**09**. **Natural Products and Toxinology**

**09.001 Evaluation of kinetics in the cell cycle of lymphocytes *Cebus apella* exposed to carcinogen N-methyl-N-nitrosourea (MNU) and treated with Canova®**. Feio DCA[1], Muniz JAPC[2], Burbano RMR[1], Brito Junior LC[3], Lima PDL[4] [1]ICB-UFPA – Citogenética Humana, [2]MS – Primatas, [3] ICB-UFPA – Patologia Geral, Imunopatologia e Citologia, [4]CCBS – Biologia Molecular

**Introduction:** The Immune Response Modifier Canova ® (CA) is a homeopathic remedy indicated for patients with depressed immune system, since this drug appears to increase the innate immunity and induce an immune response against multiple and severe pathological conditions, including cancer. In this way, we evaluated the pattern of hematopoietic cell response in non-human primates of the species *Cebus apella* exposed to N-Methyl-N-nitrosourea (MNU) and/or CA. **Methods:** The study was approved by UFPA ethics committee on research with experimental animals (CEPAE/MED002-10). Thirteen animals were divided into 4 groups: control and three experimental groups (MNU alone (35days); MNU (35days) plus CA (3days); CA alone (3days)). The animals received MNU orally and CA by three intravenous injections. Cell cycle has been observed previously by lymphocyte culture in RPMI complete medium incubated at 37º C for 72 hours. Cells from the culture of lymphocytes were analyzed by the TestTM Cycle Kit PLUS DNA Reagent according to manufacturer's protocol, and subsequent processing of the samples in FACS Calibur flow cytometry, using system Cell Quest Pro. **Results:** The cell cycle kinetics showed significant difference only in the cells of the group exposed to carcinogen MNU alone, in 3 phases (G0/G1 - 53.16 ± 14.83), (G2 + M - 4.27 ± 3.83), and (S - 25.40 ± 13.88) compared to the negative control group (G0/G1 - 63.96 ± 5.22), (S - 22.24 ± 4.32) and (G2 + M - 7, 85 ± 2.13). **Discussion:** Animals treated with MNU alone showed a blockage on S-phase with a reduction on G0/G1 and G2 + M phases. These data corroborates with data previous related on the literature. Animals treated with MNU plus CA did not show significant changes in the cell cycle distribution when compared to CA alone, suggesting that CA treatment restored the cell cycle blockage induced by MNU to the basal level (negative control). These results corroborates with previous studies where CA treatment is related to protected cells from death and promoting cell proliferation and differentiation, direct and/or indirectly. The results suggest that the Canova® is capable to restore some hematopoietic components, protecting cells from cell cycle damage and thus can be use as adjuvant in cancer chemotherapy reducing its side-effects.

**Financial Agencies:** CNPq, CAPES, CENP and FAPESPA.

**09.002 Evaluation of the mechanisms of action involved in the gastroprotection of *Serjania marginata* in rodents**. Périco LL[1], Beserra FP[1], Ganev EG[1], Heredia Vieira SC[2], Vilegas W[2], Rocha LRM[1], Hiruma-Lima CA[1] [1]Unesp-Botucatu – Fisiologia, [2]Unesp-Araraquara – Química Orgânica

**Introduction**: *Serjania marginata* Casar. (Sapindaceae) is a medicinal species found in the Brazilian Cerrado and commonly used to treat stomach pain[1]. Phytochemical studies from this species determine the presence of saponins, flavonoids, free steroids and tannins in hydroalcoholic extract of leaves from *Serjania marginata*. The aim of this study was to investigate the possible mechanisms of action of the hydroalcoholic extract from *Serjania marginata* (HESM) in acute models of gastric ulcer in rodents. **Methods**: Male Wistar rats (180-250g, n=7-10) were used in the following experimental models: Assessment of mucus adhered to the gastric wall and ethanol-induced gastric lesions in NEM (sulphydryl depleter), L-NAME (NO synthase inhibitor). For assessment of mucus adhered to the gastric wall, a longitudinal incision was made below the xiphoid apophysis for the pylorus ligature in anaesthetized rats. Vehicle (10mL/kg), carbenoxolone (200 mg/kg) or HESM (250 mg/kg) was administered (p.o.) for 1h before the ligature. Four hours later, the animals were killed, and the glandular portion of the stomach was separated, weighed and immersed in a solution of Alcian Blue to quantify the mucus. For each sample, the absorbance at 580nm was measured in a spectrophotometer[4]. The results were expressed as concentration of mucus (µg of Alcian Blue/ grams of tissue). To investigate the involvement of endogenous sulphydryl compounds in the protective effect of HESM, NEM (10 mg/kg, i.p) or vehicle (10mL/kg, i.p) was injected 30min before the administration of HESM (250mg/kg, p.o)[3]. To investigate the possible involvement of endogenous NO in the protective effect of HESM, L –NAME (70 mg/kg, i.p) or vehicle (10mL/kg, i.p) was administered 30min before the administration of HESM (250mg/kg, p.o)[3]. The lesion area ($mm^2$) was measured through the program V-Brane Labiris. Statistical significance was determined by ANOVA followed by Dunnett´s test; levels of $p<0.05$ were considered to be statistically significant. Animal Ethics Committee Protocol Number: 359/11 UNESP. **Results and Discussion**: The pretreatment with HESM and carbenoxolone significantly increased the mucus concentration adhered to the gastric wall of rats (977.8 ± 94.66***) and (961.9 ± 108.2***), when compared to the control vehicle (465.1 ± 41.60), corresponding to an increase of 110.23 and 106.81%, respectively. Mucus is an important protection factor of the gastric mucosa, because it covers the gastrointestinal mucosa and protects against irritating agents[2]. Pretreatment of animals with NEM did not change the gastroprotective effect of HESM (170.1 ± 40.08*, inhibition of 53.93%) compared to the saline-pretreatment HESM group (102.1 ± 21.11*, inhibition of 60.6%), eliminating a possible gastroprotective mechanism. The results showed with pretreatment of animals with L –NAME, also did not change the gastroprotective effect of HESM (186.1 ± 58.4**, inhibition of 67.72%) compared to the saline-pretreatment HESM group (111.7 ± 25.45*, inhibition of 56.42%). This result also excludes an involvement of endogenous NO in the gastroprotective effect of HESM. **Financial Support**: BIOTA/FAPESP, CAPES. **References**: [1] - BOURDY, *et al*. J. of Ethnopharmacology. v. 91, p. 189, 2004. [2] - HIRUMA-LIMA, *et al*. J. of Ethnopharmacology. v. 1004, p. 215, 2006. [3] - MATSUDA, *et al*. Eur. J. Pharmacology, v. 373, p 63, 1999. [4] - RAFATULLAH, *et al*. J. Ethnopharmacol., v. 29(1), p.25, 1990.

