09. Natural Products and Toxinology

09.001 Vasorelaxant and antioxidant effect of the hydroalcoholic fraction of *Sida santaremnensis* **H. Monteiro (Malvaceae) in rodents.** Souza FM[1], Santos MEP[1], Azevedo PSS[1], Moura LHP[2], Silva Filho JC[3], Costa DA[4], Sousa BM[5], Medeiros JVR[5], Oliveira AP[1]
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Introduction: Some species of the genus Sida are used in folk medicine for the treatment of hypertension (Hansen et al, 1995; Noumi et al, 1999). The species *Sida santaremnensis* H. Monteiro (Malvaceae) is a shrub known as "Guaxuma" or "vassourinha" (Peixoto et al., 2007). In a previous study, the ethanolic extract obtained from the aerial parts of this species showed vasorelaxant effect on rat superior mesenteric artery (ARCANJO et al., 2011). **Aim:** To investigate the vasorelaxant and antioxidant activities of the hydroalcoholic fraction of *Sida santaremnensis* (Ssan-HA). **Methods**: Wistar male rats (250–300 g, n=5) were used in vitro experiment. After euthanasia (Resolution n. 1000, 2012 – CFMV), rings of mesenteric artery (1-2 mm) with and without functional endothelium were kept in Tyrode at 37°C aerated with 95% O_2 and 5% CO_2, suspended by cotton thread and attached to force transducers coupled to a data acquisition system (AVS Projects/SP) for registration of isometric tension. After 1h of stabilization (tension of 0.75 g), the rings were contracted with phenylephrine (10^{-5}M), an alpha 1 adrenergic receptor agonist. After equilibration, steady tension was evoked by phenylephrine (10^{-5}M) for rings to induce contraction of similar magnitude and Ssan-HA was added cumulatively (0,1 - 750 µg/mL). Swiss mice (25- 30 g) were used in vivo experiments and divided into 4 groups: the animals were intraperitoneally pre-treated with saline and Ssan-HA at doses of 1, 10 and 20mg / kg respectively. Four hours after treatment the animals were euthanized and the heart was removed to measure the concentration of glutathione (GSH), malondialdehyde (MDA) and hydrogen sulfide (H_2S). **Results:** The results show that Ssan-HA (0.1 to 750 µg / mL) promotes vasorelaxant effect on vascular endothelial preparations (pD2 = 1.42 ± 0.04) pre-contracted with phenylephrine of concentration- dependent manner. This effect was attenuated after removal of the endothelium (pD2 = 2.01 ± 0.05 * $p < 0.05$). Regarding the antioxidant activity it was observed that the group which was administered the dose of 1 mg / kg of Ssan-HA significantly increased GSH levels (441.7 ± 42.83 mg GSH / g of tissue) compared with the control group (saline: 151.4 ± 66.67 mg of GSH / g of tissue) while MDA levels decreased significantly after treatment in all tested doses (saline: 92.47 ± 13.93; 51.48 ± 10.69, 15.73 ± 3.64, 29.32 ± 6.39 nmol / g of tissue MDA respectively). There was also an increase in the levels of H_2S at the doses of 1, 10 and 20 mg / kg (0.52 ± 0.02, 0.50 ± 0.01 and 0.42 ± 0.04 µmol / g tissue, respectively H_2S) when compared with the control (0.30 ± 0.03). **Conclusion:** In conclusion, the San-HA fraction induces vasorelaxation dependent on the vascular endothelium. In addition to Ssan-HA induces changes in GSH levels, MDA and increase of H_2S. **Support:** UFPI/UFCG/CAPES/FAPEPI/CNPq. All experimental protocols and procedures were approved by CEEA/UFPI nº 008/12.

09.002 Hematological and biochemical effects after repeated exposure to pequi oil. Traesel GK, Menegati SELT, Villas Boas GR, Kassuya CAL, Argandoña EJS, Oesterreich SA

Introduction: Pequi (*Caryocar brasiliense*) is a Brazilian fruit rich in oleic acid, phenolics and carotenoids. In phytotherapy, it is used for the treatment of influenza, asthma and other respiratory diseases. Pharmacological studies have shown that the plant has antigenotoxic, anti-clastogenic, anti-inflammatory and hypocholesterolemic activities. Due to ethnopharmacological use, the aim of this study was to evaluate the hematological and biochemical effects after repeated exposure to pequi oil. **Methods**: Subacute toxicity test was based on the OECD protocol– Guideline 407. Wistar male and female rats received, orally, repeated doses of 125, 250, 500 or 1000 mg/kg of the oil extracted from the pulp of C. brasiliense, being treated and observed for 28 days. At the end of the observation period, the animals were euthanized and the collected blood was used for biochemical and hematological analysis. The experimental procedures were approved by the Ethics Committee in Animal Experimentation from the UFGD (protocol: 17/2015). **Results**: In order to investigate systemic toxicity or target organs by the substance tested, serum biochemical tests are necessary. In this study, liver function (AST and ALT) and renal function tests (blood urea nitrogen and creatinine) were performed. Protein profile (total protein and albumine) and metabolic biomarkers (glucose, triglycerides, overall cholesterol and HDL cholesterol) were also measured. In females, there were statistically significant differences in ALT values and urea in some treated groups when compared to the control. In males, there were statistically significant differences in ALT, total cholesterol and triglycerides values in some treated groups. However, all the values that differed significantly from the control group are within the expected normal range for the species, indicating that the variations found are not attributed to clinical significance or toxic effect of the oil but rather the own physiological animal variability. Repeated administration of a substance can cause temporary or permanent damage to the hematopoietic system. The study of hematological markers provides important information about the pathophysiological state of mammals. In this study, a complete analysis of erythrocyte, including white blood cell count and platelet parameters was carried out. In females, there was a statistical difference for the differential leukocyte in some groups. In males, there were statistical differences in MCV, MCH and differential leukocyte in some groups. Similarly as in the biochemical analysis, the variations are not biologically significant since the values are within normal range for thespecies, indicating that the pequi oil does not causeany adverse effects on circulating blood cells or on its production. **Conclusion:** These results demonstrate the absence of effects in hematological or bioquimical parameters after oral exposure to the oil of *C. brasiliense* in rats. However, additional studies in animals and humans are required in order to have sufficient safety evidence for the use of the oil in humans. **Financial support**: CAPES

09.003 Hydroalcoholic extract from inflorescences of *Achyrocline satureoides* **ameliorates dextran sulphate sodium (DSS)-induced colitis in mice by attenuation in the production of inflammatory cytokines and oxidative mediators.** Boeing T, Silva LM, Farias JAM, Somensi LB, Cury BJ, Santin JR, Andrade SF Univali – Ciências Farmacêuticas

Introduction: A*chyrocline satureioides* (Lam.) D.C. is popularly known as "Marcela" or "Macela", being used in Brazil to treat inflammatory and gastro-intestinal diseases. The present study examined the intestinal anti-inflammatory effects of the hydroalcoholic extract of inflorescences of A. satureoides (HEAS) in a model of colitis induced by dextran sulfate sodium (DSS) in mice. **Methods**: Colitis was induced by DSS (3%) in drinking water. Simultaneously, mice were orally treated with vehicle, 5-ASA (100 mg/kg) or HEAS (1-100 mg/kg). Clinical signs of colitis and colonic histopathological parameters were evaluated, along with the determination of levels of glutathione reduced and lipoperoxides (LOOH), the activity of superoxide dismutase (SOD) and myeloperoxidase (MPO) in colon. The colonic content of cytokines (TNF, IL-4, IL-6 and IL-10) also was measured. Additionally, the effects of the extract in the intestinal transit, on nitric oxide (NO) release by lipopolysaccharide (LPS)-stimulated macrophages and in diphenylpicrylhydrazyl levels were determined. **Results**: HEAS improved the colonic tissue at both macroscopic and histological levels. Mucin levels and SOD activity, as well as the LOOH, MPO, TNF-α and IL-6 accumulation in colon tissues was normalized by the HEAS administration. In addition, the extract elicited an increase in IL-4 and IL-10 levels in colon. NO release by macrophages was inhibited by HEAS and its scavenger activity was confirmed. The extract did not alter the intestinal transit in mice. **Conclusion:** Together these results placing inflorescences from A. satureioides as a source of metabolites that could be used in treatment for IBD mainly flavonoids, by attenuation in the production of inflammatory cytokines and oxidative mediators. **Financial support**: CNPQ, CAPES, FAPESC. Approval number CEUA: 033/14p.

09.004 Antiproliferative activity of *Melaleuca alternifolia***, (+) and (-)-Terpinen-4-ol.** Maccari FLR[1], Ruiz ALTG[2], Bergamo JC[1], Carvalho JE[2], Scarpa MV[1], Oliveira AG[1] [1]FCFar-Unesp-Araraquara – Ciências Farmacêuticas, [2]Unicamp – Farmacologia

Introduction: Recently, *in vitro* studies have demonstrated the effectiveness of *Melaleuca alternifolia* and isolated terpinen-4-ol in the inhibition of melanoma (M14 line), lung tumor cells (A549), breast tumor cells (MCF-7) and prostate tumor cells (PC-3)[1,2]. It is well known that the terpinen-4-ol is in the form of a racemic mixture. However, it is not clear in the literature which ones of these forms present pharmacological activity. Thus, the aim of this study was to evaluate the antiproliferative activity of *M. alternifolia*, (+) and (-)-terpinen-4-ol in nine tumor cell lines. **Methods:** The oil of *Melaleuca alternifolia* from Galena® content 38,2% of terpinen-4-ol; standard (+)-terpinen-4-ol was purchased by Fluka® content 97,6%; standard (-)-terpinen-4-ol was purchased by Fluka®, content 98.8%; RPMI 1640 culture medium from Gibco® with 5% inactive bovine fetal serum (Gibco®); streptomycin/penicillin 100 mg/mL:100 IU/mL (Nutricel®); Doxorrubicine 100mg/g (Eurofarma®). The samples were evaluated in nine human cell lines [U251 (glioma, CNS), UACC-62 (melanoma), MCF-7 (breast), NCI-H460 (lung, non-small cell), OVCAR-03 (ovarian), PC-3 (prostate), HT-29 (colon), 786-0 (kidney) and NCI-ADR/RES (ovarian expressing the multiple drugs resistance phenotype)] and one normal epithelial cell line [VERO (kidney, green monkey)]. **Results:** The values were expressed as cellular inhibition in 50% of cells (GI50). The essential oil of *Melaleuca alternifolia* demonstrated selective cytostatic activity for ovarian multidrug resistant (NCI-ADR/RES,GI50 = 31,5 µg/mL) and leukemia (K-562,GI50 = 5,2 µg/mL),moderated activity in breast tumor cell lines (MCF7, GI50 = 153,9 µg/mL) , kidney (786-0, GI50= 168,9 µg/mL), prostate (PC-3, GI50= 178,6 µg/mL) and colorectal (HT29, GI50 = 99,9 µg/mL). It also demonstrated cytostatic weak effect in melanoma cell lines (UACC-62, GI50 = 250 µg/mL), being inactive at a concentration of 250 µg/mL in lung, non-small cell (NCI-H460). The dextrorotatory isomer showed cellular inhibition in only one strain, showing selective cytostatic activity in leukemia cell line (K-562, GI50 = 8.00 µg/mL) and being inactive at the concentrations analyzed in other cell lines. The levorotatory isomer showed a selective cytostatic activity for ovarian (OVCAR-03, GI50 = 53.01µg/mL), prostate (PC-3, GI50= 71.81 µg/mL) and lung (NCIH460, GI50 = 77.50 µg/mL) cancer cell lines; being inactive for melanoma (UACC-62), kidney (786-0) e colon cell lines (HT-29). **Conclusion:** Our results showed that the oil of *M. alternifolia* showed better activity than isomers of terpinen-4-ol in different cell lines. The (+)-terpinen-4-ol, showed cytostatic activity in one cell line and the (-)-terpinen-4-ol isomer presents a moderate cytostatic activity for the prostate lines (PC-3) and lung cell lines (NCI-H460) corroborating the results described by Liu et al (2009) for the tea tree oil. Thus, will be considerable an isomer quantification in essential oil, strengthening the importance of stereochemistry in the antiproliferative activity. **References:** [1] Calcabrini, A. et al., J. Invest. Derm. v.122, p.349, 2004; [2] Liu, X. et al., Eur. Food Res. Technol. v.229, p.247, 2009. **Financial support**: Fapesp.

09.005 *Uncaria tomentosa* **improves steatohepatitis and insulin sensitivity via inhibition of irs1 phosphorylation in serine 307.** Araujo LCC, Furigo IC, Murata GM, Donato Junior J, Bordin S, Curi R, Carvalho CRO USP – Fisiologia e Biofísica

Introduction: obesity is associated to excess of fatty acids, which are stocked in the liver and skeletal muscle tissue, promoting accumulation of ectopic fat and inflammation in these tissues. These fatty acids can to activate PKCθ and TLR4 receptor of inflammation pathway, this can lead to IRS-1 phosphorylation on serine and initiate insulin resistance (William, Nat Rev Mol Cell Biol, p367, 2008; Vinolo, Am J Physiol Endocrinol Metab, p272, 2012). **Aims:** To evaluate the effect of *Uncaria tomentosa* (UT) anti-inflammatory herbal in the steatohepatitis associated to obesity and signaling pathways of insulin and inflammation in obese mice. **Methods**: diet-induced obese (DIO) C57BL/6 mice were treated daily with dry extract of UT (Herbarium®) (50 mg/kg) for 5 consecutive days. Metabolic analyzes by CLAMS, insulin tolerance test (ITT), morphometric analysis of liver and adipose tissue by histology were performed. Proteins of Insulin and inflammatory pathway were analyzed by western blot and pro and anti-inflammatory markers by polymerase chain reaction (PCR). All experimental procedures were approved by ICB/USP Ethics Committee on Animal Use (Protocol/CEUA no. 35, p30, book 3). **Results**: diet-induced obesity was accompanied by reduced Kitt (0.5 ± 0.3 *vs* 4.0 ± 0.2% * min^{-1}, obese *vs* control). Treatment with UT increased Kitt in both control (2-fold) and DIO mice (10-fold). Oxygen consumption (VO_2) in nighttime and daytime periods were reduced in the DIO mice (2575 ± 58 and 2407 ± 26 mL/kg/h) compared to controls (3082 ± 91 and 2765 ± 68 ml/kg/hr), respectively. Treatment with UT increased VO_2 in the DIO mice (2774 ± 103 and 2666 ± 71 ml/kg/h, respectively). In adipose tissue, DIO mice had area of adipocytes 3-fold increased compared to controls and treatment with UT reduced that area to approximately half in the DIO mice. Liver of DIO mice showed fat droplets (28 ± 1%) compared to control group (0%). UT reduced approximately 40% the presence of fat droplets. Proteins expression levels of insulin intracellular pathway in the liver of DIO mice (IR, IRS1, AKT, GSK3) were all reduced to 2; 3; 1; and 2-fold reduction, respectively compared to controls. Treatment with UT had no impact in the protein expression levels. However, enhanced IRS1 serine phosphorylated at serine residue 307 detected in the liver of DIO mice was reduced to the same level of detected in the control group with the treatment. Furthermore, increased protein levels of JNK and IKKβp in the DIO mice, involved in the inflammatory pathway, had 2; and 1-fold reduction, respectively, in the liver of DIO mice treated with UT. Similarly, PKCθ protein level was detected and the treatment with herbal extract induced 2-fold reduction in the liver of DIO mice. There were detected 2-fold increase of F4-80 mRNA associated to 5-fold reduction in the arginase-1 mRNA in the DIO mice compared to controls. Again, UT treatment induced a 7-fold reduction in the F4-80 mRNA, however had no impact in the arginase mRNA. **Conclusion:** *U. tomentosa* improves insulin sensitivity, increases energy expenditure, reduces the accumulation of fat in the adipose tissue, inflammatory condition in the liver and steatohepatitis. Therefore, beside *U. tomentosa* has been used in clinic because of its anti-inflammatory property, it may have an additional therapeutic effect in metabolic disorders related to insulin resistance. Keywords: obesity, inflammation, insulin resistance, fatty liver. **Financial support**: CNPq, Fapesp

09.006 Antinociceptive and anti-inflammatory effects of the bioflavonoid peltatoside and filtered hydroalcoholic fraction from *Annona crassiflora* **Mart. leaves in mice.** Oliveira CC[1], Matos NA[1], Veloso CC[1], Ferreira RCM[1], Lage GA[2], Pimenta LPS[2], Klein A[1], Romero TRL[1], Perez AC[1] [1]ICB-UFMG, [2]ICEX-UFMG

Introduction: *Annona crassiflora* Mart., popularly known as “Maroleiro”, is a tree native of the Brazilian Cerrado used in folk medicine for the treatment of inflammatory and painful diseases. Quercetin-3-O-β-D-glycopyranosil(1→6)-O-α-L-arabinoside, known as peltatoside, is a natural substance isolated from the filtered hydroalcoholic fraction of *Annona crassiflora* Mart. leaves. We proposed to assess the analgesic and anti-inflammatory actions *in vivo* of *Annona crassiflora* Mart. leaves and peltatoside. **Methods**: Swiss mice were submitted to formalin-induced nociception test, tail-flick reflex test and paw withdrawal test, to assess antinociceptive properties, and to the rota-rod test, for motor performance analyses. To evaluate anti-inflammatory properties, *Annona crassiflora* Mart. leaves was orally administered 1 h prior to the intrathoracic injection of carrageenan, zymosan, LPS, CXCL8 or vehicle in Balb/c mice and neutrophil infiltration was evaluated 4 h after injection. In order to determine the cannabinoid system role in the peripheral antinociceptive effect of peltatoside, we used: (i) AM251, CB_1 cannabinoid receptor antagonist; (ii) AM630, CB_2 cannabinoid receptor antagonist; (iii) VDM11, endocannabinoid reuptake inhibitor; (iv) MAFP, anandamide amidase inhibitor; (v) and JZL184, monoacylglycerol lipase inhibitor. Statistical analysis: One-Way or Two-Way ANOVA followed by Bonferroni post-test. **Results**: Oral pretreatment with the filtrate hydroalcoholic fraction of *Annona crassiflora* Mart. leaves decreased the licking time in the second phase of formalin test, which corresponds to inflammatory pain. The latency time (s) in the filtered-treated group in the tail-flick test was not altered, suggesting no central antinociceptive effects. The filtered-treated group did not show motor performance alteration in the rota-rod test. The filtered fraction hydroalcoholic *Annona crassiflora* Mart. leaves significantly inhibited the recruitment of neutrophils into the thoracic cavity induced by carrageenan, LPS and CXCL8, but not zymosan. The peltatoside intraplantar administration produced a local inhibition of carrageenan-induced hyperalgesia in the paw withdrawal test. AM251 antagonized the antinociceptive effect induced by peltatoside, but not AM630. VDM11, MAFP and JZL184 potentiated the peltatoside intermediate antinociceptive dose. Discussion: The experimental data show that the filtered fraction of hydroalcoholic *Annona crassiflora* Mart. leaves possesses remarkable anti-inflammatory and antinociceptive activities. Furthermore, the results suggest that peltatoside is capable of inducing antinociception through activation of peripheral CB_1 receptors, involving endocannabinoids. **Financial support**: CNPq, CAPES and FAPEMIG. CEUA Protocol Number: 51/2014.

09.007 Topical anti-inflammatory activity of *Sideroxylon obtusifolium* in experimental models of dermatitis in mice. de Oliveira FTB[1], Nunes PIG[1], Viana AFSC[1], dos Santos SM[2], Alves APNN[3], Silveira ER[2], Santos FA[1] [1]UFC – Farmacologia e Fisiologia, [2]UFC – Química Organica, [3]UFC – Clínica Odontológica

Introduction: Irritant contact dermatitis (ICD) is caused by single or repeated exposure to irritants agents. *Sideroxylon obtusifolium* (Quixaba) is popularly used in the treatment of duodenal ulcers, gastritis, chronic inflammation and diabetes. This study aimed to evaluate the topical anti-inflammatory activity of the methanolic fraction of *S. obtusifolium* (MFSO) in experimental models of ICD. **Methods**: Male Swiss mice (25-30g) were used. The project was approved by the CEPA/UFC under no.110/2014. All treatments were performed by topical route, in the right ear (20µl/ear) and the edema was assessed with a digital caliper (100.174B/Digimess®). Acute ICD was induced by topical application of TPA (12-*O*-tetradecanoylphorbol-13-acetate) (2.5µg/ear). MFSO (0.03125, 0.0625, 0.125, 0.25 and 0.5mg/ear), dexamethasone (DEXA; 0.1mg/ear) or vehicle (2% Tween 80 in distilled water) were administered immediately after TPA and the edema was assessed after 4, 6 and 24h. Subsequently, the ears were collected for quantification of myeloperoxidase (MPO) activity. Chronic ICD was induced by topical application of *Croton* oil 2.5%, on alternate days for 10 days. MFSO (0.0625mg/ear), DEXA (0.1mg/ear) or vehicle were administered on days 5, 7 and 9, immediately after *Croton* oil. On the 10th day, the ears were collected for histological analysis. A group that received only vehicle was included in the study. Results were expressed as mean ± S.E.M. $p<0.05$ was considered significant (ANOVA and Student Newman Keul's test). **Results**: Acute administration of TPA induced edema at the intervals of 4h (0.070 ± 0.004mm), 6h (0.091 ± 0.004mm) and 24h (0.076 ± 0.002mm) when compared to the vehicle group (did not present edema) and increased MPO activity (0.608 ± 0.136U/mg tissue) compared to the vehicle group (0.120 ± 0.077U/mg tissue). MFSO at all doses significantly reduced the edema at the 4h (37, 70, 50, 35 and 10%), 6h (25, 81, 58, 39 and 17%) and 24h intervals (93, 99, 96, 94 and 21%), respectively. DEXA also reduced the edema at the 4h (77%), 6h (78%) and 24h (77%) intervals. MFSO (0.0625; 0.125 and 0.25mg/ear) and DEXA were able to significantly reduce the MPO activity to 0.240 ± 0.047, 0.164 ± 0.029, 0.192 ± 0,073 and 0.174 ± 0.091U/mg tissue respectively when compared to the TPA group (0.608 ± 0.136U/mg of tissue). In ICD chronic, MFSO 0.0625mg/ear significantly reduced the edema on the 5th, 7th and 9th day (0.246 ± 0.003, 0.250 ± 0.004, 0.255 ± 0.005 mm) when compared to the TPA group (0.333 ± 0.005, 0.351 ± 0.004, 0.365 ± 0.002 mm), respectively. The same was observed with DEXA (0.245 ± 0.003, 0.231 ± 0.004, 0.227 ± 0.004mm). TPA group showed hemorrhage, hypertrophied cartilage and inflammatory infiltrate. In the MFSO group there was mild infiltration of neutrophils and rare hypertrophied cartilage extracts, while in the DEXA group the morphology of the tissue was preserved. **Conclusion:** The methanol fraction of the leaves *S. obtusifolium* presents topical anti-inflammatory activity in animal models of acute and chronic dermatitis in mice. **Financial support:** CAPES/FUNCAP/UFC.

09.008 Reproductive toxicity of males treated with different doses rosemary essential oil.
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Introduction: The Rosemary (Lamiaceae) has been the subject of scientific studies for presenting functional properties related to its essential oil. Despite the great interest in therapeutic use, there are few studies related to reproductive toxicity of this oil. Reproductive toxicity testing is recommended by ANVISA, OECD and FDA as parameters evaluated for the effects of reproductive development. **Methods**: The oil was analyzed using a gas chromatograph with mass spectrometer for identification and flame ionization detector for quantification. Male Wistar rats were divided into four groups of nine rats each: CN (negative control - Tween 80 3%), C3 (essential oil in the concentration 3%), C6 (6%) and C12 (12%). All animals were treated daily by orogastric flexible. The rats were treated prior to mating (70 days) and during mating (21 days). The measurement of body mass, feed intake and water consumption were performed daily and individually. The animals had access to commercial food Nuvilab CR1 and drinking water ad libitum. At the end of the breeding period, the animals were euthanized, where, heart, liver, kidneys, spleen, testes, epididymis, vas deferens, prostate, and seminal vesicle were collected, dissected, weighed (except vas deferens), and stored solution buffered formalin for subsequent histological analysis. Analysis of organ weight took into account the relative weight. The seminal vesicle was drained before the measured weight. Each testis was crushed and homogenized in 10 ml of 0.9% NaCl containing 0.05% Triton X-100 in the tissue chopper Fisaton 720, 600rpm for 1 minute. The same procedure was performed with the tail of each epididymis. It collected 100 µl of each macerated and placed in microtube containing NaCl 900µL 0.9%. Of this volume, was performed by counting the total number of sperm (epididymis tail) and the number of spermatids (testes) through Neubauer chamber. Data were analyzed by ANOVA and when significant difference ($p < 0.05$) was followed by the Bonferroni test. **Results and Conclusion:** the major compound identified in oil was 1,8-cineole (57.17%). There were no deaths and no other apparent signs of toxicity during the experimental period. There was no significant difference in the relative feed and water consumption of treated males before mating. Regarding the relative weight of organs, there was significant difference in the relative liver weight (between C6 and C12 groups when compared to the CN group) to the relative left kidney weight (between CN groups and C12) and the weight prostate relative (between the CN and C6). For all differences p-value was $p < 0,01$. There was no significant difference in the relative weight of other organs, either for daily sperm production and the total number of sperm. As these results are still preliminary, is necessary to evaluate the change in weight associated with histopathology. The results of the histopathological analysis are not yet ready, and want to include another study group treated with the major compound of the oil analyzed by chromatography, 1,8-cineol. **Acknowlwdgment**: The authors thank Luiz C. Klein-Júnior and Amélia T. Henriques (Pharmacognosy Laboratory and Quality Control Phytomedicine, Faculty of Pharmacy, UFRGS). Animal research ethical committee: 26988.

09.009 Frutalin induces human fibroblast migration. Sousa FD[1,2,3], Brandao da Silva AF[4], Shiwen X[2], Monteiro-Moreira ACO[3], Moreira RA[1,3], Owen J[4], Abraham J[2] [1]UFC – Bioquímica, [2]University College London – Centre for Rheumatology and Connective Tissue Diseases, [3]Nubex-RENORBIO-UNIFOR, [4]University College London – Institute of Liver and Digestive Health

Introduction: Plants lectins are proteins that can specifically recognize and reversibly bind to selective sugars in carbohydrates or glycoconjugates. Due to these inherent characteristics, lectins can interact with cell surface moieties to promote both inflammatory and anti-inflammatory actions, as well as immunomodulatory and immunostimulatory effects. *Artocarpus altilis*, popularly known as "fruta-pão" (breadfruit) is a widespread plant, common in pan-tropical regions. Frutalin (FTL) is a multilectin, belonging to the Jacalin-related lectin (JRL) family derived from *A. altilis* seeds. It has been successfully used in immunobiological research, for the recognition of cancer-associated oligosaccharides. Here, we evaluate the effect of FTL on fibroblast biology, assessing fibroblast migration and activation of the innate immune pathway TLR4. **Methods:** FTL was purified by affinity chromatography on a D-galactose-agarose column. The eluted peak was dialyzed against distilled water, lyophilized and purity assessed by SDS-PAGE. Early passage normal human skin fibroblasts (NHSF) were used to perform cell viability and migration assays. Mitomycin C (5µg/mL) was used as an anti-mitotic agent to assess whether FTL induced cell migration in the scratch assay. The ability of FTL to interact with TLR4 was evaluated using HEK-Blue™-hTLR4 cells, while its effects on NHSF protein expression was assessed by western blot analysis. **Results:** FTL is expressed as different isoforms, which mainly reflect differences in post-translational glycosylation. The SDS–PAGE showed a typical JRL family mass pattern with two bands between 15kDa and 12kDa, which correspond to a glycosylated fraction and a slightly or non-glycosylated fraction, respectively. FTL did not show cytotoxicity in a concentration range of 0.001 – 1mg/mL. When FTL was added in 10%FBS-DMEM at 50µg/mL for the migration assay the scratch was completely repaired at 48h, the NHSF migrating across the entire denuded area effecting efficient wound closure. In contrast, control scratches had only managed to migrate and repair 30% of the wound ($P<0.05$). FTL was able to potently stimulate the TLR4 pathway, similar to that observed with LPS. Finally, treated fibroblasts showed increased levels of MyD88 and p-ERK expression, and also IL-6 production. **Conclusion:** This study showed that FTL was non-cytotoxic to human fibroblasts. When tested at 50µg/mL FTL substantially increased fibroblast migration, interacting via TLR4 signalling, and was also shown to increase p-ERK and IL6 levels. As fibroblasts play a pivotal role in tissue repair, FTL may represent a potential therapeutic biomolecule for wound healing and other related skin diseases. **Acknowledgments:** This work was funded by CNPQ, Conselho Nacional de Desenvolvimento Científico e Tecnológico – Brasil.

