments reported here.

09.018 Latex proteins from *Plumeria pudica* ameliorates acetic acid-induced ulcerative colitis. Oliveira NVM, Souza BS, Moita LA, Oliveira LES, Brito FC, Barbosa ALR, Magalhães DA, Batista JA, Sousa SG, Oliveira JS UFPI

Introduction: Latex is a fluid produced by laticifer cells that is released some plant species after they suffer mechanical injury. Plumeria pudica is a laticifer plant belonging to Apocynaceae family that is widely found in northeastern Brazil. Recent studies have demonstrated that a protein fraction obtained from P. pudica latex (LPPp) have anti-inflammatory, antinociceptive and anti-diarrhoeal effects[1]. Thus, based on pharmacological properties detected in LPPp, this study aimed to evaluate the protective effect of this protein fraction on acetic acid-induced colitis in mice. **Methods:** Male mice (Mus musculus, 25-30g) were starved for 14-15h prior to the experiment. Colite was induced by intrarectal instillation of 200 µl 6% acetic acid solution[2]. Animals were treated with LPPp (10, 20 or 40 mg/kg i.p.) 1 hour before and 17hours after acetic acid injection. One hour after second LPPp treatment, animals were euthanized and the portion of distal colon was excised for evaluation of macroscopic scores of lesion, wet weight analysis and myeloperoxidase (MPO) measurement[3]. Data were expressed as mean ± S.E.M. and $p<0.05$ was considered significant (ANOVA and Student Newman Keul's test). **Results:** pre-treatment of animals with LPPp 10 mg/kg (0.28 ± 0.03 g/5cm), 20 mg/kg (0.28 ± 0.01 g/5cm) or 40 mg/kg (0.23 ± 0.00 g/5cm) reduced the colon wet weight compared to acetic acid group (0.30 ± 0.02 g/5cm). The scores of macroscopic lesion of animals treated with LPPp 10 mg/kg (11.8 ± 3.40), 20 mg/kg (13.6 ± 0.97) or 40 mg/kg (8.81 ± 1.47) were reduced when compared with the animals receiving only acetic acid (16.85 ± 2.19). In addition, different doses of LPPp were also able to reduce significantly the MPO activity, mainly the group treated with 40 mg/kg (4.29 ± 1.41 UMPO/mg of tissue) in comparison to acid acetic group (67.93 ± 9.83 UMPO/mg of tissue). Conclusions: These results suggest that LPPp presented protective effect against intestinal damage induced by acetic acid. This effect may be due to reducing macroscopic lesion and wet weight and by decreasing the neutrophils infiltration to the site of lesion. **Financial Support**: CNPq and CAPES. Animal Ethics Committee Number: 037/15-UFPI. References: [1]FERNANDES, H.B. Rev. Bras. de farmacogn. v. 25, p. 269, 2015. [2]MORRIS, G.P. Gastroenterol. v. 96, p. 795, 1989. [3]BRADLEY, P. P. Blood, v. 60, p. 618, 1982.

09.019 Toxicological assessement of proteins of *Plumeria pudica* latex in mice. Souza BS, Oliveira NVM, Moita LA, Oliveira LES, Brito FC, Oliveira JS UFPI

Introduction: *Plumeria pudica* is plant belonging to Apocynaceae known by its intense latex production. The plant is found abundantly in northeastern Brazil, where its latex is mentioned by the poor population to be used for the treatment of skin diseases and tooth pain. Recent studies have demonstrated that a water soluble protein fraction recovered from P. pudica latex (LPPp) have anti-inflammatory, antinociceptive, anti-diarrhoeal and antiulcerative properties. In these studies, the authors have demonstrated that pharmacological properties are reached when 40 mg/kg of LPPp is administered by intraperitoneal route[2]. Thus, the present study was designed[1,2,3] to assess the toxicological effects of acute and subchronic treatment of animals with continuous administration of 40 mg/kg LPPp. **Methods:** For the acute and subchronic toxicity tests, mice received a daily dose of 40 mg/kg of LPPp or saline 0,9 % (i.p.) for 10 or 20 consecutive days, respectively. Every single day throughout the treatment, animals were weighted and checked to observe mortality. At the end of the period, the blood of animals were collected for biochemical (AST and ALT levels, creatinine and urea content), hematological parameters (total and differential cell count) and animals were euthanized. The internal organs (liver, spleen and kidney) were removed, weighted used to measure the levels of reduced glutathione (GSH), malondialdehyde (MDA) and myeloperoxidase activity (MPO). Differences were checked ANOVA followed by Newman-Keuls Test. $P < 0.05$ was set as the level of significance (SEM). **Results:** No significant changes were observed in the body and organs weight of animals treated with LPPp and control saline during 10 or 20 days of administration. Total and differential leukocyte count did not present significant difference between groups treated during 10 or 20 days with LPPp when compared to saline. Blood biochemical parameters revealed significant increase of AST in the group treated with LPPp during 10 days compared to saline control. However, AST level significantly reduced after 20 days of LPPp treatment. There was no significant difference on ALT, creatinine and urea measurements among saline and PLPp treatment for 10 or 20 days. Kidney GSH level was slight higher in animals treated with LPPp during 10 days, however values returned to near normal after 20 days treatment. MDA and MPO levels in liver, spleen and kidney did not present significant difference among 10 or 20 days of LPPp treatment in relation to saline group. **Conclusion:** This study suggests that LPPp administered in the dose of 40 mg/kg have low toxicity in acute and subchronic administration. Further studies are required to provide sufficient safety evidence for LPPp use. **Financial Support**: CNPq/CAPES. This work was approved by the Animal Research Ethical Committee of UFPI (number 037/15). References:[1] Akindele, A. J. et al. J. Ethnopharmacol. 174 (2015) 582–594. [2] Fernandes, H. B. et al. Rev. Bras. de Farmacogn. 25 (2015) 269–277. [3] Li, F et al. J. Ethnopharmacol. 175 (2015) 499–508.

09.020 Antioxidant activity and vascular relaxation of selected red grape juices produced in different Brazilian regions. Britto Junior J, Leite KCS, Gil ES, Rocha ML UFG – Ciências Farmacêuticas

Introduction: Polyphenol-rich diets, food, and beverages, especially red wine and grape juice, have been shown to have a protective effect against cardiovascular diseases because of high antioxidant potential and vascular relaxing activity. In this work, we investigated the antioxidant potential of 6 commercially available red grape juices (without added sugar, water or preservative) produced in different Brazilian states: RS (2 samples: RS_1 and RS_2), RJ, GO, PR and SP. In addition, the *in vitro* vascular relaxation and the participation of endothelial nitric oxide (NO) in this response were evaluated. **Methods:** The total phenolic content was estimated using the Folin–Ciocalteu reaction (expressed as the milligram gallic acid equivalent (GAE)/mL). The antioxidant capacity of the samples was evaluated by the ABTS radical cation decolorization assay, DPPH (1,1-diphenyl-2-picrylhidrazine) assay and a novel electroanalytical approach (differential pulse voltammetry – DPV). The relaxing effects of the juice samples were analyzed using isolated rat aorta (n=6 for all protocols) prepared to isometric tension recordings in an organ bath. The pre-contracted arteries (phenylephrine, 0.1 µM) with or without L-NAME (100 µM, 30 min) were stimulated to relax by increasing juice concentration in the bath solution (0 to 30 µL/mL). **Results:** The sample from RJ and SP presented higher and lower phenolic content, respectively (2.25 ± 0.06 and 1.26 ± 0.08 µg GAE/mL, $p<0.01$). In the same way, the ABTS assay have shown better and worse results to RJ and SP samples, respectively (EC_{50}: 0.59 ± 0.11 and 1.25 ± 0.19 µL, $p<0.05$). The other samples presented similar results to ABTS as compared to RJ sample (order of antioxidant activity: GO: 0.65 ± 0.01 > RS_1: 0.83 ± 0.10 > PR: 0.90 ± 0.13 > RS_2: 0.91 ± 0.18 µL). With respect to the DPPH radical scavenging activity, it could be implied that RJ, GO, RS_1 and RS_2 samples have the same potential. However, the SP and PR samples were significantly weaker potential. Indeed, in the voltammetric profiles, the RJ sample presented bigger electrochemical index (21.69 ± 3.15 µA/V) and the SP sample showed the smaller (13.30 ± 0.52 µA/V), distinguishing as better (RJ) and worse (SP) radical scavenger activity. In the vascular studies, the relaxation induced by the samples was very disparate. Equally observed in the antioxidant analyses, the RJ sample presented superior relaxation (87.9 ± 4.8%), followed by RS_1 (71.6 ± 8.6%) > GO (56.2 ± 7.2%) > SP (39.9 ± 7.8%) > PR (39.4 ± 9.5%) > RS_2 (19.5 ± 6.2%). The NO inhibition provoked by L-NAME practically abolished ($p<0.001$) the relaxation for all samples, except to RS_2 (19.5 ± 6.2 to 15.8 ± 3.7%). **Conclusion:** The results obtained by means of spectroscopy and electroanalytical techniques were all consistent with the expected results for beverages evaluated in this study. The results obtained for the order of antioxidant activity was: $RJ>RS_1>GO>RS_2>PR>SP$. The juices were able to induce vascular relaxation indifferent degrees. Moreover, the mechanism of action also was different among the selected juices studied here. **Financial support:** FAPEG and CNPq. Research approval by Animal Research Ethical Committee (CEUA/UFG: protocol 015/2014).

09.021 Effects of the infusion of *Terminalia catappa* leaves on treatment of duodenal injury induced by ischemia-reperfusion in female rats. Ohara R, Périco LL, Rodrigues VP, Santos BB, Santos RC, Santos LC, Vilegas W, Rocha LRM, Hiruma-Lima CA Unesp-Botucatu

Introduction: *Terminalia catappa* L. is a medicinal plant known in Brazil as "chapeu de Sol" used in folk medicine against hepatitis, diarrhea and gastritis. Its major compounds are tannins, molecules with high antioxidant potential, which can be effective against ischemia-reperfusion induced lesion. This study was performed in female rats aiming to verify if there is an influence of female hormones in the healing process. **Methods:** The experimental model was performed in intact and ovariectomized female Wistar rats. The duodenal ulcers were induced by ischemia-reperfusion (I/R) according to the method described by Ueda et al[1]. The animals were divided in groups treated with infusion of *Terminalia catappa* leaves (ILTC) (30 mg/kg), lansoprazole (30 mg/kg) or vehicle (saline 0,9%; 10 mL/kg) administered orally during 6 days succeeding the reperfusion, and a Sham group. After the 6th day of treatment, the rats were killed and the duodenum was removed for analysis of biochemical parameters such as superoxide dismutase (SOD)[2], myeloperoxidase (MPO)[3], malondialdehyde (MDA)[4], catalase (CAT)[5] and reduced glutathione (GSH)[6]. The results are expressed as mean ± S.E.M. Statistical significance was determined by ANOVA followed by Student's t test or Dunnett's ($p<0.05$). **Results:** The treatment with ILTC was able to reduce MPO levels in both groups, intact (23%) and ovariectomized (17%) rats. Only in ovariectomized animals, the MDA levels increased by 15% with the treatment with ILTC. Comparing ovariectomized and intact groups, the MPO levels increased in intact animals treated with ILTC (12%). The SOD activity increased in all ovariectomized groups comparing to intact rats. The MDA levels increased with all treatments in intact animals except Sham group and the GSH levels augmented in ovariectomized animals treated with ILTC (31%). **Conclusion:** The ILTC is able to reduce MPO levels in the injury induced by ischemia and reperfusion in intact and ovariectomized groups showing an anti-inflammatory action, but did not show an antioxidant effect. **Financial Support**: CAPES Animal Research Ethical Committee: Protocol number 906 References: [1] UEDA, S. et al. Scan. J. of Gastr. v. 162, p. 55, 1989. [2] WINTERBOURN, C.C. et al. J Lab Clin Med. v. 85 p. 337, 1975. [3] KRAWISZ, J.E. et al. Gastroenterol. v. 87 p. 1344, 1984. [4] OHKAWA, H. et al. Anal Biochem. v. 95 p. 351, 1979. [5] AEBI, H. Methods Enzymol. v. 105 p. 121, 1984. [6] ANDERSON, M.E. Methods Enzymol. v. 113 p. 548, 1985.

09.022 Anticancer potential of marine microorganisms from Baixada Santista. Rigato DB[1], Chain BG[1], Souza BV[1], Domingos HV[2], Costa-Lotufo LV[3], Branco P[2], Jimenez PC[1] [1]Unifesp – Ciências do Mar, [2]ICB-USP – Farmacologia, [3]USP – Farmacologia

Introduction: According to data from WHO, by the year 2030, over 13 million deaths should occur as a consequence of cancer. Despite the current therapeutic arsenal, mortality due to this disease remains unacceptably high. Therefore, it is important to search for new molecules that provide more effective and selective anticancer treatments. The oceans are proving to be an immeasurable source of new molecules with pharmacological applications, especially among microorganisms from the diverse Actinobacteria class. Herein, this study conducted an examination of the anticancer potential of extracts produced by marine actinobacteria recovered from sediments collected in the coast of São Paulo, in the region of Baixada Santista. **Methods:** Sediment was collected at 2 points off the coast of São Paulo (1– São Vicente Marina and 2– Santos Ferry), stored in sterile whrilpack bags and frozen until processing. Sediment samples were processed by two methods prior to inoculation (M1- desiccation and stamping on agar; or M2- heating and striking on agar). Moreover, three culture media (one rich in nutrients, one intermediary and one poor) were used. Selected individualized colonies were transferred to fresh agar dishes and purified strains were grown in liquid media, under agitation during 5 to 10 days. An aliquot of this broth was homogenized in glycerol for cryopreservation while the remainder was extracted using ethyl acetate. Extracts were then analyzed for cytotoxicity against HCT-116 cells (human colorectal carcinoma) using the MTT assay at two concentrations (5 mg/mL e 50 mg/mL). Extracts that inhibited greater than 70% of cell growth in the highest concentration were considered active. Moreover, selected extracts were evaluated in a quantitative approach, tested in concentrations from 0.0032 to 50 mg/mL to determine their respective IC_{50} from a concentration x effect curve. **Results:** 36 strains were recovered from São Vicente Marina, while Santos Ferry rendered 32 strains. For location 1, 67% of strains were isolated by M2, whereas, for location 2, M1 was the most efficient. For both locations, SWA was the most competent media, recovering 61% and 44% of strains, respectively, from locations 1 and 2. Of the 68 extracts produced and tested, 24 (35%) were considered active by the qualitative approach considering the standards set herein. Location 1 yielded 16 (50%) active extracts, whereas location 2, 8 (22%). IC_{50} determined for selected extracts varied from 0.15 to 17.78 mg/mL, for BRB-172, from the São Vicente Marina, and BRB-156, from Santos Ferry. Some extracts, such as BRB-184 displayed a steep curve with a high slope (2.63), indicating a classic cytotoxic effect. On the other hand, BRB-117, among other extracts, showed a mild curve, with a lower slope (0.13) suggesting the presence of cytostatic compounds. **Conclusion:** These results have shown that the coast of São Paulo has a rich pharmacological potential stored in marine microorganisms. Nevertheless, further studies are necessary for elucidation of the molecules present in the active extracts and their mechanisms of action. **Financial Support:** FAPESP (Processo # 2015/17177-6), CNPq and CAPES.

09.023 Biotechnological potential of actinomicetes associated to ascidians and sediments collected at Brazilian oceanic islands. Velasco-Alzate K[1], Silva J[1], Del Bianco B[1], Ferreira MP[2], Maldonado GP[3], Costa-Lotufo LV[1] [1]ICB-USP – Farmacologia, [2]USP, [3]ICB-USP – Microbiologia

Introduction: Brazilian oceanic islands (Atol das Rocas, Trindade, Fernando de Noronha and São Pedro and São Paulo archipelagos) have great strategic importance for the country. For its size and isolation shelter especially fragile ecosystems, and the use of natural resources present there becomes a challenge difficult to conceptualize. These islands are potential sources of marine biodiversity with biotechnological applications. **Aim:** To evaluate the chemical profile and cytotoxic potential of Actinomycetes associated with Ascidian and sediment collected in the Brazilian oceanic islands. **Methodology:** Ascidians and sediments from the different study regions were isolated by the methods of stamping and dilution in sea water in three mediums (A1, TM, SWA). Actinomycetes-like gram positive colonies were isolated and exhausted. The selected colonies were placed in liquid A1 medium to grow. After growth, the crude extracts were extracted with ethyl acetate (EtOAC) for two hours. Cytotoxicity was evaluated by the MTT method on HCT-116 (human colon carcinoma) cells using two concentrations (5 and 50 □g/ml), and IC_{50} was obtained for those extracts considered active in the first screening. The active samples were analyzed by HPLC with the phenylpropanoids method in column C18 to obtain a chemical profile. In addition, strains with cytotoxic activity are being identified by extraction, amplification and sequencing of the 16S rRNA gene. **Results:** A total of 125 strains were isolated from the Ascidian and sediment samples. 33 strains showed cytotoxic activity in HCT-116 cells between 75 and 100% inhibition at one and/or two concentrations. 15 strains were evaluated by HPLC. Two of these (BRB 348 – IC50 5,24 and BRB 406 – IC50 10,94) have shown the most interesting profiles, and were selected for regrow and further purification. The BRB-348 strain showed a peak with a low retention time and an intensity of 11.087 mAU at different wavelengths. The BRB-406 strain showed to be more interesting with many high intensity peaks ranging from 25.248 to 29.127 mAU, possibly with the same chemical nature. **Conclusion:** Ascidians and sediments collected on the Brazilian oceanic islands are an important reservoir of Actinomycetes which contain various compounds of pharmacological interest as can be evidenced our results, where extracts isolated from bacterial strains have a high cytotoxic capacity in HCT-116 cells. **Financial support:** CAPES, FAPESP (2015/17177-6).