**09.003 Effects of the essential oil of *Croton zehntneri* and its major components, anethole and estragole, on the rat *corpora cavernosa***. Cabral PH[1], Campos RM, Fonteles MC[1], Santos CF, Lessa LMA, Cardoso JHL, Nascimento NRF[2] [1]UFC – Physiology and Pharmacology, [2]UECE

*Croton zehntneri* is an aromatic plant, popularly known as “canela de cunhã``, widely distributed in the Northeastern region of Brazil. The essential oil obtained from the leaves corresponds to 2–3% of its dry weight. The major compounds present in the essential oil of *C. zehntneri* are estragole and anethole. Adult male Wistar rats (n=6/each group) were sacrificed by thiopental anesthesia (200 mg/kg). The penis was removed and he corporal tissue was carefully dissected free from the tunica albuginea, strips were prepared and mounted under 0.3 g resting tension in 5 mL organ baths filled with warmed (37 ºC) and oxygenated (95% $O_2$ in 5% $CO_2$) Krebs solution. Following an equilibration period of 60 min, tension was induced by the addition of phenylephrine (PE ;10 µM). At the plateau of contraction, relaxation responses to cumulative concentrations of the essential oil of *Croton zehntneri* (0.001 to 1000 µg/mL) or to its major compounds estragole , anethole or methyl eugenol ($10^{-9}$ to $10^{-3}$ M) were performed. The study protocols were approved by the Ethics Committee of the Ceara State University under the protocol number 09231272-0. Anethol (1-methoxy-4-(1-propenyl)benzene), estragole (1-allyl-4-methoxybenzene), methyl eugenol (4-Allyl-1,2-dimethoxybenzene), Phenylephrine (PE), guanethidine, scopolamine, Nω-Nitro-L-arginine methyl ester hydrochloride (L-NAME), 1H-1,2,4oxadiazole[4,3-a] quinoxalin-1-one (ODQ), acetylcholine chloride, indomethacin, aristolochic acid, forskolin and dimethyl sulfoxide (DMSO) were purchased from Sigma-Aldrich Chemicals Co. (Saint Louis, MO, USA). Estragole relaxed strips pre-contracted with PE with an $IC_{50}$ of 0.6 mM (maximal relaxation 76.6%). After 30 min incubation with L-NAME an $IC_{50}$ of 1.4 mM (maximal relaxation of 43.46%), ODQ-$IC_{50}$ of 0.83mM and a maximal relaxation of 53.11%, indomethacin- $IC_{50}$ of 1.3mM (max. relaxation of 24.41%), BaCl2- $IC_{50}$ of 1.1mM (Max. 63.67%), KCl 60 mM - $IC_{50}$ of 85 nM (Max 91.94%). In regard to anethole, it also relaxed strips precontracted with PE with an $IC_{50}$ of 0.96 mM (Max 66.73%), and after pharmacological treatments with L-NAME we obtained an $IC_{50}$ of 0.47mM (max. 62.07%), ODQ-$IC_{50}$ of 1.1mM and max. 62.45%, indomethacin - $IC_{50}$ of 1.6mM (max. 35.65%), BaCl2 -$IC_{50}$ of 0.79mM (Max.58.39%), KCl- $IC_{50}$ of 0.39mM (Max. 58.39%). Neither the blockade of phospholipase $A_2$ nor the activation of PKC negatively affected the concentration-response curves to estragole or anethole. Estragole showed a tendency to increase and anethole increased the relaxation induced by electrical field stimulation. Both compounds significantly increased the levels of cAMP (estragole by 3-fold and by 2-fold when compared to control). On the other hand, only estragole was able to increase the levels of cGMP (0.5-fold). Nitric oxide released from NANC fibers is recognized as the main mediator of corpora cavernosa relaxation leading to penile erection.The main chemical messengers involved in the relaxation induced by estragol in corpora cavernosa are NO and prostanoids while the relaxation induced by anethole is mainly mediated by prostanoids. These compounds deserve further evaluation as leading compounds in the development of products to treat erectile dysfunction. Thanks: LAFCAR, SEDUC

**09.004 Beneficial effects of dicaffeoylquinic acid-rich fraction from leaves of *Arctium lappa* on gastrointestinal complications associated with *Diabetes mellitus***. da Silva LM[1], Ferreira-Maria D[1], Carlotto J[2], Cipriani TR[2], Souza LM[2], Baggio CH[1], Werner MFP[1] [1]UFPR – Farmacologia, [2]UFPR – Bioquímica