09.010 Gastroprotective activity of the anthocyanins-rich extracts and the flour from fruits of *Chrysophyllum cainito.* da Rosa RL[1], Boeing T[1], Somensi LB[1], Cury BJ[1], de Souza P[1], da Silva LM[1], de Andrade SF[1 1]Univali – Ciências Farmacêuticas

Introduction: The therapy to treat peptic ulcer is based in antisecretory drugs; which were linked to side effects and a poor healing process. Thus, the search for new therapies with fewer side effects is needed; as well as functional foods that may help in gastroprotection. **Aim:** To evaluate the gastroprotective activity of the edible fruits from *Chrysophyllum cainit*o (Sapotaceae), native from Central America and known as “abiu-roxo”. **Methods:** The methanolic extract of the peel (MEPe), seed (MES) and pulp (MEPu) of *C. cainito* fruits were obtained and its gastroprotective potential was evaluated in Swiss female mice (25-30 g) against ethanol/HCl- and indomethacin- induced gastric ulcer. The role of nitric oxide, sulfhydryl non-proteic groups, prostaglandins, alpha-2 adrenergic receptor and influences of K^+,ATP-dependent channels in gastroprotective effects also were verified. The antisecretory effects of the extracts were assessed by pylorus ligature method in mice. In a second stage of the study, the gastroprotective effect of the juice (2ml/day by seven days) and the flour (10% in the feed by seven days) from *C. cainito* fruits were evaluated in ethanol/HCl-induced gastric ulcer. **Results:** The oral administration of MEPe (3, 10 e 30 mg/kg), MES (3 e 10 mg/kg) and MEPu (10 e 30 mg/kg) reduced the gastric ulcer induced by ethanol/HCl in mice by 71.9%, 85.0%, 59.2%, 76.3%, 72.7%, 80.7% and 62.5%, respectively, compared to vehicle group (23.6 ± 5.2 mm²). The effects of the extracts against acidified ethanol also was verified by H&E staining, but only MES treated group showed increased levels of mucin content (verified by periodic acid-Schiff histochemical assay). Similarly, the intraperitoneal administration of MEPe (0.3 mg/kg), MES (0.3 mg/kg), MEPu (1 mg/kg) decreased by 74.3%, 81.2% and 58.4%, respectively, the ethanol/HCl-induced gastric lesion. The administration of indomethacin (80 mg/kg, p.o) induced gastric lesion in an extension of 9.0 ± 0.8 mm² in mice and the MEPe (3 mg/kg, p.o), MES (3 mg/kg, p.o) and MEPu (10 mg/kg, p.o) reduced by 90.1%, 85.2% and 81.7%, respectively, the ulcer lesion. In the mechanistic studies, the gastroprotective effect of MEPe, MES or MEPu was reduced in mice pretreated with L-NAME (70 mg/kg, i.p), N-Ethylmaleimide (10 mg/kg, i.p), indomethacin (10 mg/kg, i.p), yoimbine (2 mg/kg, i.p) and glibenclamide (5 mg/kg, i.p), suggesting the involvement of different routes in the antiulcer effects of the extracts. However, none of them promoted changes in acid gastric parameters in mice; and the intake of juice from the *C. cainito* fruits (2 ml/day) not promoted gastroprotective effects against acidified ethanol. On the other hand, the feed supplemented with 10% of flour from *C. cainito* fruits reduced by 71.0% the gastric ulcer induced by ethanol/HCl in mice. Phytochemical trials confirm that the extracts are rich in anthocyanins, and their potent scavenger activity was confirmed in DPPH assay. **Conclusions:** The fruits from *C. cainito* have gastroprotective potential in the form of extract or flour; therefore is a promissory source in the search for new approach to treat peptic ulcer. The effects are mediated by favoring of defensive factors on the gastric mucosa and not by antisecretory activities. **Financial support:** CNPQ, CAPES, FAPESC. **Approval number CEUA:** 005/2016.

09.011 A naphthoquinone from *Sinningia canescens* **inhibits inflammation and fever in mice.** Lomba LA, Leite MG, Souza VEP, Vogt PH, Stefanello MEA, Verdan MH, Zampronio AR
UFPR

Introduction: We have showed before that plants of the genus *Sinningia* are the source of anti-inflammatory and analgesic compounds with different mechanisms of action such as 8-metoxylapachenol and aggregatin D. This study evaluated the anti-inflammatory, anti-nociceptive and antipyretic properties of the crude extract (CE) from *Sinningia canescens*, its fractions and from the naphthoquinone 6-methoxy-7-hydroxy-α-dunnione (MHD) in male Swiss mice. **Methods**: CE, fractions and MHD were evaluated on acetic acid-induced writhing, formalin-induced nociception and carrageenan(Cg)-induced hyperalgesia and paw edema and lipopolysaccharide (LPS)-induced fever and cytokine plasmatic levels. **Results**: CE, at doses of 30 and 100 mg/kg orally reduced in the fourth hour the paw edema induced by Cg in 66% and 68%, the writhing induced by acetic acid in 60.3% and 74.8%, the second phase of nociception induced by formalin in 36.8% and 38.4% and the Cg mechanical hyperalgesia in 88.2%. CE at doses of 10 and 30 mg/kg inhibited the increase in TNF-α plasmatic concentration induced by LPS in 53% and 66%, respectively, and abolished the fever induced by LPS without affecting normal body temperature of the animals. CE did not alter the motor performance assessed by rota-rod test at 30 mg/kg and did not increase the latency in hot plate test. The dichloromethane and hexane fractions, at the doses of 2.5 and 2 mg/kg respectively, (doses based on the yield of each fraction) orally administred inhibited the formation of paw edema and hyperalgesia induced by Cg and the fever induced by LPS. MHD, a naphthoquinone found in dichloromethane and hexane fractions, was evaluated for its anti-edematogenic, antinociceptive, antipyretic and its effect on cytokines plasmatic levels. This naphthoquinone at 0.15 mg/kg, orally, reduced the edema formation induced by Cg, the mechanical hyperalgesia induced by prostaglandin E2 (PGE_2), but not by dopamine. Its antinociceptive action was not blocked by pretreatment of the animals with glibenclamide, a selective blocker of ATP-sensitive potassium channels. The compound also did not change the mechanical hyperalgesia induced by the permeable ATP analog, dibutiryl cAMP (dbcAMP). MHD inhibited the febrile response and the increase in plasma concentration of TNF-α, IL-1β and IL-6 induced by LPS. Local pre-treatment with the compound at doses of 150 and 500pg reduced the edema induced by Cg. **Conclusion:** These data suggest that the CE has an important anti-inflammatory, antinociceptive and antipyretic effect and these activities are, at least in part, related to the presence of MHD. **Financial support**: CNPq and CAPES. Animal Research Ethical Committee (protocol # 745)

09.012 Matrix metalloproteinase-9 and -2 activity is reduced by (-)-myrtenol during healing of acetic acid-induced gastric ulcer in rats. Viana AFSC[1], Nunes PIG[1], Oliveira AA[1], Viana DA[2], Braga AD[3], Santos VG[3], Lopes MTP[3], Sousa DP[4], Oliveira RCM[5], Santos FA[1] [1]UFC – Farmacologia e Fisiologia, [2]Patologia e Medicina Forense, [3]UFMG – Farmacologia e Fisiologia, [4]UFPB – Química, [5]UFPI – Farmacologia

Introduction: (-)-Myrtenol is a natural fragrance monoterpenoid structurally related to α-pinene found in diverse plant essential oils. Previous studies show that (-)-myrtenol has pharmacology activities, including sedative, anti-inflammatory, antinociceptive and gastroprotective effects. The matrix metalloproteinases (MMP-2 and MMP-9) of overexpression in gastric injury may be exploited as therapeutic targets. This study avaliated (-)myrtenol against acetic acid-induced gastric ulcer in rats associated suppression of activity matrix metalloproteinases. **Methods**: For this study, female Wistar rats (200-250g, n=6-7) kept under controlled conditions and access to food and water *ad libitum* were used. The animals were fasted for 18h, prior to assays. The animals were anaesthetized with xylazine/ketamine (5 mg/kg and 50 mg/kg, i.p.), the abdomen was exposed and 70 µl 80% acetic acid was applied to the serosal surface of the stomach for 1 min. One day after the surgery, the animals were treated orally with vehicle (0.1% tween 80 in distilled water), MYRT (50 mg/kg) or cimetidine (100 mg/kg) once a day for 7 days. A naïve group formed by normal animals without ulceration was included in the study. One day after the last drug administration, the rats were sacrificed and their stomachs were removed for histological evaluation after hematoxylin/eosin (HE) staining and for extraction of total proteins and zymography of MMP-2 and MMP-9. All experimental protocols were approved by Ethics Committee for Animal Research of the Federal University of Ceará (CEPA-UFC, nº 18/15). The results are presented as the mean ± SEM. ANOVA one way followed by the Tukey's post hoc test. Values of $p<0.05$ were considered to be significant**. Results:** In this model the gastric lesions induced by acetic acid (51.4 ± 3.6 mm^3) was decreased after 7 days by the treatment with MYRT 50 mg/kg (14.9 ± 4.1 mm^3) or cimetidine 100 mg/kg (12.9 ± 4.2 mm^3). MYRT and cimetidine in HE staining revealed significant reduction in the size of the ulcer as well as a more advanced restoration of the mucosal epithelium and few inflammatory cells compared with animals of the vehicle group that showed minimal repair, with high inflammatory exudates and an immature granulation tissue. The results of activity matrix metalloproteinase indicates that the levels of MMP-9 and MMP-2 at the ulcerated tissue of treated animals with MYRT were significantly smaller (54 and 77%, respectively) when compared to vehicle group (~100%). Similarly, the cimetidine reduced MMP-2 and MMP-9 activity for 59% and 81% respectively, compared to vehicle group (~100%). **Conclusion:** The results of this study provides evidence that orally administered (-)-myrtenol exerts healing effect against acetic acid-induced gastric ulcers via inhibition of MMP-2 and MMP-9. **Financial support**: CAPES/CNPQ/UFC.

09.013 Phytochemical analysis and hepatoprotective activity of aqueous extract in the leaves of *Solanum torvum* **Sw. (Solanaceae).** Souza GR[1], de Oliveira ACAX[2], Paumgartten FJR[2], Barbi NS[3], da Silva AJR[1] [1]IPPN-UFRJ, [2]ENSP-Fiocruz, [3]UFRJ – Farmácia

Introduction: *Solanum torvum* (ST), a plant of the Solanaceae family, is popularly known as "jurubeba". Its roots, stems, fruits and leaves are used in the Brazilian traditional medicine against hepatic and digestive conditions, as well as in culinary.[1] This report focus on the results of the phytochemical analysis of the ethyl acetate partition, obtained from the aqueous extract of leaves of ST, and on the evaluation of the hepatoprotective activity in the aqueous extract. Methodology: Aqueous extracts, prepared from 50 g of dried and powdered leaves of ST were partitioned with ethyl acetate and the organic fraction was subjected to HPLC/ESIMS (analysis using a 100 x 2.1 mm, 3 µm, RP-18 column and a linear gradient of methanol in 0.1 % aqueous formic acid mobile phase). UV detection occured at 280, 310 and 365 nm. The aqueous extract of ST leaves was evaluated for hepatoprotective activity in C57BL/6 mice (male, age: 8-10 weeks, weight: 20-25 g), distributed in the following groups (N = 7 for each group): 600 mg/kg acetaminophen (APAP) intraperitonially (i.p.); 600 mg/kg N-acetylcysteine (NAC) i.p.; 600 mg/kg or 1,200 mg/kg aqueous extract (STAE6 or STAE12, respectively) v.o.; NAC+APAP; STAE6+APAP; STAE12+APAP and their respective controls. Serum transaminases (ALT and AST, IU/L) and liver glutathione (GSH, nmol/mg protein) levels were measured. ANOVA and multiple comparison tests Dunnett and Bonferroni were applied to the results. **Results**: Evaluation of the chromatograms (retention times and UV spectra) and mass spectra obtained by HPLC/ESIMS analysis led to the identification of flavonoids and hydroxycinnamates. The mean levels of ALT and AST were as follows: APAP (ALT: 325.7 ± 80.63 and AST: 196.5 ± 35.5); APAP control (ALT: 100.0 ± 12.1 and AST: 100.0 ± 17.2); NAC (ALT: 75.3 ± 8.5 and AST: 166.2 ± 12.7); NAC control (ALT: 89.1 ± 6.3 and AST: 71.8 ± 7.3); NAC+APAP (ALT: 73.4 ± 5.2 and AST: 122.9 ± 7.6); STAE6 (ALT: 105.8 ± 17.5 and AST: 99.0 ± 20.6) and STAE12 (ALT: 69.0 ± 2.8 and AST: 73.1 ± 3.7); STAE6+APAP (ALT: 162.6 ± 28.9 and AST: 127.9 ± 23.4) and STAE12+APAP (ALT: 121.9 ± 26.4 and AST: 111.8 ± 27.3). The mean levels of GSH were: APAP: 46.1 ± 22.0; APAP control: 100 ± 30.5; NAC: 94.9 ± 40.4; NAC control: 76.4 ± 28.0; NAC+APAP: 100.9 ± 45.7; STAE6: 168.7 ± 44.0; STAE12: 505.6 ± 367.1; STAE6+APAP: 137.6 ± 72.5 and STAE12+APAP: 138.0 ± 33.8. These results showed that the treatment with the aqueous extracts provoked a statistically significant ($p < 0.05$) depression in the serum levels of the two enzymes and an increase in liver GSH levels, when compared to the group treated with APAP only. These results were not statistically significant ($p < 0.05$) to the groups controls. These results suggest that the hepatotoxicity provoked by 600 mg/kg acetaminophen treatment was reverted by the extract treatments and also when compared with the protection conferred by NAC. **Conclusion:** The aqueous extract of ST reverted the hepatotoxicity provoked by the acetaminophen treatment and proved to confer a better effect when compared with NAC. Acknowledgements: CAPES/CNPq/FAPERJ. License: LW-82/12 to the Committee on the Use of Animals (CEUA/FIOCRUZ). Reference: [1] Mors, W.B. et al. 2000. Medicinal Plants of Brazil, Ed. Robert A. DeFilipps, Reference Publications Inc.

09.014 Proteolytic fraction from *Vasconcellea cundinamarcensis* **latex shows antitumor/antimetastatic activity probable by modulation of tumor associated macrophages.** Braga AD[1], Teixeira LCR[1], Freitas KM[1], Salas CE[2], Lopes MTP[1] [1]ICB-UFMG – Farmacologia, [2]ICB-UFMG – Biochemistry and Immunology

Introduction: A proteolytic fraction (P1G10) from *V. cundinamarcensis* latex has antitumor/antimetastatic activity on 4T1 breast carcinoma model by reducing inflammation, angiogenesis and increasing tumor associated-macrophages (TAMs) activity. TAM's M2 phenotype can promote angiogenesis, remodeling of extracellular matrix and invasion of tumor cells. In contrast, M1 phenotype is capable to kill tumor cells and promote immune antitumor response (SICA et al., 2008). Our previous data shown that macrophages exposed to P1G10 sub-fraction (CMS2) were capable to kill 4T1 cells, in co-culture model, probably by increase the production of cytotoxicity mediators as ROS, NO, IL-1β, IL-6 and TNF-α, in cultured macrophages. Aim: Investigate the ability of CMS2 to reduce tumor mass and metastasis number by *in vivo* modulation of TAM's phenotype. **Methods** and **Results**: Female Balb/c mice (6/group) received 4T1 tumor cells into flank region (10^6, *s.c*) and treated with saline or CMS2 (0.3, 1.0 or 3.0 mg/kg, *s.c*) daily. At day 25, bronco-alveolar laved (BAL) was done and its leukocytes counted in hemocytometer. After mice euthanaziation, tumors were removed and lungs stained with India ink (15%) by tracheal route to visualization of metastasis. All doses of CMS2 reduced tumor weight, lung metastasis and BAL leukocyte number in around 43%, 49% and 48%, respectively. In tumor homogenate's supernatants were determined pro-inflammatory/angiogenic cytokines (ELISA), NAG-enzyme produced by activated macrophages (colorimetric enzymatic assay) and metalloproteinase activity (acrylamide/gelatin electrophoresis). Quantification of tumor cytokines (ρg/mg tumor vs control) revealed that CMS2 (3.0 mg/kg) decreases IL-1β levels at 31% (1.36 ± 0.17 *vs* 1.98 ± 0.20, $p<0.05$), VEGF at 34% (2.76 ± 0.27 *vs* 4.19 ± 0.32, $p< 0.01$), but increase IL-12 levels at 36% (9.53 ± 0.93 *vs* 6.99 ± 0.46, $p< 0.05$) and it wasn't detected any alteration in levels of TNF-α, IL-10, total TGF-β or NAG activity by CMS2 treatment. Interestingly, the metalloproteinase-2 activity was reduced at 44% ($p<0.001$). To demonstrate the involvement of macrophage in CMS2 antitumoral activity, female Balb/c mice (6/group) received 4T1 tumor cells (10^6, *s.c.*) with or without M2-macrophages ($2x10^5$*, s.c.)* and treated with saline or CMS2 daily (1mg/kg, *s.c.*). The results shown that, at day 15, CMS2 wasn't able to reduce 4T1 tumor mass comparatively to 4T1 tumor from saline treated mice. On the other hand, CMS2 reduced by 33% (0.47 ± 0.04 *vs* 0.71 ± 0.05 g –control, $p<0.01$) the tumor weight in mice bearing 4T1+M2 tumors. Statistical analysis: two groups - *t-test* and three or more groups - one-way ANOVA test, *post-test* Student-Newman-Keuls. **Conclusion:** CMS2 shows antitumor/antimetastatic activity, probably by modulation of TAMs while gives to these immune cells ability to fight against transformed cells. However, the modulation mechanisms need to be defined. SICA et al., 2008. Cancer Letter, 267:204–215. **Financial support**: CNPq, CAPES, FAPEMIG. Ethical Committee: 219/2012.

09.015 Effects of polyanions and antibotropic serum on some activities of *Bothrops leucurus* **venom.** Cons BL[1,2], Tomaz MA[1,2], Strauch MA[3], Monteiro-Machado M[1,2], Tavares-Henriques MS[1,2], Cruz JMT[1,2], Saturnino Oliveira J[4], Melo PA[1,2] [1]UFRJ – Ciências da Saúde, [2]UFRJ – Farmacologia e Química Medicinal, [3]Instituto Vital Brasil – Diretoria Científica, [4]UFS – Morfologia

Snakebites accidents from genus Bothrops are common in Brazil, specifically among plantations of cacao in the Northeast, Bahia, where is high the incidence of accidents with B. leucurus, which is well adapted to such plantations. In this snake bites are observed edema, hemorrhage and myonecrosis. We investigated the effect of polyanions (Suramin and fractionated Heparin) and antibotropic serum abilities to antagonize these in vitro activities as well as phospholipase, proteolytic, hyaluronidase, myotoxic and collagenase activities and in vivo activities as well as myotoxicity, hemorrhagic, oedema and tail bleeding. Phospholipase activity was assessed using chicken egg yolk incubated with 10 µg/mL of B. leucurus crude venom. Proteolytic assay was assessed in a solution containing azocasein incubated at concentration of 10 µg/mL of B. leucurus venom. Hyaluronidase activity was assessed using solution containing hyaluronic acid with substrate. Collagenase assay was assessed in a solution containing azocoll with substrate. Hemorrhagic lesions were induced by an intradermic injection of the venom or the venom incubated with the compounds. The in vivo myotoxicity were performed by i.m. injection of 1 mg/Kg of B. leucurus crude venom and the plasma CK activity analyzed 2 hours after the i.m. injection. Myotoxic experiments were performed in vitro, on mouse extensor digitorum longus muscle (EDL) and assessed by the increase of creatine kinase (CK) release following the exposure of muscle to the venom (25 µg/mL). Suramin 30 µM and antibotropic serum inhibited circa of 100% of the phospholipase, hyaluronidase activities. Proteolytic activity was partially inhibited of Suramin and Fractionated Heparin, but Antibotropic serum inhibited circa of 80%. In all enzymatic activities when added Antibotropic serum plus polyanions observed antibotropic serum activity potentiation. On the in vivo protocols experiments, Antibotropic serum not reduced significantly the increase of plasma CK activity induced by venom injection (n=4), but Fractionated Heparin 1 mg/Kg plus many concentrations of Antibotropic serum and Suramin (30 mg/Kg) plus Antibotropic serum 1 ml / 5 mg) were able to inhibit significantly myotoxicity in vivo activity. The in vitro myotoxic activity Antibotropic serum were able to inhibit CK release and when it was added only Antibotropic serum plus Suramin (10 mM) we observe enhancement in inhibiting in vitro myotoxic activity. The oedema index was reduced in all experimental protocols (n=4). Only Suramin (30 mg/Kg) was able to protect significantly the bleeding. Antibotropic serum inhibit in a manner dependent on the concentration hemorrhagic activity, however polyanions not interfere with serum effect. Our results are showing that Antibotropic serum and polyanions were able to inhibit some important activities of B. leucurus venom which are involved in the tissue damage. In some activities we observe potentiation of Antibotropic serum treatment when we added these polyanions. CEUA-UFRJ: DFBCICB072-04/16. **Financial support**: CAPES, CNPq, PRONEX and FAPERJ

09.016 Study of antiparasitic effect of (-)-alpha-bisabolol on epimastigote forms of *Trypanosoma Cruzi* Menezes RRPPB[1], Sampaio TL[1], Tessarolo LD[2], Canuto JA[2], Medrado KA[2], Azevedo IEP[2], Martins AMC[2] [1]UFC – Fisiologia e Farmacologia, [2]UFC – Análises Clínicas e Toxicológicas

Introduction: Chagas Disease is caused by *Trypanosoma cruzi* and affects about 8 million people worldwide. The drugs available to treat this disease present low efficacy and high toxicity. In this way, several drugs have been screened in order to identify new therapeutic strategies. (-)-α-Bisabolol is a sesquiterpene alcohol found on chamomile flowers, and presents several biological activities, including antitumoral and leishmanicidal. So, we decided to study the trypanocidal effect of (-)-α-bisabolol (BIS) on *T. cruzi* epimastigotes and investigate its action mechanism. **Methods**: 10^6 epimastigotes/mL were cultured with BIS (1000 - 31.25 µM) in sterile 96-well plates. The cell density was determined by counting in neubauer chamber after 24, 48, 72 and 96 hours. The data were analyzed by non-linear regression to determine the concentration able to inhibit 50% of parasite growth (IC_{50}). The cell death pathway was evaluated by flow cytometry, using 7-AAD (7-Aminoactinomycin D) and Annexin V-PE as markers of necrosis and apoptosis respectively after 6 hours of incubation with BIS (285 µM). The increase of cytoplasmic reactive oxygen species (ROS) induced by BIS was determined by flow cytometry, using the fluorescent probe DCF-DA (2′,7′-Dichlorofluorescin diacetate). The cells were labeled with DCF-DA (20 µM) 3 hours after addition if BIS (285 µM) and the plates were incubated protected from light until complete 6 hours of treatment. FL_1 labeling level was evaluated by the fold-change (ratio: treated/untreated cells) of the geometric mean $([(X_1).(X_2)\ldots(X_n)]^{1/n}$, where X is the fluorescence intensity of each event and n is the number of events). The effect of BIS on mitochondrial transmembrane potential was assessed in epimastigotes using rhodamine 123 (Rho 123). Briefly, epimastigotes treated with BIS (285 µM) for 6 hours were washed twice with PBS and labeled with Rho 123 (10 µg/mL) for 30 minutes in the dark. The cells were washed twice again and analyzed by flow cytometry in FL_2 channel. The decrease on Rho 123 accumulation in treated groups was analyzed by the fold-change on fluorescence emission. **Results**: BIS was able to inhibit epimastigote growth, with IC_{50}(24h) = 285 ± 35 µM; IC_{50}(48h) = 145 ± 17.5 µM; and IC_{50}(72h) = 97 ± 5.8 µM. The labeling with 7-AAD and Annexin V-PE demonstrated an increase on 7-AAD^+ cells, suggesting that BIS induces necrosis on *T. cruzi*. Also, it was observed an increase on labeling with DCF-DA and Rho 123. These results demonstrate that BIS induces both cytoplasmic and mithocondrial oxidative stress. **Conclusion:** (-)-α-Bisabolol induces cell death by necrosis with involvement of oxidative stress, both in cytoplasm and mitochondria. **Financial support**: Capes (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior) and CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico).

09.017 Acute oral toxicity of gum Arabic *Anacardium Occidentale* Silva AH[1], Rodrigues Filho JMS[1], Freitas LBN[1], Azevedo HMC[2], Ferreira MVP[3], Leal LKAM[1] [1]UFC – Centro de desenvolvimento de medicamentos e cosméticos/ Farmácia, [2]Empresa Brasileira de Pesquisa Agropecuária – Embrapa, [3]UFC – patologia e medicina legal/Medicina

Anacardium Occidentale is popularly known as cashew tree. It is a native plant to Brazil which is rustic and typical of tropical climate. Cashew's gum is a complex heteropolysaccharides especially extracted from the trunk of this specie, being applied to several areas such as Food Industry and Pharmaceutical. It may be employed in replacement of Arabic gum which is more traditionally used. There are several studies indicating its pharmacological activities and pharmaceutical technology. Therefore, preclinical essays of acute toxicity have been carried out in animals in order to evaluate the safety of its usage. Experiments were led with wistar rats which were divided into three groups: control-water 10 ml/kg; gum without ethrel – 2g/kg; gum with ethrel – 2g/kg. Animals received oral and single dose and were evaluated in what regarded their behavioral changes according to Malone's Hippocratic Screen Essay. In addition to that, biochemical and hematological tests were performed before and after the test. The rats were observed during 14 days: day 0 refers to the day before the beginning of the experiment and day 15 refers to the last day of testing. The sacrifice was performed in day 15 and the vital organs (lungs, liver, heart, kidney and spleen) were weighed and immersed in formaldehyde to later histopathological study. After statistic evaluation, the weighs of the animal's organs from group gum without etherel and with etherel did not present significant differences from the control. The group gum without etherel showed significant difference from day 0 in what regarded to the values of ALT and creatine. The group with etherel showed significant difference from day 0 in what regarded to the values of ALT, urea, hemoglobin, quantity of platelets, differential counting of white blood cell. As to behavioral evolution, no animal presented any change according to analyzed parameters. Preclinical trial of acute toxicity is important for evaluating the safety of products which are candidates for being used in society. The cashew tree gum hás been shown as safe, once the changes that were found are not significant and cannot be related to the gum. Subchronic and chronic trials of toxicity are necessary in order to better evaluate the safety of such promising product. **Financial support**: FUNCAP, CNPq

09.018 Protective effect of 2-phenylquinoline derivatives on experimentally induced gastric ulcers in mice. Breviglieri E[1], da Silva LM[1], Boeing T[1], Somensi LB[1], Benhur C[1], Gimenez A[2], Valdez IL[2], Cechinel-Filho V[1], Andrade SF[1] [1]Univali – Ciências Farmacêuticas, [2]Universidad Mayor de San Andrés

Introduction: The treatment of gastric ulcer based on antisecretory drugs is associated with side effects and ulcer remission. In light of this, alternative therapies are required and medicinal chemistry guided by natural prototypes is an important tool for this. The antiulcer potential of 2-Phenylquinoline (2-PQ, an alkaloid from bark of *Galipea longiflora*, Rutaceae) was reported previously by our research group. In the next step of our continuous research, four 2-PQ derivatives were screened for gastroprotective activities against HCl/ethanol-induced gastric ulcers in mice. AIM: The aim of this work was to prepare 2-PQ derivatives molecules and evaluate gastroprotective effects of them in order to determine structure-activity relationship from new compounds. **Methods**: Three compounds from 2-PQ were prepared, namely: 2-(4-methoxyphenyl)quinoline (1), 2,4-diphenylquinoline (2) and 2-phenylquinolin-4-ol (3). The naturally occurring in *G. longiflora,* 4-methoxy-2-phenylquinoline (4) was also included in the study. The compounds were evaluated for their gastroprotective activity in the HCl/EtOH-induced gastric lesions model in mice and ulcerated tissues were collected for biochemical analysis. **Results**: The oral administration of compounds 1, 2, 3 and 4 in mice exposed to acidified ethanol, at a dose of 30 mg/kg (which corresponds to the minimum effective dose of 2-PQ) reduced the area of gastric injury by 67.4%, 79.1%, 79.4% and 95.1%, respectively (compared to the vehicle group: 24.2 ± 8.5 mm^2). As expected, the control positive carbenoxolone (200 mg/kg, p.o) also reduced the ulcer area by 88.2%. The gastroprotective effects of compounds 1, 2, 3 and 4 (3 mg/kg) were confirmed when administered intraperitoneally; however the compound 1 was not effective in this route of administration, suggesting that structural alteration impaired its systemic action. Moreover, the gastroprotective effects displayed by all compounds were accompanied of prevention of the increased lypoperoxides levels in gastric mucosa. Nevertheless, despite the effects of both compounds by oral route, only compound 4 was able to increase the gluthatione reduced content, as well as reduced the TNF content and the MPO activity at ulcerated site. Taking into account that 2-PQ (30 mg/kg, p.o) is able to reduce in up to 57.1% the ulcer lesion induced by acidified ethanol, our results showed that structural diferences, mainly those leading to compound 4, which also occurs naturally, improved the gastroprotective potential of this alkaloid. Again, our findings confirm that the reduction in oxidative damage and in the inflammatory process on the gastric mucosa is among the gastroprotective effects evidenced. Thus, the compounds tested, mainly the structure 4 due to the best gastroprotective effect, may be a suitable option for the prevention and treatment of peptic acid diseases. **Financial support**: CNPq, CAPES, FAPESC. Approval number CEUA: 38 / 14p.