09.024 Cytotoxic Compounds from *Streptromyces* sp. Recovered from the ascidian *Euherdmania* sp. Furtado LC[1], Pinto FCL[2], Ferreira MJP[3], Pessoa ODL[2], Wilke DV[4], Costa-Lotufo LV[1] [1]ICB-USP – Farmacologia, [2]UFC – Química Orgânica, [3]USP, [4]UFC – Farmacologia e Fisiologia

Introduction: Actinomycetes take up a prominent position in research to prospect for compounds with biomedical properties, such as antibiotic, antitumor and immunosuppressive activities, along with enzymes and enzyme inhibitors of great importance to the pharmaceutical industry. This study evaluated cytotoxic potential of the extract and fractions obtained from bacterium recovered from the ascidian *Euherdmania* sp. collected on the Taíba beach, Brazil. **Methods:** Bacterium growth was conducted in 60 X 250mL of A1 broth (soluble starch, yeast extract and peptone) for 7 days under agitation of 270rpm at 25-28°C in Erlenmeyer flasks (total of 15L). After the incubation period, the culture was extracted with ethyl acetate (EtOAc) for 1 hour under agitation of 140rpm. The concentrated extract yielded 1,3g and was dissolved in 100 mL of a solution composed of methanol and water and partitioned with n-hexane and EtOAc. The acetylated fraction of the extract was fractionated by molecular exclusion chromatography, using as solvent a mixture of MeOH /CH_2Cl_2. The most active fractions, BRA-346AC and BRA-346AD, were subjected to solid-phase extraction chromatography (SPE) using a mixture of solvents of different polarities. The fractions were analyzed by High Performance Liquid Chromatography (HPLC) and these fractions showed the presence of a complex mixture of compounds. The molecular identification of the strain was based on 16S rDNA gene sequencing and comparison using the Basic Local Alignment Search Tool (BLAST) from National Center for Biotechnology Information (NCBI) database. The extract and all fractions were screened for their anti-proliferative activity on the human cell line HCT-116 (human colon carcinoma), MCF-7 (human breast adenocarcinoma) and RPE (retinal pigment epithelium) using the MTT assay. **Results:** The crude extract showed a powerful cytotoxicity against tumor cell lines, mainly HCT-116, with an average IC_{50} value of 30ng/mL. The fractions BRA-346A, BRA-346AC, BRA-346ACC, BRA-346AD and BRA-346ADC showed potent cytotoxicity, with IC_{50} ranging between 0.007 to 0.24µg/mL, where BRA-346AD was the most active. The molecular identification of BRA-346 was consistent with *Streptomyces* genus. **Conclusion:** The microorganism recovered from ascidian *Euherdmania* sp. revealed a significant biotechnological potential for the prospection of molecules with cytotoxic activity. However, broader studies are needed to better elucidation of molecules having antitumor activity. **Support:** CNPq and FAPESP (2015/17177-6)

09.025 *Aedes aegypti* salivary gland extract inhibits pruriceptive responses via histaminergic and non histaminergic pathways. Cerqueira ARA[1], Rodrigues L[1], Teixeira SA[1], Taniguchi ÉY, Muscará MN[1], Cassola AC[2], Sá-Nunes A[3], Costa SKP[1]
[1]ICB-USP – Farmacologia, [2]ICB-USP – Fisiologia e Biofísica, [3]ICB-USP – Imunologia

Introduction: The salivary gland of female *Aedes aegypti* (A. aegypt) mosquitoes contains a variety of active chemical substances that ameliorates experimental inflammatory bowel disease [1], but may also induce a mixed-type allergic response in salivary antigen challenged mice [2]. Previously we report that the female A. aegypt salivary gland extract (SGE) significantly inhibits the increased microvascular permeability and pruritus evoked by Compound 48/80 (C-48/80), thus showing a potential histaminergic -mediated pathway [3]. AIM: This study was carried out to further characterise mechanisms involved in the anti-inflammatory and anti-pruriceptive effects induced by A. aegypt SGE. **Methods**: Assessments of itch behaviour and skin oedema assay were performed with i.d. injection of test agent in a single dose: C-48/80 (10µg/site), chloroquine (25µg/site) or TRPA1 agonist allyl isothiocyanate (AITC; 1µmol/site) in a Tyrode volume of 50 □l alone or simultaneously with increased doses of SGE (1-10 µg/site) or antagonists: pyrilamine (histamine receptor antagonist; 0,1µg/site) or HC030031 (TRPA1 antagonist; 20µg/site). Mice were individually placed and the scratching behaviour was recorded for 30 min [3]. Mast cell degranulation assay was evaluated in vitro via histology with acid toluidine blue and in vivo via fluorimetric assay in response to C-48/80 alone and in presence of SGE (0.3-10µg/site). Cultured neonate rat dorsal root ganglion (DRG) neurons were used to study the effect of SGE on intracellular calcium mobilization in response to AITC and capsaicin. Data are expressed as mean ± SEM and stats were performed by ANOVA followed by Bonferroni test. $P<0.05$ was taken as significant. **Results**: The co-injection of SGE (0.3, 1 and 3 µg) with C48/80 significantly, but not dose-dependently, reduced C-48/90-induced scratching bouts by 65%, 55% and 26%. SGE (1µg) co-injected with C48/80 and pyrilamine reduced itch behaviour by 60% (n=4-5; $P<0.01$). In the presence of SGE (1 µg/site) or HC030031, chloroquine-induced itch behaviour was reduced by 67% and 70%, respectively (n=4; $P<0.001$). AITC-induced itch was reduced by 62% when co-injected with EGS (1µg) or by 54% in the presence of HC030031. The combination of SGE and HC030031 did not affect AITC-induced itch. SGE (1 – 100µg/mL) did not degranulate mast cell in vitro or affected the degranulation produced by C-48/80. Likewise, histopathological did not reveal a marked effect of SGE. When applied to DRG culture, SGE (20 µg/mL) did not affect [Ca^{2+}] mobilization or significantly affected capsaicin-induced increased [Ca^{2+}] current. **Conclusion**: We show for the first time that SGE from A. aegypti contains bioactive components capable of inactivating histaminergic and nonhistaminergic pruriceptive pathways, and independently of both stabilizing mast cells and TRPV1-mediated mechanisms. **Acknowledgments**: CAPES, CNPq, FAPESP Ethic Comitte: CEUA/ICB n° 100, book 3, page 9 References: 1. Sales-Campos et al. Int. Immunopharmacol. 26; 13 (2015). 2. Barros et al. PLoS One. 20;11(5):e0155454 (2016). 3. Cerqueira et al. SBFTE. Oct; 09.048 (2016).

09.026 The p-coumaric acid derivatives cinnamic acid and methyl cinnamate modulate migration and laminin synthesis in fibroblasts *in vitro*. Aquino FLT[1], Ferro JNS[1], Conserva LM[2], Barreto E[1] [1]ICBS-UFAL, [2]IQB-UFAL – Química e Biotecnologia

Introduction: Previous studies have reported that p-coumaric acid, a natural phenolic compound, possesses relevant pharmacological properties including antioxidant and wound-healing activity. Considering that the molecular modifications or synthesis of new compounds is vital to arrive at the best pharmacological analogue with desirable properties, this study sought to evaluate the effect of p-coumaric acid and its derivatives, cinnamic acid and methyl cinnamate, on migration and laminin production by fibroblast in vitro. **Methods:** NIH3T3 mouse fibroblast cell line cultured in supplemented DMEM medium (10% fetal bovine serum, 2 mM glutamine, and 1% gentamicin) were exposed to different concentration of p-coumaric acid and its derivatives, cinnamic acid and methyl cinnamate, and incubated for 24 h in a humidified incubator (at 37°C, 5% CO_2). Cell viability was evaluated by means of MTT assay. Cells were also treated with either p-coumaric acid, cinnamic acid or methyl cinnamate to evaluate cell migration using a classical scratch assay. In another set of experiments, laminin production in cell treated with the phenolic compounds was evaluated by immunofluorescence. All assays were performed in three independent controlled experiments. Statistical analysis was performed using two-way ANOVA with post hoc Tukey test. Differences at $p<0.05$ were considered significant. **Results:** We observed that, after 24h, all three compounds in all concentration tested (3, 10 and 30 µM) did were not show cytotoxic effects on 3T3 cell line. After 24h, cells treated with 30 µM of p-coumaric acid, cinnamic acid or methyl cinnamate showed, as compared to untreated cell, an increase in cell migration of 44%, 38% and 51%, respectively. Treatment with the three compounds at concentration of 3 and 10 µM did not significantly affect the cell migration. Furthermore, immunofluorescence analysis revealed that fibroblasts treated with cinnamic acid or methyl cinnamate (30 µM) for 24 h exhibited a significant increase ($p<0.05$) in the production of laminin as compared untreated cells. p-Coumaric acid (30 µM) did not affect basal amount of laminin in fibroblasts after 24 h of treatment. **Conclusion:** These results indicate that p-coumaric acid, cinnamic acid or methyl cinnamate, modulate cell migration. We also noted that derivatives cinnamic acid and methyl cinnamate, but not p-coumaric acid, were able to improve laminin production in fibroblasts, suggesting the molecular modification in p-coumaric acid may results in analogues with specific pharmacological effects. **Financial Support**: CNPq.

09.027 Antinociceptive and anti-inflammatory effects in rodents of lyophilized aqueous extract of P1 (**LAEP1**). Lopes KS[1], Pinheiro BG[1], Barros MA[1], Souza-Junior FJC[1], Andrade DM[1], Oliveira JP[2], Silva CYY[2], Silva MN[2], Fontes-Júnior EA[1] [1]UFPA – Pharmaceutical Sciences, [2]UFPA – Organic Chemistry

Introduction: P1 is a medicinal plant typical of regions of tropical and subtropical climate, including Brazil. In folk medicine, this plant is used to treat inflammation. **Objective:** To investigate the effects of the lyophilized aqueous extract of P1 leaves (LAEP1) in standard rodent models of pain and inflammation. **Material and methods:** LAEP1 was prepared by lyophilized infusion of the dried leaves. After the acute toxicity test (AT), antinociceptive activity was evaluated using acetic acid-induced writhing test (WT), formalin test (FT) and hot plate test (HP) in mice whereas the anti-inflammatory activity was performed by carrageenan (CPE)- and dextran (DPE)-induced paw edema tests in rats. Additionally, sedative effect of the LAEP1 in open field test (OF) has been investigated. AT (n=5/group): test group received LAEP1 orally (v.o.) at the dose 2000 mg/kg whereas control group (CG) with saline. WT (n=6/group): LAEP1 test groups (25, 75, 200 e 400 mg/kg), CG and indomethacin (10 mg/kg; v.o.). FT (n=6/group): LAEP1 (146.89 mg/kg), CG, morphine (4 mg/kg, s.c.) include these three groups associated with naloxone (0.4 mg/kg, s.c.). HP (n=6/group): LAEP1 (146.89 mg/kg), CG and morphine (10 mg/kg, s.c.). OF (n=10/group): LAEP1 (146.89 mg/kg) and CG. CPE (n=6/group): LAEP1 (146.89 mg/kg), CG and indomethacin (10 mg/kg). DPE (n=6/group): LAEP1 (146.89 mg/kg), CG and cyproheptadine (10 mg/kg). Ethical committee (CEPAE 62-2015) approved all procedures. Statistical analysis was performed using Student's t-test, and one-way ANOVA with Tukey's post hoc test. $p < 0.05$-0.001 were considered as statistically significant. **Results:** Administration of LAEP1 (2000 mg/kg) showed low toxicity profile. In WT, the LAEP1 exhibited concentration-dependent inhibition of the writhing response in 24.86, 39.59, 49.17 and 70.17% respectively, achieving a similar effect to indomethacin 10 mg/kg (73.3%), with 146.89 mg/kg as the half maximal inhibitory concentration value (IC50). LAEP1 (IC50) has only shown a antinociceptive effect in inflammatory phase of FT, with 50.1% reduction in paw licking time, and this effect did not is inhibited by naloxone. LAEP1 (IC50) did not interfere on latency time in HP, as well on spontaneous locomotor activity in OF. In CPE, LAEP1 (IC50) inhibited the edema formation at 1-5 h, presenting equivalent effect to indomethacin over time. However, it did not interfere in the development of edema in DPE. **Conclusion:** EALP1 has a significant peripheral antinociceptive and anti-inflammatory effect, confirming the traditional use of P1. This suggest that constituents of EALP1 are involved in the inhibition of inflammatory mediators. Further studies are currently underway to isolate the bioactive compounds and elucidate the mechanisms responsible for their activities. **Financial support:** UFPA, CNPq and CAPES.

09.028 Antiofidic activity of *Sphagneticola trilobata* extract. Santana PHDS[1], Cons BL[1], Patrão-Neto FC[1], Monteiro-Machado M[1], Strauch MA[1], Melo PA[1] [1]UFRJ – Farmacologia e Química Medicinal

Introduction: According to WHO, snakebites are a public health problem that can lead to death. In those cases, were it does not kill the individual, it is very common to inflict irreversible skeletal muscle damage that can evolve to limb amputation. The snake anti venom serum can prevent death, but do not completely antagonize the venom myotoxic effect (Fernandes *et al*., 2014). Besides that, the access to serum is many times limited due to governmental issues and intrinsic conservations characteristics of these serums. Due to this fact, the popular use of medicinal plants occurs millennia ago. It is well know that some plant extract from the *Asteracea* family has antiofidic activity (Wagner *et. al*, 1986), however, there is still no data on the *Sphagneticola trilobata (S.trilobata*) extract. **Methods:** The antiophidic ability of the *S. trilobata* extract was evaluated against *Bothrops jararaca*, *Bothrops jararacussu (BJU)*, *Bothrops atrox*, *Naja naja, Lachesis muta* and *Echis carinatus* venom. We perform *in vivo* experiments in male Swiss mice (25g), evaluating the myotoxic, edematogenic and hemorrhagic effects. The myotoxic effect were evaluated by measuring the increase of plasma CK activity (Melo and Suarez-Kurtz, 1988) induced by intramuscular injection of venoms alone or associated with extract 30, 100 and 300 mg/Kg. The hemorrhagic effect was induced by intradermic injection of 0.1mL of venoms (1mg/Kg) alone or associated with extract 30, 100 and 300 mg/Kg in the abdomen of mice and quantified as previously described (Melo *et al*., 1994). The induction of edema was evaluated by na intramuscular injecton of 0.1 mL venoms (1mg/Kg) alone or associated with extract at the same doses, the thigh area was measured using a pachymeter (Strauch *et. al.,* 2013). We investigated *in vitro* extract ability to antagonize crude BJU (10 µg/ml) venom effects. We tested phospholipase, proteolitic, hyaluronidase, and collagenase activities with each respective substrate. Tail bleeding experiments were performed by injecton of BJU 0.1 mg/Kg intravenous alone or associated with extract 100 and 300 mg/Kg according to the modified method of Broze et al. (2001). The evaluation of the presence coumentans in the extract was made through high performance chromatography and gas chromatography coupled to mass spectrometry. **Results:** The *S.trilobata* extract antagonize some of the snakes toxic effect. Highlights should be given to the protective effect against the hemorrhagic activities of *Bothrops jararaca*, *Bothrops atrox* and *Echis carinatus* venom. *S. trilobata* extract was able to reduce the hemorrhage caused by these venoms in 52%, 100% and 100%, respectively. The edema and the myotoxic effects caused by *BJU* venom were reduced in 23% and 77% by the plant extract. Some venom enzymatic activities were also antagonized. *S. trilobata* extract reduced 100% of the phospholipase, 22% of the hyaluronidase, 27% of the proteolitic and 26% of the collagenase activities present in the *BJU* venom. S. trilobata (300 mg/Kg) extract reduced in 71% the tail bleeding induced by BJU. Chromatographic data indicates the presence of coumestans in the extract used in this study. These substances were already found in other plant extract with anti-snake venom abilities. **Conclusion:** Thus, the extract used in our work was presented for the use of treatment and prevention of injuries generated by warping by snakes. **Supported by:** CNPq, Capes and Faperj. All the animal procedure were approved by the CEUA-CCS-UFRJ nº DFB ICB 072-4/16