**Introduction:** The impaired gastric healing and diabetic gastroparesis are common gastrointestinal complications in *Diabetes mellitus* (DM). The classic therapy to treat these disorders is ineffective in some patients and has several side effects. In light of this, therapeutic alternatives are necessary and natural products are an important source for this. *Arctium lappa*, or "bardana", is widely used in folk medicine for gastric complaints. Although gastroprotective activity of extracts from *A. lappa* roots was showed in rats (Da Silva, L.M. Food Chem Toxicol.,51:179,2013; Dos Santos, A.C.Pharm Pharmacol.,60:795, 2008), the therapeutic potential of plant leaves have not yet been explored. Thus, in this study, we aimed evaluated the therapeutic potential of *A. lappa* leaves against experimentally gastric ulcer and gastric dysmotility in diabetic rats. **Methods:** First, for the choice of fraction used, non diabetic rats were treated with Ethanolic Supernatant from Aqueous Extract (ESAE) of *A. lappa* leaves or its fractions and exposed to acute gastric lesions induced by ethanol P.A. (500 µL, p.o) Diabetes was induced in rats by a single streptozotocin administration (STZ, 50 mg/kg i.p.) 4 weeks prior to production of chronic gastric ulcers by 80% acetic acid method or 8 weeks prior to gastroparesis evaluation. After the treatment period, the gastric lesion area and the gastric motility were acessed, additional studies were performed to investigate the mechanisms involved (CEUA/UFPR, 500 and 674). **Results and Discussion:** ESAE (1-100 $mg.kg^{-1}$,p.o) reduced the ethanol-induced acute gastric lesions ($ED_{50}$ of 3.8 mg/kg) up to 90% in relation to the vehicle group (173.9 ± 19.9 $mm^2$). Discarding the possible physical barrier on the gastric mucosa, ESAE (0.1-10 mg/kg, i.p.) also inhibited acute gastric lesions. Of all fractions tested, only ethyl acetate-(EA) fraction (0.15 mg/kg, p.o. and i.p.) was able to reduce the ulcer area by 66% and 61% respectively (vehicle group: 222.2± 35.19 $mm^2$). ESAE and EA-fraction (p.o. and i.p.) prevented the reduced glutathione (GSH) and gastric mucus levels depletion in acute gastric lesions. As expected, diabetic rats induced by STZ showed hyperglycemia, weight loss, delayed gastric ulcer healing and diabetic gastroparesis. EA- fraction (0.1-10 mg/kg, 7 days, p.o.) increase the healing of chronic gastric ulcer in diabetic rats up to 68% (vehicle group: 147.3 ± 18.1 $mm^2$), accompanied by enhancement of mucus content and proliferating cell nuclear antigen immunostaining, decrease in myeloperoxidase activity and increase in GSH levels. Furthermore, chronic EA-fraction treatment (1-10 mg/kg, 6 weeks, p.o) normalized the emptying gastric levels in diabetic rats. However, EA-fraction showed no gastric acid antisecretory and no hypoglycemic activity. No sign of ESAE and EA-fraction toxicity were observed in this study. EA-fraction phytochemical analysis revelated the major presence of dicaffeoylquinic acid isomers on its composition. These results show that dicaffeoylquinic acid-rich fraction from leaves of *A. lappa* provides an alternative therapeutic source for the treatment of impaired gastric healing and gastroparesis associated with DM. Studies are being conducted to better clarify these actions. **Financial support:** CAPES

**09.005 Spleen morphology and splenic corpuscles morphometry in diabetic rats induced with streptozotocin and treated with *Azadirachta indica*, a. Juss and streptozotocin 6CH**.

Corsini TB[1], Pacheco MR[1], Amoroso L[1], Baraldi-Artoni SM[1], Machado MRF[1], Santos E[1], D'Angelis FHF[1], Rivera GG[1] [1]FCAV-Unesp-Jaboticabal – Morfologia e Fisiologia Animal

The study was approved by Ethics and Animal Welfare (CEBEA), with Protocol n°. 025471-05 and subsidized by FAPESP. The streptozotocin is diabetogenic and stimulates free radicals production, while *Azadirachta indica* A. Juss reduces glycemia. It is suggested that 6CH streptozotocin, similar to alloxan 6CH, is also hypoglycemic. For anlysing effects of these substances on spleen, 20 albino wistar male rats were used, divided into five groups of four animals each. After five days of adaptation in vivarium cages, blood was sampled (1mL), through infraorbital artery, for glycemia determination (time zero), using for this, and subsequent samplings, inhalational anesthesia with ether. After fast of 14 to 16 hours, were administered, intravenously, 35 mg/kg of streptozotocin diluted in sodium citrate buffer (pH 4,5), in cavernous sinus of penis of 16 rats anesthetized by ether. The other four rats constituted the white control group. After five days of streptozotocin administration, blood was sampled to evaluate glycemia and was observed *diabetes mellitus* induction. Thus, all animals were treated daily, for 30 days, orally (0,2 mL for each 100 grams of animal) via gavage, namely: white control group, without treatment, received only water; white diabetic control group, without treatment, received only water; group treated with aqueous extract of *Azadirachta indica*, A. Juss (10%); group treated with hydroalcoholic (70%) of *Azadirachta indica*, A. Juss (10%) and a group treated with streptozotocin 6CH. On 30st day of experiment, blood was sampled again to determine the glycemia. On the 31st day, animals were sacrificed and spleen was sampled and fixed in Bouin's solution for 24 hours and processed, for paraffin embedding, in order to obtain histological semi-serial sections, in intervals of 200 mm, thickness of 5 mm, and stained by Masson's trichrome technique for morphological and morphometric studies of splenic corpuscules. Morphological results showed that spleen was involved by a capsule of dense connective tissue, which originated septa that divided the parenchyma in incomplete compartments, called white pulp and red pulp. The white pulp was formed by the set of splenic follicles scattered in the organ, consisting in a central region, the germinative center, and a external, the crown. These follicles showed central arteriole. The red pulp showed splenic cords (Billroth cords) interspersed by the splenic sinuses. The morphometric results (area, perimeter, maximum diameter, minimum diameter and form factor) of splenic corpuscles, revealed, by Tukey test, that white control group showed the highest average in most of parameters analyzed in germinal center of corpuscles spleens, except for minimum diameter, whose highest average was found in group treated with streptozotocin 6CH. Crown morphometry of these corpuscles proved that white diabetic control presented the highest values in the most parameters, except for form factor, which had an average similar to white control group. Probably further studies, however, durable, possibily will detect splenic changes.