09.019 Pharmacological action of Crotalus durissus cascavella venom on cardiac tissue of spontaneously hypertensive rats. Simões LO[1], Alves QL[1], Jesus RLC[2], Dantas SCD[2], Barreto BC[2], Silva LLC[2], Macambira SG[2], Couto RD[3], Silva DF[2] [1]Centro de Pesquisa Gonçalo Moniz – CPqGM-Fiocruz-BA, [2]UFBA, [3]UFBA – Farmácia

Introduction: Toxins from animals are a source of natural resources for pharmacological studies. The venom from *Crotalus durissus cascavella* (CDC), can be a source of bioprospecting on new therapeutic agents with cardiovascular action but, are not fully understood the biological effects induced in cardiac tissue after a snake attack by the CDC, as well as, the possible beneficial effects of new molecules isolated from this venom. In addition, studies investigating new molecules isolated from animals are relatively few when compared to studies from plant products, then, requiring further research and deepening this area. **Aim:** To investigate the influences from CDC venom on heart activity of rats. **Methods**: All experimental procedures were approved by the local Animal use and care ethics committee – CEUA/ICS/ UFBA (72/2014). Male wistar and Spontaneously Hypertensive Rats (SHR) (250-300 g) were euthanized in CO_2 chamber, and the left and right atria were isolated and maintained in an organ bath with Krebs-bicarbonate at 37 ° C and aerated with a mixture carbogenic. After a stabilization period, CDC (0.1-30 µg/ml) was added cumulatively to the organ bath. The values were expressed as mean ± sem. For the quantitation of enzymatic activity of total creatine kinase (CK), Krebs samples were collected before and after the addition of the venom in the organ bath and quantified using a commercially available assay kit. For the realization of cardiotoxicity testing, was used Langendorff system, where they were evaluated for the presence of arrhythmias, heart rate, PR interval, intrinsecoid deflection waveform amplitude and duration of the QT interval. **Results and Discussion**: CDC induced a negative inotropic effect in both wistar and SHR animals in all concentrations tested (***$p<0.001$). Interestingly, CDC induced a negative chronotropism (*$p<0.05$) in only one concentration tested (30 µg/ml), in hypertensive animals but not in normotensive rats. The previous treatment of isolated atria with CDC venom (0.01- 30 µg/mL) did not change CK activity in krebs solution that bathed the right atria and left of Wistar and SHR, suggesting the absence of significant tissue damage. Furthermore, the CDC venom (0.1, 1 and 10 µg/ml) did not change on cardiac electrogenesis in isolated perfused rat heart using the Langendorff technique, suggesting a probable absence of cardiotoxicity in the concentrations used. **Conclusion:** These data demonstrate that cardiac effect from CDC venom can be due to a pharmacological mechanism, rather than a toxic effect, and can thus serve as a potential source of new drugs having cardiovascular action. **Financial support**: FAPESB and CNPq .

09.020 *Spirulina platensis* **improves reactivity parameters no pathway and antioxidant action** Ferreira PB[1], Brito AF[1], Silva AS[2], Silva MCC[1], Souza AA[2], Felix GS[2], Souza ILL[1], Pereira RA[2], Sampaio RS[1], Araujo LCC[3], Silva BA[4] [1]UFPB – PPgPNSB, [2]UFPB – DEF, [3]UFPB – PPgBCM, [4]UFPB – DCF

Introduction: *Spirulina platensis*, also known as *Arthrospira platensis* (Oscillatoriaceae), considered as a valuable antioxidant source is a blue-green alga helical shape, with a length of 0,2 to 0,5 mm, being cultivated on a large scale in many countries for commercial purposes and is currently receiving more attention as a potential source of nutraceuticals (1). S. platensis has been associated to improve vascular function (2), but the effect of supplementation with lyophilized powder on vascular reactivity had been not investigated. The aim was to verify the effects of *S. platensis* on vascular reactivity, biochemical parameters and oxidative stress in male Wistar rat aorta. **Methods**: male Wistar rats (250-300 g, n = 5) were divided into control group (CG) and supplemented for two months with S. platensis at doses of 50 (SG50); 150 (SG150) and 500 mg/kg (SG500). Rats were euthanized and the aorta removed and suspended in organ baths with Krebs solution, under rest tension of 1 g at 37 °C and bubbled with carbogen mixture. After stabilization, isometric contractions were recorded. To evaluate the vascular response were used phenylephrine (PHE) 10^{-9}-10^{-3} M and acetylcholine (ACh) 10^{-11}-10^{-4} M. Biochemical analysis was used to quantify levels of nitrite, malondialdehyde (MDA) and antioxidant activity. **Results**: In the functional experiments was observed that only SG500 (pD_2 = 5.6 ± 0.04) presented a significant reduction on contraction induced by phenylephrine when compared to the CG (pD_2 = 6.1 ± 0.06) and the ability of S. platensis in reducing the contractile response was eliminated in the absence of functional endothelium CG (pD_2 = 7.1 ± 0.04). In the presence of L-NAME, a NO inhibitor, the supplementation of S. platensis provided a greater contractile response in the groups CG (pD_2 = 7.1 ± 0.08), SG50 (pD_2 = 7.1 ± 0.03), SG150 (pD_2 = 7.6 ± 0.07), SG500 (pD_2 = 8.2 ± 0.03). In the relaxant reactivity, SG150 (pD_2 = 7.0 ± 0.08) and SG500 (pD_2 = 7.3 ± 0.02) presented an increase in the relaxant potency, with shift from the curve to the left, compared to the CG (pD_2 = 6.4 ± 0.06). The key role of NO was noticed since a significant increase in nitrite production in the SG150 and SG500 was observed. The MDA production was reduced in SG150 and SG500, approximately 80%, while the oxidation inhibition percentage was increased by about 50%, indicating a possible antioxidant action. **Conclusions**: the present study demonstrated that the chronic supplementation of S. platensis reduced contractile response to PHE in male rat aorta and at doses of 150 and 500 mg/kg induced a higher relaxant reactivity to ACh and these effects are accompanied by an increase in nitrite concentration, indicating involvement of the NO pathway, by a reduction of oxidative stress and increased antioxidant activity. Sources of Research and Financial Support: CAPES, CNPq, UFPB. Ethical Committee in Animal Use of UFPB: Protocol 1101/11 **References**: 1. KHAN, Z., Current Pharm. Biotec., v. 6, p. 373, 2005. 2. BRITO, A.F., Doctoral Thesis, UFPB, 2014.

09.021 Biophysical and biological properties of small linear peptides derived from crotamine Dal Mas C[1], Pinheiro D[2], Campeiro JD[1], Oliveira V[3], Oliveira EB[4], Miranda A[3], Perez KR[3], Hayashi MAF[1] [1]Unifesp-EPM – Farmacologia, [2]Unifesp-EPM, [3]Unifesp-EPM – Biofísica, [4]FM-USP – Bioquímica e Imunologia

Introduction: Crotamine is a peptide isolated from the venom of the South American rattlesnake *Crotalus durissus terrificus*, positively charged and composed by 42 amino acid residues. Among the activities described for this toxin, crotamine shows antifungal and antibacterial activity which are dependent of interaction with negatively charged membranes associated with their lytic activity on negatively charged membranes compared to neutral net charge vesicles. The crotamine has also the ability to translocate and permeabilize lipid membranes acting as a cell-penetrating peptide (CPP). **Aim:** To identify the minimum structure of crotamine necessary for the antimicrobial properties and the interaction with mimetic membranes, this project aimed to study the properties of highly positively charged synthetic short linear peptides C1 and C2, derived from crotamine primary sequence, maintaining the cysteines, in the presence or absence of the reducing agent, DTT, on membrane model systems with different phospholipid compositions. **Methods:** The antimicrobial activity was monitored by antimicrobial growth inhibition assay in liquid medium, against the following microorganisms: *Candida albicans* ATCC 757 (clinical isolate), *C. krusei* ATCC 6258, *C. parapsilosis* ATCC 22019 and *C. glabatra* ATCC 90030. The analysis of the interaction of peptides derived from the crotamine with mimetic membranes with phospholipids positively and/or negatively charged, was performed using Nanoparticle Tracking Analysis (NTA) with NanoSigth equipment (NanoSight Ltd.), which allows to evaluate the percentage of particles according to their average diameter and to evaluate the secondary structure of the fragments C1 and C2 in the presence of liposomes, it was used the Circular dichroism (CD) (JASCO International Co. Ltd.). This techniques was used to determine the behavior of the mimetic membranes composed of POPC:POPG in the ratio 50 mol% in the presence of native crotamine and/or its peptide fragments C1 and C2, in the absence of DTT. **Results:** Our results suggest that peptides C1and C2 shows higher antimicrobial activity than the native crotamine, and P1 and P2 (analogues peptides with substitution of the cysteine by serine), for some strains and in some specific conditions. We demonstrated here that the presence of cysteine residues highly influenced the antimicrobial activity. The interaction of C1, C2 peptides and native crotamine occurred rather with negatively charged membranes than with neutral membranes as observed in the NTA. The C2 peptide showed higher interaction with membranes than C1 and promoted aggregation of lipossomes. Analysis by CD further suggests that this interaction with lipid membranes does not promote structuring of these peptides, although in the presence of DTT, C2 peptide undergoes changes in its structure in the presence of negatively charged membranes. **Ethical Committee:** UNIFESP/EPM 171905/13. **Financial Support:** FAPESP, CNPq and CAPES

09.022 Anti-inflammatory and antinociceptive activity of an isolated naphthoquinone from *Sinningia reitzii* Barbosa FL[1], Silva AS[2], Stefanello MEA[2], Zampronio AR[1] [1]UFPR-Farmacologia, [2]UFPR

Introduction: Previous studies in our laboratory have shown that the genus Sinningia presents several compounds with significant anti-inflammatory, and/or antinociceptive activities. For instance, 8-metoxilapachenol isolated from Sinningia allagophyla reduced the edema and the mechanical hyperalgesia while aggregatin D isolated from Sinningia aggregata reduced only mechanical hyperalgesia induced by carrageenan (Cg). The aim of the present study was to evaluate the anti-inflammatory and antinociceptive effects of a naphthoquinone (SRD15B-B) isolated from another species Sinningia reitzii. **Methods:** Male Swiss mice (± 25 g, n= 5-8 per group) were locally (intraplantar) treated with SRD15B-B (5-500 pg), vehicle, dipyrone (Dip, 320µg) or dexamethasone (Dex, 30ng) 15 min before de injection of carrageenan (Cg, 300µg) into the hind paw. Edema formation and mechanical hyperalgesia were evaluated using a digital micrometer and Von Frey filaments, respectively. Additionally, the antinociceptive effects of SRD15B-B were evaluated in the hyperalgesia induced by prostaglandin E2 (PGE2, 100ng), Dopamine (DOP, 3µg) or dybutiryl cAMP (dbcAMP, 5 µg) injected directly into the hind paw. **Results:** The intraplantar injection of SRD15B-B 50, 150 and 500 pg dose-dependently reduced the edema formation by 23%, 38% and 53%, respectively while Dex (positive control) reduced the edema in 56%. The injection of Cg in the paw also induced mechanical hyperalgesia. The intraplantar treatment with SRD15B-B 5, 15 and 150 pg reduced the mechanical hyperalgesia induced by Cg by 6%, 98% and 100%, respectively while Dip (positive control) reduced the hyperalgesia by 98%. The SRD15B-B (15pg) significantly reduced PGE2 and DOP-induced mechanical hyperalgesia by 91% and 100%, respectively. However, the same treatment did not change the dbcAMP-induced mechanical hyperalgesia. **Conclusion:** These results suggest that the naphtoquinone SRD15B-B has an important anti-inflammatory and antinociceptive effect, since it reduced the edema and mechanical hyperalgesia induced by Cg. Its antinociceptive effect seems to be different from classic non-steroidal anti-inflammatory drugs and it may interfere in some step between G-protein-coupled receptor activation and cAMP formation. **Financial support:** CNPq and CAPES. CEUA protocol Nbr. 937.

09.023 Effect of a standardized extract of *Baccharis trimera* **(Less) DC. On DSS-induced acute colitis in mice** Silva RV[1], Nogueira FM[1], Silva JDP[1], Tanae MM[1], Landman G[2], Lima-Landman MTR[1], Lapa AJ[3], Souccar C[1] [1]Unifesp-EPM- Farmacologia, [2]Unifesp-EPM- Patologia, [3]Unifesp-EPM& UEA- MA – Farmacologia

Introduction: Inflammatory bowel disease (IBD) is a disorder characterized by a chronic and recurrent inflammation that affects the gastrointestinal tract. The disease involves genetic, immune and environmental components and manifest in two main forms: ulcerative colitis (UC) and Crohn's disease (CD). Both UC and CD present similar effects that include diarrhea, rectal bleeding, abdominal pain weight loss, and fever, but with distinct immunological and pathological aspects. Because of the relapsing-remitting nature of IBD, the available drug therapy has been ineffective for the healing of patients. The plant *Baccharis trimera* (Less.) DC (Asteraceae), popularly known as "carqueja", is popularly used to treat gastrointestinal and cardiovascular disorders, inflammation and diabetes. The presence of constituents endowed with gastroprotective, anti-inflammatory and antioxidant activities have been confirmed in the plant extract. This work was aimed to evaluate the effects of a standardized extract of *B. trimera* on acute dextran sodium sulfate (DSS)-induced colitis in mice. **Methods**: The aqueous extract (AE) of the aerial parts of *B. trimera* was partitioned with n-butanol (3 x 0.2 L) and the resulting butanol fraction was lyophilized after evaporation of the organic solvent, providing the standardized extract (FB_{Bt}). Male C57Bl/6 mice (3-months old) were given tap water (control, C), or 2.5% DSS in their drinking water for 5 days and plain water in the next 48 h (DSS-mice). Intestinal inflammation was assessed by clinical symptoms, body and colon weights, colon length, histological analysis of colon sections and determination of myeloperoxidase (MPO) activity. The parameters of gastric acid secretion were determined in intact pylorus-ligated mice. **Results**: Intraduodenal injection of FB_{Bt} (0.5 g/kg) to pylorus-ligated mice reduced the volume (71%) and total acidity (75%) of gastric secretion compared to control values (0.74 ± 0.31 mL and 7.27 ± 3.47 mEq[H^+]/L/4h, respectively, n=6), while the pH was increased by 1.5 units. A lower concentration of FB_{Bt} (0.1 g/kg) did not affect the parameters of acid secretion. Mice treated with DSS (5-7 days) presented bloody diarrhea and decrease in the body weights by 13% relatively to the initial values (C: 22.8 ± 0.3 g, n=9). The colon weight and colon length were decreased by 16% and 9% of control values (253.6 ± 5.8 mg and 68.2 ± 0.9 mm, respectively; n=6). However, the tissue MPO activity was increased by 72% of control (C: 7.11 ± 1.56 mUn/g tissue). Oral treatment of DSS-mice with 0.5 g/kg FB_{Bt} did not significantly change the DSS-induced effect on the body and colon weights, but the tissue MPO activity was reduced by 56%. **Conclusion:** The results indicate that at a dose effective as antacid, the standardized extract of *B. trimera* produced a mild anti-inflammatory effect on DSS-induced colitis in mice. **Financial support**: CNPq and CAPES Animal Investigation Ethics Committee Protocol Nº 6469270514

09.024 Evaluation of the antihypertensive effect of a phenolic-rich fraction of syrah red wine from São Francisco Valley Region Figueiredo EA[1], Alves NFB[1], Braga VA[1], Oliveira EJ[2]
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Introduction: Hypertension is the most important risk factor for cardiovascular disease. Studies have demonstrated an association between the consumption of food and/or beverages rich in phenolic compounds and the reduction of the risk of cardiovascular diseases. The wine is a drink made from fermented grapes, presenting high levels of polyphenols. **Objective**: To investigate the antihypertensive effect of a fraction rich in phenolic compounds obtained from fractionation of Syrah red wine from São Francisco Valley region (FrSySFV). **Methods**: The total phenolic content of FrSySFV was determined by Folin-Ciocalteu reagent according to Waterhouse, A. L., 2003, with gallic acid as a standard, analyzed in triplicate and expressed as milligrams of gallic acid equivalents/100 milligrams fraction (mg GAE/100mg). We used twenty-four spontaneously hypertensive rats (SHR, 250-300g) divided into 3 different groups: SHR+ saline (n=8); SHR + FrSySFV (50 mg/Kg) (n=8); SHR + FrSySFV (100 mg/Kg) (n=8) and treated with the respective daily doses by gavage, during fifteen consecutive days. All protocols were approved by the Animal Care and ethic Committee of the Federal University of Paraiba (CEUA/CBiotec no. 0601/13). Twenty-four hours after treatment, animals were anesthetized with ketamine and xylazine (75 and 10 $mg \cdot kg^{-1}$, intraperitoneal, respectively). A Polyethylene tube (PE-10 connected to PE-50) was implanted in abdominal aorta through femoral artery for arterial pressure recordings. Twenty-four hours after catheter implantation, mean arterial pressure (MAP) and heart rate measurements were performed using a pressure transducer coupled to an acquisition system (PowerLab; ADInstruments, Castle Hill, NSW, Australia) connected to a computer installed with LabChart 5.0 software (ADInstruments). Comparisons among groups were performed using 1-way ANOVA followed by Bonferroni post hoc test. **Results:** The total phenolic content was 58.45 ± 0,01 mg GAE/100mg. SHR + FrSySFV (50 mg/Kg) and SHR + FrSySFV (100 mg/Kg) groups presented lower MAP compared with SHR + saline group (146.1 ± 4.062 N=7, 126.5 ± 5.322 N=8 vs 159.0 ± 3.891 N=7, respectively). This reduction was dose-dependent. **Conclusion:** These results suggest that FrSySFV induce an antihypertensive effect *in vivo* and this effect may be related to the content of phenolic compounds present in fraction. **Financial support**: CNPq

09.025 Neuromuscular activity of *Micrurus surinamensis* **(Aquatic Coral Snake) venom in avian and mammalian preparations *in vitro*** Schezaro-Ramos R[1], Floriano RS[1], Silva Junior NJ[2], Rodrigues-Simioni L[1], Rowan EL[3], Hyslop S[1] [1]FCM-Unicamp – Farmacologia, [2]PUC-Goiás – Biologia, [3]University of Strathclyde – Pharmacy and Biomedical Sciences

Introduction: Neurotoxicity, the hallmark of coral snake (*Micrurus* spp.) venoms, is mediated by presynaptic (PLA_2) and postsynaptic (three-finger toxins; 3-FTx) neurotoxins. *Micrurus surinamensis* differs from other *Micrurus* spp. in being aquatic and feeding primarily on fish. In this work, we compared the neuromuscular activity of *M. surinamensis* venom in chick biventer cervicis (BC) and mouse phrenic nerve-diaphragm (PND) preparations *in vitro*. **Methods:** PND preparations suspended in Tyrode solution and BC preparations suspended in Krebs solution were stimulated indirectly or directly (in the presence of 8.16 □M d-tubocurarine) in the presence of venom (0.1-30 µg/ml) or physiological solution alone. Contractile responses to exogenous acetylcholine (ACh, 1 mM), carbachol (CCh, 20 µM) and KCl (40 mM) were obtained in BC preparations. Venom phospholipase A_2 (PLA_2) activity was assayed colorimetrically. The results were expressed as the mean ± SEM. Statistical comparisons were done with Student´s *t*-test or ANOVA with the Tukey-Kramer post-test; $p<0.05$ indicated significance. **Results:** *M. surinamensis* venom produced concentration-dependent blockade in both preparations ($p<0.05$). The minimum concentration for partial blockade in PND after 60 min was 3 µg/ml (45 ± 10%; n=4; $p<0.05$), while the time for 90% blockade (t_{90}) with 30 □g/ml was 7.2 ± 1.7 min (n=4). In BC, the minimum concentration for partial blockade was 0.3 µg/ml (42 ± 11%; n=6; $p<0.05$), while the t_{90} with 30 □g/ml was 8.0 ± 1.2 min (n=6). In PND, the blockade was totally reversible by washing, even 1 h after total blockade, but was irreversible in BC with venom concentrations >10 □g/ml ($p<0.05$). The blockade was partially and temporarily reversed with 2.9 µM neostigmine [29 ± 6% (n=3) and 28 ± 3% (n=3) with 10 □g of venom/ml in PND and 1 □g of venom/ml in BC, respectively; $p<0.05$] and 230 µM 3,4-diaminopyridine [61 ± 11% (n=3) and 62 ± 10% (n=3) with 10 □g/ml in PND and 1 □g/ml in BC, respectively; $p<0.05$]. Venom did not affect contractures to exogenous KCl in BC, but partially inhibited those to ACh and CCh at concentrations of 0.1-1 □g/ml; concentrations >3 □g/ml caused complete inhibition ($p<0.05$). With 0.3 □g/ml, the ACh-induced contracture was inhibited before neuromuscular blockade and was totally reversed by washing ($p<0.05$). Venom (10-30 □g/ml) did not affect contractile responses to direct stimulation in either preparation. The venom had no PLA_2 activity. **Conclusions:** These results indicate that *M. surinamensis* venom caused neuromuscular blockade in both preparations, with BC being more sensitive. This blockade was essentially via inhibition of post-synaptic nicotinic receptors (probably via 3-FTx). The venom showed no direct myotoxicity on skeletal muscle. **Financial support:** CAPES, CNPq, FAPESP (RSF, grant no. 2014/24409-8) **Ethical approval:** Committee for Ethics in Animal Use (UNICAMP, protocol no. 3477-1).

09.026 BJ-PI2, a P-I Class Metalloproteinase from *Bothrops jararaca* Venom, causes thrombocytopenia without affecting coagulation parameters in anesthetized rats.
Tamascia ML[1], da Silva IRF[1], Baldissera Jr L[1], Huaco FDT[1], Hyslop S[1] [1]FCM-Unicamp – Farmacologia

Introduction: BJ-PI2 is a P-I class non-hemorrhagic metalloproteinase isolated from the venom of *Bothrops jararaca*. This protein has fibrinogenolytic activity *in vitro* and prolongs the plasma recalcification time. In this work, we examined the ability of BJ-PI2 to affect coagulation parameters and circulating platelet number in rats. **Methods:** BJ-PI2 was purified using a combination of gel filtration and ion-exchange chromatography. Male Wistar rats (350-400 g) were anesthetized with isoflurane (2% in air) and a carotid artery was cannulated for blood pressure measurement. A femoral vein was cannulated for injection of venom or BJ-PI2 in 100 □l that was washed in with 100 □l of 0.9% saline. Blood pressure, heart rate and electrocardiogram (ECG) were monitored continuously (PowerLab software, ADInstruments, Australia). For blood sampling, rats were cannulated as described above and blood (500 µl) was collected from the carotid into plastic tubes containing 3.8% sodium citrate and commercial bothropic antivenom at 0, 1, 5, 15, 30, 45, 60 and 120 min. Platelets were counted manually by light microscopy in a Neubauer chamber. The activated partial thromboplastin time (APTT), prothrombin time (PT) and fibrinogen concentration were measured with commercial kits in a semi-automatic coagulometer. Platelet-rich plasma was obtained by centrifuging whole blood (200 g, 15 min) and the platelets were washed using 10 mM citrate buffer (pH 6.0). BJ-PI2 (10 µM)- and thrombin (100 mU/ml)-induced platelet aggregation was evaluated using a two-channel aggregometer. The results (mean ± SEM) were analyzed using ANOVA followed by the Tukey test, with $p<0.05$ indicating significance. The protocols were approved by an institutional Committee for Ethics in Animal Use (CEUA/UNICAMP, protocol no. 2253-1). **Results:** BJ-PI2 and venom caused hypotension that was much more rapid and intense with venom (in mmHg: from 110 ± 3 to 92 ± 1 at 65 ± 19 min, 110 ± 2 to 82 ± 6 at 87 ± 15 min and 107 ± 1 to 52 ± 3 mmHg at 18 ± 6 min, for 0.1 and 0.3 mg/kg of BJ-PI2 and 0.1 mg/kg of venom, respectively; n=3-5; $p<0.05$ vs. pre-venom values). There were no changes in ECG parameters and heart rate decreased only with venom (0.1 mg/kg) (from 398 ± 2 to 317 ± 10 beats/min). Circulating platelets decreased markedly with BJ-PI2 (0.3 mg/kg) and venom (0.1 mg/kg) (from 573 ± $40x10^6$/ml to 308 ± $15x10^6$/ml and 31 ± $3x10^6$/ml at the end of the experiment, for control, BJ-PI2 and venom, respectively; n=3; $p<0.05$ vs. pre-venom values). Venom (0.1 mg/kg) consumed all fibrinogen 5 min after injection, whereas BJ-PI2 (0.3 mg/kg) was not fibrinogenolytic *in vivo*. Pasma was incoagulable 15 min after venom injection, whereas BJ-PI2 had no effect on the APTT and PT clotting time. BJ-PI2 (10 µM) caused platelet aggregation *in vitro* to a similar extent as thrombin (100 mU/ml). **Conclusion:** BJ-PI2 caused delayed hypotension and thrombocytopenia in anesthetized rats, without consuming coagulation factors. This protein also induced platelet aggregation *in vitro* by mechanisms that are yet to be determined. **Financial support:** CAPES, CNPq.