09.029 Pharmacological Potential of the 4'-O-Methylepigallocatechin, a flavonoid, for the treatment of Alzheimer's Disease. Veloso CC[1], Matos NA[2], Netto GPL[3], Rodrigues VG[4], Duarte LP[4], Takahashi JA[4], Matildes BLG[4], Klein A[2], Giusti-Paiva A[5], Souza GG[3] [1]UFAM – Ciências Farmacêuticas, [2]UFMG – Farmacologia, [3]Unifal – Fisioterapia, [4]UFMG – Química, [5]Unifal – Fisiologia

Introduction: The development of more efficient AChE inhibitors and anti-inflammatory agents, which act mainly in brain, has been considered as an effective approach to be applied for treating Alzheimer's disease (Liu *et al*., 2013). Neuroinflammation constitutes in an Alzheimer's disease pathogenesis (Heneka *et al*., 2015). Therefore, in the present work the flavonoid 4'-*O*-methylepigallocatechin, isolated from leaves of *Maytenus imbricata*, was investigated in relation to the *in vitro* AChE inhibitory activity and *in vivo* anti-inflammatory activity. **Methods:** Adult male *Swiss* mice and female Balb/c mice (20-25g) were used in the experiments. Experimental procedures were approved by the Ethics Committee for Animal Use of the Federal University of Alfenas (protocol number: 683/2015). The evaluation of nociceptive threshold was performed by carrageenan induced mechanical allodynia test (*Von Frey* filaments). For evaluation of the anti-inflammatory activity, female Balb/c mice (20-25g) were divided into experimental groups. Vehicle (DMSO 5% in saline, 10 ml/kg) or 4'-*O*-methylepigallocatechin (2, 6 and 20 mg/kg) was orally administered 1 h before the intrapleural injection of carrageenan (200 µg/100µl) or phosphate buffered saline (PBS, 100µl). The positive control group received dexamethasone (0.5 mg/kg, i.p.) 30 min before the inflammatory stimulus. Statistically significant differences among the groups were calculated by the application of an analysis of variance (ANOVA) followed by Bonferroni's test, with the level of significance set at $P < 0.05$. All results were expressed as Mean ± Standard Error of Mean (SEM) of 4-6 animals. The *in vitro* AChE inhibitory activity of 4'-*O*-methylepigallocatechin was evaluated using a 96-well microtiter plate following the Ellman´s method (Ellman *et al*., 1961). **Results:** 4'-*O*-methylepigallocatechin exhibited significant *in vivo* anti-inflammatory activity in the pleurisy model. Carrageenan induced neutrophil migration in pleurisy mice 24 h after i.pl. injection when compared to PBS-treated mice ($P < 0.001$), while 4'-*O*-methylepigallocatechin abolished this recruitment in all doses tested ($P < 0.001$), as well as dexamethasone reduced the number of infiltrating neutrophils ($P < 0.001$). However, 4'-*O*-methylepigallocatechin did not change the nociceptive threshold in the carrageenan induced mechanical allodynia test (*Von Frey* filaments) in all doses tested. 4'-*O*-methylepigallocatechin presented AChE inhibition with percentage of inhibition (%) of 63,38 ± 2,34. These results present perspectives for more accurate tests to prove the activity of this substance against Alzheimer's disease. **Conclusion:** In this work it was observed that the flavonoid 4'-*O*-methylepigallocatechin have AChE inhibition property and anti-inflammatory activity. The results open possibilities to the employment of this compound as drug leads to be used in the treatment of Alzheimer's disease. **Financial Support** and acknowledgments: CAPES PNPD. References: Ellman, G. L. et al (1961). Biochem. Pharmacol. 7, 88–95. Heneka, M.T. et al (2015). Lancet Neurol. 14, 388e405, http://dx.doi.org/10.1016/S1474- 4422(15)70016-5. Liu, J.-Q. et al (2013). Org. Lett. 15, 1580–1583.

09.030 Effect of heparin on acute cutaneous lesions induced by *Bothrops jararacussu* venom in mice. Borges PA[1], Strauch MA[2,1], Patrão-Neto FC[1], Nogueira TA[3], Oliveira FL[5], Melo PA[1], Calil-Elias S[5] [1]ICB-UFRJ – Farmacologia e Química Medicinal, [2]IVB, [3]UFF – Ciências Aplicadas a produtos para Saúde, [5]ICB-UFRJ – Proliferação e Diferenciação Celular

Introduction: Bothrops snake are responsible for many accidents in Brazil that induces local myonecrosis, edema, hemorrhage and dermonecrosis. Several studies show that *polyanions such as heparins* are effective in counteracting the myotoxic effects by interact with a large number of proteins in the inflammatory process, thereby limiting cellular activation and tissue damage. **Methods:** We induced a mouse skin wound by *Bothrops jararacussu* venom injection (3.0 mg/kg; n=4-6 animals), and observed an epidermal necrosis, inflammatory reaction 7 days after the inoculation. Mice were treated during the first five days with subcutaneous application of 50 µL fractionated heparin (10mg/Kg - Enoxaparin) or vehicle (physiologic saline solution - PSS - 0.9% NaCl). At 1, 3 and 7 days blood and bone marrow was collected and at group of mouse were euthanized under anesthesia (CEUA Protocol DFBCICB072-04/16). During these days, the skin was removed and processed for Immunohistochemistry and histological approach and different analysis. **Results:** After different days of venom injection the histological analysis showed, an inflammatory infiltrate, intense cell proliferation, vascular congestion, and hypodermis disorganized. Also the venom induces a significant increase in epidermal, dermal and hypodermal thickness. Heparin treatment prevented the epidermal (3 and 7 days post-injury) and dermal (3 days post-injury) thickness increase, and did not change significantly hypodermal thickness. Our observations demonstrate that *B. jararacussu* venom induced an intense cellular response 72 h after the venom injection in the skin. In the blood and bone marrow, the venom induced an increase of all analyzed myeloid cells, such as monocytes, immature and mature neutrophils, and heparin treatment was effective in preventing it. **Conclusion**: These data showed that *B. jararacussu* venom induced skin wound, associated with inflammatory reaction and heparin treatment counteract the inflammation and improves the healing. Reference: 1-Herrera et al., Negl PLoS. 2016 Trop Dis Apr 1;10(4); 2- Monteiro-Machado et al., Toxicon. 2015 May;98:20-33; 3- Patrão-Neto et al., Toxicon. 2013 Jul;69:55-64 **Financial Support**: CNPq; CAPES; FAPERJ

09.031 Acute oral toxicity of *Minthostachys mollis* (Benth.) Griseb and antispasmodic activity in rat ileum. Rojas J[1], Arroyo J[1], Ortiz J[2], Palomino M[3], Paredes A[4] [1]Universidad Nacional Mayor de San Marcos – Farmacologia, [2]Universidad Nacional mayor de San Marcos – Fisiologia, [3]Universidad Nacional Mayor de San Marcos – Química, [4]Universidad Nacional Mayor de San Marcos – Medicina

Introduction: *Minthostachys mollis* (Benth.) Griseb is an aromatic sub-shrub known in Peru with the popular name "muña". In traditional Peruvian medicine, the infusion of this plant is used to treat inflammation, cough, bronchitis and digestive disorders. It is essential to establish the safety of this medicinal plant and scientifically validate its pharmacological properties, so the objective was to determine the acute toxicity of aqueous extract (EAc-Mm) and essential oil (AE-Mm) as well as the antispasmodic effect in ileum of rat. **Methods:** Acute toxicity was evaluated in albino rats treated with a single dose of 2000 mg / kg body weight of AE-Mm and EAc-Mm. At the conclusion of the experiment, the animals were sacrificed and necropsy and macroscopic and microscopic anatomopathological study of the organs were performed. For the determination of the antispasmodic activity, the rat ileum was used in an organ bath. AE-Mm and EAc-Mm were added cumulatively during the 1.0 □M acetylcholine-induced tonic contraction phase. **Results:** At the single dose of 2000 mg / kg body weight of AE-Mm, the rats showed immediate signs of toxicity and died within 36 to 72 hours. With EAc-Mm, no signs of toxicity were observed. In the microscopic examination of the lung, inflammatory infiltrate was observed, predominantly lymphocytic with severe hemorrhage and presence of macrophages with hemosiderin. At the concentration of 37.5 µg / mL AE-Mm, the contraction percentage was zero ($p < 0.001$) (100% relaxation). At the concentration of 7.5 mg / ml EAc-Mm the percentage of contraction was 15.69 ± 8.0 ($p < 0.001$). Pre-incubation with L-NAME modified the AE-Mm relaxing response. **Conclusions:** AE-Mm presents moderate oral toxicity (LD50 = 500 mg / kg), whereas EAc-Mm is classified as non-toxic. Both AE-Mm and EAc-Mm have a relaxing effect on rat ileum. The nitric oxide signaling pathway would be involved in bowel relaxation. This would provide the scientific evidence that supports the use of this plant in traditional medicine for the treatment of abdominal spasms. **Financial Support**: Vice-rector of research from the National University of San Marcos, Peru. License number of the Ethics Committee: 0262 (date: April 26, 2016)

09.032 Vaginal cream containing curcumin as a promising antifungal for the treatment of vulvovaginal candidiasis. Santos AJA[1], Silva EL[1], Peixoto FN[1], Pires LMN[1], Sakamoto RY[1], Silva SC[1], Amorim YM[1], Pinto FCH[2], Araujo MGF[1] [1]UFSJ-Centro Oeste, [2]UFSJ-Dom Bosco

Introduction: Vulvovaginal candidiasis (VVC) is the substantial cause of lower genital infections in women, affecting 75% of all women, at least once during their lifetime[1]. *Candida albicans* is the main agent that causes VVC. Despite the advances in antifungal therapy, the growing resistance among isolates of *Candida* has been reported[2]. Curcumin is well-known to have therapeutic potential due to its antioxidant, anticarcinogenic and antimicrobial activities and some studies showed that curcumin has antifungal potential against different human pathogens[3,4]. Once the antifungal potential of curcumin is notable, the purpose of this study was to evaluate the in vivo antifungal activity of a vaginal cream containing curcumin in the treatment of vulvovaginal candidiasis in a vaginal infection animal model. **Methods:** The anticandidal activity of curcumin was investigated against *C. albicans* (ATCC 10231) by broth microdilution assay[5]. Then, a vaginal cream formulation containing three different concentrations of curcumin was developed and the effect in the treatment of VVC was performed in an immunosuppressed and estrogen-treated rat model[6] (ethical approval protocol 012/2015). The in vivo assay was performed using female Wistar rats that were intravaginally inoculated with 0.1 ml of *C. albicans* (5.0×10^7 yeast/ml). Since the infection was established, the animals were treated, once a day, with 0,1 mL of the vaginal cream, during six days. At the end of treatments, vaginal sections were longitudinally removed for histological analysis. **Results:** Curcumin showed a minimum inhibitory concentration value of 1000 mg/L. In addition, in the in vivo model of VVC, the groups treated with the cream containing curcumin showed a progressive reduction in the number of infected animals and the reduction of the vaginal fungal burden was significant after six days of treatment with the different doses. Histological analyses of the vaginal mucosa sections showed that the animals treated with 1% showed absence of stratum corneum in the canal and presented tumefied cells as signs of tissue reaction associated with the infection; however, reduction in mucosal inflammatory infiltrate was observed. **Conclusion:** Curcumin could be considered as a promising effective antifungal agent in the treatment of vulvovaginal candidiasis. **References:** 1. Achkar JM et al. Clin. Microbiol. Rev. 23, 253, 2010. 2. Tapia CV et al. Mycopathologia. 182, 339, 2017. 3. Martins CVB et al. J. Antimicrob. Chem. 63, 337, 2009. 4. Neelofar K et al. Can. J. Microbiol. 57, 204, 2011. 5. CLSI - Clinical and Laboratory Standards Institute. 2008. 6. Araújo MGF et al. Med. Mycol. 51, 673, 2013. **Financial support:** FAPEMIG and UFSJ **Ethical approval protocol**: 012/2015 CEUA-UFSJ

09.033 MTHP-induced endothelium-independent vasodilatation in thoracic aorta rat: **Role of calcium channels**. Souza Neta OAC[1], Dourado TMH[1], Sarmento DM[1], Albuquerque JSS[1], Travassos RA[2 1]UFPB, [2]UFPB – Biologia Celular e Molecular

Introduction: Isoquinoline are an important heterocyclic aromatic alkaloids formed due the fusion of the benzene ring to the pyridine ring and are commonly known as benzopyridines. These classes possess many pharmacologically active substances displaying a broad range of biological activity (Awuah, J. of Org. Chem., v. 75, p. 5627, 2010). Thus, the objective of this study was to evaluate the mechanism of vasorelaxant action of 1-(3-methoxy-4-hydroxyphenyl)-7-methoxy-1,2,3,4, tetrahydroisoquinoline alkaloid (MTHP) in rat aorta in the absence of functional endothelium. **Methods**: Male Wistar rats (*Rattus norvegicus*) were obtained from Bioterium Prof. Thomas George of IPeFarM/UFPB. All rats were euthanized by decapitation with guillotine. The aortic rings about 3-5 mm wide were obtained from the thoracic aorta. To obtain isometric responses, the rings were individually suspended on stainless steel rods in organ baths (10 mL) containing Krebs solution (pH = 7.4) at 37 ºC, bubbled with 95% O2 and 5% CO2 mixture and resting tension of 1 g. The relaxation was expressed as the reversal percentage of the initial contraction elicited by contractile agent and EC50 values were obtained by nonlinear regression. All procedures were approved by the UFPB Ethics Committee on Animal Use (Protocol/CEUA nº 0605/13). **Results:** MTHP relaxed significantly and concentration-dependent aortic rings in the absence of functional endothelium pre-contracted with 80 mM KCl (EC50 = 4.6 ± 0.7 x 10^{-5} M, n = 3), the relaxing potency of MTHP not changed when compared to the relaxation curve with rings pre-contracted by 3 x 10-7 M of PHE (EC50 = 5.7 ± 1.1 x 10^{-5} M, n = 5), suggesting a common mechanism for these two contractile agents, indicating a possible participation of voltage-operated calcium channels (Ca_V). However, in the relaxation curve obtained by the MTHP in a pre-contracted aortic rings with S-(-)-Bay K8644 (EC50 = 1.2 ± 0.2 x 10^{-4} M, n = 5), its potency was decreased about 2.6 times, confirming a participation of Ca_V. **Conclusion:** This study shows that endothelium-independent, Ca^{2+} influx contributes to the vasodilatory effect of MTHP in rat aorta. **Key Words:** MTHP, calcium channels, aorta, isoquinoline. **Financial support:** UFPB/CNPq

09.034 From popular use to preclinical validation: **A study of the healing activity of hydroalcoholic extract from the leaves of *Eugenia punicifolia* (Myrtaceae) in rodents**. Périco LL[1], Rodrigues VP[1], Ohara R[1], Santos BB[1], Santos RC[2], Vilegas W[3], Rocha LRM[1], Santos C[4], Hiruma-Lima CA[1] [1]IBB-Unesp – Fisiologia, [2]USF – Farmacologia e Gastrenterologia, [3]Unesp-Litoral Paulista, [4]FCLAr-Unesp

Introduction: *Eugenia punicifolia* is an Amazonian medicinal plant popularly used in the treatment of inflammation, wounds and infections. The aim of this study was to evaluate the curative role of the hydroalcoholic extract from the leaves of *E. punicifolia* (HEEP) in female Wistar rats. **Methods:** The gastric ulcers were induced by ischemia-reperfusion (I/R) according to the method described by Ueda et al[1]. HEEP (125 mg/kg), lansoprazole (30 mg/kg) or saline (10 mL/kg) were administered during 6 days to determinate the healing effects of the subacute treatment. After treatment, the rats were killed and the stomach removed for analysis of lesions areas (mm^2) and biochemical parameters such as: superoxide dismutase (SOD)[2], myeloperoxidase (MPO)[3], malondialdehyde (MDA)[4], catalase (CAT)[5] and reduced glutathione (GSH)[6]. The results were expressed as mean ± S.E.M. and statistical significance was determined by ANOVA followed by Dunnett's test ($p<0.05$). **Results:** The results show that the treatment with lansoprazole and HEEP during 6 consecutive days healed the gastric ulcers decreasing the lesion area (68.80% and 52.83%, respectively, $p<0.01$ and $p<0.05$) when compared with control group treated with vehicle. Our results indicate that HEEP administered for 6 days presents healing effects against the I/R induced lesions increasing GSH levels (0.35x, $p<0.0001$) and SOD activity (0.8x, $p<0.01$). After 6 days of treatment, HEEP did not alter the activity of MPO (a marker of inflammation) and CAT (antioxidant) or levels of MDA (a marker of lipid peroxidation) when compared with the group treated with vehicle. **Conclusion:** HEEP probably acts through antioxidant (GSH and SOD) action against gastric I/R injury in females Wistar rats, corroborating, thereby, with an indication of this popular plant for wounds and infections. **Financial Support**: FAPESP-BIOTA (at process number - 2009/52237-9) and FAPESP (at process number – 2015/ 14797-3). Animal Research Ethical Committee (number 675). References: [1] Ueda, S. et al. Scan. J. of Gastro., v.162, p.55, 1989. [2] Winterbourn, C.C. et al. J.Lab. Clin. Med., v.85, p. 337, 1975. [3] Krawisz, J.E. et al. Gastroenterology, v. 87, p. 1344, 1984. [4] Ohkawa, H. et al. Anal Biochem., v.95, p. 351, 1979. [5] Aebi, H. Methods Enzymol, v. 105, p. 121, 1984. [6] Anderson, M.E. Methods Enzymol, v. 113, p. 548, 1985.