**09.006 Evaluation of the antioxidant mechanism of ethanolic *Azadirachta indica* (Neem) extract**. Takayama KS[1], Souza CR[1], Baracat MM[1], Casagrande R[1], Georgetti SR[1] [1]UEL – Ciências Biológicas

**Introduction:** There is an increasing interest on antioxidants, particularly those from natural sources and capable of preventing the deleterious effects of free radicals in human disease. Neem leaves contain multiple compounds such as limonoids, nonterpenoids, phenolics, and flavonoids that may work simultaneously and/or synergistically to target multiple pathways and suppress the tumor cell growth (Mahapatra et al., 2012). In this sense, there is also increasing need for methods for estimating the efficiency of antioxidants. The aim of this study was to evaluate the antioxidant mechanism of the ethanolic extract of neem using the following in vitro methods: scavenging capacity of DPPH• free radical, inhibitory activity over Fe+2 ion-induced lipid peroxidation (LPO) and chelating iron. **Material and Methods:** The extract of the dried minced leaves of neem were obtained by turbo extraction using 80% ethanol as a solvent. The hydrogen donating ability of the neem extract, to DPPH was determined by the change in absorbance at 517nm (Georgetti et al., 2008). LPO was assayed as malondialdehyde formation by $Fe^{+2}$-citrate mitochondria system (Georgetti et al., 2006). The iron-chelating activity was determined using the bathophenantroline (BPS) assay (Casagrande et al., 2006). The IC50 (concentration that inhibits 50%) of the neem extract was determined using GraphPad Prism software. **Results and discussion:** The maximum activity of the extract in the DPPH assay was obtained at the concentration of 4µL/mL (82%) with an IC50 of 0.893µL/mL. The inhibition of LPO was concentration-dependent with an IC50 of 1,165µL/mL. The $Fe^{2+}$-chelating activity was concentration-dependent and the maximum activity was observed at the concentration of 10µL/mL (93%) with an IC50 2,32µL/mL. **Conclusion:** The results suggest that the hydroethanolic extract of neem has antioxidant activity by mechanisms related to hydrogen donation (DPPH assay), inhibition of LPO and iron chelation. Therefore, the present data suggest the neem extract merits further in vitro and in vivo studies to determine its usefulness to inhibit oxidative stress. **References:** Biswas et al. Current Science, vol.82, p.1336, 2002. Casagrande et al. AAPS PharmSciTech; 7 (1) Article 10, 2006 Georgetti, S.R., et al., LWT, vol.41, p.1521, 2008 Georgetti et al., Eur J Pharm Biopharm, vol.64, p.99, 2006 **Acknowledgements**: Fundação Araucária and CNPq, Brazil

**09.007 The NO/sCG pathway involvement in vasorelaxant effect of *Lippia origanoides* ethanol extract on rat mesenteric artery**. Campelo RT[1], Carvalho GD[1], Moura LHP[1], Sousa TO[2], Citó AMGL[2], Arcanjo DDR[1], Oliveira AP[1] [1]NPPM-UFPI, [2]UFPI – Química

**Introduction**: The *Lippia origanoides* H.B.K (Verbenaceae) is an aromatic shrub native of Central America and northern South America commonly known as "Oregano-del-Monte", "Salva-de-Marajó" or "Alecrim-d'Angola". It is an apiarian plant used as a spice in cooking and in the folk medicine to treat gastrointestinal, respiratory and skin disorders as a topical lotion (Pascual et al., *J. Ethnopharmacol.*, 76, 201, 2001). The main identified components of its essential oil are the monoterpenes carvacrol and thymol, which also showed antimicrobial, antiparasitic, insecticidal, gastroprotective, antihypertensive and vasorelaxant activity (Dambolena et al., *Toxicon*, 51, 37, 2008; Camurca et al., *Vet. Parasitol.*, 148, 288, 2007; Isman et al., *Crop. Prot.*, 19, 603, 2000; Santos et al., *J. Essent. Oil Res.*, 16, 504, 2004). Thus, this study concerns the investigation of the vasorelaxant effect induced by the ethanol extract obtained from the leaves of *Lippia origanoides* (Lo-EtOH) and the possible underlying mechanisms on rat superior mesenteric artery rings. **Methods:** Male Wistar rats (250-350g) were used for all experiments (Animal Research Ethics Committee/UFPI no. 015/2012). After euthanasia procedure, the superior mesenteric artery was removed and cleaned from the connective tissue and fat. Mesenteric rings (1 to 2 mm) were obtained and suspended by cotton threads in organ baths containing 10 ml of Tyrode's solution, at 37°C and gassed with carbogenic mixture (95% $O_2$ and 5% $CO_2$). The isometric tension was recorded by a force transducer coupled to a data acquisition system (AECAD 1604, AQCAD 2.8.0., AVS Projects, SP, Brazil). The endothelium integrity was verified by relaxation to acetylcholine (10 µM) in rings pre-contracted by phenylephrine (10 µM), as described by Oliveira et al. (Oliveira et al., *Vascul. Pharmacol.*, 44, 338, 2006). After 30 minutes, Lo-EtOH (0.1 - 243 µg/mL) was cumulatively added on the phenylephrine ($10^{-5}$ M)-induced vasoconstriction. All values were expressed as mean ± S.E.M. Student's t-test and ANOVA-one way Bonferroni post-test were used in the data analysis and results were considered significant when $p<0.05$ (GraphPad™ Prism 5.0). **Results and Discussion:** The Lo-EtOH (0.1 - 243 µg/mL) produced a concentration-dependent vasodilation ($pD_2$ = 0.75 ± 0.06; n= 6) in endothelium-intact rings pre-contracted with phenylephrine, which was attenuated in endothelium-denuded rings ($pD_2$ = 0.99 ± 0.05; n=6, $^{**}p<0.01$ *vs* E+). Endothelium-dependent vasodilation induced by Lo-EtOH was strongly reduced by L-NAME (100 µM), a nitric oxide (NO) synthase inhibitor ($pD_2$ = 1.62 ± 0.03; n=6, $^{***}p<0.001$ *vs* E+); ODQ (10 µM), a selective inhibitor of soluble guanylate cyclase ($pD_2$ = 1.01 ± 0.04; n=6, $^{**}p<0.01$ *vs* E+); and atropine (1 nM), a non-selective muscarinic receptor antagonist ($pD_2$ = 1.09 ± 0.03; n=6, $^{***}p<0.001$ *vs*E+). Therefore, this finding suggests the involvement of NO/sCG pathway in the Lo-EtOH-induced vasorelaxant effect. **Keywords:***Lippia origanoides,* mesenteric rings, nitric oxide **Financial Support:** This work was supported by UFPI/FAPEPI/CNPq.