09.027 Fruit juice, a rich source of polyphenols, induces endothelium-dependent relaxations in mesenteric arteries and antioxidant activities Assis KS[1], Almeida AJPO, Monteiro LS, Azevedo FLAA, Maciel PMP[1], Machado NT[1], Ribeiro TP[1], Medeiros IA UFPB – Ciências Farmacêuticas

Introduction: The fruit-containing beverages, such as fruit juices, are rich sources of polyphenols have the ability to induce potent endothelium-dependent relaxations and free radical scavenger activity, increasing their vascular protection.[1-2] **Objective:** The aim of this study was to evaluate the ability of lyophilized fruit juices of the *Myrciaria cauliflora* (JMC), *Spondia luta* L (JSL) and *Spondias tuberosa* (JST) to induce antioxidant activities and endothelium-dependent relaxations in mesenteric arteries and, if so, to determine the role of their total phenolic content and composition. **Methods and Results** All protocols of this study were approved by the CEUA (nº 1405/13). The results showed a higher total phenolic from 9.88 ± 0.55µg GAE/mg, 16.88 ± 0.18µg GAE/mg, 13.72 ± 0.25µg GAE/mg, content as well as antiradical $DPPH^{\bullet}$ scavenger activity (91.69 ± 0.23%, 19.55 ± 0.15%, 14.01 ± 0.15%) in *Myrciaria cauliflora* (JMC), *Spondia luta* L (JSL) and *Spondias tuberosa* (JST). In 10 µmol/L phenylephrine (PE)-pre-contracted mesenteric artery rings JMC, JSL and JST (10 to 5000 mol/L), caused a concentration-dependent relaxations responses maximum relaxation (MR= 101.14 ± 9.92 %, EC_{50}= 852.85 ± 105.77, n = 6; MR= 121.64 ± 15.42, EC_{50}= 566.60 ± 123.01, n =4; MR=100.74 ± 5.1%, EC_{50}=273.37 ± 100.48, n=7, respectively). Vascular response was assessed after removal of the endothelium, the vasorelaxation elicited by JMC, JSL and JST was attenuated (MR= 89.77 ± 4.14 %, EC_{50}= 1621.42 ± 358.87.,n = 4; MR= 102.30 ± 2.61, EC_{50}= 1014.05 ± 100.48, n =8, MR=98.69 ± 4.83%; EC_{50}= 1099.84 ± 157.99, n=7, $P < 0.05$). In small mesenteric arteries of control and L-NAME-induced hypertensive rats sections (14 µm) were incubated the redox-sensitive fluorescent dye dihydroethidium (DHE, 2.5 µM) for 30 min at 37°C. In some experiments, hypertensive rats sections with a pretreated with JMC, JSL and JST (500, 1000 mol/L) for 15 min before the addition of DHE. The hypertensive sections of small mesenteric artery was significantly increased the formation of superoxide anion (15.75 ± 0.62, 22.65 ± 0.97 %, n=4) and pretreated with JMC, JSL and JST was significantly reduced ROS production (13.99 ± 0.61, 16.59 ± 1.24, 17.70 ± 1.50 %, n=4) and (11.41 ± 1.39, 14.39 ± 1.86, 16.28 ± 1.73 %, n=4), respectively. **Conclusion** Altogether, these findings indicate that fruit juices have the ability to induce potent endothelium-dependent relaxations, and antioxidant activities, that this effect is related to their quantitative phenolic content. **Financial Support: CNPq and CAPES** **References:** 1. AUGER, Cyril et al. Food & function, v. 2, n. 5, p. 245-250, 2011. 2. AUGER, Cyril et al. Journal of medicinal food, v. 18, n. 1, p. 128-136, 2015

09.028 Investigation of Spamolytic Activity of the *Croton echioides* Ball. (Euphorbiaceae)

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[1]UFPB – PIVIC/CNPq, [2]UFPB – PIBIC/CNPq, [3]UFPB – PPgPNSB, [4]UFRPE – DCM, [5]UFPB – DFP

Introduction: *Croton echioides* Ball. (Euphorbiaceae) is popularly known as "quebra-faca", "catinga-branca", "canela-de-velho" or “catinga-de-porco” (Novello, Rev. Bras. Farmacogn., v. 22, p. 946, 2012). Its distribution is restricted to the Brazilian territory, especially in the semiarid, cerrado and caatinga-cerrado transitional areas (Silva, Rodriguésia, v. 60, p. 879, 2009). It is used in popular medicine to treat gastrointestinal tract disorders, like indigestion (Silva, Rev. Caatinga., v. 25, p. 130, 2012). Furthermore, according to Silva studies this species has pharmacological activities such as antidiarrheal (XXVI FeSBE/Rio de Janeiro-RJ, 2011). Other species of this genus have shown spamolytic activity on guinea pig ileum such as C. rbamnifolius, C. rhamnifolioides (Randau, Lecta-USF, v. 20, p. 61, 2002), C. nepetaefolius (Fundam. Clin. Pharmacol., v. 18, p. 539, 2004) and tocolytic activity on sheep's uterus (Pereira, Rev. Bras. Farmacogn., v. 22, p. 522, 2012). Therefore, this study aimed to investigate a possible spasmolytic activity of ethanolic extract from Croton echioides stem (CE-$EtOH_C$) on guinea pig ileum and rat uterus. **Methods**: Guinea pig of both sexes (Cavia porcellus, 300-500 g) and female wistar rat (Rattus norvegicus, 150-250 g) were used. Tissues were removed and suspended in organ baths under appropriate conditions for each experimental protocol and isotonic contractions were monitored. The results were statistically analyzed by the Student’s t-test or one-way ANOVA followed by Bonferroni’s post-test when appropriate (n = 5). The values were expressed as the mean and standard error of the mean. **Results**: On guinea pig ileum, CE-$EtOH_C$ (27, 81 and 243 µg/mL) inhibited in a concentration-dependent manner the phasic contractions induced by both carbachol (CCh) 10^{-6} M (E_{max} = 95.5 ± 0.5%) and histamine 10^{-6} M (E_{max} = 100%), being more potent to histamine (IC_{50} = 36.7 ± 2.6 µg/mL) when compared to CCh (IC_{50} = 53.0 ± 2.3 µg/mL). Additionally, CE-$EtOH_C$ (9, 27, 81 and 243 µg/mL) showed inhibitory effect, in a concentration-dependent manner, phasic contractions induced by both oxytocin 10^{-2} IU/mL (E_{max} = 100%) and CCh 10^{-5} M (E_{max} = 96.5 ± 1.1%) on rat uterus, being more potent to oxytocin (IC_{50} = 19.0 ± 2.7 µg/mL) when compared to CCh (IC_{50} = 56.6 ± 7.0 µg/mL). **Conclusions**: The CE-$EtOH_C$ showed a non-selective spasmolytic activity on guinea pig ileum and rat uterus, described by the first time on literature, and thus, represents a therapeutic potential further choice for the treatment of health problems such as diarrhea, dysmenorrhea and miscarriage. In addition it is necessary further studies to characterize its mechanism of action on these smooth muscle models studied. **Financial support**: CAPES, CNPq, PPgPNSB/UFPB. Research approval by Ethical Committee on Animal Use of UFPB: 069/15.

09.029 Effects of the association of crotamine and thioridazine in mice skeletal muscle contraction evaluated in ex vivo assay Porta LC[1], Lima SC[1], Duarte T[1], Campeiro JD[1], Oliveira EB[2], Rodrigues T[3], Godinho RO[1], Hayashi MAF[1] [1]Unifesp-EPM – Farmacologia, [2]FCFRP-USP – Bioquímica e Imunologia, [3]UFABC – Ciências Naturais

Introduction: Crotamine (CR), one of the main component of the rattlesnake *Crotalus durissus terrificus* venom, has been studied by our group due to its antitumor effect, in addition to other properties as the anthelmintic, antiparasitic and antimicrobial activities described. All these effects may be mainly determined by its amphiphilicity, which may also underlie the CR capacity to disrupt acidic vesicles, as lysosomes and depolarize mitochondrial membranes. However, the ability to immobilize the hindlimbs of rodents was the principal biological property that led to the identification and characterization of CR from the snake venom. Interestingly, the cytotoxic and antitumoral effects of an atypical phenothiazine antipsychotic thioridazine (TR) are also dependent of targeting intracellular organelles, as mitochondria and lysosomes, as similarly described for CR. Co-administration of these compounds in *in vivo* experiments showed that TR potentiates the CR-induced hindlimb immobilization while CR potentiates the TR sedative, suggesting that these compounds may potentially act in a common pathway, which would explain the mutual potentiation effects. Therefore, the objective of the present work was the evaluation of the effects of CR and/or TR in the contraction of skeletal muscle in *ex vivo* assay, aiming to understand this mutual potentiation effects and eventually identify the common molecular pathways shared by these two apparently unrelated compounds. **Methods**: The contraction of diaphragm of Swiss mice was monitored using a PowerLab® (AD Instruments) system and the program PowerLab® Chart®. The contraction was induced by transmural electrical stimuli, with 2 ms of duration, frequency of 0.1 Hz and supramaximal voltage. Aiming to avoid the interference of acetylcholine signaling, the diaphragm was pre-treated with d-tubocurarine (10 µM), before the addition of CR (30 nM), TR (1 µM), or vehicle (water) used as paired control. **Results**: The basal contraction force of the muscle was increased by 94 ± 8% in the presence of crotamine (CR). On the other hand, thioridazine (TR) reduced the contraction force of the muscle by 11 ± 7%. The treatment with TR, 30 min after addition of CR, increased in 49 ± 3% the twitch contraction force. On the other hand, pre-treatment with CR, 30 min prior the addition of TR, reduced in 29 ± 13% the contraction force.**Conclusion:** The results presented herein showed that, after co-administration of CR and TR, the prevailing effect is determined by the compound firstly added into the muscle preparation. Furthermore, in contrast to the *in vivo* observations, no potentiation effect could be observed in the *ex vivo* assay. Thus, we believe that the effects observed in both *ex vivo* and *in vivo* assays can involve the same molecular pathways as, although showing opposite effects in the *ex vivo* experiments, TR and CR are still interfering the activity of each other in isolated skeletal muscle preparations. **Financial support**: FAPESP, CNPq and CAPES. Approval by ethical committee CEUA Nº 7971160315.

09.030 Effect of four categories of yellow maca aqueous extract (Lepidium meyenii) from Huallanca (Ancash) on testis, epididymis and deferens vas sperm count in experimental animals. Sanchez SL, Gonzales GF Universidad Peruana Cayetano Heredia -

Introduction: Consumption of *Lepidium meyenii* hypocotyls (Maca), a native plant of the Central Andes of Peru, has important effects on male and female fertility. For the first time the biological value of Maca cultivated in the Northern Peruvian Andes is published. The objective of this study is to evaluate the effect of different categories (cataloged as well from the first quality to the fourth one according to the size of hypocotyls); the effect of different pH (acid, natural and alkali) and the effect of routes of administration (orogastric vs intraperitoneal). As a biological response, sperm count was evaluated in testis, epididymis and deferens vas in Swiss strain mice. **Methods**: Four different sizes were used (Yellow Maca categories of MGAT1P1530 area (Torres Parcela Regalado farm) from Huallanca district, Bolognesi Province, Ancash Department, located at 4250 msnsm. pH, glucose and total polyphenols were evaluated of four categories of Maca. Three bioassays were performed considering normal pH, pH acidified with hydrochloric acid (pH=4) and pH alkalized with sodium hydroxide (pH=8). For each bioassay, 35 mice were used, which were administered with distilled water (control), an standardized atomized extract of Black Maca (positive control) and aqueous extracts of four categories with a daily dose of 273 mg/kg bw (1 mg of maca per kilogram of body weight) during 3 days with a volume of 0.5 mL per animal and the effect of two routes of administration (orogastric and intraperitoneal) was also evaluated. After treatment mice were sacrificed evaluated daily sperm production in testis, and sperm count in epididymis and deferens vas. $P < 0.05$ was considered as significant. **Results**: First Category of Yellow Maca showed the highest levels of total polyphenols. First and Second category had the most acidic pH and better biological activity. Aqueous extracts of first and second category of maca with acid pH had a significant effect on sperm count in all reproductive organs, followed by the aqueous extract with natural pH, while the alkali aqueous extract did not show a significant effect ($P > 0.05$). The most effective treatment route was orogastric, yielding a high sperm count ($P < 0.05$) in contrast to intraperitoneal ($P > 0.05$). **Conclusion:** Aqueous extract of first category of maca with acid pH showed the best effect on sperm count on reproductive organs and the best route of administration was orogastric, suggesting that the gastro-intestinal passage promotes the production of active principles. The budget for this research was obtained from funds of “Círculo de Investigación en Plantas con Efectos en Salud” through FONDECYT. All study procedures were performed according to Guide for the Care and Use of Laboratory Animals, National Institute of Health in the United States. The approval of the Institutional Ethics Committee of Universidad Peruana Cayetano Heredia was requested. The process number is 65965.

09.031 Evaluation of the effects caused by different concentrations of Aflatoxin B_1 in jundiás (*Rhamdia quelen*) by hematologic evaluations. Barbosa CK, Soares RL, Régio RR, Iachinski EA, Araújo CMTD, Rocha DCC, Ribeiro DR, Anater A, Pimpão CT PUCPR – Medicina Veterinária

Introduction: The naturally occurring aflatoxins in corn, in animal feed and corn-based foods possibly contribute to problems related to the health of humans and animals infected by consuming these products, which are dependent on the intake of aflatoxin concentration. Clinical signs and diagnosis of this type of poisoning are not accurate and often result in considerable economic losses in livestock production. **Objective:** The aim of this study was to determine the possible deleterious effects on jundiá fed contaminated feed containing different levels of aflatoxin B_1 (AFB_1) through hematologic evaluations. **Methods:** The Ethics Committee on Animal Use PUCPR approved this project under the protocol number 886 – 2nd version. 624 jundiás fingerlings were used, divided into 4 different groups (GI – 0; GII – 45; GIII – 90 and GIV – 180 µg $AFB_1.kg^{-1}$ in the feed) and randomly divided into 24 aquariums (n=26 fingerlings/aquarium) and fed for 56 consecutive days. Blood samples were taken on days +28, +42 and +56 days of the experiment. They were evaluated erythrocyte and leukocyte parameters of these animals. For statistical analysis was used ANOVA followed by Bonferroni test or Kruskal-Wallis test followed by Dunn's test. **Results:** No significant differences were observed ($p>0.05$) in erythrocyte parameters between different groups. There was a significant increase ($p<0.05$) in the total leukocytes, lymphocytes, special granulocytic cells, neutrophils and platelets GII and GIV in relation to GI on days +28 and +42, but there was a reduction ($p<0.05$) in these parameters at day +56, showing that these animals respond to poisoning in the first, but with increasing time of infection, the immune system goes into depletion. However, GIII showed a reduction in these values ($p<0.05$) compared to GI on days +28 and +42 ready demonstrating ineffectiveness of the immune system and on day +56, there was an increase of these values ($p<0.05$), demonstrating a reaction or adaptation to the toxic agent. **Conclusion:** According to these data, can be conclude that AFB_1 affects the immune system jundiá and probably compromise the productive performance of the species. **Keywords:** Intoxication; Erythrocyte parameters; Leukocyte parameters; Productive performance; Mycotoxins.

09.032 Evaluation of the immunomodulatory effect of essential oil obtained from *Eremanthus erythropappus* McLeish Rich In α-bisabolol and α-bisabolol isolated towards lymphocytes obtained from mice bearing experimental autoimmune encephalomyelitis *in vitro.* Silva SK[1], Alves JV[1], Silva CA[1], Silva AM[2], Rovarotto CF[3], Silva GAA[3], Silva IRS[1], Santos LMB[3], Farias AS[3], Rocha-Parise M[1] [1]UFG, [2]Instituto Federal Catarinense, [3]Unicamp

Introduction Multiple Sclerosis (MS) is an autoimmune, chronic, inflammatory and demyelinating disease of the Central Nervous System[1]. It is probably mediated by $CD4^+$ T cells, but a regulatory subset of $CD4^+$ cells (T_{REG}) is thought to be involved in the control of MS progression[2]. Experimental autoimmune encephalomyelitis (EAE) is used to study MS, featuring inflammation and demyelination as MS[3].There is not a cure for MS and the available drug treatment nonspecifically suppress the immune response, exerting side effects[4]. So, the search for better drugs with anti-inflammatory properties, i.e. stimulating T_{REG} cells is needed. Alpha-bisabolol (α-B) rich oil from *Eremanthus erythropappus* (EE) wood and α-B isolated, due to α-B anti-inflammatory properties[5], may be promising for MS treatment. The aim of the study was to find the concentration of α-B rich oil from EE and α-B capable to maintain lymphocytes viability in EAE, and check if this concentration is able to increase the number of T_{REG} cells. **Methods** EAE was induced in C57BL/6 mice by immunization with MOG_{35-55} antigen with Freund's complete adjuvant and by Bordetella pertussis toxin after 48h. Mice were observed to analyze the clinical evolution and at the onset of EAE, were sacrificed and had their axial lymph nodes removed. The obtained cells were cultivated and then incubated for 24h with concentrations of EE essential oil rich in α-B and sole α-B ranging from 200 to 1.563µg/mL for the cytotoxicity evaluation through the reduction test of 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide (MTT)[6]. Flow cytometry technique was employed to characterize T_{REGs}, by using the anti-CD3, CD4, CD25 and FoxP3 antibodies. **Results** Both EE essential oil and α-B, after 24h incubation, presented a concentration-dependent cytotoxicity, being 6.25µg/mL the common lowest concentration capable of keeping total lymphocytes viability. In this concentration, only EE essential oil stimulated a significant increase ($p<0.05$) in the relative number of T_{REGS}, showing that other substances in the oil are involved in the observed effect. **Conclusion** Overall data showed an immunoregulatory property of EE essential oil but further studies, mainly in vivo, are necessary to evaluate this effect and its overall security.

09.033 Evaluation of acute and subacute toxicities of the aqueous extract of *Chrysobalanus icaco*. Silva NM[1], Rios ACM[1], Carvalho VMF[1], Neto PPM[1], Guerra ASHS[1], Melo MCS[1], Ribeiro NE[1], Carvalho-Júnior CHR[1], Oliveira TB[1], Silva TG[1] [1]UFPE – Antibióticos

Introduction: Plants are used as a therapeutic resource since the beginning of men's history. Despite of the technical and scientific advances, phytotherapy remains as an optional treatment for several diseases. In Brazil, the specie *Chrysobalanus icaco* (Chrysobalanaceae), popularly known as "guajerú", has several biological properties, such as antioxidant, anticancer, hypoglycemic, anti-inflammatory and antinociceptive. However, there are no records regards its toxicity. Therefore, the main goal of this work was to evaluate the acute and subacute toxicities of the aqueous extract of *C. icaco* leaves (AeCi). **Methods:** To access acute toxicity, female swiss mice (*Mus musculus*) were used (OCDE 423, 2001) and approved by the Committee for Ethics in Animal Research nº 23076.016550/2016-38. The mice were divided into two groups (n=6): control group received saline (v.o), and the treated group received AeCi (2,000 mg/kg; v.o.). Following, the mice were observed individually in the first 1 h, 2 h, and 14 days after drug administration to analyze the presence of clinical signs of toxicity or death. On the 14th day the animals were anesthetized with ketamine/xylazine (2:1; i.p.), and the blood was collected for haematological and biochemical analysis. Liver, kidney, and spleen were removed, analyzed macroscopically, and weighted. The subacute toxicity test followed OCDE 407 (2008) guidelines: repeated doses during 28 days. The mice were divided into 10 groups (n=5/group/sex). The control group received saline (v.o), the groups treated received AeCi (100, 200, or 400 mg/kg), and the satellite group received 400 mg/kg of AeCi for 28 days and kept alive for more 14 days without treatment to detect delayed toxic effects. On the 28th day, the animals were anesthetized and followed the steps accordingly the acute toxicity test. **Results:** In the acute toxicity test, the AeCi did not lead the animals to death, nor any acute toxicity effects were observed. Water and food consumption had no difference between the groups. Liver, kidney and spleen had no significant morphological alterations regarding of aspects or color, as well as the relative weight had no difference between the groups. The extract at the dose of 2000 mg/kg did not show toxicity for blood cells and did not change the biochemical parameters of the mice, since there was no statistical significance. In the subacute toxicity test we did not observe death of the animals treated with AeCi during 28 days. A small weight decrease of the body weight was noticed for both female and male mice treated with AeCi when compared to control group. However, this reduction cannot be due to the toxic effects of the substance, since weight loss was inferior to 20%. In addition, no statistical difference was found in the haematological and biochemical profiles, also there was no macromorphological alterations and organ weight. **Conclusion:** The results show that the aqueous extract of *Chrysobalanus icaco*, in the administrated doses, has low toxicity, not presenting significant toxic effects when administrated by oral route. **Financial support**: FACEPE, CAPES and CNPq. **References**: OECD. **Guideline: 423**. p. 1, 2001. OECD. **Guideline: 407**. p. 1, 2008.

09.034 Effect of *Allium cepa* **L. extract in lung and pancreas of diabetic rats streptozotocin-induced.** Lemos LIC, Medeiros MA, Silva FS, Abreu BA, Bortolin RH, Rezende AA, Medeiros KCP

Diabetes Mellitus is a chronic metabolic disease characterized by hyperglycemia secondary to the reduction in circulating insulin levels or a tissue deficit of the effects of this hormone. Diabetes mellitus type I (DMI) is an autoimmune disease that results in the destruction of the beta cells, usually leading to absolute insufficiency of insulin and consequently to hyperglycemia that is associated with long-term damage, dysfunction and failure of various organs, including the pancreas and lung (BENZADÓN, 2014). The onion (*Allium cepa* L.), in the preparations and known worldwide, has been used in research that has a focus on diabetes, as an alternative treatment, checking its potential hypoglycemic and systemic beneficial effect, as it has anti-inflammatory and antioxidant components (LEE, 2013) . The aim of this study was to evaluate the treatment effect of *Allium Cepa* L. extract in rats induced with streptozotocin. **Methods**: 26 Wistar rats were used and DMI was induced by streptozotocin (40mg / kg i.p ..). *Allium cepa* L. extract (400 mg / kg, V.O.) was administered daily for 30 days after installation of the DM. Clinical, biochemical profile, morphology and morphometry pancreatic and lung were the parameters analyzed in this study. **Results**: Clinically, diabetic animals showed polydipsia (723 ± 109), weight loss (18 ± 12), hyperglycemia (413 ± 38) and increased lipid profile (91 ± 7) and treatment with the *Allium cepa* L. extract could decrease significantly cholesterol (64 ± 5) in diabetic animals and helped in preventing sudden loss weight (9 ± 6), but was not effective in reducing blood glucose. As for the morphological aspect, the treatment with the extract was able to improve pancreatic atrophy of diabetic animals. As well, helped in improving the thickness of the alveolar septa, decreased inflammatory infiltrate and presence of macrophages. But the extract did not cause a significant improvement in fibrosis in the lungs of diabetic rats. **Conclusion:** The acute treatment *Allium cepa* L. extract was shown to reduce cholesterol and regeneration ability of pancreatic beta cells by an unknown mechanism, and further improvement of some pulmonary alterations that are found in diabetes. Thus, the *Allium cepa* L. extract can be considered a promising product for future clinical applications, associated or not with other therapies. BENZADÓN, M. et al. Actualización en el diagnóstico de la diabetes, v.16, n.4, p. 1, 2014. IDF DIABETES ATLAS 7th- Edition, 2015. LEE, C. et al. I*n vivo* Investigation of Anti-diabetic Properties of Ripe Onion Juice in normal and Streptozotocin-induced Diabetic Rats. Prev Nutr Food Sci. v.18, n.3, p. 169, 2013 Financial Support: PROPESQ/UFRN/CNPq Research approved by the Animal Research Ethical Committee of Federal University of Rio Grande do Norte (process number: 054/2014).

09.035 Oceanapia sp. sponge also presents dual effect on intestinal motility in mice

Figueiredo IAD[1], Pereira JC[2], Ferreira SRD[2], Moreno GTA[1], Oliveira FRMB[1], Santos BVO[2,3], Silva BA[2,3], Cavalcante FA[2,4] [1]PIBIC/UFPB, [2]PPgPNSB/UFPB, [3]DCF/UFPB, [4]DFP/UFPB

Introduction: Marine natural products have attracted the attention of researchers due to its potential as source of new medicines (Movahhedin, Iran J Pharm Res, v. 13, p. 515, 2014). Oceanapia sponges present around 100 species distributed on tropical worldwide seas (Van Soest, World Porifera Database, 2015) and there are few studies relating the pharmacological effects of this sponges. According to Pereira et al. (CIFARP/Ribeirão Preto-SP, 2015), the ethanolic extract from Oceanapia sp. (OC-EtOH) showed both spasmolytic and spasmogenic actions on guinea pig ileum. Thus, the aim of this study was to investigate a possible antidiarrheal or laxative effect of the OC-EtOH in mice. **Methods**: Initially, behavioral screening and evaluation the acute toxicity in mice (n = 6) were performed according to OECD guideline no. 423 (OECD, guideline for testing of chemicals n. 423, 2001). For in vivo assays, mice (n = 6) were divided into the following groups: negative control (saline 10 mL/kg plus Cremophor® 0.01%, p.o.), positive control (loperamide 10 mg/kg or atropine 2 mg/kg, p.o.) and OC-EtOH (various doses, p.o.). Then, the effect of OC-EtOH on castor-oil induced diarrhea, normal intestinal transit and castor-oil induced intestinal transit in mice were analyzed. **Results**: In acute toxicity assay, OC-EtOH (2000 mg/kg, p.o.) did not induce toxicity signs in female mice under experimental conditions and the 50% lethal dose was estimated at about to 5000 mg/kg according to OECD 423 guide. Since natural products with dual effect are cited on scientific literature as potential agents to treat gastrointestinal disorders as diarrhea and constipation (Mehmood, Dig Dis Sci, v. 56, p. 1460, 2011), we decided to investigate a possible antidiarrheal activity of the OC-EtOH. The extract produced antidiarrheal effect in dose-dependent manner, being 2 fold more potent for inhibiting liquid stools (ED_{50} = 189.1 ± 13.6 mg/kg) than the total defecation frequency (ED_{50} = 387.7 ± 21.6 mg/kg). Interestingly, the extract increased the normal intestinal transit (ED_{50} = 477.6 ± 14.8 mg/kg); however, in castor oil induced-diarrheic animals the OC-EtOH reduced the intestinal transit (ED_{50} = 93.30 ± 7.2 mg/kg). **Conclusion:** In conclusion, the present study demonstrated for the first time that Oceanapia sp. sponge has lower acute toxicity and inhibitory effect on the castor oil-induced diarrhea. OC-EtOH also presents a dual effect on in vivo experiments by increase the normal intestinal motility and decrease the castor oil-induced intestinal motility. Therefore, this study indicates a potential medicinal usage of the Oceanapia sp. sponge on intestinal conditions as diarrhea and/or constipation. **Financial support**: CNPq, CAPES, PgPNSB/CCS/UFPB. Research approval by Ethical Committee in Animal Use of UFPB: Protocol 146/2015.

09.036 Chemoprotector potential of the flavonoid hesperidin in the carcinogenesis model induced by 1,2-dimethylhydrazine in mice C57/BL6 Machado JLP[1], Nascimento LNS[1], Cordeiro PGA[1], Lopes MSP[1], Paz APS, Aires WC[2], Vierira V[2], Serquetto PL[3], Novaes R[4], Hamoy M[1], Mello VJ[1] [1]UFPA – Farmacologia e Toxicologia de Produtos Naturais, [2]UFPA, [3]Universidade Federal de Juiz de Fora – UFJF, [4]Unifal

Colorectal cancer occupies a place of global importance due to its high incidence and a large pool of lifestyle, particularly as regards eating habits. Experimental studies support the hypothesis that both its establishment and its prevention are directly associated with the intake of compounds that are carcinogenic and chemopreventive effects, respectively. Within this perspective phytochemicals that show protective biological properties as Flavonoids may have to be excellent candidates for chemoprevention of this pathology. This study aimed to evaluate the potential of quimioprotetor Hesperidin in experimental carcinogenesis induced by 1, 2-dimethylhydrazine (DMH) in C57 / BL6 mice. Materials and methods: We used the C57 / BL6 mice that received the inducer agent at a dose of 20 mg / kg for 10 weeks (n = 12 per group). Treatment with hesperidin (orally at the doses 10, 100 and 200 mg / kg) was started from the first dose 1, 2-DMH being performed 2 times per week and completed 20 weeks after the first dose. Immediately after euthanasia was made count and photographic record of polyps / lesions present in the segments of intestine of C57 / BL6 mice. This experiment was approved by the research ethics committee animal protocol 00002/2012-I. **Results**: Treatment with Hesperidin in doses 100 and 200 mg / kg was able to increase the body weight when compared to control after 17 weeks and 5 weeks ° the significance level of the data was verified trough analysis of variance (ANOVA) followed by Dunnett's test ($p<0,05$), respectively. Increased survival was observed in all treated groups, with no loss of animals, in contrast, was observed death of 12.5% of the control animals. The reduction in polyp formation / lesions present on mice intestine segments C57 / BL6 mice was 45 %, 55 % and 66 % respectively in the treatment with doses 10, 100 and 200 mg / kg, the significance level of the data was verified trough analysis of variance (ANOVA) followed by Dunnett's test ($p<0,05$) and ($p<0,001$) . **Conclusion:** The study shows the effect quimioprotetor dose dependent in this experimental model. Financing was provided by conselho nacional de desenvolvimento cientifico e tecnológico. Keywords: Quimioproteção , mice C57 / BL6, Hesperidin, colorectal carcinogenesis.