09.035 Vasorelaxant effect of neryl acetate in rat thoracic aorta. Carvalho EF, Gadelha KKL, Oliveira DMN, Magalhães PJC UFC – Fisiologia e Farmacologia

Introduction: Neryl acetate (NAc) is an oxygenated monoterpene found in the essential oil of several plant species such as *Citrus aurantium*, *C. limon*, *C. aurantifolia* and *Helichrysum italicum*. The essential oil of these plants are known by its antioxidant, anticoagulant and antitumor properties, and some of them are reported as alleviative agents used in the treatment of cardiovascular symptoms. For that reason, we investigated herein the vasorelaxant effects of NAc in rat thoracic aorta. **Methods:** Male Wistar rats (250 - 300 g) from our institutional vivarium were the source from which rings of thoracic aorta were obtained after euthanasia (Ethics Committee approval #60/2015). Isolated aorta was sectioned in rings (3 - 5 mm length each) that were incubated at 37°C in Krebs-Henseleit solution (pH 7.4) under bubbling with carbogen mixture (95% O_2, 5% CO_2). Tissues were connected by cotton threads to force transducers that were coupled to a data acquisition system for recordings of isometric tension. The addition of acetylcholine (ACh, 1 µM) on the steady state of a sustained contraction induced by phenylephrine (PHE, 0.1 µM) served to test the integrity of the vascular endothelium in the aortic rings. Whether a ACh-induced relaxation was higher than 80%, the endothelium was considered functional. **Results:** Added cumulatively on the steady state of sustained contractions elicited by PHE (1 µM), NAc (1 - 2000 µM) induced a vasorelaxant effect with EC_{50} values (geometric mean [confidence interval 95%]) of 601.0 [403.6 - 894.9] µM (n = 6) in preparations with intact endothelium (E+). In endothelium-denuded aortic rings (E-), the EC_{50} values were 708.6 [457.3 - 1098.0] µM (n = 6), which did not reveal significant difference when compared with values from E+ preparations ($P > 0.05$, Mann-Whitney). In E+ preparations, the EC_{50} values to relax KCl-elicited contractions (276.0 [182.4 - 417.6] µM; n = 10) were significantly lower than EC_{50} values to relax PHE ($P < 0.05$, Mann-Whitney). In 60 mM KCl-contracted E+ preparations treated with indomethacin (10 µM) or in E- aortic rings, the EC_{50} values for the relaxing effects of NAc were 355.6 [231.5 - 546.0] µM (n = 8) and 504.7 [318.4 - 799.8] µM (n = 6), respectively, which were without statistical significance when compared to E+ control values ($P > 0.05$, Mann-Whitney). In E+ preparations contracted with 80 mM KCl, the EC_{50} values for the relaxing effects of NAc were 901.7 [532.2 - 1527.9] µM (n = 7), which were significantly higher than those recorded on E+ preparations contracted with 60 mM KCl ($P < 0.05$, Mann-Whitney). In isolated E+ preparations maintained under resting tonus, NAc (1 - 2000 µM; n = 9) induced no contractile or relaxing effect. **Conclusion:** NAc possesses vasorelaxant properties on rat isolated aortic rings. Its vasorelaxant effects did not depend on the integrity of the endothelial layer nor involved a putative prostaglandin release. As NAc was more potent to relax KCl- than PHE-contracted preparations, it is probable that its relaxant actions involved a preferential inhibitory action against voltage-operated pathways. Such hypothesis is reinforced by the fact that its vasorelaxant potency decreased when the contraction was induced by a higher KCl concentration (80 *vs.* 60 mM). **Financial Suport**: UFC/CAPES/CNPq Commission of ethics in animal research (CEPA/UFC 60/2015)

09.036 Biopolymer Extracted From Exudate of *Anadenanthera colubrina* var. cebil (Griseb.) Altschul (Angico Gum) displays antidiarrheal therapeutic potential in mice. Araújo TSL[1,2], Nicolau LAD[3,1], Sousa NA[1,2], Souza LKM[1,2], Araújo S[1], Sousa FBM[1,2], Oliveira AP[1], Nogueira KM[1], Iles B[1], Pacheco G[1], Medeiros JVR[1,2] [1]UFPI – Farmacologia da Inflamação e Desordens Gastrintestinais, [2]Renorbio, [3]UFC – Fisiologia e Farmacologia

Introduction: Biopolymers extracted from traditional trees of northest of Brazil have been extensively studied for their diverse biotechnological potentialities and biological activities in gastrointestinal tract (Araújo TSL, J Ethnopharmacol, 174, 299, 2015; Carvalho NS, Drug Dev Res, 76, 144, 2015). Thus, the purpose of this study was to evaluate the antidiarrheal potential and safety assessment of angico gum (AG), a biopolymer obtained from exudate of Anadenanthera colubrina tree. **Methods:** Initially, the antidiarrheal activity of AG was evaluated for castor oil-induced acute diarrhea and enteropooling. Albino (Swiss) mice (20-25g) were pretreated with AG (30, 60, and 120 mg/kg, p.o.), and after 1 h, was administered castor oil (10 ml/kg, p.o.). Loperamide (5 mg/kg, p.o.), was used as a standard drug for diarrhea. Animals were placed in cages lined with filter paper and observed for 3 h for the presence of diarrhea defined as watery (wet), unformed stool. The effects of AG (60 mg/kg, p.o.) on gastrointestinal transit and Na^+-K^+-ATPase activity were then examined. Subsequently, the effect of AG (60 mg/kg, p.o.) on secretory diarrhea induced by cholera toxin (CT) and Enterotoxigenic Escherichia coli (ETEC) was investigated. In addition, an acute toxicity test was conducted in accordance with OECD guideline 423. **Results:** Angico gum (30, 60, and 120 mg/kg) reduced significantly ($P<0.05$) the diarrheal severity (33.711%, 61.180% and 73.341%, respectively), decreasing the frequency of defecation and the total number of wet feces produced upon administration of castor oil. The intestinal fluid accumulation (enteropooling) was also reduced by AG (60 and 120 mg/kg) pretreatment (56.766% and 59.398%, respectively). In addiction AG (60 mg/kg) increased Na^+-K^+-ATPase activity in the intestinal mucosal cells and significantly ($P<0.05$) reduced gastrointestinal transit (43.661%) compared with the control group. In the model of fluid secretion in 1µg-cholera toxin-treated intestinal closed loops in live mice, AG (60 mg/kg) significantly inhibited the intestinal fluid secretion (51.306%) and decreased Cl^- ion loss. AG (60 mg/kg) also reduced diarrhea induced by ETEC (51.610%) and prevented weight loss in the animals. Moreover, AG did not induce any toxicity signs. **Conclusion:** These results suggest that AG is a possible candidate for the treatment of diarrheal illnesses, however further study will be necessary to evaluate the mechanisms involved in the antidiarrheal effect of AG. **Financial support and acknowledgments:** CNPq and FAPEPI. This study was approved by Federal University of Ceará ethics committee (n° 11/2013).

09.037 Antifungal activity and mechanism of action of monoterpene linalool on *Candida albicans* strains of pulmonary origin. Silva ACL[1], Silva DF[1], Diniz-Neto H[1], Sousa JP[2], Lima EO[1] [1]UFPB – Farmacologia e toxicologia de produtos naturais, [2]UFPB – Análises Clínicas

Introduction: With the increasing occurrence of infections by fungal resistant strains, several substances have been tested in order to obtain new antifungal drugs replacing the conventional pharmacotherapy. Among then, monoterpenes have been considered potentially candidates (QUINTAS JR. Phytotherapy Research 27(1) 1-15, 2013; SOBRAL et al. The Scientific World Journal 2014(1) 1-35, 2014). Many pharmacological activities, such as antifungal, are related to the monoterpene linalool (ALVIANO et al. Oral microbiology and immunology 20(2) 101-105, 2005). The aim of this work was to investigate the antimicrobial potential of linalool with *Candida albicans* strains from pulmonary origin. **Methods:** The antifungal activity was determined by the Minimum Inhibitory Concentration (MIC) using the microdilution technique in double-concentrated RPMI-1640 or SDB in 96-well plates. A total of six strains of *C. albicans* were used: five from pulmonary origin, part of the collection of maintained library at Laboratório de Pesquisa de Atividade Antibacteriana e Antifúngica de Produtos Naturais e Sintéticos Bioativos., and one standard strain ATCC 60193. All the stains were suspended in NaCl 0,9%, adjusted to the 0.5 tube of McFarland scale and diluted to an initial inoculum at 10^5 CFU/mL. The test product was successively diluted from the concentration of 1024 µg/mL up to 2µg/mL. The linalool MIC was evaluated according to the following criteria: MIC at 50-500 µg/mL (strong/optimal activity) and MIC at 600-1500 µg/mL (moderate activity). The assay to evaluate the Minimum Fungicidal Concentration (CFM) of linalool was performed with aliquots of 10µL of the corresponding dilutions: MIC, MICx2 and MICx4, transferred into 100 µl of RPMI-1640 contained new cell culture plates. CFM was considered the lowest concentration in which there was no yeast growth in the culture medium. Both assays were performed in duplicate. Amphotericin B (100 µg/mL) was used as a positive control. In order to verify the action mechanism in fungal cells, two strains, LM-32 and ATCC 60193, were tested with sorbitol (0.8 M) and ergosterol (400 µg/mL) using microdilution method in duplicate. The MICs of linalool were compared in the absence and presence of both compounds. The increase of the linalool MIC in the presence of sorbitol or ergosterol compared to the control indicated whether the monoterpene would act at the cellular wall or membrane level, respectively. **Results:** Linalool showed a MIC at 32 µg/mL and CFM of 64 µg/mL, respectively, among 50% of strains. Concerning the action mechanism assay, MIC in the presence and absence of sorbitol and ergosterol were at 128 g/mL, respectively, to *C. albicans* ATCC-60193. Surprisingly, MIC at 32 µg/mL were also observed in the presence and absence of both compounds to *C. albicans* LM-32. **Conclusion:** Monoterpene linalool has a strong activity against pulmonary *Candida albicans* as well as to the standard strain. However, the mechanism of this event was neither involving membrane nor fungal cell wall rupture. Further studies will be need in order to determine whether it may occur when the linalool has already assimilated by the yeast. Finantial Support: CNPq, CAPES, PgPNSB/CCS/UFPB

09.038 Methyl cinnamate, a natural phenolic compound, inhibits elastase-induced emphysema in mice. Silva LMP[1], Ferro JNS[1], Souza TNC[1], Melo LEJ[1], Conserva LM[2], Barreto E[1] [1] ICBS-UFAL, [2]IQB-UFAL

Introduction: Pulmonary emphysema is characterized by irreversible airflow obstruction, inflammation, oxidative stress imbalance and lung remodeling, resulting in reduced lung function and a lower quality of life. Phenolic compounds are plant metabolites with potential anti-inflammatory and antioxidant effects that have been used in folk medicine. Our aim was to determine whether treatment with methyl cinnamate, a natural phenolic compound, interferes with the development of lung emphysema. **Methods**: Intranasal saline or elastase (2UI) was administered to C57BL/6 mice (CEUA/UFAL License 085/2015); the animals were then treated with methyl cinnamate (MC, 1, 10 and 50 µmol/kg) or vehicle once a day after the sixteenth day until 20 day. Analyses were carried out at 24h after the last treatment. We evaluated inflammatory profile in bronchoalveolar lavage (BAL) fluid. The lungs were removed to evaluate inflammatory infiltration and alveolar enlargement. In addition, the effect of MC on cell viability and reactive oxygen species production by TNF-α-stimulated A549 cells was evaluated by MTT assay and NBT assay, respectively. Statistical analysis was performed using two-way ANOVA with post hoc Tukey test. Differences at $p<0.05$ were considered significant. **Results**: In elastase-treated animals, treatment with MC at the doses 1, 10 and 50 µmol/kg reduced counting of total leukocyte in the BAL of 4.02±1.10 $x10^4$ cells to 1.71±0.20 $x10^4$, 1.40±016 $x10^4$ and 1.15±0.17 $x10^4$ cells, respectively. After treatment with MC at the doses 1, 10 and 50 µmol/kg, The IL-6 levels on BAL fluid from elastase-treated animals was inhibited in 75%, 62% and 66%, respectively. Histological lung analysis showed that elastase-stimulated group presented an alveolar enlargement and infiltration of inflammatory cells in the alveoli, parameters that were inhibited ($p<0.01$) by treatment with MC at all doses tested. In vitro experiments we observed that MC was non-toxic and reduced the production of reactive species. **Conclusions**: These results demonstrated the anti-inflammatory effect of methyl cinnamate by reduce levels of IL-6 and inflammatory cells into BAL and also in the lung. Moreover, MC attenuates the remodeling of the lung parenchyma caused by elastase in mice. In addition, MC suppresses the production of reactive oxygen species in A549 cells, suggesting their effect on oxidative stress. **Financial Support**: CNPq

09.039 Ultralow concentration piericidin A1 changes phenotype of tumor cells. Florêncio KGD[1], Wilke DV[1], Costa-Lotufo LV[2], Pinto FCL[3], Oliveira FAS[1], Pessoa ODL[3], Rocha DD[1] [1]UFC – Fisiologia e Farmacologia, [2]ICB-USP, [3]UFC – Química Orgânica

Introduction: Natural products play an important role in pharmacology because of the notorious contribution to the development of new drugs and pharmacological tools. Piericidins are produced almost exclusively by actinomycetes and have promising biological and pharmacological activities. Piericidin A1 (PA1) inhibits complex I of electron transportation chain. **Methods:** In this study, we investigated the effects of PA1 on proliferation and migration of tumor cell lines (HCT-116, human colorectal carcinoma and B16-F10, murine metastatic melanoma). PA1 was isolated from actinomycete BRA-399, recovered from the sediment of Fernando de Noronha Archipelago, was identified as belonging the genus *Streptomyces* based on the 16S rRNA gene sequence. To evaluate PA1 effects on tumor cells, we used different approaches after 72h incubation using a stunning wide concentration range, from 0.1 attomolar (aM) to 12.0 micromolar (□M). Colorimetric methods MTT [1] and SRB [2] allowed the measurement of metabolism and protein content respectively. Flow cytometry assays were performed to measure cell number, morphology and membrane integrity. Wound healing *in vitro* assay (scratch assay) and confocal microscopy were performed to evaluate migration properties and characteristics respectively. In addition, it was evaluated the influence of prior treatment with PA1 using sub lethal concentration of 0.5 picomolar (pM) on the sensitivity of tumor cells to an antitumor chemotherapic (doxorubicin). **Results:** PA1 caused complete tumor cell inhibition of HCT-116 and B16-F10 in □M concentration as observed by MTT and SRB assays. However PA1 depicted a sustained inhibition of ~60% until incredible ultralow concentrations (in aM range) on HCT-116 cells after 72h incubation. Because of these unprecedented results, it was not possible to calculate inhibition concentration mean values for HCT-116 (IC_{50}). B16-F10 did not present such cytostatic profile going from total inhibition in □M concentrations to a mild or no inhibition in aM to nanomolar (nM) concentrations. These assays were repeated 6 times in triplicate. Accordingly, the flow cytometry assays, on HCT-116 cells, depicted decreased ($p<0.05$) cell counting at concentrations from aM to □M and membrane damage starting at 3.6 nM. B16-F10 cell counting decreased from nM to □M range. Treatment with PA1 increased the cell migration rate in B16-F10, as well as induced morphological alterations compatible with greater migratory activity cells. Finally, cells pre-treated with PA1 showed higher IC_{50} values on doxorubicin treatment. **Conclusion:** PA1 depicted unprecedented potency against on tumor cell lines (HCT-116 and B16-F10) on causing inhibition of metabolism and proliferation. However, sub lethal concentrations of PA1 increased cell migration and IC_{50} values of doxorubicin. **Financial Support**: CNPq References: [1] Mosmann, T., J. Immunol. Methods, 65: 55-63, 1983 [2] Skehan, P., J Natl Cancer Inst., 4;82(13), 1990