**09.008 Vasorelaxant effect of the ethyl acetate fraction from *Mimosa caesalpiniifolia* flowers extract in rat mesenteric artery**. Moura LHP[1], Campelo RT[1], Santos MEP[1], Rezende Junior LM[1], Silva-Filho JC[1], Monção NBN[2], Citó AMGL[2], Oliveira RCM[1], Arcanjo DDR[1], Oliveira AP[1] [1]NPPM-UFPI, [2]UFPI – Química

**Introduction**: The *Mimosa caesalpiniifolia* Benth (Fabaceae) popularly known as "sansão-do-campo", "unha-de-gato" or "sabiá", is a widespread species from the Brazilian Caatinga region. The bark and flowers are commonly used in treatment of inflammations and hypertension, respectively (De Albuquerque, J. Ethnopharmacol.**,** v.114, p.325, 2007). Accordingly, previous studies have demonstrated the vasorelaxant effect of ethanol extract from flowers. Them, considering the extract fractionation as an important step in the obtention of isolated bioactive compounds, the present study aimed to investigate the vasorelaxant property of a ethyl acetate fraction from *M. caesalpiniifolia* flowers extract (Mc-EtOAc) and the possible underlying mechanisms. **Methods:** Male Wistar rats (270 ± 30 g) were used for all experiments (Animal Research Ethics Committee/UFPI - 015/2012). After euthanasia procedure, the superior mesenteric artery was removed and cleaned from the connective tissue and fat. Mesenteric rings (1-2 mm) were obtained and suspended by cotton threads in organ baths containing 10 ml of Tyrode's solution, at 37°C and gassed with carbogenic mixture (95% $O_2$ and 5% $CO_2$). The isometric tension was recorded by a force transducer coupled to a data acquisition system (AECAD 1604, AQCAD 2.8.0., AVS Projects, SP, Brazil). The endothelium integrity was verified by relaxation to acetylcholine (10 µmol/L) in rings pre-contracted by phenylephrine (10 µmol/L) described by Oliveira et al. (Oliveira A P, Vascul. Pharmacol., 44; 338, 2006). All values were expressed as mean ± S.E.M. Student's t-test and ANOVA-one way Bonferroni post-test were used in the data analysis and results were considered significant when $p<0.05$ (GraphPad™ Prism 5.0). **Results and Discussion:** Mc-EtOAc (0.1 - 750 µg/mL) promoted a concentration-dependent vasorelaxation on tonic contractions evoked by phenylephrine (Phe) (10 µmol/mL) in endotelium-intact ($pD_2$ = 1.90 ± 0.04, n=5) or endothelium-denuded ($pD_2$ = 2.02 ± 0.04, n=5) mesenteric artery rings. A similar effect was obtained in preparations pre-contracted with KCl 80 mM in absence of endothelium ($pD_2$ = 2.62 ± 0.05; n=6). Moreover, the Mc-EtOAc (81, 243, 500 and 750 µg/mL) inhibited contractions induced by cumulative addition of phenylephrine ($10^{-9}$ – $10^{-5}$ M) in a concentration-dependent manner. Likewise, in a $Ca^{2+}$-free depolarizing medium Mc-EtOAc inhibited $CaCl_2$ ($10^{-6}$ – $3x10^{-2}$ M)-induced contractions and promoted a concentration-dependent rightward shifting of the concentration-response curves, indicating that Mc-EtOAc inhibited the contractile mechanisms involving extracellular $Ca^{2+}$ influx. These results demonstrate that Mc-EtOAc induces vasodilatation of rat superior mesenteric artery which probably mediated by $Ca^{2+}$ channel block. **Key Words:***Mimosa caesalpiniifolia;* mesenteric artery; vasorelaxation **Financial Support:** This work was supported by UFPI/FAPEPI/CNPq.

**09.009** ***Vochysia bifalcata***: **Biological activity for a reforestation species**. Horinouchi CDS, Mendes DAGB, Soley BS, Cabrini DA, Otuki MF UFPR – Farmacologia