09.037 *In vitro* **antibacterial activity of plant extracts on pathogens of clinical importance.**
Melo BO[1], Maia HS[1], Nascimento OMO[1], Silva TFC[1], Carmo MS[1], Bomfim MRQ[1] [1]Universidade Ceuma – Programa de Pós-Graduação

Introduction: The popular use of plants for medicinal purposes is common in Brazil, mainly in the poorest states, such as those in North and Northeast regions. Generally, the population cultivates in the backyards different species. Plants can be also purchased freely in markets and fairs in vacant urban lots. These plants are rich in substances capable of alleviate pain in general, heal wounds, cure diarrhea and cough, combat parasites, among others. In this regard, adding the scientific confirmation to therapeutic practice can bring many benefits, especially to low-income communities. This study aimed to evaluate the antimicrobial properties of hydroalcoholic extracts from leaves of the following plant species: *Bauhinia forfic*ata Link (cow foot); *Jatropha gossypiifolia* L (bellyache bush) and *Himatanthus drasticus* (frangipani). **Methods:** The leaves were collected in the morning (between 8 and 10 hours), washed and placed in an oven at 45 ° C until complete dryness. Each dried material was proceeded to obtain powder and then subjected to extraction using 70% ethanol for ten days with twice daily homogenization. After this period, the macerated were filtered through filter paper and concentrated until complete removal of the solvent on a rotating evaporator at 50 °C. The extracts were solubilized in sterile ultrapure water and filtered on filter with a pore size of 20 micrometers. Phytochemical analysis for detection of secondary metabolites was performed. The antimicrobial activity was determined against *Staphylococcus aureus* (ATCC 25923), *Pseudomonas aeruginosa* (ATCC 27853), *Salmonella enterica typhimurium* (ATCC 14028), *Listeria monocytogenes* (ATCC 15313) *Enterococcus faecalis* (ATCC 19433); *Klebsiella pneumoniae* (ATCC 10031) and *Candida albicans* (ATCC 18804). Each microorganism was plated on culture plate with Mueller-Hilton agar and yeast in Sabouraud agar, and incubated at 35 ° C for 24 and 48 hours, respectively. After the incubation period suspension of microorganisms were prepared with turbidity equivalent to 0.5 McFarland tube ladder (1.5×10^8 CFU/mL). The antimicrobial action of each extract was evaluated using agar diffusion assay (diameter of the inhibition zone) and broth microdilution assay (for determination of the minimum inhibitory concentration; MIC). **Results and Conclusion:** *B. fortificata* extract showed activity against Gram-positive bacteria: *L. monocytogenes* (MIC 20 mg/mL) and *S. aureus* (MIC 5 mg/mL) and gram-negative (*P. aeruginosa* (MIC 10 mg/mL). The extract from *J. gossypiifolia* only showed activity against *S. aureus* (65.6 mg/mL). On the other hand, the extract from *H. drasticus* showed antimicrobial activity against *L. monocytogenes* (MIC 20 mg/mL) *K. pneumoniae* (MIC 10 mg/mL) and *C. albicans* (MIC 40 mg/mL). In this study it is evident the importance of developing new studies for the isolation and identification of the active ingredients responsible for the antimicrobial activity demonstrated *in vitro*, as well as their potential use in the pharmaceutical industry. **Keywords:** Antimicrobial properties, Hydroalcoholic extracts, Phytochemical analysis, Medicinal plants. This work was supported by Fundação de Amparo à Pesquisa e Desenvolvimento Científico do Maranhão (FAPEMA) and Universidade Ceuma.

09.038 Antimicrobial activity of *Piper bogotense* **against** *Salmonella cholerae**-suis*** **and** *Staphylococcus aureus* **and the effect of fertilization changes on its metabolome.** Rincón-Aceldas S[1], Botero-Villegas N[1], Gonzáles-Bernal V[1], Coy-Barrera E[1] [1]Universidad Militar Nueva Granada – Laboratorio de Química Bioorgánica, Facultad de Ciencias Básicas y Aplicadas

Introduction: *Piper* is one of the largest genera of angiosperms, belonging to the Piperaceae family, and comprises many species with economical, ecological, ethnobotanical and ethnomedicinal interest in tropical areas. The bioactivity and pharmacological uses of plants from this genus has been reported at different levels with interesting potential [1]. On this context, several antimicrobial metabolites had been reported from *Piper* species, but there is a lack of information regarding the bioactivity of *P. bogotense* (endemic in Bogota plateau), as well as on the metabolome variability depending on substrate changes. Thus, as part of our interest on naturally-occurring antimicrobials, crude extracts from *P. bogotense* were evaluated against two bacterial strains (*S. cholerae-suis* and *S. aureus*) and this activity was correlated to the chemical composition by LC/MS-based metabolic profiling for identifying bioactives [2]. Themetabolome variability of *P. bogotense* was also studied when the fertilization scheme was modified as parameter of standardization of the antimicrobial potential of *P. bogotense*. **Methods:** *In vitro* growth inhibition of ethanolic extracts of leaves, stems and roots of *P. bogotense* plants was evaluated against *S. cholerae-suis* and *S. Aureu s*on Müeller-Hinton medium with paper disks impregnated with different concentrations of extracts (10, 5 and 1mg/mL).The bacterial growth was determined with ImageJ® for estimating the inhibition area. **Results** were statistically analyzed by Shapiro-Wilk, ANOVA, and Tukey tests. Chemical characterization of extracts was performed by LC-MS using a Shimadzu Prominence UFLC. In order to study the metabolome differences in *Piper bogotense* extracts, propagated plants were fertilized with Hoagland solution varying nitrogen content (standard, 1/2 and 1/4). Plant material from the different treatments was collected in three periods and ethanolic extracts were then prepared by ultrasound-assisted extraction. Chromatographic data were pretreated and imported to SIMCA® for corresponding multivariate analysis. Thus, Principal Components Analysis (PCA)-derived Score Plots and Loadings-line were used to establish the metabolome correlations. **Results and Conclusions:** Crude extracts of leaves, stems and roots of *P. bogotense* plants showed *in vitro* antimicrobial activity against *S. cholerae-suis* and *S. aureus* at different levels in a dose-response manner. Several metabolites were found to be correlated with the activity by metabolic profiling. The effect of nitrogen variations in *P. bogotense* at early growth stages reveals differences in the chemical profiles within a non-linear behavior, indicating the metabolome of *P. bogotense* is sensitive to substrate changes. This plasticity could be useful in further studies for induced production of bioactive metabolites.*The present work is a product derived by the Project INV-CIAS-2050 financed by Vicerrectoría de Investigaciones at UMNG - Validity 2016.* **References:** 1. Dwivedi, V.*et al*. 2014. *J PharmacognPhytochem*, 3(4), 93. 2. Yuliana, N. D.*et al.* 2011. *Phytother Res*, 25(2), 157.

09.039 Metabolic profiling-based identification of antioxidants from bacterial endophytes isolated from *Genista monspessulana* Botero-Villegas N[1], Coy-Barrera E[1] [1]Universidad Militar Nueva Granada – Laboratorio de Química Bioorgánica, Facultad de Ciencias Básicas y Aplicadas

Introduction: *Genista monspessulana* (Fabaceae family) is a plant characterized by its easy spreading to form dense shrubbery, being therefore considered as an invasive species [1]. For invasion and protection purposes, this plant can produce novel and unique secondary metabolites or require strong interactions with other organisms such as endophytes. This kind of organisms establishes a specific association with its host for mutual benefits. Many endophytes allow protecting its host against cell death [2], since a positive effect between host-endophyte occurs to induce high levels of compounds (e.g., antioxidants), which directly or indirectly counteract to harmful effects through free radicals or oxidants, avoiding alteration of cell functions [3]. Thus, as part of our research on antioxidants of natural origin, a set of endophytes were isolated from different plant structures and the resulting extracts were evaluated for their antioxidant capacity. **Methods:** Endophytes were isolated from plant structures such as leaves, pods and stems of *G. monspessulana*. A massive seeding of explants was performed in nutritive agar and the resulting isolated bacterial colonies were transferred to nutrient broth, centrifuged and stored in glycerol. The endophytes were reactivated and placed into liquid cultures (LC) for growing. LC was then separated into supernatant and pellet by centrifugation and filtration. Supernatant was directly extracted using ethyl acetate using a liquid-liquid extraction. Pellet was lyophilized and then extracted using ethyl acetate. Antioxidant capacity of resulting crude extracts was evaluated through DPPH-radical scavenging capacity assay. Additionally, extracts were also profiled by LC/MS using a UFLC Shimadzu Prominence system. Radical scavenging results were analyzed by Shapiro-Wilk, ANOVA, and Tukey tests. Chromatographic data were pre-treated and imported to SIMCA® for corresponding multivariate analysis. Thus, Principal Components Analysis (PCA)-derived Score Plots and Loadings-line were used for identification of antioxidant compounds. **Results and Conclusions:** Twenty bacterial endophytes were isolated and sixteen of them were found to have antioxidant activity. UFLC-DAD-derived profiles of the extracts from liquid cultures of endophytes exhibited a large number of related compounds. PCA-derived score plots exhibited four groups: group 4 comprised extracts with the highest antioxidant capacity obtained and group 1 involved the lowest ones. Labeling by Gram staining indicated that *G. monspessulana* have a highest population of Gram(-) bacteria, but this classification was found to be non-related to metabolic profiles. OPLS-derived score plots let to the identification of a set of compounds to be correlated to antioxidant capacity. The present untargeted metabolomics exploration of endophytes from this invasive plant resulted in an excellent approach for antioxidants finding from nature. *The present work is a product derived by the Project INV-CIAS-2050 financed by UMNG - Validity 2016.* **References:** 1. Alarcón, E.P. et al. 1997. *Rev Colomb Quim,* 26(2), 987. 2. Abello, J. et al. 2006. *Rev Corpoica,* 7(2), 55. 3. Kinsella, J. et al. 1993. *Food Technol,* 47, 85.

09.040 Trypanocidal effect of violacein from *Chromobacterium violaceum* Canuto JA[1], Azevedo IEP[1], Menezes RRPPB[2], Batista AH[1], Nogueira PCN[3], Grangeiro TB[4], Silveira ER[3], Nogueira NAP[1], Martins AMC[1] [1]UFC – Análises Clínicas e Toxicológicas, [2]UFC – Fisiologia e Farmacologia, [3]UFC – Química Orgânica e Inorgânica, [4]UFC – Biologia

Introduction: The World Health Organization estimates that approximately 7 to 8 million individuals are infected with *Trypanosoma cruzi* worldwide. The treatment of Chagas disease has limited efficacy and side effects that limit patient tolerability and compliance. The search for new therapeutic alternatives from biodiversity has increased significantly in recent years. Violacein (VIO), a bacterial pigment produced by *Chromobacterium violaceum,* has shown several biological actions and among them, antiulcer, antitumor, antiviral, and antiparasitic action. In this study, we assessed the effects of VIO on the evolutionary forms of *Trypanosoma cruzi.* **Methods**: Epimastigotes were cultured in liver infusion tryptose (LIT) medium at 28 °C in the presence of VIO (0.97; 1.9; 3.9; 7.8; 15.62; 31.25; 62.5; 125; 250 ; 500; 1000μM) for 24, 48 and 72 hours. Trypomastigotes obtained after infection in LLC-MK2 cells were resuspended in 2% DMEM medium of FBS and incubated with VIO (0.97; 1.9; 3.9; 7.8; 15.62; 31.25μM) for 24h. Amastigotes were cultured on circular glass slides within culture plates containing LLC-MK2 cells and treated with violacein (4.97 and 9.94 μM). All experiments were performed in triplicate (n = 3). For comparison of the experimental groups, ANOVA test was used with Dunnett's post-test, using $p < 0.05$ as significance criterion. **Results**: In epimastigotes, the substance showed trypanocidal action, with an IC_{50} value of 51.39; 104.7 and 67.78μM at 24, 48 and 72h of treatment, respectively. In trypomastigotes, IC_{50} was 4.97μM at 24 hours. The analysis of amastigotes reduced the percentage of infected cells and their survival rates at 24 and 48 hours, at concentrations of 4.97 and 9.94 uM, respectively. **Conclusion:** VIO showed trypanocidal effects on all forms of the parasite evolutionary cycle, suggesting that this substance is a promising alternative to the development of new trypanocidal drugs. **Financial support**: Capes (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior) and CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico).

09.041 Antioxidant activity of extracts obtained from red grape pomace. Karling M, Merlin N, Bicas TC, Carpes ST, Oldoni TLC UTFPR – Química

Introduction: Grapes, its derivatives and by-products are considered sources of phenolic compounds, which represent a class of bioactive compounds with antioxidant potential [1], [2], [3]. In order to extract the bioactive compounds from different samples, various techniques have been employed because many factors can affect the extraction process, mainly the polarity of the solvents used. Thus, the aim of this study was to develop a successive extraction from by-product of the red grape pomace using solvents with different polarities and test the antioxidant activity (AA) of the extracts by two *in vitro* assays. **Methods**: The red grape pomace (*Vitis labrusca* – variety bordeaux) from the red wine processing was obtained in a winery in 2014 in the city of Mariópolis, Parana, Brazil. After collection, the sample was freeze-dried, grounded and stored at - 6°C until analysis. The extraction was performed at room temperature and the solvents used were added in the following order: hexane (E-HEX), dichloromethane (E-CH_2Cl_2), ethyl acetate (E-ACETATE), acetone (E-ACETONE), ethanol (E-EtOH) and ethanol:water 50:50 (v/v) (E-EtOH50). Solvents were replaced each 24 h during 3 days. After that the extracts were evaporated in a rotary evaporator and lyophilized under controlled temperature and pressure. For 2,2-diphenyl-1-picrylhydrazyl hydrate (DPPH) free radical scavenger analysis [4], and 2-2'-azino-di-(3-ethylbenzthiazoline sulfonic acid) (ABTS) method [5] extracts were weighed, solubilized and diluted to concentrations that ranged from 200 mg L^{-1} to 3000 mg L^{-1}. Assays were performed in triplicate. The Tukey´s test was performed using STATISTICA 8.0 software. **Results**: The comparison between the averages calculated for the extracts from the ABTS method indicated a significant difference between all analyzed extracts. When the AA was evaluated by the DPPH method, only E-CH_2Cl_2 and E-HEX extracts showed no significant difference between the averages. The extract E-EtOH50 showed the highest antioxidant potential in both ABTS (1419 ± 67 µmol Trolox g^{-1} of dry sample) and DPPH (1159.8 ± 57 µmol trolox g^{-1} dry sample) free radical scavenger Methods: However, the extract that has the lowest activity, for both methods, was the E-HEX extract, with values of 14.76 ± 0.75 and 34.67 ± 0.88 µmol Trolox g^{-1} for DPPH and ABTS, respectively. **Conclusion:** The extracts obtained with solvents of medium and high polarity presented the best responses to AA by both methods, which indicates that this by-products of the wine industry is a promising source of compounds with antioxidant activity. There are few studies with successive extraction technique for extraction and concentration of bioactive compounds from red grape pomace, which emphasizes the importance of this study. References: [1] Karacabey e Mazza, Food Chem, 119, 343, 2008; [2] Leyva-Corral et al., LWT - Food Sci Tech, 65, 228, 2016; [3] Rana et al., Food Sci Hum Well, 4, 180, 2015; [4] BRAND-WILLIAMS et al., Leb. Technol., 28, 25, 1995; [5] RE et al., Free Radi Bio & Medic, 26, 1231, 1999. **Acknowledgments:** The authors acknowledge grants and fellowships from CNPq (Process 476635 / 2013-6) and Capes, Central de Análises and PPGTP (UTFPR - Pato Branco).

09.042 Evaluation of the copaiba oil (*Copaifera reticulata*) on the healing process on the bladder of rats. Rocha IRO[1,2], Feitosa-Júnior DJS[2], Carvalho LTF[2,3], Brito CN[2], Moreira RA[2], Barros CAV[2] [1]CESUPA, [2]UEPA – Cirurgia Experimental, [3]UFPA

Introduction: Although the tissue healing happens similarly in different tissues, some organs have their peculiarities. In the case of bladder, this is an organ with a little collagen synthesis and the healing process becomes difficult by the presence of urine. So, the search for new treatments which can improve and speed up the healing process on the bladder becomes necessary, as well as increase knowledge related to their collagenous, acute and chronic inflammation. The World Health Organization (WHO) recognizes the importance of phytotherapy for treatment, cure and prevention of diseases suggesting that is a viable and considerable alternative. One of the main medicinal plants used on the Amazon region is copaiba, whose effects have been tested and found effective in various activities, such as anti-inflammatory, healing and antimicrobial. Faced with the need to improve the healing process on the bladder and the actions attributed to the copaiba oil, this study aims to evaluate copaiba oil on the healing process of surgical incisions on the bladder of rats in an experimental comparative study. **Methods**: This study was approved by the Ethics Committee of Animals Use (CEUA) of State University of Pará (UEPA). 13 male Wistar rats (Rattus norvegicus) were used, weighing between 250-300g and 110-130 days old. They were randomly distributed in three study groups: Sham group (ShG); Control group (CG) and Copaiba group (CpG). All of them underwent a median abdominal incision, with an 1cm cistotomy, followed by one plan suture with three separated stitches of poliglecaprone 25 4-0. On the CG animals, was injected 1ml/kg of saline solution directly on the suture line and on the CpG, the copaiba oil was injected in place of the saline solution, in single dose 0,63ml/kg. Euthanasia was made by anesthetic overdose on the 7th day after surgery. **Results**: The microscopic evaluation revealed a trend to more severe acute inflammation process on the CpG. In this same group, a more significant giant cells reaction (p=0.0236) could be seen, as far as the evidence of vascular neoformation (p=0.0236) on the 7th day. **Conclusion:** The use of copaiba oil in CpG showed no difference in healing process when compared to the CG and demonstrated greater inflammatory reaction including giant cells reaction and neovascularization. CEUA protocol's: 25/2015. **References:** APPEL, S. Can Vet J.**,** v.53, p.303, 2012. BOCHNER, R. Rev Bras Plantas Med**,** v.14, p.537, 2012. CARMONA, G.B. et al. Acta Cir Bras, v.28, p.430, 2013. DE OLIVEIRA NOGUEIRA, E. Braz J Vet Res An Sci, v.49, n.4, p.293, 2012 PIERI, F.A. Arq. Bras. Med. Vet. Zootec., v.64, n.1, 2012. LUCENA, P. L. H. et al. Acta Cir. Bras., v. 21, p. 46, 2006. YAMAGUCHI, M.H. Rev Sau e Pesq, v.5, p.137, 2012.

09.043 Pharmacological Screening of *Zornia Brasiliensis* Vogel. (Leguminosae) on different smooth muscle models. Oliveira FRMB[1], Figueiredo IAD[1], Silva ARLFC[1], Ferreira SRD[1], Silva ADS[2], Tavares JF[1], Cavalcante FA[1 1]UFPB, [2]UFAL

Introduction: *Zornia genus* (Leguminosae) contains about 80 species distributed in tropical and subtropical regions of the world (Mohlenbrock, Webbia, v. 16, p. 1, 1961). Zornia brasiliensis Vogel. is a herbaceous species, popularly known as "urinária", "urinana" or "carrapicho", and it is used in the traditional medicine for the treatment of gastrointestinal disorders (Diniz, I Congresso Brasileiro de Extensão Universitária/ João Pessoa - PB, 2002). According to Oliveira, the ethanol extract of the aerial parts from Zornia brasiliensis (ZB-EtOH$_{AP}$) has antidiarrheal effect due to inhibition of intestinal motility in mice (IX Congresso Brasileiro de Farmacognosia, Goiânia – GO, 2013), and spasmolytic activity on guinea pig ileum by voltage-gated calcium channel blockade (IX Reunião Regional da FeSBE, João Pessoa-PB, 2014). In addition, other species of Zornia has also shown spasmolytic activity on other smooth muscle models, like Z. venous (Rojas, Phytomedicine, v. 2, p. 51, 1995) and Z. diphylla (Rojas, Phytomedicine, v. 6, p. 367, 1999) that have spasmolytic activity on rat ileum. Thus, based on the chemotaxonomic criteria and on the fact that *Zornia brasiliensis* already showed spasmolytic activity on guinea pig ileum, the aim of this study was to investigate the spasmolytic effect of ZB-EtOH$_{AP}$ on guinea pig trachea, rat uterus and aorta. **Methods**: Guinea pigs (*Cavia porcellus*, 300-500 g) of both sexes and Wistar rats (Rattus norvegicus, 150-250 g) were used. Tissues were removed and suspended in organ baths, under appropriate conditions for each experimental protocol. Isotonic and isometric contractions were monitored and recorded. All results were expressed as the percentage of the mean ± standard error of the mean and analyzed using Student's t test or one-way variance analysis followed by Bonferroni's posttest, as appropriate. The difference between the means were significant when $p < 0.05$. All data was analyzed using GraphPad Prism® software version 5.01. IC_{50} and EC_{50} values were calculated by nonlinear regression analysis. **Results**: ZB-EtOH$_{AP}$ relaxed carbachol-precontracted guinea pig tracheal rings containing epithelium (1-729 µg/mL, n = 5), presenting EC_{50} = 30.4 ± 6.1 µg/mL and E_{max} = 130.3 ± 8.9%. On rat uterus, ZB-EtOH$_{AP}$ (9 - 243 µg/mL, n = 5) showed concentration-dependent inhibitory effect against phasic contractions induced by both carbachol 10^{-5} M (IC_{50} = 53.1 ± 13.1 µg/mL) and oxytocin 10^{-2} UI/mL (IC_{50} = 67.8 ± 5.0 µg/mL) in equipotent manner, with values of E_{max} = 100%. In addition, ZB-EtOH$_{AP}$ also relaxed phenylephrine-precontracted rat aortic rings in presence of endothelium (0.1-729 µg/mL, n = 5), showing EC_{50} = 18.7 ± 3.9 µg/mL and E_{max} = 96,1 ± 2,4%. **Conclusions**: This study was carried out to assess the spasmolytic effect of the ZB-EtOH$_{AP}$ on guinea pig trachea, rat uterus and aorta. ZB-EtOH$_{AP}$ showed non-selective activity on the different tissues and for the different agonists tested, presenting higher potency on rat aorta. In addition, on rat uterus, ZB-EtOH$_{AP}$ seems to act in a common pathway step for both CCh and oxytocin. **Financial support**: CAPES, CNPq, PPgPNSB/CCS/UFPB. Research approval by Ethical Committee on Animal Use of UFPB: protocol 069/15.

09.044 Leishmanicidal evaluation of extracts and isolated compounds from propolis collected in the São Francisco River Valley Region, PE and their effects on the inhibition of topoisomerases (LCTOPIB And HTOPIB). Silva LB[1], Cavalcante GM[2], Silva JKS[1], Dias GS[1], Silva ES[3], Yamamoto SM[3], Camara CA[2], Silva TMS[2], Moreira MSA[1] [1]UFAL- Ciências Biológicas e da Saúde, [2]UFRPE, [3]UNIVASF

Introduction: Leishmaniasis is a neglected anthropozoonosis present in 98 countries, including Brazil, which is responsible for causing various clinical manifestations. The control, prevention, and treatment has been limited, so new pharmacological studies have been proposed aiming at the development of a new drug candidate for leishmaniasis. This study aimed to evaluate the leishmanicidal activity and the effects of extracts and isolated compounds on the human (hTopIB) and *Leishmania chagasi* (LcTopIB) topoisomerases. **Methods:** The substances and extracts used in this study were derived from propolis, namely: the extract (EEtOH) the fractions (FrHex), (FrAcEOt), (FrMeOH), and the major flavonoids naringenin and isorhamnetin (0.1 to 100 µM). The viability assay on J774.A1 macrophages and promastigote forms of *L.chagasi* was performed using the MTT assay. It was also observed the effect of substances on the *L.chagasi* amastigote intracellular form, in which it was, assessed the parasitic load in infected macrophages. The flavonoids naringenin and isorhamnetin were subjected to the assay of inhibition of *Leishmania chagasi* (LcTopIB) and human (hTopIB) topoisomerases at concentrations of 100-3.12 µM. **Results and Conclusion:** In the viability assay on the host cell, it was observed that the tested substances showed no toxicity to J774.A1 macrophages. EEtOH and FrAcEOt caused inhibition of *L.chagasi* promastigote growth, with $IC_{50\ of}$ 4.2 ± 0.9 and 6.6 ± 0.3 µM, respectively. The flavonoids naringin and isorhamnetin exhibited IC_{50} of 5.1 ± 1.7 and 2.4 ± 0.9 µM, respectively, against *L.chagasi* amastigotes. In the topoisomerase inhibition assay, naringenin (25 µM) and isorhamnetin (100 µM) were able to inhibit the *L.chagasi* (LcTopIB) topoisomerase with IC_{50} of 4.6 ± 1.0, these compounds were, however, not able to inhibit the human topoisomerase (hTopIB). The results revealed that the compounds derived from propolis may be used in subsequent studies of leishmanicidal activity since they showed significant effects on the growth of promastigote and amastigote forms of *L. chagasi* and did not cause toxic effects on macrophages. Moreover, naringenin and isorhamnetin inhibited the LdTopIB activity and did not inhibit the hTopIB activity. The results indicate that these compounds are active on *L. chagasi* and suggest the conduction of in vivo tests. **Financial support:** INCT-INOFAR, CNPq, LAFI (UFAL), LaBioFito (UFPRE), FAPEAL, CAPES.