09.040 Anti-inflammatory and antinociceptive activities of cashew gum (*Anacardium occidentale*) in mice. Silva DPB[1], Lino RC[1], Cardoso CS[1], Florentino IF[1], Pereira-Junior MA[2], Fernandes KF[2], Costa EA[1] [1]UFG – Farmacologia, [2]UFG – Bioquímica

Introduction: Pain and inflammation diseases significantly influence the lifestyle of millions of people and existing therapies aren't always effective and can cause several adverse effects. Medicinal plants appear as an important tool in the search for new drugs more safe and effective. In this study was evaluated the antinociceptive and anti-inflammatory activities of hydroalcoholic extract of cashew gum (HECG), as well as its mechanisms of action. **Methods**: The animals used were adult female *Swiss* mice weighing 35 - 40g (n = 8 per group). The antinociceptive and anti-inflammatory effects of LQFM008 were evaluated using the methods of acetic acid-induced abdominal writhing, formalin-induced pain, carrageenan-induced paw edema and pleurisy and hyperalgesia induced by carrageenan or PGE_2. All the experimental protocols were approved by the Research Ethics Committee of the UFG (Protocol Nº. 057/15). **Results and Discussion**: The treatment with HECG (75, 150 or 300 mg/kg, p.o.) decreased in a dose-dependent manner the number of writhing by 14%, 40% and 55% respectively, when compared to the vehicle (94.1 ± 3 writhing). HECG (150 mg/kg, p.o.) reduced only the second phase of formalin-induced pain test, reducing the licking time by 33% compared to the vehicle 10 mL/kg (188.1 ± 8.5 seconds). In the test of paw edema induced by carrageenan, treatments with HECG (150 mg/kg, p.o.) reduced the edema at four hours of the test by 13, 19, 25 or 24%, respectively compared to the vehicle (Difference between the paws 135 ± 1.7; 136 ± 3.4; 125 ± 3.7 and 114 ± 3.1µL, respectively). In the test of pleurisy induced by carrageenan, treatments with HECG (150 mg/kg, p.o.) reduced polymorfonuclears migration by 40% compared to the vehicle (6.619 ± 0.33 polymorfonuclears cells x 10^6/mL) and increased the mononuclears migration by 56% compared to the vehicle (2.153 ± 0.14 mononuclears cells x 10^6/mL). This same treatment also reduced the myeloperoxidase activity by 46% compared to the control group (159.1 ± 19.5 mU/mL) and the levels of IL-1β and TNF-α cytokines by 34 and 50%, respectively compared to the vehicle (IL-1β: 386.6± 20.1 pg/mL and TNF-α: 87.4 ± 6.8 pg/mL). Furthermore, HECG (150 mg/kg, p.o.) reduced the difference of nociceptive threshold between the non-inflamed and inflamed paw of animals in response to mechanical stimulus in the four hours of the test by 41, 33, 36 or 39%, respectively compared to the vehicle (Difference of nociceptive threshold 164 ± 8.2; 152 ± 3.6; 136 ± 4.3 and 138 ± 3.9 g, respectively). However, in the animals received PGE_2 in the paw, the treatment with HECG (150 mg/kg, p.o.) did not alter significantly the difference of nociceptive threshold between the non-inflamed and inflamed paw. These results suggest that HECG, at dose used, possess antinociceptive effect dependent of anti-inflammatory activity. Moreover, the effects of HECG in the hyperalgesia induced by carrageenan or PGE_2 suggest that anti-inflammatory effect of this plant may involve the inhibition of the cyclooxygenases or phospholipase A_2 enzymes. **Financial Support**: CAPES and CNPq

09.041 Lipid-lowering and antiatherogenic effects of *Echinodorus grandiflorus* (Cham. & Schltdl.) Micheli. in rabbits . Gasparotto FM[1], Lourenço ELB[2], Gasparotto Junior A[1], Kassuya CAL[1] [1]UFGD – Ciências da Saúde, [2]Unipar – Farmácia

Introduction: Dyslipidemia and atherosclerosis are the leading causes of death and disability in Western countries. The process consists of chronic and progressive alterations in arterial wall characterized by inflammatory and fibroproliferative response (Buckley et al., 2015). Considering the impact of this disease to humans, in recent decades there was a great interest in the research of medicinal plants and their extracts in medication therapy. Recent researches have shown that extracts of *Echinodorus grandiflorus* (Cham. & Schltdl.) Micheli. features cardiovascular benefits especially by its popular use in the treatment of hypertension (Prando et al., 2016). **Aim:** Evaluate the hypolipemiant and antiatherogenic effects of ethanol soluble fraction obtained from *E. grandiflorus* (ESEG) in New Zealand rabbits submitted to cholesterol-rich diet (CRD). **Methods:** Dyslipidemia and atherogenesis were induced by the administration of CRD (1% cholesterol) for 8 weeks. The ESEG was administered orally at doses of 10, 30 and 100 mg/kg, once a day, for four weeks, starting from the 5nd week of CRD. The gain in body weight were measured weekly over the eight week study. Blood was collected and samples were analyzed at time zero and at the end of each month to measure the levels of triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and very low-density lipoprotein cholesterol (VLDL-C). At the end of the experiments it was withdrawn the aorta and its direct branches to perform pathological study. **Results:** The CRD induced dyslipidemia and major structural changes in the aortic wall. The treatment with ESEG was able to prevent the increase of TC, LDL-C, VLDL-C, triglycerides, and increase HDL-C New Zealand rabbits. Moreover, macroscopic lesions were significantly reduced in ESEG -treated rabbits. **Conclusion:** This study demonstrated that ESEG reduces the serum lipids when orally administered to New Zealand rabbits. In addition, it was able to prevent arterial thickening induced by CRD. **References:** Buckley, M. L. et al. The influence of dysfunction signaling and lipid homeostasis in mediating the inflammatory responses during atherosclerosis. Biochim Biophys Acta, v.1852, p. 1498- 1510, 2015. Prando, T.B. et al. Involvement of bradykinin B2 and muscarinic receptors in the prolonged diuretic and antihypertensive properties of *Echinodorus grandiflorus* (Cham. & Schltdl.) Micheli. Phytomedicine. v. 23, p. 1249-1258, 2016. **Financial Support**: PROAP – UFGD, FUNDECT, CNPq, CAPES Animal Research Ethical Committee: process 08/2015 - CEUA/UFGD

09.042 Antinociceptive and anti-inflammatory effect of the dichloromethane extract from the roots of *Arrabidaea brachypoda* (DC.) bureau and its role on asic and TRPM8 receptors. Rodrigues VP[1], Périco LL[1], Ohara R[1], Santos RC[2], Vilegas W[3], Rocha CQ[4], Rocha LRM[1], Hiruma-Lima CA[1] [1]IBB-Unesp, [2]USF, [3]Unesp-Câmpus do Litoral Paulista, [4]UFMA

Introduction: *Arrabidaea brachypoda* roots are used in the treatment of kidney stones and joint pain in the southeast and northeast of Brazil. This study evaluated the antinociceptive and anti-inflammatory activity of the dichloromethane extract from the roots of *A. brachypoda* (DEAB) and it's safety. **Methods:** For the acute toxicity test and Hippocratic screening[1, 2] of the DEAB male and female Swiss mice were used. They received DEAB (2000 mg/kg, p.o.) and vehicle (saline 0.9%; 10 mL/kg, p.o.). In all other models only male mice were used. The antinociceptive activity of DEAB was evaluated through the formalin test[3] three doses of DEAB were used (10, 30 and 100 mg/kg, p.o.), vehicle was used as negative control, morphine (2.5 mg/kg, s.c.) as a positive control for the early phase and piroxicam (30 mg/kg, p.o.) for the late phase. The antinociceptive DEAB mechanisms of action related to acid-sensing ion channels (ASIC) and transient receptor potential (TRP) channels were investigated. The time (seconds) animals spent licking their right hind-paw was used as the nociception indicator. To assess the anti-inflammatory activity of the DEAB ear edema induced by xylene[4] and arachidonic acid[5] were performed. In both models the treatments were DEAB (10, 30 and 100 mg/kg; p.o.), vehicle (p.o.) and dexamethasone (5 mg/kg, i.p.). Results are expressed as mean ± S.E.M. Statistical significance (p<0.05) was determined by Student´s *t*-test or one-way ANOVA followed by Dunnett's test. **Results:** The administration of DEAB only exhibited a mild analgesia in both male and female mice during the Hippocratic screening, otherwise it didn't display any sign of toxicity. In the formalin test only the DEAB dose of 30 mg/kg decreased the nociceptive behavior in both early (50%) and late (43%) phases as well as their respective positive control (morphine 72%; piroxicam 47%) when compared to vehicle-treated group. The investigation of ASIC and TRP receptors in the antinociceptive activity revealed that DEAB acts on TRPM8 (39%) and ASIC (58%) it decreased the licking time when compared to the control group in both models. In the inflammatory models, the DEAB was able to decrease edema induced by xylene with all doses tested (51%; 60% and 79%) however the extract had no effect in the arachidonic acid model. **Conclusion:** The DEAB presents an anti-inflammatory and antinociceptive effect. Although the anti-inflammatory activity mechanisms remains unknown, the antinociceptive effect of the DEAB acts on TRPM8 and ASIC receptors. **Financial Support**: FAPESP-BIOTA (2009/52237-9) and CAPES All Experiments were previously approved by the ethics committee for use of experimental animals (IB/UNESP), protocol 728. References: [1] Souza-Brito, ARM, Manual de ensaios toxicológicos in vivo: ciências médicas, 15, 1994. [2] Malone, MH et al., Llooydia, 25:320, 1962. [3] Hunskaar, S et al., Pain, 30:103, 1987. [4] Swingle, KF; et al., Arch Int Pharmacodyn, 254:168, 1981. [5] Young, JM et al., J Invest Dermatol, 82:367, 1984.

09.043 Modulating activity of the alga Chlorella in impaired glucose tolerance and type-2 diabetic patients. Castro TCL, Martins F, Torello CO, Queiroz MLS FCM-Unicamp – Farmacologia

Chronic inflammation is involved in the pathogenesis of insulin resistance being characterized by increased circulating levels of proinflammatory cytokines such as TNF-α and IL-6, in addition to reduced levels of IL-10 (anti-inflammatory cytokine)[1-2]. This chronic inflammatory state may impair the mechanism of normal glucose tolerance triggering impaired glucose tolerance (IGT) and type-2 diabetes (T2D) [3-4]. Although several drugs are available for the treatment of these conditions, the disadvantages of conventional therapy[5] lead to the search for alternative therapies, particularly natural products[6]. In this context, the alga Chlorella (CV) is an alternative and natural agent that acts as a biological response modifier by directly modulating the production of cytokines[7-8]. Thus, our objective was to evaluate the effects of CV in the production of pro- and anti-inflammatory cytokines in IGT and T2D patients. Volunteers with T2D (n=25) and IGT (n=20) from Diabetes Group of the Centro de Saúde da Comunidade (CECOM), University of Campinas, Brazil, received oral doses of 3 g CV daily for 12 months. Serum levels of IL-10, TNF-α and IL-6 were quantified by sandwich enzyme-linked immunosorbent assay (ELISA) before use of CV (T0), after 6 (T6) and 12 (T12) months using CV. Data were analyzed for statistically significant differences using Wilcoxon t test. The results showed that the alga significantly ($P<0,05$) decreased serum levels of IL-6 and TNF-α at T6 and T12, in both groups IGT and T2D. There was a significant increase ($P <0.05$) of IL-10 at T6 in IGT and T2D groups. Our findings demonstrate that CV was able to restore the balance in the disturbed cytokine network in IGT and T2D, in which the unbalance of pro- and anti- inflammatory cytokines dictates the emergence and evolution of the pathological process. It seems that the supplementation with CV is promising in IGT and T2D, since it reduces the patient's inflammatory profile. **References:** (1) Lottenberg et al., *Einstein (Sao Paulo)* 8:254; 2010. (2) Shoelson et al., *J Clin Invest.*116:1793; 2006. (3) Goldfine et al., *Clinical Chemistry* 57:162; 2011. (4) Stumvoll et al., *Lancet* 365:1333; 2005. (5) Chang et al., *Evid Based Compl Altern Med.* 2013:378657; 2013. (6) Kibiti & Afolayan, *Pharmacogn Mag*. 11:S258; 2015. (7) Queiroz et al., *Food Chemical Toxicology* 49:2934; 2011. (8) Torello et al., *EC Nutrition* 5.1:1037; 2016. **Sources of Research Support:** FAPESP, CAPES and CNPq. We thank collaborators from CECOM/UNICAMP. Human Research Ethical Committee (**CAAE:** 30981114.4.0000.5404)

09.044 Anti-inflammatory potential of aqueous extract and polysaccharide fraction from *Thuja occidentalis Linn*. in reducion of COX-2, iNOS and pro-inflammatory cytokines in mice. Fonseca AMV[1], Silva IS[2], Nicolau LAD[3], Sousa FBM[4], Silva RO[3], Oliveira AP[5], Araújo S[5], Nogueira KM[5], Souza LKM[4], Araújo TSL[4], Alencar MS[5], Costa ACB[5], Pacheco G[5], Medeiros JVR[5] [1]IESVAP, [2]ICB-UFMG, [3]UFC, [4]Renorbio, [5]UFPI

Introduction: The most commonly drugs used to treat inflammatory conditions were associated with low efficacy therapeutic and adverse effects. The aim this study was investigated the anti-inflammatory effect of aqueous extract (AE) and the polysaccharide fraction (PLS) from *T. occidentalis* L. in mice. **Methods:** The AE and PLS were used in experimental models of paw edema induced by carrageenan (Cg), histopathological and immunohistochemical analyses. In a mouse peritonitis model, myeloperoxidase (MPO) activity, and levels of cytokine, nitrite, glutathione (GSH) and malondialdehyde (MDA) were evaluated. In addition, the vascular permeability and gastric toxicity were analyzed. **Results**: The Cg promoted the formation of 3h edema (0.128 ± 0.01 ml). The pretreatment with AE and PLS 3, 10, and 30 mg/kg i.p. significantly reduced the edematogenic response, and the maximum effect was observed after a dose of 3 mg/kg of both (0.05 ± 0.05 mL; and 0.03 ± 0.01 mL, respectively). In histological evaluation the Cg administration, exhibit marked inflammatory infiltrates. However, the pretreatment with AE and PLS significantly decreases neutrophil infiltration. The immunohistochemical analysis also showed decreased their expression of the immunostaining for iNOS and COX-2. Cg administration produced a significant (15.6 ± 0.5 U/mL of peritoneal exudate) increase in MPO activity. The pretreatment with AE and PLS significantly reduced MPO activity (6.9 ± 0.4 U/mL and 7.8 ± 0.7 U/mL, respectively). Pretreatment with AE or PLS also significantly reduced the levels TNF-α (220.0 ± 58.8 and 173.8 ± 45.1 pg/mL, respectively) and IL-6 (7680 ± 2458 and 7780 ± 1620 pg/mL, respectively), when compareted with the Cg group: TNF-α (478.3 ± 68.6 pg/mL) and IL-6 (24542 ± 7586 pg/mL). The AE and PLS also decreased the MDA concentration (4.66 ± 0.5 and 3.64 ± 0.49 nmol/mL, respectively vs Cg group 15.48 ± 0.44 nmol/mL) and maintained the GSH levels (118.6 ± 1.1 µg/mL and 127.1 ± 2.2 µg/mL, respectively vs Gg group 94.6 ± 13.3 µg/mL). The AE and PLS reduced significantly the nitrite concentration (0.27 ± 0.03 and 0.25 ± 0.04 µM, respectively), when compared the Cg group (0.84 ± 0.02 µM). The pretreatment with AE significantly reduced the vascular permeability (24.4 ± 5.4 µg/mL exudate). However, the PLS did not significantly reduce the vascular permeability (61.9 ± 2.0 µg/mL exudate), when compareted with Cg group (68.7 ± 5.7 µg/mL exudate). The gastric toxicity was conducted in comparison with indomethacin, that promoted gastric damage (2.1 ± 0.1 mm) and significantly increased MPO activity (2.21 ± 0.09 UMPO/mg of gastric tissue). Though, the AE and PLS (300 mg/kg) did not cause gastric damage (0.20 ± 0.04 and 0.10 ± 0.02 mm, respectively) or change MPO activity (0.09 ± 0.04 and 0.07 ± 0.05 UMPO/mg of tissue, respectively). **Conclusion:** The AE and PLS from *T. occidentalis* L. reduced the inflammatory response by inhibiting vascular and cellular events, inhibiting pro-inflammatory cytokine production, and reducing oxidative stress. Furthermore, they did not induce gastric toxicity at high doses. **SUPPORT**: CNPq and FAPEPI. CEP UFPI: Protocol Nº 66/10