**Introduction:** *Vochysia bifalcata* is a native Brazilian tree usually employed for economic purposes in the reforestation of destroyed areas and in the manufacture of wood products (Negrelle, R.R.B. Acta sci, Bio, sci. 29:29, 2007). In order to encourage the exploration of other parts of the plant, the aim of this study was to evaluate the activity of the crude extract of leaves from *V. bifalcata* in animal models of skin inflammation. **Methods:** Female Swiss mice (20-30g) were used. Extract activity was evaluated in animal models of TPA or croton oil-induced ear edema. Phlogistic agents, extract (0.03 to 1.0 mg/ear) or dexamethasone (0.1 mg/ear), as a positive control, were dissolved in 20 µL of acetone and applied on the inner right ear. IL-6 and TNF-α skin levels were quantified 6 hours after TPA application (2.5 µg/ear). Extract (0.03 – 1.0 mg/ear) or dexamethasone were applied immediately after TPA. In chronic model, croton oil (0.4 mg/ear) was applied in alternate days for 9 days, the extract topical treatment (1.0 mg/ear, 2x/day) started after 4$^{th}$ day and the edema was measured daily. Animals were euthanized and samples were collected for further analysis (myeloperoxidase (MPO) and N-acetylglucosaminidase (NAG) activity, histological and immunohistochemical analyses). To verify possible corticoid-like side effects, animals were topically treated for 7 days (2x/day) with extract (1.0 mg/ear) or dexamethasone. In the 8$^{th}$ day, lymphoid organs and skin atrophy were assessed. All animal procedures were approved by the Institutional Ethics of our University (n. 390). **Results**: *V. bifalcata* and dexamethasone were able to inhibit inflammatory parameters in both ear edema models. Extract (0.1-1.0 mg/ear) completely reverted TPA-induced cytokines increased levels, while dexamethasone (0.1 mg/ear) completely inhibited TNF-α levels and inhibited 79.4 ± 5.4% of IL-6 levels. In chronic model, extract (1.0 mg/ear) inhibited ear thickness and weight showing inhibition of 70.2 ± 5.6% and 42.6 ± 2.7%, respectively while dexamethasone (0.1 mg/ear) inhibited 89.1 ± 1.8% and 77.3 ± 1.9%. MPO and NAG activity also was reduced by extract (1.0 mg/ear) in 55.1 ± 7.3% and 23.7 ± 4.4%, respectively, and dexamethasone (0.1 mg/ear) in 96.0 ± 3.4% and 49.0 ± 9.6%, suggesting inhibition of leukocyte migration. Inhibition of cell infiltration was confirmed by histological analysis where extract (1.0 mg/ear) and dexamethasone (0.1 mg/ear) reduced in 52.7 ± 3.6% and 81.0 ± 1.4%, respectively. Also, croton oil promoted an increase of epidermis thickness and both extract (1.0 mg/ear) and dexamethasone (0.1 mg/ear) were able to reduce this increase in 50.8 ± 4.4% and 31.5 ± 3.9%, respectively. PCNA-positive cells were quantified by immunohistochemistry. Both extract (1.0 mg/ear) and dexamethasone (0.1 mg/ear) inhibited the increase of PCNA-positive cells in 55.0 ± 2.0% and 76.6 ± 4.1%, respectively. Unlike dexamethasone, extract application during 7 days, did not cause skin atrophy or alteration of lymphoid organs. **Discussion:** In summary, according with these findings *V. bifalcata* leaves is a potential source of new topical anti-inflammatory agents. These medicinal purpose aggregates an admirable value to a native tree of great social, economic and ecological importance. Further investigation is necessary to elucidate the mechanism and support efficacy and security of this plant. **Support:** CAPES, CNPq/RHAE and Fundação Araucária.

**09.010 Active fractions of *Celtis iguanaea* (Jacq.) Sargent (Cannabaceae)**. Sousa LV, Oliveira LP, Silva DPB, Florentino IF, Nascimento MVM, Costa EA UFG – Farmacologia de Produtos Naturais

**Introduction:** *Celtis iguanaea* (Jacq.) SARGENT (CANNABACEAE) popularly known as ``esporão de Galo`` is native to cerrado. It has small flowers, flexible branches and armed with thorns. Leaf extract prepared in the form of tea is used for body pains, asthma, colic and indigestion. Previous results from our laboratory showed that oral treatment with the ethanolic leaf extract of esporão de Galo (EEEG) reduces the number of writhing induced by acetic acid, possesses antinociceptive property in the first and second phases of the formalin test as well as antiedematogenic activity in a model of ear edema induced by croton oil. In carrageenan-induced pleurisy there was a reduction in cell migration and protein exudation. A reduction in the concentration of TNF in pleural exudate suggests its involvement in the anti-inflammatory effect of EEEG. These effects are dose dependent. The aim of our present study was to identify the active fractions responsible for the anti-inflammatory and antinociceptive effects of this plant species. **Methods:** The leaves of the plant were collected in the municipality of Hidrolândia-GO, desiccated at 40 ° C, pulverized, subjected to maceration for seven days with ethanol 96 º GL and concentrated in the rotary evaporator up to 10% of the initial volume. 14.12 g of EEEG, after drying, was solubilized in water and fractionated sequentially with hexane, dichloromethane, ethyl acetate to yield: hexane fraction (HF), dichloromethane fraction (DF), ethyl acetate fraction (EAcF) and aqueous fraction (AF). We used adult male Swiss mice (35 - 40g). Formalin-induced pain, croton oil-induced ear edema and carrageenan-induced pleurisy were seen, cell migration and protein exudation by Evans blue were used. All experimental protocols were approved by the Research Ethics Committee of the UFG (Protocol No. 104/2008). **Results and Discussion:** After fractionation, DF (9 mg / kg, p.o.) treatment decreased the licking time of formalin-induced pain in the first (control 60 ± 4.4 s; FD 44± 3.5 s) and second ( control 180 ± 8.3s; FD 140 ± 14 s) phases; the EAcF (16 mg / kg, p.o.) only reduced nociception in the second phase (81 ± 14 s). The same treatment with the EAcF was able to significantly reduce edema of the ear 14.9 ± 0.7 to 9.5 ± 0.86 mg, the number of migrated leukocytes / ml 4.6 ± 0.68 ($10^6$) to 1.95 ± 0.18 ($10^6$) and protein exudation from 8.09 ± 1.79 to 1.99 ± 0.39 µg/mL. Previous data showed that EEEG has an antinociceptive and anti-inflammatory, meanwhile, in this work we show that active principles responsible for analgesic activity are concentrated in dichloromethane fraction while ethyl acetate fraction retains those with anti-inflammatory effect. Further studies become imperative towards identification of the responsible molecules and clarify their mechanisms of action. **Financial Support:** CAPES, CNPq, FAPEG