09.045 Spasmolytic Effect of essential oils from *Mesosphaerum suaveolens* **(L.) Kuntze and** *Medusantha martiussi* **(Benth) on guinea-pig ileum and rat aorta** Barros BC[1], Souza ILL[2], Ferreira PB[2], Costa VCO[3], Silva MS[2,4], Silva BA[2,4] [1]UFPB – PIBIC, [2]UFPB – PPgPNSB, [3]UFPB – IPeFarM, [4]UFPB – DCF

Introduction: The plants play a key role in pharmacological research and health protection (Newman, J. Nat. Prod., v. 75, p. 311, 2012), highlighting the genus Hyptis (Lamiaceae), used in folk medicine as spasmolytic agents (Basílio, Acta Farm. Bonaer., v. 25, p. 518, 2006). In addition, there are some pharmacological activities attributed to species of Hyptis as hypotensive (Santos, Fitoterapia, v. 78, p. 186, 2007), antiulcer (CALDAS, J. Ethnopharmacol., v. 137, p. 886, 2011) and spasmolytic (Souza, J. Med. Plants Res., v. 7, p. 2436, 2013; Costa, Phytochem. Lett., v. 8, p. 32, 2014). Therefore, we animed to investigate a possible spasmolytic activity of essential oils obtained from Mesosphaerum suaveolens (MS-EO) and Medusantha martiussi (MM-EO) on guinea pig ileum and rat aorta. **Methods**: Guinea pig (Cavia porcellus) of both sexes (300-500 g) and male Wistar rats (Rattus norvegicus) (250-300 g) were used. The guinea pig ileum and rat aorta were removed, cleaned and suspended in organ baths under appropriate conditions. Both isotonic and isometric contractions were monitored by force transducer. **Results** were expressed as mean and standard error of mean and analyzed by Student's t-test or one way ANOVA followed by Bonferroni's post-test, as appropriated. **Results**: On guinea pig ileum, MS-EO (3-729 µg/mL, n = 5) and MM-EO (9-729 µg/mL, n = 5) antagonized in a equipotent and concentration-dependent manner the phasic induced by both 10^{-6} M histamine (IC_{50} = 49.7 ± 2.3 and 56.6 ± 4.4 µg/mL, respectively) and 10^{-6} M carbachol (CCh) (IC_{50} = 67.1 ± 4.2 and 70.6 ± 8.6 µg/mL, respectively), suggesting an action in a common step of the signaling pathway of these contractile agents, which could be the voltage-gated calcium channels (Ca_V) blockade. On rat aorta, MS-EO (1-729 µg/mL, n = 5) and MM-EO (1-729 µg/mL, n = 5) relaxed in a equipotent and concentration-dependent manner the rat aortic rings pre-contracted by 3 x 10^{-7} M in both presence (EC_{50} = 239.3 ± 67.9 and 132.8 ± 46.9 µg/mL, respectively) and absence (EC_{50} = 130.2 ± 25.8 and 126.3 ± 34.1 µg/mL, respectively) of functional endothelium. However, MM-EO presents lower efficacy than MS-EO in both presence (E_{max} = 59.4 ± 11.1 and 93.9 ± 9.2%, respectively) and absence (E_{max} = 43.9 ± 4.1 and 101.9 ± 3.2%, respectively) of functional endothelium. Analyzing the vasorelaxation promoted by both essential oils in the presence/absence of epithelium it suggests that these relaxations seem not to be related to endothelium-derived relaxing factors (EDRF). **Conclusion:** Therefore, we concluded that both essential oils present spasmolytic activity on guinea pig ileum and rat aorta, and the vasorelaxant effect seems not to involve EDRF. Moreover, these data contribute to the pharmacological study of Lamiaceae family and hyptis genus. **Financial support**: CNPq, CAPES, PPgPNSB/UFPB. Research approval: Ethical Committee on Animal Use of UFPB (048/2015).

09.046 Macroscopic and histological evaluation of vital and reproductive organs of rats after subacute exposure to the aqueous extract of *Alibertia edulis* **leaves.** Menegati SELT[1], Traesel GK[1], Lima FF[1], Castro LHA[1], Souza RIC[1], Santos AC[1], Oesterreich SA[1], Vieira MC[1]
[1]UFGD

Introduction: Alibertia edulis, popularly known as “marmelo do Cerrado”, is a native plant from the Brazilian Cerrado. It has ornamental potential and its fruits are a food source for the locals. Its anti-hypertensive, hypoglycemic, diuretic and anti-tumor potential is currently being studied as the tea leaves is popularly used for these purposes. The aim of the study was to evaluate the toxicological profile of the aqueous extract from the leaves of A. edulis in rats. **Methods:** The experiments were performed in accordance with the OECD protocol (guideline 407) and were approved by the Ethics Committee in Animal Experimentation from the UFGD (protocol: 29/2015). Four different doses (125, 250, 500 and 1000 mg/kg) of the aqueous extract of A. edulis leaves (AEAE) were administered by gavage to male and female rats for 28 consecutive days. A satellite group received the maximum dose (1000 mg/kg) for 28 days and remained untreated for 14 more days in order to observe reversibility, persistence, or delayed occurrence of toxic effects. A sixth group was used as control to which saline (1 ml/kg) was also daily administered. At the end of the experiment, the vital organs (heart, lung, kidney, liver and spleen) and reproductive organs (testes, epididymis, uterus and ovary) were isolated, weighed, dissected and then inspected for any macroscopic and histopathological changes. A histological assessment was also done to brain of one animal from all groups in order to investigate the presence of histological lesions due to central nervous system toxicity. **Results:** There was a significant difference in the weight of kidneys from the female rats treated with doses of 125 and 500 mg/kg of the AEAE when compared to the control. However, no macroscopic and histological alterations evidencing the presence of toxicity were found. Moreover, the change of the weight of kidneys did not occur in groups that received the highest dose, which confirms that this sign was not dose dependent. There was also a significant difference in the relative weight of the ovaries of rats treated with 125 and 1000 mg/kg of the AEAE when compared to the control. Nevertheless, since the control of the estrous cycle was not performed, weight variation of the reproductive organs was expected. Macroscopic analysis in all doses of the AEAE showed no changes in vital and reproductive organs of the treated animals. Likewise, the histological assessment showed no signs suggestive of toxic effects. These toxic signs would be characterized by congestion, leukocyte infiltration, extravasation of blood, degeneration, necrosis, apoptosis and fibrosis in the organ tissues analyzed histologically. **Conclusion:** These results provide valuable data on the toxic profile of A. edulis on macroscopic and histological parameters. Therefore, further assessments are required in order to proceed to clinical studies of this plant. Acknowledgments: FUNDECT, CNPq and CAPES.

09.047 Study of the gastroprotective activity of menthofuran in rodents. Alves NM[1], Martins MCC[2], Nunes PHM[2], Brito AKS[1], Sousa SS[1], Freitas MCL[2], Medina HC[2], Garcez AM[2], Pacheco JFR[2], Santos RS[1], Fernandes HB[2], Oliveira IS[1], Nunes ASS[1] [1]UFPI – Bioquímica e Farmacologia, [2]UFPI – Biofísica e Fisiologia

Introduction: Several monoterpenes have popular indication for the treatment of gastrointestinal disorders, worms and respiratory problems, in addition to having analgesic, anti-inflammatory, antifungal, antiseptic and antispasmodic activities. Studies which evaluate the gastroprotective activity of monoterpene menthofuran. In preliminary experiments conducted by our group the menthofuran showed antiulcerogenic effect on gastric ulcers induced by ethanol. **Objective:** To evaluate the effect of menthofuran (MF) on acid secretion and mucus content of the, non-protein sulfhydryl groups (GSHNP) and catalase activity of the gastric wall in rats underwent ligation of pylorus. **Methods:** The protocols were performed after approval by the Ethics Committee on Animal Experimentation (CEEA/UFPI), under the protocol number 086/15. 086/15. Male wistar rats (*Rattus norvegicus*) (n = 7 animals / group) weighing between 180-250g in solid fasting for 24 h, they were anesthetized with intramuscular administration of ketamine 50 mg / kg and xylazine 5mg / kg association. After the anesthesia a longitudinal incision of about 2 cm was induced in the abdominal wall to the stomach location, ligation of the pyloric sphincter and intra duodenal injection vehicle, (Tween 80 1%, 0.5 mL/100 g), menthofuran 50 mg/kg (MF-50) or 100 mg/kg (MF-100) or carbenoxolone 250 mg/kg (Carb-250). After 4 hours the animals were sacrificed, the stomaches were removed and the gastric contents were collected for the determination of volume, pH (potentiometric) and total acidity (titration with 0.05 N NaOH). From each animal were removed stomach body fragments joined to spectrophotometric determination of mucus content (MA, µg/g), concentration of GSHNP and catalase activity. The data (mean ± E.P.M) were analyzed by analysis of variance (ANOVA) followed by Tukey test. **Results:** Compared to vehicle (3.26 ± 0.16), MF-50, significantly increased the pH (5.62 ± 0.47), while MF-50 (3.42 ± 0.11) and Carb 250 (4.30 ± 0.51) did not produce significant changes statistically. As the total acidity of gastric juice, MF-50 (6.98 ± 1.6) as well as Carb 250 (14.5 ± 1.5) significantly reduced the acidity. However, MF-100 did not cause any change in the total acidity (17.68 ± 1.20) when compared to vehicle (22.64 ± 0. 16). There was a significant decrease in the mucus content in groups MF-50 (397. 10 ± 8.97) and MF-100 (338.20 ± 24.37), while in the group Carb-250 there was a significant increase in this parameter (702.5 ± 59.84) when compared to the vehicle group (573.10 ± 33.51). There was no difference in catalase activity between the groups treated with MF-50 (2.40 ± 0.16) and MF-100 (3.32 ± 0.09). There was also no change in the activity of this enzyme in the group Carb-250 (3.05 ± 0.15) in relation to the vehicle (2.87 ± 0.28). **Conclusion:** The results show that the gastroprotective effect of menthofuran activity associated with antissecretória, but monoterpene not increased mucus content of the gastric wall and did not alter the activity of catalase and levels of GSHNP. Keywords: Essential oil; Monoterpene; Gastric secretion.

09.048 Anti-pruritic and anti-inflammatory effects of the salivary gland extract of the mosquito *Aedes aegypti* **in mice dorsal skin.** Cerqueira ARA[1], Rodrigues L[1], Teixeira SA[1], Muscará MN[1], Sá-Nunes A[2], Costa SKP[1] [1]ICB-USP – Farmacologia, [2]ICB-USP – Imunologia

Introduction: Itch is known as an irritating sensation that triggers a desire to scratch can be often an intractable condition. Anti-histamine drugs and mast cells inhibitors are the most common drugs used to treat acute itch; however, they are ineffective against chronic itch or non-histaminergic pathway, such as proteases activated receptors type -2, -4 (PAR-2; -4) and mas-related G protein-coupled receptor (Mrgpcr) families [1]. By comparison, the saliva of hematophagous insects, such as the *Aedes aegypti* female mosquitoes, most known as Zika or yellow fever mosquito, contains a variety of pharmacologically active substances, including anti-hemostatic enzymes, peptides and proteins with anti-inflammatory or immunomodulatory activity [2]. Whether active components in the salivary gland extract (SGE) of *Aedes aegypti* may counteract the normal itch reaction to injury produced by histaminergic or non-histaminergic pathway in vertebrate hosts is unknown. **Methods:** SGE preparation: salivary glands from adult female *A. aegypti* mosquitoes were dissected and the protein concentration was measured and stored at -80°C. Itch behaviour or skin oedema assay was performed in the shaved dorsal skin of male adult BALB/C mice (23-25g) anaesthetised with isoflurane. The mast cell degranulator compound 48/80 (10µg/site), PAR-2 receptor agonist SLIGRL (40nmol/site) or Mrgpcr receptor agonist chloroquine (100µg/site) was intradermally injected (i.d.) alone or simultaneously with increased doses of SGE (0.3 – 10 µg/site), and scratching behaviour was recorded during 30 min and expressed as bouts of scratching. Skin plasma protein extravasation and neutrophil accumulation (measured as mileloperoxidase acitivity - MPO) was assessed in distinct groups of mice by the extravascular accumulation of i.v. injected ^{125}I (100 µl, 0,037 MBq/µg) and increased MPO activity in the skin, respectively, in response to C48/80 alone and co-injected with SGE (0.3 - 10 µg/site) [3]. Data are presented as mean ± SEM. Stats are performed by ANOVA plus Dunnett test. $P<0.05$ was taken as significant. **Results**: Either C48/80, SLIGRL or chloroquine markedly increased itching frequency in the mouse dorsal skin. C48/80 also led to a potent plasma extravasation and increased MPO activity compared to Tyrode. SGE (0.3 - 3 µg) significantly, but not dose-dependently, reduced C48/80-induced scratching bouts by 71, 63 and 38%, respectively. SLIGRL or chloroquine-induced itch was inhibited by 45% and 60% (n=5-6; $P<0.001$) via co-injection with SGE, respectively. C48/80-induced plasma extravasation was significantly reduced by 10□g of SGE, but the increased MPO activity was not. **Conclusion:** We show the first evidence that SGE from *A. aegypti* contains bioactive components capable to inhibit histaminergic/non-histaminergic pruriceptive pathways in addition to exert a protective effect against mast cell-mediated inflammation. The SGE anti-pruritic responses might also illustrate some of ways this particular mosquitoes has adapted to the challenges of vertebrate bites. **Acknowledgments**: CAPES, CNPq, FAPESP. Ethic: CEUA/ICB n° 100, book 3, page 9 1. Nat. Neurosci. 17; 175 (2014). 2. Int. Immunopharmacol. 26; 13 (2015). 3. Vascul. Pharmacol. 45; 209 (2006).

09.049 Effect of *Euterpe oleracea* Mart extract (açaí) on aerobic exercise training rats. Soares RA, Bem GF, Costa CA, Santos IB, Carvalho LCRM, Okinga A, Oliveira BC, Mello JSMF, Cordeiro VSC, Rocha APM, Ognibene DT, Moura RS, Resende AC UERJ

Introduction: The chronic exercise training results in adaptation of skeletal muscle to the increased metabolic demand. Adjustments in vascular control mechanisms play an important role in increasing blood flow to the muscle during and after exercise. On the other hand, the increase in reactive oxygen species may occur as a result of increased oxygen uptake. Previous studies from our group demonstrated that the hydroalcoholic extract from the seeds of açaí (ASE) has antioxidant and vasodilator properties. Thus, the aim of this study was to evaluate if treatment with ASE, rich in polyphenols improves chronic exercise training. **Methods:** Wistar rats were divided in four groups: Sedentary (standard diet and water for 4 weeks), Sedentary+ASE (standard diet + ASE 200 mg/kg by intragastric gavage for 4 weeks), Training (standard diet and water, subjected to exercise training for 4 weeks) and Training+ASE (standard diet + ASE 200 mg/kg subjected to exercise training for 4 weeks). The test consisted of an exercise protocol on a treadmill, with initial speed of 3 m / min, increased to 4m / min every three minutes until exhaustion of the animal, at which no longer maintains the racing standard. The animals trained for 4 weeks, 5 times per week with duration of 30 minutes per session. The training intensity was 60% of the maximum speed reached during maximal incremental test. Blood glucose and lactate were measured in plasma by glucose and lactate meter (Accutrend Plus - Roche). The vasodilator effect of acetylcholine (ACh, 1-1000 pmol) was studied in perfused mesenteric arterial bed (MAB) pre-contracted with norepinephrine (NE, 30 mM). The vascular reactivity to NE (1-1000 nmol) was also evaluated. **Results:** The distance (m) and exercise time (min) were significantly increased in the Training+ASE (27.8 ± 2.4 and 367.5 ± 23.5, respectively; $P<0.05$) in relation to the Training group (18.4 ± 1.2 and 272.9 ± 17.9, respectively). The increased lactate levels (mmol/L) in training animals (3.2 ± 0.2) were reduced by treatment with ASE (2.3 ± 0.2; $P<0.05$). The glucose (mg/DL) levels were not different between groups. The endothelium-dependent vasodilator effect of ACh was not different between Training and Training+ASE groups, but was greater in Traning *vs* Sedentary in a small dose (1pmol: 24 ± 2.7 *vs* 12 ± 1.1; respectively $P<0.05$), as well as, in Training + ASE *vs* Sedentary + ASE (1pmol: 27 ± 1.8 *vs* 18 ± 1.9 and 10pmol: 55 ± 1.7 *vs* 42 ± 4.3; respectively, $P<0.05$). The vascular reactivity to small doses of NE was reduced in Training *vs* Sedentay (1 nmol: 15 ± 1.7 *vs* 23 ± 2.8 and 10nmol: 48 ± 5 *vs* 67 ± 5; respectively, $P<0.05$) and in Training+ASE vs Sedentary (1nmol: 9 ± 1.4 *vs* 23 ± 2.8 and 10nmol: 41 ± 5 *vs* 67 ± 5; respectively, $P<0.05$). **Discussion:** ASE increased the distance and exercise time in rats subjected to exercise training, suggesting an important beneficial effect of the extract on the performance of this animals. The reduction of vascular resistance may probably promote better oxygenation of the muscle, reducing the production of lactate and muscle fatigue. **Financial Support:** CNPq and FAPERJ. **Ethics Committee:** The experiments were approved by the Ethics Committee of Animal Experiments of the UERJ (protocol: CEUA/058/2012).

09.050 Spasmolytic action mechanisms of the total glycoalkaloids fraction from *Solanum Crinitum* Lam. (Solanaceae) fruits on guinea pig ileum. Ferreira SRD[1], Souza ILL[1], Moreno GTA[2], Oliveira FRMB[2], Figueiredo IAD[2], Silva TMS[3], Cavalcante FA[4] [1]UFPB – PPgPNSB, [2]UFPB – PIBIC/CNPq, [3]UFRPE – DCM, [4]UFPB – DFP/PPgPNSB

Introduction: Solanum crinitum Lam. (Solanaceae), popularly known as "jurubeba", "fruto-de-lobo", “jurubeba-grande” or “lobeira” (Moura, Sci. For., v. 37, p. 143, 2009), is used to treat diabetes (Araújo, Rev. Bras. Farmacogn., v. 20, p. 666, 2010), liver (Simões, Farmacognosia: da planta ao medicamento. 6. ed. Porto Alegre, p. 1102, 2010) and veneral diseases (Fagg, J Etnofarmacol, v. 161, p. 18, 2015) and showed antifungal (Souza, Congresso Nacional de Botânica, Belo Horizonte-MG, 2013), antibacterial (Essien, Pharm. Bio., v. 4, p. 474, 2012), antitumor (Cornelius, J. Braz. Chem. Soc., v. 21, p. 2211, 2010), antioxidant activities (Azevedo, Simpósio de Plantas Medicinais, Manaus–AM, 2004), among others. In previous studies the total glycoalkaloids fraction from S. crinitum (TGF-SC) showed antidiarrheal effect in mice by changed intestinal motility and spasmolytic activity on guinea pig ileum, showed high inhibitory potency in both phasic and tonic histamine-induced contractions, suggesting that TGF-SC may be acting in histaminergic receptor level (Ferreira, SBFTE, Fortaleza-CE, 2014). Thus, the aim of this study was to investigate spasmolytic action mechanism of TGF-SC on guinea pig ileum. **Methods**: guinea pig (343.8 ± 10.6 g) both sex were used. After euthanized, the gut was removed and the ileum was suspended in organ baths under appropriate conditions, and isotonic and isometric contractions were recorded. All results were expressed as the percentage of the mean ± standard error of the mean (S.E.M.) and analyzed using Student’s t test or one-way variance analysis (ANOVA) followed by Bonferroni’s posttest as appropriate and analyzed using GraphPad Prism® software version 5.01. **Results**: in the presence of the fraction (9, 27 and 81 µg/mL), the cumulative contractions induced by histamine (n = 5) were inhibited with reduction of the E_{max} of 100% (control) to 89.1 ± 4.4; 47.3 ± 2.8 and 0%, respectively, indicating that the TGF-SC probably acts on histaminergic receptors in non-competitive manner on guinea pig ileum. In the presence of CsCl (5 mM), non-selective blocker of K^+ channels (n = 5), the TGF-SC relaxing potency did not change (EC_{50} = 23.6 ± 3.5 µg/mL), and the involvement of these channels was discarded. To verify the effect of the fraction on the Ca^{2+} release of intracellular stores (n = 3) experiments using circular layer of the ileum were performed and it was observed that the fraction antagonized phasic contractions induced by histamine 10^{-5} M (IC_{50} = 9.0 ± 1.7 µg/mL), and negatively modulate the release of Ca^{2+} to exert their spasmolytic effect. **Conclusion:** TGF-SC spasmolytic activity involves non-competitive antagonism type pseudo-irreversible of histamine receptors and negative modulation calcium release of intracellular stores. **Financial support**: CNPq, PPgPNSB/CCS/UFPB. All the experimental protocols were approved by Ethical Committee in Animal Use UFPB (Protocol 107/2015).

09.051 Copaiba oil effects associated with microneedling in the skin of rats. Carneiro FRO, Botelho NM, Palheta CSA, Alho BCN, Garcia da Silva PR, Pereira da Silva WM, Silva AMF, Souza RMT, Dias DV, Martins Neto ES, Banna de Oliveira MH, Bengtson KL, Dórea MA, Couteiro RP

Introduction: The microneedling is a technique used in the production of collagen and as drug delivery. The copaiba oil has healing effects and anti-inflammatory drugs that have been demonstrated in various animal models. So, this study aims to evaluate the effect of copaiba oil associated with microneedling in the skin of rats. **Methods**: 30 rats were used and divided into 6 groups of 5 animals each: microneedling group 14 days (MAG14) and 30 days (MAG30) microneedling group and mineral oil 14 days (MAOM14) and 30 days (MAOM30) with oil application, and microneedling group and copaiba oil 14 days (MAOC14) and 30 days (MAOC30) with application of copaiba oil. The histopathological parameters were collagen, fibroblasts and vessels and were classified as absent (0), mild (1), moderate (2) or heavy (3). **Results**: There was a statistically significant difference between the groups MAGxMAOMxMAOC compared to collagen with 14 ($p = 0.0091$) and 30 days ($p = 0.0357$) and fibroblasts 30 days ($p = 0.0357$). The MOC30 days group showed a greater production of collagen and fibroblasts. **Conclusion:** The copaiba oil associated with microneedleling was able to stimulate the production of collagen and fibroblasts in the skin of rats. **Financial support** acknowledgments: no one. The Ethical Committee on Use of Animals approved the research, protocol 18/2015. **References:** DODDABALLAPUR, S. J. Cutan Aesthetic Surgery. v. 2, p. 110-1, 2009. LIMA, E. V. A. Surg Cosmet Dermatol. v. 5, p. 110-4, 2013.KALIL, C. L. P. Surg Cosmet Dermatol. v. 79, p. 144-8, 2015. BUDAMAKINTLA, L. J Cutan Aesthet Surg. v. 6, p. 139-43, 2013. SAHNI, K. J Cutan Aesthet Surg. v. 6, p. 123-34, 2013. MAJID, I. J Cutan Aesthet Surg. v. 2, p. 26-30, 2009. LIEBL, H. J Am Col Clin Wound Spec. v. 3, p. 2-6, 2013. EL-DOMYATI, M. J Clin Aest Derm. v. 8, p. 36, 2015. BRITO, M. B. Act Cir Bras. v. 15, p. 1-7, 2009. MONTES, L. V. Natureza on line. v. 7, p. 61-7, 2009. FRANCISCO, S. G. Femina. v. 33, p. 89-93, 2015. GARCIA, R. F. Saúde e Pesquisa. v. 5, p. 10-13, 2012. YASOJIMA, E. Y. Ar Bras Cirur Dig. v. 28, p. 186-189, 2015. VIEIRA, R. C. Pesq. Vet. Bras. v. 28, p. 358-66, 2008. ZEITTER, S. Burns. v. 40, p. 966-73, 2014. LEE, H. J. Ann. Dermatol. v. 26, p. 584-91, 2014. LIEBL, H. J. Am. Col. Clin. Wound. Spec. v. 4, p. 2-6, 2014. ESTEVÃO, L. R. M. Act. Cir. Bras. v. 28, p. 863-69, 2013. VIEIRA, R. C. Pesp Vet. Bras. v. 28, p. 358-66, 2008.

09.052 Effect of copaiba oil (*Copaifera officinalis*) **at bone integration of flocculated resin-castor oil** (*Ricinus communis*) **on rats jaw.** Peres ACR[1], Brito MVH[1], Pontes FSC[1], Oliveira LCM[1], Ramos SR[2], Yamanaka CM[1], Rodrigues FMS[1], Afonso NR[2], Bengtson KL[2], Oliveira MHB[2] [1]UEPA, [2]CESUPA

Introduction: Defects with bone mass loss are generally treated with bone autografts. Even with the techniques already established, the grafts have some disadvantages, like morbidity of donor area, chronic pain and vascular lesions during de surgery. The use of medicinal plants for therapeutic purposes is common in Amazonia, and copaiba is the biggest choice because have the anti-inflammatory, healing and others effects. In this way, the objective of the study was evaluating the effects of copaiba oil (*Copaifera officinalis*) at bone integration of flocculated resin-castor oil (*Ricinus communis*) on rats jaw. **Methods**: This study was approved by the Ethics Committee of Animals Use (CEUA) of State University of Pará (UEPA). 50 male rats (Rattus norvegicus, Wistar) were submitted to the procedure in order to create the jaw defect. They were randomly distributed in five groups: control group (GC), flocculated resin-castor oil group (GM), flocculated resin-castor oil with topic copaiba oil group (GMCLoc), flocculated resin-castor oil with oral copaiba oil group (GMCOr) and flocculated resin-castor oil with oral Meloxicam group (GMM). Radiographs of the jaw defect area were taken from each animal to analyze the bone formation. The euthanasia was performed after 30 days after the procedure and the jaw of each animal was removed for histological analysis. The bone formation was analyzed by the radiograph and histological aspects. **Results**: The osteoclast activity was observed in two groups: GMCLoc ($p = 0,04$) and GMM ($p = 0,04$). Osteoblasts were present in GMCLoc ($p = 0,04$) and GMCOr ($p = 0,009$). Inflammatory cells were more evident in groups: GC ($p = 0,04$), GMCLoc ($p = 0,04$) and GMM ($p = 0,03$). The bone formation was observed, related to the density, in groups GC ($p = 0,04$) and GMCLoc ($p = 0,03$). With the contrast, it was observed in GMCLoc ($p = 0,03$) and GMM ($p = 0,04$). **Conclusion:** The groups GMCLoc and GMCOr showed, statistically significant, better bone integration than the other groups. GC and GMCLoc presented with better radiographic density and GMCLoc and GMCOr showed better contrast. Key-Words: Bone integration, Copaiba oil, Castor oil. REFERENCES: Pinheiro TC, Rev. bras. ortop. vol.43 no.10, 2008. Veiga Junior, V.F, O gênero copaifera L. Química nova, v.25, n.2, p.273-286, 2002. CEUA Protocol number: 40/2014

09.053 Profile of phenolic antioxidants from *Moringa oleifera* **Leaves** Merlin N[1], Karling M[1], Morales RGF[2], Oldoni TLC[1] [1]Universidade Tecnológica Federal do Paraná – UTFPR, [2]Empresa de Pesquisa Agropecuária e Extensão Rural de Santa Catarina (Epagri), Estação Experimental de Itajaí

Introduction: *Moringa oleifera* leaves have a wide variety of phenolic compounds, especially flavonoids [1, 2]. Since there are few investigations on the antioxidant activity (AA) of *M. oleifera* grown in Brazil, the aim of the present study was to evaluate the profile of phenolic compounds from leaves extracts of this species, collected in Itajaí – Santa Catarina, by HPLC-DAD, and its AA, by an *in vitro* assay. **Methods:** Plant identification was performed and a voucher specimen (HPB 483) was deposited at the Herbarium of UTFPR, campus Pato Branco. *M. oleifera* leaves were dried in an oven at 40-45 °C and were ground. Successive extraction was carried out at room temperature, under shaking. Solvents were added in the following order: hexane (E-Hex), dichloromethane (E-CH_2Cl_2), ethyl acetate (E-EtOAc), acetone (E-Ace), ethanol (E-EtOH) and 50% ethanol (E-Hydro). Each solvent was replaced four times. Extracts were evaporated in a rotary evaporator and E-Hydro was also lyophilized. AA was determined, in triplicate, by the ABTS free radical scavenging method [3]. The determination of phenolic profile was performed on a Varian 920 liquid chromatograph, using a C18 Agilent column (250 x 4,6 mm, 5 µm), wich was maintained at 30 °C, and a diode array detector. 10 µL of extracts, prepared in a concentration of 15 g L^{-1}, were injected. The mobile phase was a mixture of water:acetic acid (98:2, v/v) (solvent A) and acetonitrile:water:acetic acid (40:58:2, v/v) (solvent B), with a flow rate of 1 mL min^{-1}, in a gradient mode. Identification was made by comparison of the absorption spectrum in the ultraviolet region and of the retention time with standards of phenolic acids: gallic, vanillic, caffeic, coumaric, ferulic and salicylic; flavonoids: catechin, epicatechin, rutin, myricetin and quercetin; and the stilbene *trans*-resveratrol. **Results:** Five of the phenolic standards were identified in at least one of the extracts: two monophenols, gallic and caffeic acids; and three flavonoids, epicatechin, rutin and quercetin. The lowest AA were observed for E-Hex and E-CH_2Cl_2 (149,04 ± 15,03 and 191,34 ± 5,33 µmol Trolox/g extract, respectively), results that should be related to the chromatographic profiles shown by both extracts, with few low intensity signals. On the other side, E-Hydro showed the best AA (789,54 ± 45,74 µmol Trolox/g extract) and, also, a profile with high intensity signals. Moreover, the diversity of chromatographic signals observed for E-EtOAc, E-Ace, E-EtOH and E-Hydro suggests that *M. oleifera* leaves have various bioactive compounds. **Conclusion:** Extracts showed distinct chemical profiles, proving the extraction capacity of solvents with different polarities. Together, the AA and the chromatographic profiles of E-EtOAc, E-Ace, E-EtOH and E-Hydro suggest the potential of *M. oleifera* leaves, grown in Itajaí, as a source of bioactive molecules. **References:**

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Acknowledgments: The authors acknowledge grants and fellowships from Capes and Fundação Araucária, Central de Análises and PPGTP (UTFPR - Pato Branco).