09.045 Marine microorganisms from the north coast of São Paulo are a promising source of anticancer compounds . Rigato DB[1], Domingos HV[2], Chain BG[1], Souza BV[1], Falcão GC[1], Branco P[2], Costa-Lotufo LV[2], Jimenez PC[1] [1]Unifesp – Departamento de Ciências do Mar, [2]Universidade de São Paulo – USP – Departamento de Farmacologia

Introduction: In the last decades, natural products of marine origin have gained attention of the field of pharmacology, mainly related to new anticancer chemotherapy. Despite available treatments and much success, cancer continues to take a large mortality toll and, therefore, the demands for new remedies are ever increasing. Microorganisms of the class Actinobacteria, due to their distinct secondary metabolism, are a traditional source of bioactive molecules, many of which have been developed into drugs. Still, such bacteria inhabiting the vast and diverse marine environment remain underexplored for their biomedical potential. Thus, the aim of this study was to bioprospect the anticancer potential of extracts produced by marine actinobacteria recovered from sediments of the Northern coast of São Paulo. **Methods:** Sediment was collected across 8 locations on the north coast of São Paulo State, including Bertioga, São Sebastião and IlhaBela, stored in sterile plastic bags and frozen. Sediment processing took place under the aseptic conditions provided by a laminar flow hood, where samples were handled by two methods prior to inoculation (M1- desiccation and stamping on agar; or M2- heating and striking on agar), and plated on three culture media with increasing nutritional levels (SWA, TMA and A1). Individualized colonies were transferred to fresh agar dishes and repeatedly subcultured until pure. These strains were then grown in liquid broth, extracted with ethyl acetate, and analyzed for cytotoxicity at 5 e 50 mg/mL against the HCT-116 cell line (human colorectal carcinoma), by the MTT assay. Extracts that repressed over 70% of cell growth at the highest concentration were considered active and tested in a quantitative approach, over varied concentrations (0.0032 – 50 mg/mL), to obtain their respective IC_{50}.**Results:** A total of 173 strains were isolated from the 8 sediment samples collected. A comparable number of strains were isolated from either method. However, the poorest media, SWA, was responsible for recovering 48% of these strains. 59 extracts tested were considered positive for cytotoxicity in a qualitative approach, which amounts to 34% active extracts. In Araçá Beach, 45% of extracts were found cytotoxic, the highest percentage of active extracts yielded per location. IC_{50} calculated for selected extracts varied over 1000-fold, from 0.013 to 20.13 mg/mL, for BRB-058 and BRB-178, respectively. For the highly cytotoxic extracts derived from strains BRB-191 (Itaguaré Beach) and BRB-248 (São Sebastião's Cove), IC_{50} could not be obtained, as it may be below the lowest concentration tested. **Conclusion:** Additional chemical and biological studies are crucial for further elucidating the active principals present in these extracts. However, the results herein have shown that the microorganisms from the northern coast of São Paulo have a relevant biomedical potential. **Financial Support:** FAPESP (Processo # 2015/17177-6), CNPq and CAPES.

09.046 Effect of the hexane fraction of Punica granatum leaves in the oxidative stress induced in septic mice Sousa NCF[1], Simone AT[2], Araújo MC[1], Figueiredo IFS[1], Pereira DMS[1], Mendes SJF[1], Silva BRS[1], Silva LCN[1], Muscará MN[2], Fernandes ES[1] [1]Ceuma, [2]USP

Introduction: Oxidative stress plays an essential role in sepsis, as it regulates the production of inflammatory mediators such as oxygen reactive species, pathogen phagocytosis and lysis. Excessive activation of pro-oxidant pathways leads in turn, to the activation of anti-oxidant systems including the thioredoxin and glutathione systems (Flores et al., 2012). Drugs that regulate oxidative stress may be useful for the treatment of sepsis. *Punica granatum* L. is a plant used in the folk medicine due to its potential anti-inflammatory properties. Recent studies have reported these actions for *P. granatum* extracts or derived compounds. However, little is known of the effects of *P. granatum* extracts or fractions. **Aims:** Here, we investigated the actions of a hexane fraction (HF) obtained from the leaf hydroalcoholic extract of this plant in oxidative stress by using a murine model of sepsis induced by cecal ligation and puncture (CLP). **Methods:** Male C57Bl/6 mice received either FH (100 mg/kg, p.o.) or vehicle, 1h prior to CLP induction. Sepsis was induced by ligation and puncture of the ceccum following laparotomy. Sham-operated mice were used as controls. Twenty hours after sepsis, animals were culled and the peritoneal lavage samples were collected for analysis of the activation of oxidative stress enzymes. All experiments were approved by the CEUA-UNICEUMA. **Results:** FH increased the activation of superoxide dismutase, catalase and thioredoxin reductase whilst reducing hydrogen peroxide production by peritoneal cells obtained by septic mice. No significant changes differences were observed in glutathione activation in the same animals. On the other hand, when administered in sham-animals, FH caused reduction of the activation of catalase and glutathione peroxidase, while increasing thioredoxin reductase activation levels. These changes did not affect hydrogen peroxide production by cells from sham-mice. **Conclusions:** HF regulates the activation of key oxidative stress enzymes in sepsis leading to reduced production of hydrogen peroxide, an essential molecule in the host´s response to infection. This effect may be either detrimental or beneficial depending on the stage of sepsis and may affect disease outcome.

09.047 Investigation of anticancer potential of Neoteredo Reynei's microbiota through metagenomics and culturing approaches. Brito TL, Wilke DV, Silva AB, Pessoa ODL, Silva AT UFC – Farmacologia

Microorganisms from special ecological niches, such as the marine invertebrate symbionts, are a source of diverse and structurally unique bioactive natural products. For instance, the Teredinidae family, known as shipworms, evolved a novel digestive strategy to thrive feeding on wood by hosting gammaproteobacterial endosymbionts of the clade Teredinibacter (1). Genome mining of T. turnerae type strain T7901 confirmed its nutritional role and also revealed the potential for production of bioactive metabolites (2), latter confirmed by the characterization of biosynthetic gene clusters (BGCs) for tartrolon antibiotics (3) and turnebactin triscatecholate siderophore (4). Besides that, unpublished works with Teredinidae symbionts have shown their ability to produce substances with high cytotoxic activity. In the present work we performed culture independent (metagenomics) strategies to prospect the BGCs from shipworm associated microbiomes and also evaluated the anticancer potential of crude extracts from Teredinidae's bacterial isolates. Specimens of Neoteredo reynei shipworm species were collected at the Coroa Grande estuary, RJ, Brazil, and freshly processed for metagenomic DNA extraction of tissues from the digestive tract (digestive glands, intestine and gills). Metagenomic samples were shotgun-sequenced at MiSeq (Illumina), and processed for quality control, assembling and microbial genome-binning, resulting on the recovery of 2 high-quality Teredinibacter near genomes. In silico screening for BGCs with AntiSMASH revealed that both binned genomes contain candidate clusters for biosynthesis of complex polyketides, nonribossomal peptides, arylpolyenes, bacteriocins, and terpenes. The bacteria culturing from same tissues homogenates leads to a collection of 137 isolates, from which, 49 were submitted to fermentation with liquid broth, followed by chemical extraction with ethyl acetate. The cytotoxicity of crude extracts was evaluated against a colorectal cancer cell line (HCT-116) through the SRB assay (5) after 72h incubation. From the 49 extracts screened, 35% depicted potent cytotoxic activity, with IC_{50} values ranging from 0.59 to 60.00 ng/ml. Through metagenomics and culture approaches the present work confirmed the not fully explored potential of Teredinidae molluscs symbionts, including strains of the Teredinibacter clade as source of bioactive molecules. **Financial Support**: CNPq. **References**: 1. O'Connor RM, PNAS, vol. 111, no. 47, 2014. 2. Yang JC, PLoS ONE 4(7): e6085, 2009. 3. Elshahaw SI, PNAS, vol. 110 no. 4, 2012. 4. Andrew Han, PLoS ONE 8(10): e76151, 2013. 5. Skehan P, J Natl Cancer Institute, vol 82, no. 13, 1990.

09.048 Biochemical and biological characterization of *Leptodeira annulata* (Banded Cat-Eyed snake; Dipsadidae) venom. Torres-Bonilla KA, Panunto PC, 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. In this work, we investigated the biochemical profile and some biological activities of *L. annulata* venom. **Methods:** The electrophoretic profile of the venom was analyzed using SDS-PAGE in 12%. Proteolytic, estereolytic, elastolytic and phospholipase A_2 activities were examined using colorimetric assays and zymogram gels. The effects of the inhibitors EDTA and 1,10-phenanthroline, PMSF and AEBSF (10 µM to 10 mM) and the pH and temperature profiles were studied using azocasein. Fibrinogenolytic activity was determined by SDS-PAGE. The venom was fractionated by RP-HPLC and the peaks were tested for activities. The coagulant activity and the influence on the plasma recalcification time were examined using rat citrated plasma. The cross-reactivity of *L. annulata* venom with commercial antivenoms was assessed by ELISA. The hemorrhagic activity and the role of inhibitors was determined in rat dorsal skin. The results were expressed as the mean ± SD and comparisons were done using ANOVA with the Tukey-Kramer test and $p<0.05$ indicating significance. **Results:** SDS-PAGE of venom (30 µg) showed protein bands in the region of 15-75 kDa. Zymography (3-30 µg) revealed caseinolytic and gelatinolytic activities in different bands. The caseinolytic activity of *v*enom was very similar to that of *B. moojeni* and greater than that of *B. jararacussu*, with pH and temperature optima of 8.0 and 37 ºC, respectively. This activity was strongly inhibited by EDTA or 1,10-phenanthroline but not by PMSF or AEBSF. The venom (1-30 µg) was not active towards BA*p*NA and TAME. The venom was more active towards the elastasic natural substrate than towards the synthetic one. The venom (50 µg) was not very active towards hide powder azure. Venom (1-20 µg) showed low PLA_2 activity compared to *Bothrops* venoms. RP-HPLC of the venom yielded 34 peaks (peaks 10-21 showed PLA_2 activity and peaks 26-32 proteolytic activity). *L. annulata* venom (1-20 µg) did not clot rat citrated plasma even after 5 min at 37 ºC. *L. annulata* venom (5-10 µg) reduced the extent of coagulation by ~30% and delayed the plasma recalcification time by ~3 min. The latter finding agreed with the ability of venom to degrade the Aa-chain of fibrinogen, whereas the Bb- and g-chains were unaffected, as assessed by SDS-PAGE. This fibrinogenolytic activity was inhibited by 10 mM EDTA or 1,10-phenanthroline, but not by 10 mM PMSF or AEBSF. The minimum hemorrhagic dose was 92.2 µg and EDTA or 1,10-phenanthroline inhibited this activity. ELISA showed that *L. annulata* venom reacted most with antivenom raised against venom from *Bothrops* spp. species, followed by coral snakes (*Micrurus* spp.) and rattlesnakes (*Crotalus durissus terrificus*). **Conclusions:** *Leptodeira annulata* venom had no esterolytic activity but contained PLA_2 and proteolytic activities. The venom was devoid of coagulant activity, but was anticoagulant (via the fibrinogenolytic activity) and caused hemorrhage. The proteolytic, fibrinogenolytic and hemorrhagic activities were mediated by metalloproteinases. The venom cross-reacted with different antivenoms, indicating partial immunological identity with components from other snake venoms. **Financial support:** CAPES, CNPq. **Ethical approval:** Institutional Committee for Ethics in Animal Use (CEUA/UNICAMP, protocol no. 4479-1/2017).

09.049 Antitumor potential of bacteria associated to *Zoanthid Palythoa caribaeorum* from Trindade Island, Brazil Ferreira KQ[1], Oliveira FAS[1], Pinto FCL[2], Pessoa ODL[2], Sahm BDB[3], Costa-Lotufo LV[3], Wilke DV[1] [1]UFC – Farmacologia e Fisiologia, [2]UFC – Química Organica, [3]ICB-USP – Farmacologia

Introduction: The marine Brazilian Exclusive Economic Zone (EEZ) is comparable in size and biodiversity of the amazon rain forest, however studies on its biodiversity and bioactive molecules are scanty. EEZ comprises five oceanic islands, among those, Trindade Martins Vaz, which lacks studies on the pharmacological potential. Several studies depict antitumor potential of the zoanthid Palythoa caribaeorum. Additionally, growing evidences suggest the microorganisms role in the production of active molecules isolated from marine invertebrates. Then, this study aimed to evaluate the cytotoxic activity of the microorganisms associated to P. caribaeorum collected in Trindade Vaz island. **Methods:** bacteria strains were isolated through streaking method. These strains were cultivated in A1 broth (soluble starch, yeast extract and peptone), for 7 days under agitation of 150rpm at 25-28°C in Erlenmeyer flasks and submitted to chemical extraction with organic solvent Ethyl Acetate (AcOEt). The antiproliferative effects against a human colorectal carcinoma cell line (HCT-116) were tested by MTT [3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide] assay (2) with extract concentrations ranging from 0.00012 to 1 ug/ml after 72h incubation. The inhibitory concentration mean (IC50) values and their 95% confidence intervals (CI 95%) were obtained by non-linear regression of normalized data. The strains identified on 16S Ribosomal DNA (rDNA) gene sequencing and comparison using the Basic Local Alignment Search Tool (BLAST). **Results:** The five bacteria isolated were added to MicroMarin bacteria bank and called BRA-479, BRA-480, BRA-481, BRA-489 and BRA-490. The IC50 values of extracts were BRA-479 is 450 ng/mL, BRA-480 is 9ng/mL, BRA-481 is 11ng/mL, BRA-489 is 23ng/mL and BRA-490 is 13 ng/mL. BRA-481 was identified as Streptomyces sp. and BRA-489 Alcanivorax sp. Chromromycins were found in all extracts identified through to LC-MS analysis followed by dereplication using AntiMarin. Chromomycins are promising molecules with antibiotic and antitumoral activities (3). **Conclusion:** Extracts obtained from bacteria associated to P. caribaeorum from Trindade Vaz island were highly cytotoxic. Chromromycins are at least partially responsible for the bioactivity observed in BRA-480 and BRA-489, in which Cromomycin A2, cromomycin A3 and desmethylchromomycin A2 are more predominant. **Financial Support**: CNPq. References 1.Costa-Lotufo, L.V. Quim. Nova,32:703,2009 2.Mosmann, T. J.Immunol.M, 65:55,1983 3.Lombó, F. Appl. Microbiol.B., 73:1,2006

09.050 Antimalaric activity *in vitro* of essential oils of *Piper marginatum* Jacq. (**Piperaceae**). Moraes-Castilho J, Silva EBS, Cirino-Lopes JM, Silva NC, Pires-Moraes TM, Ferreira-Castro KC, Pires-Moraes W UFOPA – Farmacologia Experimental

Introduction: Malaria is a parasitic, tropical disease and is considered one of the greatest social and economic problems in the world. Among the main drugs used in the treatment are chloroquine, primaquine, quinine, artemisinin and its derivatives, and some antibiotics such as doxycycline, clindamycin and tetracycline. With the emergence of resistant parasites, lack of an effective vaccine, the great endemic malaria has become an increasingly obvious health problem. Taking into account the great biodiversity of the Amazon and the potential of medicinal plants used in traditional medicine, including *Piper marginatum* Jacq., Which according to the literature has been used in the treatment of malaria **Objective:** This project aims to evaluate the pharmacological antimalarial potential of the essential oil of *Piper marginatum* Jacq. In order to contribute to the knowledge of the species and possible use as a pharmacological instrument for the treatment of malaria, as a possible tool in the search to solve the problem of parasitic resistance. **Methods:** In order to evaluate the antimalarial activity, the essential oils were submitted to in vitro schizonticidal tests with *Plasmodium falciparum* considered traditional microtests. In order to investigate the cytotoxicity of *P. marginatum* essential oil, assays were performed using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazol bromide (MTT), thus determining LC50 (minimum lethal concentration capable of Inhibits the growth of cells by 50%). The selectivity index of essential oil was determined by the ratio of cytotoxic activity to antimalarial activity. **Results:** The LC50 of leaf essential oil was 4.94 µg/mL for *P. falciparum* sensitive strains and LC50 of 5.14 µg/mL for resistant chloroquine strains. The essential oil of the branches had LC50 of 5.34 µg/mL and 5.54 µg/mL for sensitive and resistant strains, respectively. The preliminary evaluation of the antimalarial activity showed that the essential oil of the leaves had better activity when compared to the essential oil of the branches against *P. falciparum*. **Conclusion:** According to the results obtained we can infer that both the essential oil obtained from the leaves qunato the essential oil of the branches of the species Piper marginatum Jacq. Have significant antimalarial activity against Plasmodium falciparum, sensitive and resistant strains, where we verified that the LC50 values presented are below 5.60 µg/mL, characterizing the plant species as a possible alternative tool in the treatment of the disease.