**09.011 Effect of ethyl acetate fraction of *Harpagophytum procumbens* on cell viability *in vitro***. Schaffer LF[1], Peroza LR[2], Alves SH[1], Fachinetto R[1,2], Wagner C[1] [1]UFSM – Farmacologia, [2]UFSM – Ciências Biológicas: Bioquímica Toxicológica

**Introduction**: *Harpagophytum procumbens*, popularly known as devil's claw, is a plant widely used in the treatment of diseases of inflammatory origin. The anti-inflammatory effects of *H. procumbens* have been studied; however, its mechanism of action is not well elucidated (van Wyk, 2008; Wegener, 2000). It is known that excess of reactive oxygen and nitrogen species may contribute to increasing tissue damage due to inflammation (Reuter et al., 2010). In the present study, we examined the effects of ethyl acetate fraction (rich in of phenolic compounds) of *H. procumbens* against cell damage (in brain cortical slices) induced by different pro-oxidants (Iron sulphate and Sodium Nitroprusside). **Methods**: Cross-sectional slices of rat cerebral cortex (0.4 mm thickness) were obtained using a McIlwain Tissue Chopper. To verify cell viability it was performed MTT assay (Rigon et al., 2008). The concentrations of the fraction used for the tests ranged from 100, 200 and 400 µg/ml. The total protein content in slices was determined by the method of Lowry et al (1951), using bovine serum albumin as standard. Protein content was used to calculate the estimation of cell viability. Experimental protocol was approved by internal ethical commission of UFSM under the number 025/2011. Results: In our study, the results of MTT assay showed that *H. procumbens* ethyl acetate fraction had the ability of avoiding significantly ($p<0.01$) a decrease on cell viability in a concentration dependent manner induced by both pro-oxidant used which are able to generate reactive species, installing the oxidative process and leading to cell death. Discussion: Our results showed that the H. procumbens ethyl acetate fraction was able to protect against loss of cell viability induced by pro-oxidant agents *in vitro*. Thus, a possible antioxidant activity can also be related to potent anti-inflammatory effect of *H. procumbens*. However, more studies must be performed to investigate its mechanism of action with the aim of exploring the whole therapeutic potential of this plant. **References:** Lowry, O.H. et al. J. Biol. Chem. v. 193, p.265, 1951. Reuter, S. et al. Free Radic. Biol. Med. v.49, p.1603, 2010. Rigon, A.P. et al. Neurotoxicology. v.29, p.727, 2008; van Wyk, B.E. J Ethnopharmacol. v.119, p.342, 2008. Wegener, T. Herbal Gram. v.50, p.47, 2000. Sources of financial support: CNPq/CAPES/FAPERGS/DECIT/SCTIE-MS/PRONEM #11/2029-1

**09.012 Evaluation of crude extracts of Norte-Fluminense plants in the process of cutaneous wound healing in rats**. Rodrigues AAM[1], Magalhães JF[1], Castro AB[1], Leal ICR[2], Muzitano MF[2], Raimundo JM[1], Bonavita AG[1] [1]UFRJ – Laboratório Integrado de Pesquisa, [2]UFRJ – Produtos Naturais

**Introduction:** Wound healing is a complex process which involves a sequence of molecular events aiming restoration of injured tissue. It has been divided into three overlapping phases: inflammatory, proliferative and remodeling. Due to some diseases, such as diabetes mellitus, wound healing can be compromised, and of studies for new drugs that can interact with the injured tissue and accelerate the healing process is necessary. Natural products derived from plants play an important role on treatment of diseases and various plant species has been studied to identify new therapeutic agents. Considering also that plants are unlimited sources of potentially active substances, many of them are used to aid healing. This work aims to search and evaluate the wound healing activity of crude extracts of *Passiflora mucronata*, *Peplonia asteria*, *Ocotea notata* and *Kielmeyera membranacea* obtained from the botanical species from the Jurubatiba National Park, located in the Norte Fluminense (RJ). **Methods:** Female Wistar rats, weighing 230 g, were anesthetized and had their backs shaved, followed by sterilization with alcohol solution [70%]. Then a wound measuring 1 cm² was made and the animals placed in individual cages for 24h. The animals were divided into five groups: i) control (vehicle-DMSO treated), ii) treated with extract of *P. mucronata*, iii) treated with extract of *P. asteria*, iv) treated with extract of *Ocotea notata* v) treated with extract of *K. membranacea*. Animals were topical treated for three consecutive days, 1 time a day at a dose of 0.6 mg/site. The freeze-dried extracts were diluted in DMSO on the day of the experiment. Wound healing was evaluated using photographs taken during the period of 1, 3, 5, 7, 10, 14 and 21 days, and reduction of the wound area was calculated using the ImageJ program considering 100% the total open wound area. All exepriments were approved by Animal Care Ethical Comission of our institution under protocol MACAE003. **Results and Discussion:** Treatment with extract of *P. mucronata* had a significant effect on the reduction of wound area (39.7 ± 1.8%) compared with untreated animals (57.5 ± 6.7%) at the 5th day. At the same day the extract of *P. asteria* also demonstrated wound healing activity (40.2 ± 8%) when compared with control (57.7 ± 7.3%), while extracts *Ocotea* and *K. membranacea* showed no significant activity. Out results suggest a possible healing action of the extract of *P. mucronata* and *P. asteria* and more studies are being provided to better identify these effects. **Financial Support:** FAPERJ, UFRJ

**09.013 Rhamnogalacturonan from *Acmella oleracea* (L.) R.K. Jansen: gastroprotective and ulcer healing properties**. Ferreira DM[1], da Silva LM[1], Mendes DAGB[1], Nascimento AM[2], Iacomini M[2], Cipriani TR[2], Santos ARS[3], Werner MFP[1], Baggio CH[1] [1]UFPR – Pharmacology, [2]UFPR – Biochemistry and Molecular Biology, [3]UFSC – Physiological Sciences