09.054 Phytochemical and toxicological effects of *Euphorbia tirucalli* Linneau latex. Uchôa MBR[1], Figueiredo CSSS[1], Fernandes ES[1], Silva LCN[1], Grisotto MAG[1] [1]Ceuma

Introduction: *Euphorbia tirucalli* L. belongs to the Euphorbiaceae family, found mainly in Africa and America, which comprises more than 7500 species, is one of the most important in Brazilian flora, due to the presence of a variety of metabolites with potential for tumor treatment (VALADARES 2006). Considering the empiric use of this species by the Brazilian population for treatment of cancer, parasite diseases and even AIDS, there is scarce information about its toxicity and effectiveness. In this this scenario, the objective of this work was to investigate phytochemical and toxicological effects of *Euphorbia tirucalli* Linneau latex. **Methods**: The phytochemical analysis was performed according to Upadhyay and Kumar (2010). Totoxicity was evaluated in *Artemia salina* leach model according to Meyer (1982). Citotoxicity analysis were carried out by treatment of Swiss female mice with diluted latex (50, 100, and 150 □L/L) with daily doses of 10 ml/Kg, for 15 days. **Results:** Phytochemical analysis showed the presence of anthocyanins, anthocyanidins, flavones, flavonols, xanthones, flavonoids, hydrolysable tannins, condensed tannins and resins. Latex toxicity to *A. salina* was dose dependent and lethal dose median (LD_{50}) concentration was 80,59µl/L. Repeated treatment with diluted latex did not cause changes in body weight and temperature in experimental mice, however repeated treatment with latex for 15 days caused liver steatosis with multifocal infiltrate varying from mild to moderate intensity in groups treated with 100 or 150 □L/L. Splenic histopathology, showed increase of megakaryocytes, edema and multifocal depletion of white pulp in group treated with 150 □L/L. **Conclusion:** Given the broad empirical use of *E. tirucalli* L. in treatment of cancer, parasite diseases and AIDS, this work suggests a potential risk of its use for the general population. Nevertheless, further studies are needed to confirm and extend these findings.

09.055 L-Amino acid oxidase from *Bothrops jararaca* snake venom induces cytotoxicity and apoptosis in rat lung macrophages. Pereira BB, Panunto PC, Fonseca FV, Torres-Huaco FD, Hyslop S Unicamp – Farmacologia

Introduction: Snake venom L-amino acid oxidases (LAAO) exert a variety of biological activities, e.g., cytotoxicity, induction of apoptosis and edema and inhibition of platelet aggregation, but their action on macrophages remains poorly understood. In this work, we examined the cytotoxicity and apoptotic activity of LAAO from *Bothrops jararaca* snake venom on rat lung macrophages. **Methods:** Macrophages were isolated from male Wistar rats (~300 g) using standard procedures and allowed to adhere to 96-well plates (24 h at 37 °C). Cytotoxicity was examined based on the neutral red reduction assay, release of free radicals (H_2O_2, reactive oxygen species - ROS and nitric oxide - NO) and lipid peroxidation. Apoptotic activity was evaluated by caspase -3, -8 and -9 activity, alteration of mitochondrial membrane potential and increased expression of Bax and Bid. In all experiments, the cells were incubated with LAAO (75 U/ml) for 2 h (1 h for lipid peroxidation) and, when required, co-incubated with superoxide dismutase (SOD; 40 U/ml), catalase (CAT; 100 U/ml), N^{w}-L-nitroarginine methyl ester (L-NAME; 1 mM) or aminoguanidine (AG; 500 µM). **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 LAAO reduced macrophage viability to 34 ± 5% (mean ± SEM; n=3; $p<0.05$ vs. control cells). Co-incubation with SOD, CAT, L-NAME or AG significantly attenuated cytotoxicity by 58 ± 1%, 96 ± 2%, 95 ± 1% and 54 ± 1%, respectively (n=3; $p<0.05$ vs. LAAO alone). LAAO induced macrophage H_2O_2 production (maximal at 10 min: 5.02 ± 0.2 µM); co-incubation with CAT attenuated this production to 1.88 ± 0.5 µM (n=3; $p<0.05$ vs. LAAO alone). The release of ROS by LAAO (fluorescence intensity: 52441 ± 2003) was attenuated by SOD (23889 ± 1925), CAT (17022 ± 1126), L-NAME (14159 ± 688) and AG (18798 ± 779) (n=3; $p<0.05$ vs. LAAO alone). LAAO induced the release of NO (0.52 ± 0.003 µM) that was attenuated to 0.36 ± 0.03, 0.16 ± 0.02 and 0.08 ± 0.03 µM by CAT, L-NAME and AG, respectively (n=3; $p<0.05$ vs. LAAO alone). Lipid peroxidation caused by LAAO (7.05 ± 0.39 µmol MDA/mg protein) was partially reduced by SOD, CAT, L-NAME and AG to 4.61 ± 0.13, 4.25 ± 0.79, 4.53 ± 0.13 and 4.38 ± 0.82, respectively, after 1 h (n=3; $p<0.05$ vs. LAAO alone). Incubation with LAAO increased caspase-3 (1.54 ± 0.01 µmol protein/min/ml), -8 (3.34 ± 0.80) and -9 (3.20 ± 0.16) activity compared to control cells; this increase was abolished by SOD, CAT, L-NAME and AG. LAAO decreased the mitochondrial membrane potential (fluorescence intensity: 7850 ± 645 vs. control 16250 ± 743); this decrease was prevented by CAT, L-NAME and AG (fluorescence intensities of 15813 ± 1488, 12505 ± 2585 and 12778 ± 2089, respectively; n=3). LAAO increased Bax and Bid expression (assessed by western blotting) compared to control cells. **Conclusion:** *Bothrops jararaca* LAAO is cytotoxic and apoptotic to macrophages via mechanisms that involve free radical production and oxidative stress. **Financial support:** CAPES, CNPq, FAPESP. **Ethical approval:** Institutional Committee for Ethics in Animal Use (CEUA/UNICAMP, protocol no. 2694-1).

09.056 Short-term carcinogenesis evaluation of a medicinal plant used by Brazilian Unified Health System (SUS). Palozi RAC[1], Lívero FAR[1], Traesel GK[1], Tirloni CAS[1], Gasparotto Júnior A[1] [1]UFGD – Ciências da Saúde

Introduction: Brazil has a great variety of medicinal plants distributed throughout its territory. Many of these plants are used by population without scientific validation of its efficacy and safety. Among them is *Casearia sylvestris* Swartz, a plant with an extensive distribution in tropical and temperate regions around the world, popularly known in Brazil as guaçatonga. In traditional medicine, its leaves are used for treating cardiovascular diseases, among others. Furthermore, *Casearia sylvestris* Swartz is one of the Brazilian plants listed as of interest by Brazilian Unified Health System. Besides recent preclinical studies described important cardiovascular protective effects and absence of acute and prolonged toxicity, no studies evaluated if this species can induce carcinogenesis. Until a few years ago, only long-term animal bioassays (18-24 months), involving lifetime studies on animals, were used to evaluated carcinogenesis, which besides demanding a long time, require a large number of animals, substantial resources and expensive laboratory animal upkeep. Batteries of short-term assays (1-3 months) have been developed as inexpensive and rapid screening tools for mutagens and carcinogens. Moreover, the result of this test is considered equivalent to the predictive value of a long-term study and reduces the number of animals used in experimentation. Thus, we **e**valuated the carcinogenic properties of crude extract obtained from this specie (MECS) in rats. **Methods**: Leaves were obtained from plants of an experimental botanical garden and authenticated as *Casearia sylvestris* Swartz. The cultivation is located at an altitude of 620-650 m under the following coordinates: S 25º03'28''- W 53º52'37''. The crude extract was prepared by maceration (1:5 w/v) from methanol/water (70:30 v/v) at room temperature for fifteen days. After removing the organic solvent, the concentrated extract was dried in lyophilizer. For the tests we used male and female Wistar rats (n = 8-10) maintained under controlled conditions. Body weight gain, chow and water consumption were weekly accompanied and the animals were daily treated (by gavage for 12 weeks) with 50, 250 or 500 $mg.kg^{-1}$ of MECS or vehicle. Twice daily, morbidity and mortality were monitored. In the end, rats were anesthetized and blood and bone marrow samples were collect for mutagenicity evaluation, through micronucleus test and comet assay (OECD, 2014a; 2014b). All vital organs were removed to determine the relative weights, gross pathology and histopathological analyses. **Conclusion:** Prolonged treatment with MECS did not induce any signs of mutagenesis and carcinogenesis in rats. Thus, together with previous scientific researches with this species, our data indicate the safety of the prolonged use proposed by the Brazilian Unified Health System. **Financial support:** CAPES, CNPq and FUNDECT. **CEUA-UFGD:** The institutional committee for the animal care # 11/2015 approved all the procedures. **References:** OECD (2014)a. Test No. 474: Mammalian Erythrocyte Micronucleus Test, Organization for Economic Co-operation and Development Publishing. OECD (2014)b. Test No. 489: In Vivo Mammalian Alkaline Comet Assay, Organization for Economic Co-operation and Development Publishing.

09.057 Neuromuscular and hemodynamic responses to *Micrurus lemniscatus lemniscatus* **(South American Coral Snake) venom.** Floriano RS[1], Schezaro-Ramos R[1], Pereira BB[1], Panunto PC[1], Dias L[1], da Silva Jr NJ[2], Rowan EG[3], Hyslop S[1] [1]Unicamp – Farmacologia, [2]PUC-Goiás – Biologia, [3]University of Strathclyde – Pharmacy and Biomedical Sciences

Introduction: *Micrurus lemniscatus lemniscatus* is a coral snake found in the Brazilian Amazon states of Amapá, Maranhão and Pará and occasionally causes envenomation in humans. In this work, we examined the neuromuscular activity of *M. l. lemniscatus* venom in mouse phrenic nerve-diaphragm (PND) preparations and investigated the hemodynamic responses to venom in anesthetized rats. **Methods:** PND preparations incubated with venom (0.1-30 µg/ml) or physiological Tyrode solution alone were used for myographic and electrophysiological experiments. Male Wistar rats (350-450 g) were anesthetized with isoflurane (2% in air); the left carotid artery was cannulated for blood pressure measurement and a femoral vein was cannulated for venom injection (0.1 and 0.3 mg/kg). The results were expressed as the mean ± SEM, with $p<0.05$ indicating significance (Student's *t*-test). **Results:** In PND preparations, venom caused irreversible (by washing) time- and concentration-dependent neuromuscular blockade, with complete blockade at ≥10 µg/ml within 60 min (times for blockade with 3 and 30 µg of venom/ml: 50% – 32.2 ± 7.6 min and 8 ± 1 min; 90% – 54.1 ± 5.4 min and 16.2 ± 1.6 min; n=4). Venom (3 µg/ml) had a biphasic effect on the frequency of miniature end-plate potentials (MEPPs)/min [from 32.6 ± 2.2 (t_0) to 49.3 ± 4.4 (t_{15}; $p<0.05$) and 19.9 ± 5.2 (t_{60}; $p<0.05$), n=5], but did not significantly affect the MEPP amplitude (t_0: 1.28 ± 0.13, t_{15}: 1.09 ± 0.22 and t_{60}: 1.17 ± 0.22 mV). Venom (10 µg/ml) did not alter the diaphragm muscle resting membrane potential (DRMP: -85.8 ± 2.7 mV *vs.* -82 ± 0.8 mV after 60 min; n=5) or prevent depolarization by carbachol (20 mM) (-58.1 ± 6 mV *vs.* -59.5 ± 8.7 mV before and after venom addition, respectively; n=5). Venom (10 µg/ml) did not significantly affect the amplitude of the compound action potential (CAP) in mouse sciatic nerve [from 10.7 ± 1.2 mV (t_0) to 8.8 ± 1.3 mV (t_{30}), n=4]. Venom caused immediate hypotension that was maximal within the first minute [MAP: from 103 ± 4 to 56 ± 4 mmHg (46 ± 3.2% decrease) for 0.1 mg/kg and 98 ± 3 to 63 ± 4 mmHg (35 ± 1.5% decrease) for 0.3 mg/kg, $p<0.05$, n=4]; both doses were lethal after 20-40 min. There were no significant changes in the electrocardiogram (ECG), heart rate or respiratory rate. **Conclusion:** *M. l. lemniscatus* venom produced potent irreversible neuromuscular blockade in PND preparations. The lack of effect on CAPs and DRMP, without affecting post-synaptic receptors (responses to Cch), indicated that the neurotoxicity was restricted to motor nerve terminals. The biphasic effect on the MEPP frequency suggested the presence of presynaptic toxins. The lack of effect on the cardiac (ECG, heart rate) and respiratory parameters suggested that the venom-induced hypotension involved a predominantly vascular action. **Financial support:** CAPES, CNPq, FAPESP (RSF, grant no. 2014/24409-8). **Ethical approval:** Committee for Ethics in Animal Use (CEUA/UNICAMP, protocol no. 3477-1).

09.058 Effects of batroxase, a metalloprotease isolated from *Bothrops atrox* snake venom, over the hemostasis of rats. Jacob-Ferreira AL[1], Menaldo DL[1], Sartim MA[1], Sampaio SV[1]
[1]FCFRP-USP – Análises Clínicas, Toxicológicas e Bromatológicas

Introduction: Snake venoms are a great source of bioactive molecules that can be used as model of new drugs for the treatment of different pathological processes. Toxins that may interfere in hemostasis have received considerable attention in recent years, due to their importance in brain- and cardiovascular diseases. This study aimed at the evaluation of the thrombolytic and antithrombotic activity of Batroxase, a P-I metalloprotease from *Bothrops atrox* venom. **Methods:** Fibrin(ogen)olytic activity of Batroxase was evaluated *in vitro*. Batroxase's thrombolytic and antithrombotic activities *in vivo* were studied on a model of venous thrombosis in rats, based on two of the Virchow's Triad: alterations in normal blood flow, with partial stenosis of the inferior vena cava, and vessel wall injury with ferric chloride at 10% for 5 min. Bleeding time was assessed by tail bleeding assay. **Results:** Batroxase presented fibrinolytic and fibrinogenolytic activities, which were inhibited by alpha 2-macroglobulin. Batroxase presented thrombolytic activity *in vivo* in a concentration-dependent manner, with 12 mg/kg of the metalloprotease causing a thrombus reduction of 80%, a thrombolytic activity very similar to the one observed for the positive control Alteplase 10mg/kg (85%). In this protocol, the tail bleeding time was not altered by the administration of Batroxase, while it increased 3.5 times with Alteplase. This dose of Batroxase was also tested for its antithrombotic capacity. Batroxase 12mg/kg reduced the thrombus formation in 81%, a result similar with the one obtained with heparin 25U (85%). However, in this protocol, Batroxase as well as Heparin, increased 3 times the tail bleeding time. **Conclusion:** Batroxase presents thrombolytic and antithrombotic activities *in vivo*, with a possible therapeutic potential. The inactivation of the metalloprotease by alpha 2-macroglobulin may reduce its activity, but also its potential side effects, as seen for bleeding time on the thrombolytic protocol. **Financial Support:** FAPESP; NAP-TOXAN-USP. This study was approved by the Ethics Committee on Animal Use of Ribeirão Preto campus, University of São Paulo, protocol number 12.1.1809.53.2.

09.059 Effects of *Euterpe oleracea* **Mart. (açaí) extract on metabolic changes associated with obesity: role of renin angiotensin system.** Bem GF[1], Santos IB[1], Costa CA[1], Carvalho LCRM[1], Cordeiro VSC[1], Soares RA[1], Costa GF[1], Okinga A[1], Medeiros AF[1], Romão MH[1], Rocha APM[1], Ognibene DT[1], Moura RS[1], Resende AC[1 1]UERJ

Introduction: Obesity is a worldwide disease that is accompanied by several metabolic abnormalities such as hypertension, hyperglycemia and dyslipidemia. The production of renin–angiotensin system (RAS) components by adipocytes is exacerbated during obesity, contributing to the systemic RAS and its consequences. Polyphenols possess anti-inflammatory, antioxidant and vasodilator activities. Our group demonstrated that the hydro-alcoholic extract of the açaí stone extract (ASE) rich in polyphenols induces vasodilator and antioxidant effects in different experimental models. Thus, the aim of this study was to evaluate the effect of treatment with ASE and the drugs that interfere with RAS such as: enalapril (ENA) and telmisartan (TEL) on metabolic disorders observed in an experimental model of obesity. **Methods:** Fifty male C57BL/6 mice were separated in five groups. The control group was fed a standard diet (10% fat) and four other groups were fed a high fat diet (HF) for 3 months and were divided into: HF group, HF+ASE group (ASE 300 mg/kg^{-1}), HF+ENA group (ENA 30 mg/kg^{-1}) and HF+TEL group (TEL 10 mg/kg^{-1}). The animals received these treatments by intragastric gavage. The body weight, food intake and weight of visceral adipose tissue were evaluated in balance precision scale. Glycemia was measured with a glucometer. Blood pressure was measured by plethysmography. Lipid profile was determined by kit and the expression of AT1 receptor in visceral adipose tissue homogenates were determined by western blotting. Adipocyte hypertrophy was examined histologically. **Results:** The increased ($p<0,05$) body weight in HF group was reduced ($p<0,05$) by treatment with ASE and ENA. Food intake was not different among groups. Glycemia, sistolic and diastolic blood pressure were increased ($p<0,05$) in HF group. The treatment with ASE, ENA and TEL prevented ($p<0,05$) these alterations. HF and HF+TEL groups showed increased ($p<0,05$) total cholesterol levels, which was prevented ($p<0,05$) by treatment with ASE and ENA. Triglycerides and VLDL levels were reduced ($p<0,05$) in HF+ASE and HF+ENA groups when compared to HF and HF+TEL groups. Weight of visceral adipose tissue was increased ($p<0,05$) in HF and HF+TEL groups. The treatment with ASE and ENA prevented ($p<0,05$) the gain of the body fat. HF and HF+ENA groups showed increased ($p<0,05$) expression of AT1 receptor. This protein content was reduced ($p<0,05$) in HF+ASE and HF+TEL groups compared to HF and HF+ENA groups. The adipocyte size was higher in HF group and treatment with ASE and ENA reduced this hypertrophy. **Conclusion:** Our findings indicate that similar to enalapril, ASE protects against deleterious effects of the HF diet, including obesity, hyperglycemia and hypertension. These beneficial effects of ASE may involve the reduction of lipid profile, body fat mass, and probably the modulation of RAS. These preclinical studies open a possibility for oral administration of ASE in the treatment of obesity. **Financial Support:** CNPq and FAPERJ. **Animal Research Ethical Committee:** The experiments were approved by the Ethics Committee of Animal Experiments of the UERJ (protocol: CEUA/034/2015).

09.060 Effect of chronic administration of *Marrubium vulgare* **in neonates calves.** Schlemper V[1], Soares EL[1], Schlemper SRM[1], Roman Junior WA[2] [1]UFFS – Medicina Veterinária, [2]Universidade Comunitária da Regia de Chapecó – UNOCHAPECÓ – Curso de Farmácia

Introduction: *Marrubium vulgare* (Labiateae) is a medicinal plant that has important pharmacological effects such as antispasmodic, analgesic and antiedematogenic in rodent models, mainly attributed to its phytochemical compound diterpene marrubiin (Schlemper et al., Phytomedicine, 7: 103, 1996; Popoola, et al., Molecules, 18: 9049, 2013). Although its therapeutic effects were previously studied, the scientific investigation of a possible preclinical toxicity of this plant had not been carried out yet. **Methods**: Jersey weaned calves (5-10 days, n= 6 - 8), weighting 15 to 20 kg, remained under adaptation for 7 days in individual stalls. They received colostrum during 5 days after birth, and from the day 6, they received 2.0 liters of milk with 50% of milk replacer in the morning and in the evening, which were incorporated 500 ml of M. vulgare infusion in increasing doses (1, 2, 4 and 8 $g.kg^{-1}$, 10 days each) to the studied group and equal amount of water to the control group. Calf feed was introduced from the fifth day ad libitum and animals were deprived of fodder for the maintenance of the nonfunctional rumen via esophageal groove, to the gastrointestinal absorption of the plant active principles. To carry out haematological/biochemical tests, blood samples were obtained through jugular vein puncture. Through erithrogram, the red blood cells counting and the determination of hemoglobin concentration with an automated blood cell counter was performed. Hematocrit measurement was made in a centrifuge (12.500 rpm/5 minutes). Mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC) were calculated through standard formulas. For white blood cells count, leukocytes were taken in automated blood cell counter and the differential through stained by quick Panoptic method and microscopic analysis. Serum biochemical test was made through kinetic method in semiautomatic analyzer to evaluate aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), total protein and albumin for hepatic alterations, and the metabolites urea and creatinine to verify the renal function. **Results**: Chronic administration of M. vulgare infusion inhibited significantly neutrophil ($P < 0.01$ and maximal inhibition [MI] of 59.33 ± 4.91%) and monocytes ($P < 0.05$ and MI of 56.01 ± 11.05%) counts up to the dose of 8 $g.kg^{-1}$. Enzymes tests (AST and GGT), proteins, albumin, as well as urea and creatinine, had no alteration. **Conclusion:** The model proposed is suitable for preclinical tests in monogastric animals and may use parameters of toxicity and phytochemical compounds detection in blood. M. vulgare administered orally and chronically did not show adverse health effects in calves. Moreover, plant infusion inhibited neutrophils and monocytes circulating, suggesting an immunomodulatory effect in high doses. Financial Support: Federal University of Fronteira Sul-UFFS. Experimental protocols were approved by Animal Research Ethical Committee under No. 23205.004981/2013-40.

09.061 Hydroalcoholic crude extract from *Citrus reticulata* **Blanco (HCE-CR) reduces hyperalgesia in a model of colitis induced by DSS in mice.** Piovezan AP[1,2], Gysemans BM[3], Lisbôa MEM[3], Magnago RF[4], Duarte ECW[5], Cargnin-Ferreira E[6] – [1]LaNEx-UNISUL, [3]UNISUL – Medicina-UNISUL, [5]UFSC, [6]IFSC – Histological Markers

Introduction: Results obtained in our laboratory have shown that HCE-CR possess anti-nociceptive and anti-inflammatory actions in CFA-model in mice. DSS-induced colitis is an inflammatory condition of the colon associated to referred hyperalgesia in hindpaws of animals. **Aims:** The present study evaluated possible anti-hyperalgesic effect for HCE-CR in DSS-induced colitis in mice. **Methods**: Colitis (COL) induction was performed in Swiss mice (n= 8-12/group) fed with filtered water solution containing 3% dextran sulfate sodium (DSS) *ad libitum* for 5 days period. Solutions were replenished each 2 days and on 6th and 7th days they received tap water to drink. Behavioral analyzes were conducted within this period of 7 days to assess mechanical referred hyperalgesia with von Frey filaments, with basal values measured before starting DSS-induction. On days 3rd-5th, after basal values measures, different groups of animals were pre-treated with vehicle (saline, 10ml/kg s.c.) or different doses of HCE-CR (30 or 100 mg/kg) and 1h after they were evaluated once more to observe effects of the treatment on hyperlagesic response. Mechanical allodynia was assessed by paw withdrawal in response to 10 applications (%) of von Frey filament (0.4 g). Project was approved by CEUA-UNISUL (15.010.4.03.IV). Data are presented as mean ± SEM, Two way ANOVA followed by Bonferroni ($p \leq 0.05$). **Results:** On the 4th day after beginning of the induction, DSS-induced COL promoted elevation in the frequency of response to von Frey filaments (76,0 ± 11,7 % of response) in relation to control group (17,1 ± 6,8 % of response). In the other hand, an anti-hyperalgesic effect was observed in groups of animals treated with HCE-CR, in both doses tested (30 mg/kg: 42,9 ± 11,1 or 100 mg/kg: 20,0 ± 7,6 % of response). **Conclusion:** These data shown that treatment with HCE-CR can modulate pain processes in an animal model of DSS-induced colitis in mice. **Financial support**: CNPq, FAPESC, UNISUL (Brazil).

09.062 Anti-inflammatory and toxicological potential of hydrolyzed extract of *Agave sisalana* Santos L, Ondaera GK FCLAs-Unesp-Assis – Ciências Biológicas

Introduction: It is already described that the juice extracted from *Agave sisalana*, sisal, presented high concentrations of steroidal sapogenins, precursor molecules of steroid anti-inflammatories (Ding Y, Phytochem, 28, 2787, 1989). However, the knowledge about the sisal`s pharmacology is limited. Therefore, this project aimed to analyze the anti-inflammatory effect and the toxicological profile of acid hydrolysis extract (AHE) of sisal in order to ensure its use. Furthermore, as the steroidal sapogenins represents the saponins' lipophilic portion, the concentration of saponins was analyzed in the AHE. **Methods:** The sisal juice, liquid portion resulting from shredding of its leaves, was used to prepare the AHE. For this, the sisal juice was subjected to acid hydrolysis with sulfuric acid, heating and precipitation. The anti-inflammatory effect of AHE (50, 100 and 200 mg/kg) was evaluated through the paw edema test induced by carrageenan (CPE) (Winter CA, Soc Exp Biol Med, 111, 544, 1962). The acute anti-inflammatory phase was measured in 1, 2, 3 and 4 hours after the carrageenan injection, and the chronic phase in 24, 48, 72 and 96 hours. The acute toxicity (AT) of the AHE, in single dose of 2000 mg/kg, was determined during 14 days by the observation of behavioral and physiological parameters and possible toxicity signs manifestation. In the study of repeated doses toxicity (RDT), animals were treated once a day, for 14 days, with the doses of 200, 400 and 800 mg/Kg. In this test, the same analyses of behavior and physiology were performed and the biochemical analysis of blood was executed. All treatments were performed orally in *Wistar* rats (n=6/group) after approval by the ethics committee - process 04/2013. The concentration of saponins was determined by spectrophotometric analyses. Data were expressed as mean ± SEM. The statistical significance was determined by the Anova followed by Duncan test ($p< 0.05$). **Results:** In the CPE the AHE 200mg/Kg significantly reduced paw edema (mL) in all the evaluated times, with inhibition of 64,27% (0.31 ± 0.03) of edema in 4 hours after the carrageenan injection (1%) and of 82,71% (0.05 ± 0.01) in 96 hours after. The dose of 2000 mg/Kg did not promote death of treated animals in the study of AT. In the study of AT and RDT the behavioral and physiological parameters were not modified. The biochemical analysis of AHE, 200mg/Kg, performed in the RDT study, presented reduction of 46,48% in the serum levels of uric acid (1.98 ± 0.18) and of 74,95% (134.50 ± 6.63) of glutamic oxaloacetic transaminase. The spectrophotometric analysis of AHE revealed that in the concentration of 0,35 mg/mL, this extract presented a proportion of 52,85% of saponins. **Conclusion:** The results obtained showed that the AHE at the dose of 200 mg/kg presented powerful anti-inflammatory activity. In the toxicological study, the signs of toxicity were not observed and no deaths occurred. The spectrophotometric analysis showed high concentration of saponins and suggested that the antiedematogenic effect of the AHE may be related to the presence of steroidal sapogenins obtained during the process of chemical hydrolysis. However, new studies will be carried out for a better comprehension of the anti-inflammatory activity observed by us. **Financial support and acknowledgments:** FAPESP; FUNDUNESP; SECTI-BA.