09.051 Antihypertensive and cardioprotective effects of *Cuphea carthagenensis* (Jacq.) J. F. Macbr. in a renovascular hypertension model associated with ovariectomy. Schaedler MI[1], Tirloni CS[1], Palozi RAC[1], Silva AO[1], Vasconcelos PC[1], Lívero FAR[2], Araújo VO[2,3], Gasparotto Junior A[1] [1]UFGD – Toxicologia e Farmacologia Cardiovascular, [2]Unipar – Farmacologia e Toxicologia de Produtos Naturais

Introduction: Hypertension is a worldwide economic and health problem wich affects 1,13 billion of people (WHO, 2013). The female population is the most affected by this problem at the age of 50 years, because the abrupt fall of the hormone estrogen, being an important group for studies about cardiovascular diseases (Mozaffarian et al., 2015). Despite this great problem, many people have little access to traditional medicines and therefore make use of medicinal plants. Among these *Cuphea carthagenesis* (Jacq.) J. F. Macbr. deserve attention (Bolson M. et al., 2015) . Despite the great use by the Brazilian population as an anti-hypertensive and cardioprotector drug, there is no studies wich prove these effects. This way, we propose evaluate the possible antihypertensive and cardioprotective effects of a purified aqueous extract obtained from *C. carthagenensis* (ESCC) using two-kidney- one-clip (2K1C) hypertension in ovariectomized Wistar rats. **Materials and Methods:** The purified aqueous extract from *C. carthagenensis* was obtained (from dry leaves) by infusion (1:10 w/v). The infusion was treated with 3 volumes of EtOH, which gave rise to a precipitate and an ethanol soluble fraction (ESCC). 2K1C hypertension and ovariectomy were surgically induced (Lasota et al., 2004; Umar et al., 2010). The ESCC was administered orally at dose of 30 mg/Kg, once a day, for 28 days, starting from the fifth week after the surgery. Enalapril (15 mg/kg) was used as standard antihypertensive drug. Two groups, one with renovascular hypertension and ovariectomy (positive control) and another SHAM-operated (negative control) were used as controls. Each group had n=10. Diuretic activity (with urine collection in metabolic cages for 8 hours) was evaluated on days 1, 7, 14, 21 and 28 after beginning of treatments. At the end of the experiments the systolic (SBP), diastolic (DBP), and mean arterial pressure (MAP), besides heart rate (HR) were registered. Furthermore, vascular reactivity to phenylephrine, acetylcholine and sodium nitroprusside was evaluated in mesenteric vascular bed. **Results:** The data obtained showed that prolonged treatment with the ESCC (30 mg/kg) reduces significantly the SBP in 2K1C-ovariectomized Wistar rats (positive control: 117.8 ± 8.3 mm Hg; ESCC 30 mg/kg: 91,1 ± 4,1 mm Hg; $p < 0.05$). Moreover, the groups treated with ESCC (30 mg/kg) presented lower vascular responsivity to phenylephrine (10 nmol) (48.1 ± 13.08 mm Hg versus 102.0 ± 3.80 mm Hg), and a significantly higher response to acetylcholine (3 pmol) (-20.5 ± 2.84 mm Hg versus -7.89 ± 2.37 mm Hg) when compared to the positive control. All other parameters evaluated did not present significant alterations. **Conclusion:** This study showed that ESCC obtained from *C. carthagenensis* was able to reduce SBP after prolonged treatment. In addition, the ESCC prevented the endothelial dysfunction induced by renovascular hypertension associated with ovariectomy. **References:** Lasota A., Roczniki Akademii Medycznej w Biaymstoku, 49, 29, 2004. Mozaffarian D., Circulation 131, 29, 2015. Umar A., Hypertens Res, 33, 727, 2010. WHO (World Health Organization). High blood pressure: a public health priority. World Health Day, 2013. **Financial support:** FUNDECT and CNPq. **CEUA:** 46/2016.

09.052 Role of the NO-cGMP pathway on the sustained antihypertensive effects of *Acanthospermum hispidum* DC. on ovariectomized rats with renovascular hypertension. Palozi RAC, Schaedler MI, Tirloni CAS, Silva AO, Gasparotto Junior A
UFGD – Ciências da Saúde

Introduction: Recently, evidence shown significant differences between the genesis and the development of cardiovascular diseases between men and women. At large, women are more affected, especially hypertension, after a pronounced drop in estrogen levels, a fact that usually occurs after menopause. However, preclinical studies for this specifically population are very restricted. Newly, we have shown that the purified aqueous extract from *A. hispidum* (ESAH), a medicinal plant used in the Brazilian Pantanal region, has a significant acute hypotensive effect in male Wistar rats. Despite the widespread use, its prolonged diuretic and antihypertensive activities have not yet been scientifically evaluated. Thus, we investigated the prolonged diuretic and antihypertensive activities of *A. hispidum* in rats ovariectomized with renovascular hypertension (2K1C), to simulate part of the woman population over 50 years old. **Aim:** Evaluate possible mechanisms involved in the sustained antihypertensive effects of ESAH on 2K1C-hypertension in ovariectomized (OVX) rats. **Materials and Methods:** 2K1C and OVX were surgically induced. The ESAH was administered orally at doses of 30, 100 and 300 mg/kg, once a day, for 28 days, from the 5nd week after the surgery. Enalapril and hydrochlorothiazide were used as standard drugs. Diuretic activity was evaluated on days 1, 7, 14, 21 and 28 of treatment. At 28th day, the systolic (SBP), diastolic (DBP), mean arterial pressure (MAP) and heart rate (HR) were registered. Serum levels of thiobarbituric acid reactive species, nitrosamine, nitrite, aldosterone, vasopressin, and ACE activity were measured. Moreover, the role of NO and prostaglandins in the vasodilator response of ESAH on mesenteric bed was also investigated. **Results:** The data obtained showed that the positive control group presented a increase in SBP (144 ± 5.3 vs 111 ± 3.7 mmHg), DBP (103 ± 2.8 vs 82 ± 2.9 mmHg), MAP (110 ± 3.8 vs 92 ± 2.8 mmHg), and HR values (251 ± 12 vs 202 ± 4.6 bpm) when compared to the SHAM group. Prolonged administration of ESAH-30 mg/kg was able to reduce SBP, DBP, and MAP to 90 ± 5.5, 71 ± 4.4, and 77 ± 5.5 mmHg, respectively, while HR levels were reduced to 165 ± 7.7 bpm. This effect induced by ESAH is associated with a reduction of oxidative and nitrosative stress, in addition to a possible increase in the bioavailability of NO. Additionally, an important NO-dependent vasodilator effect was observed in mesenteric vascular bed, a finding that indicates a potential mechanism for the cardiovascular effects of ESAH. **Conclusion:** A 28-day-ESAH-treatment reduces the arterial pressure in 2K1C-OVX rats. These effects are associated with an antioxidant and antinitrosant action, activating the NO/cGMP pathway in resistance arteries. **Financial support:** CNPq and FUNDECT **Animal Research Ethical Committee**: nº 45/2015-CEUA/UFGD **References:** A. Sarma, "Assessing and Modifying Coronary Artery Disease Risk in Women," *Curr Treat Options Cardiov Med*,vol.19, n.51, pp.1, 2017. Bieski, I.G.C.; “Ethnopharmacology of Medicinal Plants of the Pantanal Region (Mato Grosso, Brazil),” Evid Based Complementary Altern Med, vol. 2012, Article ID 272749, 36 pages, 2012. doi:10.1155/2012/272749 Tirloni, C.A.S. "Ethnopharmacological investigations of the cardio-renal properties of a native species from the region of Pantanal, state of Mato Grosso do Sul, Brazil," J Ethnopharmacol, vol. 206, pp. 125, 2017.

09.053 Cytotoxicity of BjcuL, a Galactose-binding Lectin from *Bothrops jararacussu* Snake Venom, in J774A.1 macrophages. Pereira BB, Panunto PC, Hyslop S Unicamp – Farmacologia

Introduction: Snake venom carbohydrate-binding lectins exert a variety of biological activities, including hemmaglutination, mitogenic activity in lymphocytes, modulation of platelet aggregation, inflammation and edema and apoptosis in different cell lines. However, their action on macrophages remains poorly understood. In this work, we examined the cytotoxicity of BjcuL, a galactose-binding lectin from *Bothrops jararacussu* snake venom, in the macrophage cell line J774A.1. **Methods:** J774A.1 macrophages obtained from the Rio de Janeiro Cell Bank (BCRJ) were cultured in 96-well plates in DMEM medium in a 5% CO_2 atmosphere for 24 h at 37 °C prior to use. For the experiments, the cells were incubated with BjcuL (100-1000 ug/ml) for 24 h and cytotoxicity was assessed using the MTT assay. In some experiments, the influence of incubation time with BjcuL (6, 16 and 24 h) was also examined. Reactive oxygen species (ROS) production was evaluated using the fluorochrome DCFH-DA and lipid peroxidation was measured with the thiobarbituric acid assay. The involvement of reactive species in BjcuL-induced cytotoxicity was assessed by co-incubating macrophages with BjcuL (1 mg/ml) and catalase (CAT; 300 U/ml), superoxide dismutase (SOD; 120 U/ml), N^{w}-L-nitro-arginine methyl ester (L-NAME; 10 mM), aminoguanidine (AG; 5 mM), lactose (LAC; 2 mM) or antivenom (AV; 1:5 antivenom:BjcuL ratio) for 16 h. The results were expressed as the mean ± SEM and statistical comparisons were done using one-way ANOVA followed by the Tukey-Kramer test. A value of $p<0.05$ indicated significance. **Results:** Incubation with *B. jararacussu* venom (0.1-1000 µg/ml) reduced macrophage viability to 90.2±1.2%, 84.8±1.3%*, 63.2±1.4%*, 12.9±3.9%* and 2.5±0.7%* for 0.1, 1, 10, 100 and 1000 µg/ml, respectively, after 24 h (n=3; *$p<0.05$ vs. control cells). BjcuL (100-1000 µg/ml) was also cytotoxic, with the two highest concentrations, 300 and 1000 µg/ml, reducing cell viability to 62.3±5.8%* and 33.4±8.2%*, respectively (n=3; *$p<0.05$ vs. control cells). Incubation with BjcuL (1 mg/ml) reduced macrophage viability to 62.1±6.9%*, 40.3±1.9%* and 34.7±1.8%* after 6 h, 16 h and 24 h, respectively (n=3; *$p<0.05$ vs. control cells). Co-incubation of macrophages with BjcuL (1 mg/ml) plus SOD, CAT, L-NAME, AG, LAC and AV significantly attenuated cytotoxicity by 71±3%*, 79±3%*, 77±0.6%*, 93±3%*, 98±4%* and 85±0.6%*, respectively (n=3; *$p<0.05$ vs. BjcuL alone). The stimulation of ROS production by BjcuL (1 mg/ml; fluorescence intensity: 58848±4774) was attenuated by SOD (34880±2187*), CAT (20698±3343*), L-NAME (30273±3691*), AG (38727±2442*), LAC (27801±3907*) and AV (38498±459*) (n=3; *$p<0.05$ vs. BjcuL alone). Lipid peroxidation caused by BjcuL (1.3±0.08 µmol MDA/mg protein) was partially attenuated by SOD, CAT, L-NAME, LAC and AV to 0.9±0.03*, 0.7±0.01*, 0.9±0.02*, 0.6±0.1* and 0.37±0.01*, respectively, after 16 h (n=3; *$p<0.05$ vs. BjcuL alone). **Conclusion:** BjcuL is cytotoxic to J774A.1 macrophages via mechanisms that involve free radical production and oxidative stress. **Financial support:** CAPES, CNPq, FAPESP.

09.054 Beta-Cyclodextrin enhanced antioxidant effect of (-)-linalool, a monoterpene present in Rosewood essential oil, in gastric lesion models Silva FV[1], Sousa SS[2], Fernandes HB[1], Oliveira IS[1], Viana AFSC[3], Araújo AAS[4], Quintans-Júnior LJ[5], Oliveira RCM[1] [1]Renorbio-UFPI – Biotechnology, [2]UFPI – Pharmacology, [3]UFC – Pharmacology, [4]UFS – Pharmacy, [5]UFS – Neuroscience and Pharmacological Assays í

Introduction: (-)-Linalool (LIN) is one monoterpene constituent of essential oils obtained from the plant species *Aniba roseadora* Ducke, among others. It has shown several promising pharmacological activities such as a modulator of central nervous system, antinociceptive and anti-inflammatory activities in animal models. Thus, the incorporation of cyclodextrins, especially β-CD, has emerged as an important tool to improve the physicochemical and biological properties of several monoterpenes. This study aimed to evaluate the potential antioxidant of this monoterpene in uncomplexed (LIN) and complexed (LIN-βCD) forms. **Methods:** The induced acute gastric lesions in mice (n = 5 animals/group) orally (0.2 mL/animal) with absolute ethanol. Vehicle (NaCl 0.9%), LIN or LIN-βCD (5; 10, 20 or 40 mg/kg) or carbenoxolone (100 mg/kg) were administered orally 1 h prior to application of the agent. In the antioxidant activity protocols, the lowest dose of uncomplexed LIN and with significant gastroprotective activity (10 mg/kg) was used. Both the stomachs removed from the animals of the Sham group and the groups treated orally with vehicle, LIN or LIN-βCD (10 mg/kg), were used to quantify the following parameters: determination of non-protein sulfhydryl groups and myeloperoxidase activity. The experimental protocols were approved (CEEA-UFPI 096/14). All data are expressed as mean ± SEM/ANOVA/Tukey's test were used to determine the significance between groups (*p<0.05). **Results**: Pretreatment with LIN at a dose of 10 mg/kg did not alter the levels of gastric contents NP-SH (221.98 ± 11 µg/g protein) compared to the vehicle group after induction of absolute ethanol ulcer. Unlike, the LIN-βCD at the dose of 10 mg/kg exhibited a significantly increased rate of gastric contents NP-SH (454.22 ± 24* µg/g protein) compared to vehicle; myeloperoxidase activity assessment (MPO) in stomachs of animals pretreated with vehicle (7.13 ± 1.2 U/mg* tissue) was significantly higher when compared to Sham group (2.7 ± 0.7 U/mg tissue). Stomachs pretreated with LIN (1.6 ± 0.7 U/mg* tissue) or LIN-βCD (0.8 ± 0.3 U/mg* tissue) in the dose of 10 mg/kg showed a reduction in MPO activity wen compared to vehicle group. **Conclusion:** These data show that the gastroprotective activity of uncomplexed monoterpene and complexed into β-cyclodextrin is probably related to the increased antioxidant activity. LIN-βCD was shown to have a more potent antioxidant effect when compared to LIN, revealing that the incorporation of the monoterpene in β-cyclodextrin improves its antioxidant profile. **Financial Support:** CNPq/CAPES/UFPI.