09.063 Acute cutaneous lesions induced by *Bothrops jararacussu* snake venom in mice: Antagonism by heparina. Borges PA[1], Nogueira TA[2], Oliveira FL[3], Calil-Elias S[4], Melo PA[3,5]
[1]UFRJ – Farmacologia e Química Medicinal, [2]UFF, [3]UFRJ, [4]UFF – Ciências Aplicadas a Produtos para Saúde, [5]Farmacologia e Química Medicinal

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. **Objectives:** We investigated the skin wound induced by *Bothrops jararacussu* venom injection in mice and the effect of regular Heparin. **Methods:** Adult Swiss mice received intradermal injection of 100 µl of *B. jararacussu* crude venom s (5 µg/g). Control group received saline and one group received treatment with heparin (10 mg/kg).Blood samples were collected for at different times. The animals were euthanized in accord to the IACUC guide (DFBCICB072-04/16) and the skin removed for analysis. **Results:** The venom injection induced epidermal necrosis, inflammatory infiltrate, intense cell proliferation, vascular congestion, and hypodermis disorganization, and a significant increase in epidermal, dermal and hypodermal thickness at 1, 3 and 7 days after the inoculation. 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 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. **Conclusions:** These data showed that *B. jararacussu* venom induced skin wound, associated with inflammatory reaction and heparin treatment counteract the inflammation and improves the healing. Support from CNPq; CAPES; FAPERJ

09.064 Characterization of the Anti-Helicobacter pylori activity of semi-synthetic Pyrogalloyl-flavan-3-ols obtained from polymeric proanthocyanidins of *Peumus boldus* leaves and Avocado Peels. Pastene E[1], Parada V[1], Torres E[1,2], Avello M[1], Alarcon J[3], Zuñiga F[4], Saavedra A[1], Aranda M[5], Garcia A[2] [1]Universidad de Concepción – Laboratorio de Farmacognosia, Facultad de Farmacia, [2]Universidad de Concepción – Microbiología, Facultad de Ciencias Biológicas, [3]Universidad del Bio-Bio – Facultad de Ciencias Básicas, [4]Universidad de Concepcion – Bioquímica Clínica e Inmunología, Facultad de Farmacia, [5]Universidad de Concepcion – Ciencia y Tecnología de Alimentos, Facultad de Farmacia

Introduction: H. pylori (Hp) infects the gastric epithelium and its presence is related with gastric pathologies like gastritis, MALT lymphoma and peptic ulcer. Urease help Hp to neutralize the acidic environment of the stomach, allowing it to survive for decades. Although urease is important during early stages of colonization, recently has been established that carbonic anhydrase (CA) of this bacterium acts cooperatively with urease, helping to neutralize the pH by means of bicarbonate production. Regarding this latter, currently we are conducting a program for the screening and design of new polyphenol-based anti-Hp compounds. In this step of the study we particularly evaluate the anti-Hp effects of semi-synthetic derivatives prepared by nucleophlic attack of proanthocyanidins (PACs) with pyrogallol. **Methods**: Two semi-synthetic derivatives of natural catechins were prepared from proanthocyanidins (PACs) of Boldo leaves and avocado peels. Through acid-catalyzed cleavage and depolymerization of such PACs, formed carbocations were attacked with pyrogallol, giving adducts of catechin and epicatechin, respectively. Compounds were purified by preparative CPC (Arizona system C) and HPLC. Identity was confirmed by HPLC-DAD-ESI-MS/MS. Anti-H. pylori effects were assessed by diffusion in agar (ATCC 43504 strain) and inhibition FITC-labeled bacteria adherence to AGS cells. Antioxidant and anti-inflammatory effects in H. pylori-infected AGS cells were evaluated by DCFDAH and IL-8 levels. Finally, using in silico approaches (Docking) the most probable binding mode of these compounds is proposed. **Results**: Synthesis and purification of two pyrogalloyl derivatives of catechins were successfully achieved using CPC and HPLC Methods: **Introduction** of groups harboring three phenolic hydroxyls on the catechins structure increase its cellular antioxidant activity compared with the parental flavan-3-ol (catechin). Such derivatives also were able to reduce both the adherence of Hp to AGS cells and the IL-8 secretion in Hp-infected cells (> 80%). These compounds behave mainly as anti-inflammatory agents and moderated inhibitors of urease and carbonic anhydrase. Moreover, Docking experiments suggest that such inhibition differ from the classical zinc-binding observed in sulfonamides (e.g. acetazolamide). **Conclusions**: Currently, these preliminary results lead us to propose that these derivatives could be interesting candidates for development of new molecules. Our results suggest that these semi-synthetic compounds could be used as chemical framework for the design of new drugs that help to the prevention and treatment of the colonization by H. pylori and the inflammatory damage exerted upon gastric mucosa (Grants: Fondecyt 1150948; Fondequip N° EQM 130209 y Fondequip N° EQM150025).

09.065 Effects of Açaí seed extract (*Euterpe oleracea* Mart.) on maternal and fetal changes in experimental preeclampsia. Silva AS, Carvalho LCRM, Costa CA, Bem GF, Nunes DVQ, Menezes MP, Soares de Moura R[1], Resende AC[1], Ognibene DT UERJ – Farmacologia

Introduction: The hydroalcoholic extract of the açaí seed (ASE) is rich in polyphenols that are known to reduce the incidence of cardiovascular diseases. This study was designed to determine the protective effects of ASE on the deleterious effects observed in experimental preeclampsia, a condition where reduced nitric oxide production and increased oxidative stress are present. **Methods:** The experimental preeclampsia was induced in pregnant Wistar rats (3 months) by the administration of L-NAME (60mg/kg/day), a nitric oxide synthase inhibitor, from 14th to 20th day of pregnancy. We evaluated the effects of concomitant treatment with ASE (200mg/kg/day) on maternal cardiovascular changes and fetal growth restriction induced in this model. Both L-NAME and ASE were administered in drinking water. There were 4 groups: L-NAME (LN); L-NAME+ASE (LN+ASE); Control (C); Control+ASE (C+ASE). Hemodynamic parameters were evaluated once a week during pregnancy (days 0, 7, 14, 19). Urine (24h) was collected on the 19th day of pregnancy to assess microalbuminuria. On the 20th day of pregnancy, rats were anesthetized with thiopental (70mg/kg; i.p.), the number and weight of alive fetus as well as total placental mass were evaluated. In norepinephrine-preconstricted mesenteric arterial bed (MAB) was evaluated the vasodilator responses of acetilcholine (Ach), bradykinin (BK) and angiotensin II (AngII). **Results:** The results showed that L-NAME induced an increase in systolic blood pressure at the end of pregnancy compared to control groups and ASE was able to prevent the development of hypertension in this model (mm Hg; C:113 ± 2,9/ C+ASE:116 ± 1,8/ LN:160 ± 3,6/ LN+ASE:124 ± 2,1). There was an increase in maternal microalbuminuria in LN group compared to control groups and ASE restored this parameter (mg/24h; C:0,037 ± 0,020/ C+ASE:0,038 ± 0,017/ LN:0,122 ± 0,025/ LN+ASE:0,035 ± 0,014). In LN group, a significant reduction in fetus weight was observed relative to control groups and ASE normalized this parameter (g; C:3,4 ± 0,2/ C+ASE:3,3 ± 0,1/ LN:2,7 ± 30,1/ LN+ASE:3,3 ± 0,1). In the same way, ASE was able to ameliorates the reduced total placental mass in LN group (g; C:5,1 ± 20,2/ C+ASE:4,8 ± 0,2/ LN:3,8 ± 0,2/ LN+ASE:4,8 ± 0,1. In addition, the vasodilator responses induced by acetylcholine (100pmol: C:73,6 ± 4,8/ C+ASE:66,7 ± 4,2/ LN:38,7 ± 5,7/ LN+ASE:58,8 ± 5,2), bradykinin (100nmol: C:47,5 ± 1,7/ C+ASE:47,6 ± 5,3/ LN:28,8 ± 3,6/ LN+ASE:48,8 ± 6,9) and angiotensin II (100nmol: C:45,4 ± 3,9/ C+ASE:40,1 ± 5,5/ LN:18 ± 2,5/ LN+ASE:30,8 ± 1,6) were significantly lower in MAB from LN group than in other groups. **Conclusion:** The results suggest that ASE prevents the maternal hypertension development and endothelial dysfunction as well as fetal growth restriction in the experimental model of preeclampsia induced by L-NAME. **Financial Support:** FAPERJ e CNPq. **Animal Research Ethical Committee (IBRAG-UERJ):** n° 035/2015.

09.066 Anti-obesity and hipogycemic effect of *Myracrodruon urundeuva.* Calou IBF, Veloso FKS, Ribeiro DES, Araújo MC, Lima GS, Negreiros HA, Lima LAR, Lopes JP, Viana GSB

Introduction Obesity has been significantly increasing worldwide, and environmental factors such as excessive food intake and sedentary lifestyle are the main factors related to the genesis of this disease. The use of hypercaloric or hyperlipidemic diets has been used as a model of obesity induction in animals, because of its similarity to the genesis and metabolic responses caused by obesity in humans. It has been shown that prolonged administration of extracts rich in tannins causes a strong reduction of lipids and consequent anti-obesity effect (Liu et al., 2005). Natural antioxidants such as flavonoids, tannins and phenols has received increasing attention from researchers because of its properties of disease prevention and health promotion, reducing oxidative damage they cause damage to DNA, lipid peroxidation and inflammatory processes. From the above, this study aimed to analyze the effect of standardized extract of *Myracrodruom urundeuva* (SEMU) in an obesity experimental model induced by hipercaloric diet, since it has tannins as major components, and anti-inflammatory and antioxidandes attested activities (CALOU et al., 2014). **Methods:**The experiment consisted of four experimental groups (normal control(NC) , hipercaloric diet (HD), HD + SEMU 20mg/kg (13 weeks, p.o) and HD + SEMU 40mg/kg (13 weeks, p.o)). Except the normal control group, all animals received the hipercaloric diet *ad libitum* for 13 weeks. The effects of the HD and SEMU treatment were analyzed in terms of **body weight gain**: through the weekly weighing; **morphometry of adipocytes:** at the end of experiment, abdominal fat was dissected to manufacture of histological slides, stained with HE (40x);cell area mensuration through the Image J® program) and **Glucose tolerance:** once a month through a small puncture on the tail.**Results:** In the beginning of the experiment, animals weighed 21,91g ± 0.64. At the end, the HD group showed a weight gain of 23,70g ± 0,88, that's much higher than that found in NC (18,30 ± 0,92). SEMU20 and 40 mg/kg, showed significantly less weight gain than DG (20,70 ± 0,91; 17,99 ± 0,86, respectively). After a month undergoing calorie diet, animals showed increse glycemia (126,4 mg/dl ± 9,384),when compared to NC (102,3 mg/dl ± 7,261). Goups SEMU 20 and 40mg/kg, showed a decrease in glycemia compared to HD group (122,5 ± 7,621;113,4 mg/dl ± 4,823, respectively). At the last month, the glycemia found in the HD, NC and treated groups were: 135,2 ± 7,137; 126, 8 ± 7,446; 135,2 ± 6,629 (20mg/kg) and 123,7mg/dl ± 11,08 (40mg/kg), clearly demonstrating the increase in glycemia caused by diet as well as the extract potential in decrease blood glucose, particularly at the highest dose. In the morphometry of adipocytes , the cells size were: HD: 198129 μm^2 ± 4446 ; NC: 53735 μm^2 ± 3895; SEMU 20: 57863 μm^2 ± 5918 and SEMU 40: 93427μm^2 ± 7243. **Conclusion:** SEMU can reverse metabolic changes occasioned by hYpercaloric diet. **Financial support**: CNPq. Aprovval by Animal Research Ethical Committee (ESTÁCIO/FMJ): 2014.1 – 004

09.067 Characterization of the phenolic compounds, free radical scavenger and vasorelaxant activities induced by lyophilized grape skins waste extracts. Albuquerque JGF[1], Basilio IJLD[1], Assis VL[1], Almeida AJPO[1], Meireles BRLA[2], Codeiro AMTM[3], Veras RC[1], Ribeiro TP[1], Medeiros IA[1] [1]UFPB – Ciências Farmacêuticas, [2]UFCG – Ciência e Tecnologia Agroalimentar, [3]UFPB – Tecnologia e Desenvolvimento Regional

Introduction: Polyphenols and other phenolic compounds extracted from the grape pomace from the wine production of Petit verdot (*Vittis vinifera* L. of the São Francisco Valley Region) should gain important visibility in face of its application as a grape byproduct with yield of compounds of great antioxidant potential, which are suitable for use as ingredient in foods, pharmaceutical, and cosmetics industries. To better evidence the phenolic composition we performed a comparative analysis with the lyophilized grape skins waste (GSW) extract compared to the fresh ones (GSF). **Methods and Results:** All protocols were approved by CEUA-UFPB nº 1505/13. The results showed a higher total phenolic content as well as antiradical $DPPH^{\bullet}$ scavenger activity in GSW compared to GSF. HPLC analysis identified seventeen different phenolic compounds in GSW and fifteen in GSF. In 10 µmol/L phenylephrine (PE)-pre-contracted mesenteric artery rings, GSW or GSF (10 to 1000 mol/L), caused a concentration-dependent relaxations with significantly attenuated responses (maximum relaxation = 96.9 ± 4.4 %; EC_{50}= 80.0 ± 14.9, n = 5, and 100.0 ± 3.7 %; EC_{50}= 768.0 ± 99.4, n=7, respectively). After removal of the endothelium, the vasorelaxation elicited by GSW was attenuated (maximum relaxation = 103.0 ± 6.1%; EC_{50}= 545.0 ± 146.8; $P < 0.05$; n = 4). Endothelium-dependent response was assessed in the presence of L-NAME to prevent the endothelial formation of NO, and charybdotoxin + apamin to inhibit EDHF-mediated responses. In these conditions, GSW significantly attenuated the responses (maximum relaxation = 97.1 ± 12.1; EC_{50}= 495.2 ± 93.8, n = 4). **Conclusion:** In conclusion, these results demonstrate that GSW is rich in phenolic compounds with potent antioxidant activity *in vitro*. In addition, these data suggest that the GSW induces endothelial-dependent vasorelaxation, probably via NO pathway and greater powerful than GSF. Finally, GSW could be proposed as a high-value by-product for the winemaking industry with significant financial and environmental gains. **Financial support:** CNPq and CAPES.

09.068 Antimicrobial activity of essential oil of *Pelargonium odoratissimum* (L) L`Hér (Geraniaceae) Pombo LM, Borrego P

Introduction: *Pelargonium odoratissimum* species (Apple pelargonium) belongs to the family Geraniaceae. In their chemical composition, flavonoids such as quercetin, kaempferol and myricetin are present, the essential oil of the leaves is rich in methyl eugenol, limonene and fenchone (1). The whole plant is an aromatic herb with astringent, tonic and antiseptic effects. Internally, it is used in the treatment of weakness, gastroenteritis and control bleeding. Externally, it is used to treat skin conditions, injury, neuralgia and throat infections (2). **Methods:** From leaves and flowers of the species *P. odoratissimum*, the essential oil was obtained by hydrodistillation (yield of 0.3% m/v); the chemical composition was determined by gas chromatography coupled to mass spectrometry (GC-MS), comparing the retention index and mass spectral (3) with the data reported in the literature. The antimicrobial activity measured as the Minimum Inhibitory Concentration (MIC) was performed by the microdilution method in microplates of 96 wells using the MTT (3-[4,5 dimethylthyazol-2-yl] -2,5-diphenyltetrazolium bromide) as indicator of the viability. **Results and Conclusions:** It was determined the presence of 4 monoterpenes, 20 sesquiterpenes and some oxygenated compounds including 7 esters and one acid, which constitute about 74% of the total oil relative composition. The identified monoterpenes represent 22,60% of the composition of the essential oil, in which the main components founded were geraniol (12,69%) and citronellol (8,99%). The essential oil showed activity on all tested microbial strains. The highest activity was found for *Staphylococcus aureus*, *Proteus mirabilis*, *Aspegillus brasiliensis* and *Candida albicans* with a MIC < 3.9 µg/mL. It was found less inhibitory activity, but not least, against *Trichophytum rubrum* (MIC = 62.5 µg/mL) and *Trichophytum mentagrophytes* (MIC = 125 µg/mL). **Financial Support:** The present work is a product derived from the 2707_PROY_12539 Project financed by Fundación Universitaria Juan N Corpas, Bogotá (Colombia). **Ethical Considerations:** The study was approved by the Ethics Committee (No risk - Resol 8430/93) **References:** 1. Andrade MA, Cardoso MG, Batista LR, Freire JM, Nelson DL. Antimicrobial activity and chemical composition of essential oil of *Pelargonium odoratissimum.* Brazilian J Pharmacogn. 2011;21(1):47–52. 2. Bussmann RW, Malca-García G, Glenn A, Sharon D, Chait G, Díaz D, et al. Minimum inhibitory concentrations of medicinal plants used in Northern Peru as antibacterial remedies. J Ethnopharmacol. 2010;132(1):101–8. 3. Adams RP. Identification of Essential Oil Components by Gas Chromatography / Mass Spectrometry. In: Identification of Essential Oil Components by Gas Chromatography / Mass Spectrometry In Identification of Essential Oil Components by Gas Chromatography / Mass Spectrometry. 4th Editio. Illinois: Allured Publishing Corporation; 2007. p. 401.

09.069 *Conyza trihecatactis* **and** *Ageratina vacciniaefolia* **exhibit a high cytotoxicity activity on mammalian tumoral cells** Borrego P, Pombo LM, Robles J, Hernandez J, Rojas L

Introduction: *Conyza trihecatactis* and *Ageratina vacciniaefolia* (Asteareaceae), are ruderal plants growing in the Sumapaz and Cruz Verde paramo (Colombia) situated at an altitude of 3000-3200 masl. These species are used in traditional medicine as antipyretic, diaphoretic, for rheumatism treatment, and gastrointestinal disorders (1,2). **Methods:** For the evaluation of the cytotoxic activity of the species *Conyza trihecatactis* and *Ageratina vacciniaefolia*, from the aerial parts of the species the complete ethanolic extracts and fractions were obtained with solvents in order of increasing polarity. The evaluation of the cytotoxic activity was performed by the MTT method (3) on tumor cell lines of human (MCF-7) and murine (TSA and 4T1) breast cancer, and additionally, on a line non tumorigenic fibroblast of murine origin (3T3). **Results and Conclusions:** The dichloromethane fraction of *C. trihecatactis* (CD) showed the highest cytotoxic activity with an IC50 of 36,23 µg/mL for 4T1, 47,81 µg/mL for TSA, 46,05 µg/mL for MCF-7 and 70,67 µg/mL in 3T3 fibroblasts. From this fraction a mixture of flavonoids (CMF) was obtained, identified as apigenin and hispidulina, which presented a marked cytotoxic effect on MCF-7 with an IC50 of 23,50 µg/mL. Fractions obtained from *A. vacciniaefolia* showed IC50 greater than 150 µg/mL on the tumoral cell lines evaluated and greater than 180 µg/mL on line 3T3 fibroblast. In the chloroform fraction from *A. vacciniaefolia* (AC) four terpenoid compounds were identified, which showed similarity in the retention time (t_{ret}) and the mass spectrum, comparing to the compounds isolated and determined in other studies for this species (1) . The present work is a product derived from the 2707_PROY_12539 Project financed by Fundación Universitaria Juan N Corpas, Bogotá (Colombia). **Ethical Considerations:** The study was approved by the Ethics Committee (No risk - Resol 8430/93) **References:** 1. Hernández JM. Diterpenos de *Ageratina vacciniaefolia*, *Conyza trihecatactis* y *Gnaphalium graveolens* y evaluación del efecto antiinflamatorio y citotóxico. Pontificia Universidad Javeriana; 2013. 2. Pedrozo J. Química y Propiedades antimicrobianas de plantas autoctonas de Paramos Colombianos. Pontifica Universidad Javeriana; 2001. 3. Rojas L. Evaluación de la actividad citotóxica de los extractos y fracciones de pulpa y semillas de Annona muricata sobre líneas celulares tumorales y normales. Universidad Distrital Francisco Jose de Caldas; 2015.

09.070 Antibacterial activity of *Thymus vulgaris* L., *Origanum vulgare* L and *Minthostachys mollis* (Benth.) Griseb's essential oils in combination with EDTA on methicillin-resistant *Staphylococcus aureus* Rojas J, Ruiz J, Almonacid R, Ortiz J, Palomino M, Huaroto L, Collahua E

Introduction: Bacterial resistance to antibiotics is increasing day by day both in the community and in the hospital. It has a significant impact on morbidity and mortality rates and on the financial burden that is associated with it. According to the World Health Organization (WHO), antimicrobial resistance is a global problem that requires urgent action. In addition, the increased commercial trades and the international travels allow resistant microorganisms to spread quickly to other continents in which they were not resistant previously. The searching of active agents against MRSA is justified, and natural resources are a potential alternative for the solution of the problem. The objective was to determine the antibacterial activity of *Thymus vulgaris*, *Origanum vulgare* and *Minthostachys mollis's* essential oils (EOs) in combination with ethylenediaminetetraacetic acid (EDTA) on methicillin-resistant *Staphylococcus aureus* (MRSA). **Methods:** The EOs' chemical composition was determined by gas chromatography coupled with mass spectroscopy (GC-MS). Clinical isolates of MRSA were obtained from the "Dos de Mayo" National Hospital in Lima, Peru. The inhibitory activity on MRSA was determined by disk diffusion method and Minimum inhibitory concentration (MIC) by the microdilution colorimetric method in 96-well plates. **Results:** The main components of *Thymus vulgaris'* EO were thymol (46.47%), □-terpinene (20.27%) and p-cymene (15.80%); from *Origanum vulgare*'s EO were □-terpinene (21.17%), (-)-4-terpineol (12.61%) and cis-β-terpineol (12.18%); and from *Minthostachys mollis'* EO were pulegone (33.48%) and menthone (26.68%). The *Thymus vulgaris'* EO presented inhibition halo diameters of 32.23 ± 1.70 mm, and *Thymus vulgaris* + EDTA had inhibition halo diameters of 32.47 ± 2.06 mm, both significantly higher compared to 30 mcg of cefoxitin, which had inhibition halo diameters of 17.60 ± 0.68 mm ($p < 0.01$). The MIC of *T. vulgaris* against MRSA was 0.625 µl/mL. *Origanum vulgare* and *Minthostachys mollis's* EOs were resistant to MRSA. **ConclusionS:** The *Thymus vulgaris'* EO has in vitro antibacterial activity against MRSA and if it is asociated with EDTA has not a synergic effect. **Financial support**: Universidad Nacional Mayor de San Marcos. Research approval by the Ethical Committee of the Medicine Faculty of Universidad Nacional Mayor de San Marcos (N° 152-15).

09.071 Investigation of mechanism action spasmolytic of essential oil from *Lippia alnifolia*

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Introduction: *Lippia alnifolia* is a native and endemic specie of Brazil used on folk medicine to treat wounds or skin burns. Medicinal plants of the genus Lippia has been indicated for the treatment of diseases of the respiratory and digestive systems, and infections in general. **Objetives:** The aim of this work was to investigate the mechanism of action of *L. alnifolia* essential oil on the spasmolytic activity in guinea-pig isolated trachea (OLA). **Materials and Methods:** The experimental protocols were established in accordance with CEUA/UNIVASF (protocol # 0006/021014). Guinea-pig isolated trachea (n= 3 to 5) was incubated in 10 ml chambers in an organ bath system filled with a Krebs' solution at 37°C and constant oxygenation by 1h and tension settled for 1g. Cumulative concentrations of OLA (1-729 µg/mL) were added after the induction of the contraction by 1 µM carbachol or 10 µM histamine in order to investigate the spamolytic effect. To elucidate the OLA mechanism of action a set of experiments were performed both in the presence and absence of 2 mM 4-aminopyridine (4-AP), 5 mM tetraethylammonium (TEA), 3 µM glibenclamide (GLIB), 5 mM cesium chloride (CsCl), 10 µM N-nitro-L-arginine methyl ester (L-NAME), 10 mM indometacin (IND), 3 µM propanolol (PROP), 3 µM dexamethasone (DEX), 100 µM hexamethonium (HEX), and 25 µM methylene blue (BLUE). Data are presented as means ± standard error of the mean (SEM) and was analyzed using GraphPad Prism® Software (v.5). The concentration that caused 50% of the relaxation (EC_{50}) in guinea-pig isolated trachea was calculated by non-linear curve fitting. Statistically significant differences were calculated using non-parametric test t or one-way ANOVA and the post-hoc Tukey's multiple comparison test. **Results:** OLA had as majors constituents carvone (60%) and limonene (6.1%). In terms of airway smooth muscle relaxation OLA was more potent on induced contractions by with histamine (EC_{50} = 5,45 ± 0,90 µg/mL) than carbachol (EC_{50} = 53,65 ± 3,90 µg/mL). The relaxing potential of OLA after contractions induced by histamine in the presence of modulators of the pathway nitric oxide(BLUE and L-NAME), neuronal nicotinic receptor antagonist (HEX) and nonselective inhibitor of potassium channels (CsCl) had not change when compared whith relaxation in the absence of these blockers. However, EC_{50} of OLA in the presence of 4-AP (20.24 ± 5.211 µg/mL), GLIB (24.74 ± 5.690 µg/mL), TEA (46.38 ± 16.83 µg/mL), DEX (59.75 ± 19.84 µg/mL), IND (96,31 ± 9,433 µg/mL) and PROP (58,71 ± 18,67 µg/mL) showed significant increase in comparison with EC_{50} in the absence (5,45 ± 0,90 µg/mL). **Conclusions:** The essential oil from *L. alnifolia* present spasmolytic activity on activity in guinea-pig isolated trachea. Spasmolytic effect, possibly involving different pharmacological targets. The OLA may be involved in the activation of potassium channels, modulation of the pathway arachidonic acid and also acting as β-adrenergic agonist. Research approval by the Ethics Committee on Animal Use (CEUA/UNIVASF process number: 0006/021014). **Financial Support**: FACEPE/UNIVASF

09.072 Toxicological evaluation of the methanol extract of *Pentaclethra macroloba* in rats
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Introduction*: Pentaclethra macroloba* (Fabaceae) popularly known as “pracaxi”, is an original species of the Amazon, used in folk medicine for snake bites, wound healing ulcers, dermal scarring after caesarean birth as well as insecticidal. The aim of this study was evaluate the preclinical acute toxicity of the methanol extract of the *Pentaclethra macroloba* (EMPM). **Methods**: A preliminary cytotoxicity test of the extract using *Artemia salina* Leach was conducted to obtain the median lethal concentration (LC_{50}).Then it was evaluated the acute toxicity as established in the RE 90/2004 of the Agência Nacional de Vigilância Sanitária (ANVISA). Was used 24 Wistar rats (*Rattus norvegicus albinus*), which acutely received the EMPM (2000 mg/kg, po). General signs of toxicity, as well as weight gain, water intake, feed intake and verification of the lethal power of the extract were observed for 14 days after exposure. On the 15^{th} day, blood samples of the animals were collected for the purpose of determination of hematological and biochemical parameters, and then they sacrificed for macroscopic analysis, calculation of the relative mass of vital organs (heart, liver, lungs and kidneys). Numerical results were expressed as mean ± standard error of mean. Differences between groups were determined using analysis of variance (ANOVA) and method of Turkey. Hematological determinations were analyzed by Student’s t-test. For the test with *A. saline* was used the statistical method of PROBIT and the program Microcal Origin 6.0. All protocols were approved by the ethics committee on research on number 006/2015. **Results** and Discussion: LC_{50} determined by bioassay using *A. salina* was 738,53 µg/mL., Indicating that the EMPM has low toxicity. The extract of *P. macroloba* did not induce death in the animals, behavioral changes or significant changes in weight gain, water intake and feed intake when compared with control groups. However, the relative mass of the male lungs ($p = 0.0408$) and kidneys males ($p = 0.0383$) and kidneys of females ($p = 0.0396$) showed a significant difference. The blood profile there was only an increase in platelet count in males treated compared to the control ($p<0.001$). There was no change in the biochemical parameters of the treated animals. The results show that the methanol extract of *Pentaclethra macroloba* has low potential acute toxic (2000 mg/kg, orally), suggesting that it has a good safety in use in biological system, although differential sensitivity between the sexes on certain parameters. However, toxicity studies, sub-chronic and chronic are needed to elucidate the toxicological profile of EMPM. **Financial support:** CNPq/PIBIC