09.055 Gastroprotective effect of sedum dendroideum leaves infusion on acute ethanol-induced gastric lesions in rats. Luz BB[1], Maria-Ferreira D[2], Dallazen JL[1], Oliveira AF[2], Cipriani TR[2], Werner MF[1] [1]UFPR – Farmacologia, [2]UFPR – Bioquímica e Biologia Molecular

Introduction: *Sedum dendroideum* popularly known as "bálsamo", is a succulent plant widely used ornamentally. In folk medicine is commonly used for the treatment of gastrointestinal disorders, (DE MELO *et al*., **J. ETHNOPHARMACOL.** 102, 217; 2005), and the ethnopharmacological use involves the consumption of fresh leaves as salad or an infusion prepared by soaking the leaves in hot water. Therefore, our aim was investigate the gastroprotective effect of an infusion prepared with leaves of *Sedum dendroideum* (ISD). **Methods:** The gastroprotective effect of infusion (ISD) was evaluated using acute gastric lesions induced by ethanol (ROBERT *et al*., *Gastroenterology* 77, 433; 1979). Fasted female Wistar rats were pre-treated orally with vehicle (V: water 1ml/kg), omeprazole (O: 40 mg/kg), ISD (80, 160 or 320 mg/kg) or with the ISD mean ID_{50} of 19 mg/kg by intraperitoneal route. After 1 h of pre-treatments, all animals received orally 1 ml ethanol P.A., and following 1 h were euthanized with an overdose of thiopental (100 mg/kg, i.p.). The stomachs were removed, opened along the greater curvature and cleaned with saline for the quantification of lesion area by planimetry. The protective factors of the gastric mucosa (mucus and glutathione levels (GSH)) were also analyzed. All experiments were conducted in agreement with the "Guide for the Care and Use of Laboratory Animals" (8th ed, 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**: The treatment with ISD (80, 160 and 320 mg/kg, p.o.) significantly reduced the gastric ulceration induced by ethanol in 33, 40 and 63% respectively when compared with the control group (V: 187.6 ± 22.41 mm^2). In addition, ISD (80, 160 and 320 mg/kg, p.o.) was also able to preserve the gastric wall mucus content in 40, 43 and 38% (V: 1805.1 ± 121.7 µg alcian blue/g of tissue). Concerning the antioxidant parameter, ISD 320 mg/kg prevented in 42% the GSH levels when compared to the control group (V: 1037.1 □ 165.5 µg GSH/g of tissue). In relation to the positive control, omeprazole prevented in 94% the formation of ulcers and in 44 and 47 % the depletion of the level of GSH and mucus content respectively. Interestingly, the gastroprotective effect was maintained when ISD 19 mg/kg was administrated by intraperitoneal route, reducing in 81% the gastric ulcer formation when compared with control group (V: 220.4 ± 37.2 mm^2), discarding the formation of a physical protective barrier on the gastric mucosa. In addition, ISD (19 mg/kg, i.p.) preserve the gastric wall mucus in 30% and GSH levels in 57%, in comparison to the control group (V: 2398.5 ± 204.3 µg alcian blue/g of tissue; V: GSH: 1012.5 ± 150.7 µg GSH/g of tissue). **Conclusion:** Collectively, our results reinforce and prove the therapeutic and ethnopharmacological use of *Sedum dendroideum* infusion against gastric lesions, showing the involvement of the mucus and GSH protective factors. Furthermore, we conclude that the maintenance of mucosal integrity promoted by "bálsamo" occurs independent to the formation of a mechanical barrier in the gastric mucosa. **Financial Support:** CAPES

09.056 Evaluation of the acute toxicity and gastroprotective activity of hesperetin in animal models. Silva SL[1], Guedes JM[1], Formiga RO[1], Pessoa MMB[1], Barros MEFX[1], Vasconcelos RC[2], Araujo AA[2], Batista LM[1] [1]UFPB, [2]UFRN

Introduction: Hesperetin is a natural aromatic organic compound. It is classified as a flavonoid belonging to the class of flavanones that occur either in the free form (aglycone) or bound to sugar residues (glycosides/heterosides), in plant species. The objective of this study was to evaluate the acute toxicity, the gastroprotective activity, as well as, to determine the immunomodulatory activity and antioxidant of hesperetin. **Methods:** The animals used on the toxicological assay were male Swiss mice (Mus musculus) (n=3), weighing 25-35 g. They were treated with 10 mL/kg of 0.9% saline solution (control group) and with the test substance hesperetin (300 and 2000 mg/kg) (Almeida R. N. Rev. Bras. Cienc. Farm, 80, 72, 1999), all orally. After treatment, a behavioral assessment was undertaken (30 min, 1, 2, 3, 4, 24 and 48h) and mice were evaluated during 14 days over water and feed consumption. For the assessment of the gastroprotective activity the ethanol-induced gastric ulcer model was used (Morimoto Y. J. pharmacol, 57, 495, 1991). Wistar rats (Rattus norvegicus) (n=6-8), weighing 180-250g were pre-treated with 10 mL/kg of 0.9% saline solution (negative control), carbenoxolone 100 mg/kg (positive control) and hesperetin (25, 50, 100 and 200 mg/kg - v.o). After 1 hour, gastric lesions were induced by the administration of absolute ethanol. The animals were then euthanized after 1 hour, the stomachs were collected and ulcerative lesion area (ULA) were determined (mm^2) using the software AVSOFT Bioview®. Gastric portions were stored for further analysis of antioxidant (MDA and GSH) and immunomodulatory activity (IL-1β and TNF-α). Data were analyzed using unpaired "t" student test for the acute toxicological evaluation. For the antiulcer protocol, antioxidant and immunomodulatory determinations data were analyzed using ANOVA, followed by Dunnett's/Tukey test. **Results:** No deaths were observed in the groups treated with hesperetin (300 and 2000 mg/kg). Thus, it was possible to verify that hesperetin LD_{50} is 5000 mg/kg or more - if configured in category 5. Besides, there were no significant changes in the final weight, water and feed consumption and on the organ index (heart, kidney, spleen and liver) of hesperetin treated groups, when compared to control group. In the ethanol-induced gastric ulcer model, the results showed a reduction of ULA ($p<0.001$), in all tested doses (25, 50, 100 and 200 mg/kg) in 42.64, 64.13, 71.5, 70.53% respectively, when compared to the negative control group. The results for the antioxidant assay demonstrated a restoration in GSH levels ($p<0.001$), as well as, a decrease in MDA levels ($p<0.001$) in the hesperetin treated groups (100 and 200 mg/kg), when compared to the negative control group. In the evaluation of immunomodulatory effect, the results presented a reduction of proinflammatory cytokines IL-1β ($p<0.01$) and TNF-α ($p<0.0001$) levels, in the hesperetin treated groups (100 and 200 mg/kg), when compared to the negative control group. Conclusions: Thus, the results demonstrated that hesperetin presents low toxicity and gastroprotective activity, which is linked to antioxidant and immunomodulatory effects. Acknowledgments: CNPq/CAPES/PgPNSB/UFPB. Ethics Committee (CEUA/UFPB): Protocol number 0118/2016.

09.057 Rhamnogalacturonan for the management of pain in ulcerative colitis. Maria-Ferreira D[1], Dallazen JL[1], Barbosa BL[1], Nascimento AM[2], Cipriani TR[2], Baggio CH[3], Werner MFP[1] [1]UFPR – Farmacologia, [2]UFPR – Bioquímica, [3]University of Calgary – Chronic Diseases

Introduction: Ulcerative colitis (UC) is a chronic disorder characterized by relapsing inflammation of the colon and abdominal pain is a common complaint in up to 70% of patients experiencing the initial onset or exacerbation of the disease. The conventional therapies (corticosteroids, aminosalicylates and immunomodulators) have side effects and high cost, leading the search for new alternative therapeutic strategies. Accordingly, the polysaccharides are in a remarkable scenario exhibiting important pharmacological activities as anti-inflammatory in gastric ulcer models (Maria-Ferreira *et al*., 2014) and antinociceptive (Moreno *et al*., 2016). In addition, we already showed that the polysaccharide rhamnogalacturonan (RGal) isolated from *Acmella oleracea* has potent anti-colitis activity (Maria-Ferreira, D. *et al*., JRV AWARD first place, 47º SBFTE, 2015). Here, we investigate the antinociceptive effects of RGal in a dextran sulfate sodium (DSS)-induced colitis model in mice and in normal mice. **Methods:** Colitis was induced by administration of DSS for 5 days followed by 2 days of water. The animals were orally treated with vehicle (water, 1 ml/kg) or RGal (10 mg/kg) daily. After 7 days, gastrointestinal transit was measured and visceral allodynia was evaluated by von Frey filaments. The colons were collected, measure and used for oxidative stress analysis. Antinociception was evaluated in normal animals through abdominal pain induced by intraperitoneal injection of 0.6% acetic acid and intracolonic injection of 0.5% mustard oil or 0.1% of capsaicin. The locomotor activity was evaluated in open field test (CEUA/BIO-UFPR: 863, 721, 1005). **Results and Discussion:** RGal reduced the colitis score ~ 46% and protected mice from weight loss ~ 51% at day 8 when compared to the DSS group. Also, it prevented the reduction of colon length (9.1 ± 0.2 cm), maintained the intestinal transit ~ 52% and reduced the withdrawal response to mechanical stimulation of the abdomen when compared to the DSS group. Further, RGal prevented the depletion of GSH, restore the GST and SOD levels and decreased the LOOH when compared to the DSS group (GSH: 130 ± 6.8; GST: 10484 ± 463.3; SOD: 49.8 ± 2; LOOH: 22.3 ± 0.5). In normal animals, acetic acid increased the writhing in the control group (53.3 ± 4.8), while RGal treatment decreased the response by 47 and 71% (v.o. and i.p., respectively). Interestingly, naloxone treatment blocked the antinociceptive responses induced by RGal (47.1 ± 5.1). In addition, RGal v.o. and i.p. decreased the leukocyte infiltration in 90 and 98%, respectively, when compared to the control group (4.9 ± 0.7). Intracolonic administration of mustard oil or capsaicin increased the nociceptive behaviors in 159% and 72% when compared to the control group (mustard oil: 16 ± 0.9 and capsaicin: 21.1 ± 5.4). Furthermore, RGal treatment (v.o. and i.p.), reduced the nociceptive responses by 51% and 87% (mustard oil), and 52 and 60% (capsaicin), when compared to the control group. RGal did not alter animal locomotion. **Conclusion:** Collectively, we demonstrated that RGal reduced the severity of DSS colitis in mice and restored the normal intestinal transit homeostasis. Besides, RGal decreased the abdominal pain with the involvement of opioid system, TRPV1 and TRPA1 receptors. Thus, RGal may represent a promising molecule for drug development to the management of pain in UC. **Support:** CAPES, CNPq

09.058 Toxicity induced by bee venom (*Apis mellifera*) antagonized by polyanion (Fucosylated chondroitin sulfate – fucCS). Cons BL[1], Tavares-Henriques MS[1], Monteiro-Machado M[1], Strauch MA[2], Teixeira-Cruz JM[1], César MO[1], Peçanha TSC[1], Patrão-Neto FC[1], Mourão PAS[3], Melo PA[1] [1]UFRJ – Farmacologia e Química Medicinal, [2]IVB, [3]HUCFF-UFRJ – Tecido Conjuntivo

Introduction: Massive bee venom envenomation induces intense local pain, tissue damage, and systemic alterations like increase in capillary permeability and hemoconcentration. In the last years, bee attacks and death has increased in Brazil. There is no substance clinically in use able to direct antagonize bee venom toxicity. Fucosylated Chondroitin Sulfate (fucCS) is a glycosaminoglycan isolated from a sea cucumber that has antithrombotic and anticoagulant properties. Recently, we showed that fucCS is able to antagonize myotoxicity and inflammatory response induced by *Bothrops jararacussu* venom and its isolated phospholipase toxins (bothropstoxin-I and bothropstoxin-II). Thus, we evaluated if fucCS is able to antagonize bee venom toxicity. **Methods and Results:** Mice (25 ± 5 g) were used to perform *in vivo* experiments. Hemathocrit, cardiotoxicity (plasma CKmb) and lethality experiments were performed using *A. mellifera* crude venom (10 mg/kg) alone or associated to fucCS (1-10 mg/kg). Intraplantar edema induced by bee venom (3 µg/paw) challenge with fucCS (0.3-3 µg) was evaluated using a digital caliper. All experiments were approved by the Committee of Animal Use of the Rio de Janeiro Federal University (DFBCICB 026). It was observed that fucCS completely abolish lethality, venom hemoconcentration cardiotoxicity when mixed with fucCS (10 mg/kg) in a dose dependent manner. FucCS was also able to partially inhibit (60% with 0.3 µg) paw edema induced by bee venom. **Conclusion:** FucCS shows strong ability in antagonize important *in vivo* toxicity induced by bee venom crude venom. These results can be used to help in elucidate venom mechanism of action. Thus, fucCS became a promising candidate that maybe can be useful clinically in future to treat massive bee venom envenomations. **Keywords:** Bee venom, toxicity, cardiotoxicity, fucosylated chondroitin sulfate. **Financial Support:** CNPq, CAPES, FAPERJ and PRONEX.

09.059 Evaluation of the intestinal anti-inflammatory activity from green propolis extract in a model of colitis in mice induced by dextran sulfate sodium. Silva RCMVAF, Costa APM, Perondi G P, Bolda LNM, Somensi LB, Souza P, Andrade SF, Silva LM Univali – Ciências Farmacêuticas

Introduction: Ulcerative colitis (UC) is a chronic inflammation disease restrict to the mucous layer which affects the large intestine upwardly from the rectum to the colon. The pathogenesis of UC is not well understood and the current therapy includes a large numbers of drugs, many with side effects, high cost and sometimes with inefficient response. Therefore, this study aimed to investigate the anti-inflammatory effect of hydroalcoholic extract from green propolis (HEGP) in mice with colitis induced by dextran sulfate sodium (DSS). **Methods:** Colitis was induced by addition of 3% (w/v) DSS (MW: 40,000) in drinking water *ad libitum* for 5 days. Control-colitic group was treated once a day, for 7 days, with vehicle (water, 10 mL/kg). HEGP-treated colitic group received the extract (300 mg/day) once a day for seven days. The positive control agent used in this experiment was 5-aminosalicylic acid (5-ASA), administered at a dose of 100mg/kg (p.o) once a day for 7 days in colitic animals. Noncolitc group did not received DSS in drinking water. The treatment with vehicle or extract started simultaneously with the DSS administration. The effects of the extract were evaluated through clinical parameters (loss of weight, diarrhea and, the presence of blood in the stool), microscopes (histology and mucins quantification) and biochemical analysis (reduced glutathione (GSH) and lipid hydroperoxide (LOOH)). **Results:** Our results indicated that HEGP had anti-inflammatory activity, and was able to reduce the clinical signs of the diseases ($p<0,001$). In addition, HEGP maintained the length of the colon as well as preserved the architecture of the villi and, reduced the deleterious effect promoted by the DSS on the intestinal tunics. Furthermore, the mucins reduction was minimal when compared to others groups ($p<0,001$), maintaining the epithelium protection. GSH levels were also preserved in the colon of the animals treated with HEGP (300 mg/kg). **Conclusion:** The hydroalcoholic extract from green propolis demonstrated anti-inflammatory activity in the DSS-induced colitis model by the maintenance of intestinal mucin barrier and reducing the oxidative stress. We are currently investigating the potential therapeutic from green propolis and the contribution of anti-inflammatory activity of HEGP against intestinal inflammatory processes. All procedures were approved by the Institutional Ethics Committee of UNIVALI (protocol number: 04 16p). **Financial support:** Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, CAPES, Brazil; Conselho Nacional de Desenvolvimento Científico e Tecnológico, CNPq, Brazil. UNIVALI

09.060 Conservation among venoms PLA2 molecules as basis for development of pan-PLA2 antibodies. Strauch MA[1,2], Corrêa-Netto C[1], Araújo RT[1], Brazil-Más L[1], Monteiro-Machado M[3], Leitão-Araújo M[4], Foguel D[5], César MO[3], Calvete JJ[6], Migowski ERC[1,7], Melo PA[3], Zingali RB[5] [1]IVB, [2]UFRJ, [3]ICB-UFRJ, [4]FZB-RS – Ofiologia, [5]UFRJ – Bioquímica Médica, [6]IBV-CSIC [7]UFRJ – Puericultura e Pediatria

Martagão Gesteira Polyclonal antibodies have been used for over a century for the treatment of snakebite envenoming. New strategies and approaches to understand how antibodies recognise and neutralise snake toxins represent a challenge to generate next-generation antivenoms. The neurotoxic activity of *Micrurus* venom is mainly due to two distinct proteins families, 3FTx and PLA_2. Structure conservation among protein family members may represent an opportunity to generate neutralizing monoclonal antibodies against family-conserved epitopes. In this work, we sought to produce a set of monoclonal antibodies against the most toxic components of *M. altirostris* venom. To this end, the venom was fractionated, its major toxic proteins identified, and used to generate a panel of five monoclonal antibodies. The specificity of these mAbs was characterised by ELISA and antivenomics. Three and two mAbs recognised, respectively, 3FTx and PLA_2 epitopes. The PLA_2-specific monoclonal antibodies cross-reacted with all PLA_2 molecules of *M. altirostris* venom and inhibited their catalytic activity. The anti-PLA_2 mAbs showed paraspecificity against, and neutralized the activity of PLA_2 molecules from *Naja naja* venom. Epitope conservation among venom PLA_2 molecules offers the opportunity of generating pan-PLA_2 antibodies. **Financial Support**: Faperj, Cnpq