**Introduction:** *Acmella oleracea* (L.) R.K. Jansen (bas. *Spilanthes oleracea*; syn. *Spilanthes acmella* var. *oleracea*) is a plant of the Asteraceae family and popularly known as "jambu", "agrião bravo" or "agrião do Pará". In northern Brazil (Amazon region), it is commonly used as ingredient for food and in traditional medicine for the treatment of several disorders. Indeed, some biological activities have been described for *A. acmella*, such as anesthetic, anti-inflammatory, analgesic and antipyretic. Recently, our group showed that rhamnogalacturonan (RGal), a polysaccharide isolated from *A. oleracea*, protected the gastric mucosa against acute lesions induced by ethanol in rats, with an ED50 of 1.5 mg/kg when administered by oral route. For this reason the aim of this study was to investigate the gastric protective and healing effects of RGal in acute and chronic experimental models of gastric ulcer in rats. **Methods:** Fasted female Wistar rats were treated with vehicle (water or saline, 1 ml/kg) or RGal (0.01-1 mg/kg, i.p.) before induction of gastric lesions by ethanol P.A. and at the moment of pylorus ligature (0.1-10 mg/kg, i.d. or 10 mg/kg, p.o. or 1 mg/kg, i.p. of RGal). After that, gastric mucus levels were measured in ethanol-induced lesions. Chronic gastric ulcers were induced with 80% acetic acid and vehicle (1 ml/kg) or RGal (1-30 mg/kg) were orally administered for seven days, twice a day, starting on the second day after injection of acetic acid. Following treatment, immunohistochemical analysis of proliferating cell nuclear antigen (PCNA) and mucin histochemistry was performed in acetic acid-induced gastric ulcer. Besides, reduced glutathione (GSH), lipid hydroperoxides (LOOH), superoxide dismutase (SOD) and glutathione *S*-transferase (GST) activities, myeloperoxidase (MPO) and cytokine (TNF-α, IL-1β and IL-10) levels were determined (CEUA/BIO-UFPR; approval number 473-B). **Results and Discussion:** Intraperitoneal treatment of animals with RGal (0.01-1 mg/kg) protected the gastric mucosa against acute lesions when compared to control group (C: 151.7 ± 25.7 $mm^2$), restoring the mucus levels to 1397.7 ± 90.2, 1196.6 ± 89.5 and 1179.5 ± 154.5 µg of Alcian Blue/g of tissue. In the chronic ulcer model, oral administration of RGal (1-30 mg/kg) accelerates the gastric ulcer healing, reducing in 43, 55, 73 and 60% the area of lesion, accompanied by increasing of cellular proliferation and gastric mucus content (155% and 60%, respectively), reducing inflammatory parameters (TNF-α: 56%; MPO: 54%) and oxidative stress (GSH: 69%; LPO: 49%; SOD: 36%; GST: 40%) when compared to the control group (data regarding the dose of 10 mg/kg). In addition, the repeated 7 days-treatment of animals with RGal did not show alterations of clinical and behavioral symptoms, body and organs weights or plasmatic biochemical parameters. **Conclusion:** Collectively, these results showed that RGal has interesting antiulcerogenic and gastric healing activities and could constitute an attractive molecule of interest for the development of new antiulcer agents. **Financial support:** CAPES

**09.014 Effect of hesperidin methyl chalconhe in acute lung injury induced by LPS**. Domiciano TP[1], Staurengo-Ferrari L[1], Casagrande R[2], Verri Junior WA[1] [1]UEL – Ciências Patológicas, [2]UEL – Ciências Farmacêuticas

**Introduction:** Naturally occurring chalcones and their synthetic analogues display wide spectrum of biological activities. Several of them, which have been approved for clinical trials, have shown one or more pharmacological activities. Hesperidin methyl chalcone (HMC) is widely used in preparation of pharmaceutical formulations which are used for chronic venous disease symptoms[1]. Inflammation is a complex biological response triggered by harmful stimuli and is associated with many pathophysiological conditions such as adult respiratory distress syndrome. In response to inflammatory stimuli resident cells release proinflammatory molecules, including cytokines IL-1, IL-6 and TNFα[2] to recruit leukocytes. Animal models utilizing LPS-induced injuries provide important information about the events which cause sepsis and pulmonary damage. HMC substituents and structural features in common with other flavonoids having antioxidant and anti-inflammatory activities, thus, it is also possible that HMC presents similar effects[2]. In the present study, it was investigated the effect of HMC in LPS-induced acute lung injury model. **Methods** For acute lung injury induction, male Swiss mice, were anesthetized with chloral hydrate 4% and thereafter administered by, intranasal instillation, 10 µg of LPS diluted in 50 µL of PBS or 50 µL of PBS for control group. Mice received HMC per oral treatment (10, 30, 100 and 300 mg/kg) or vehicle (water) 1 hour prior LPS administration. Mice were sacrificed 24 hours after LPS instillation and the bronchoalveolar lavage fluid (balf) was obtained by washing the lung with 1 ml PBS through cannulation of the trachea. The number of total leukocytes, mononuclear and polymorphonuclear cells present in balf was determined by optical microscope. The levels of IL-1, IL-6 and TNFα were determined in the balf by ELISA. The experimental protocol was approved by the Ethics Committee and Animal Experimentation (process number 9776.2012.93). **Results and Discussion:** LPS induced significant increase of total leukocytes and neutrophils in the balf compared to saline group. It was observed that $HMC_{300}$ treatment significant decreased the total leukocyte numbers in balf by 72.5%, when compared to LPS group. A significant decrease in the number of neutrophils was also observed in the HMC treated groups ($HMC_{100}$=56.9%; $HMC_{300}$=64.9% $P<0.05$). LPS also induced significant cytokine production compared with saline group. Cytokine levels of IL-1beta (75.3%), IL-6 (67.9%) and TNFalpha (68.6%) were significantly lower in the $HMC_{300}$ group compared with LPS group.. These results indicate that HMC reduces the LPS-induced leukocyte recruitment to the lungs by inhibiting cytokine production. Therefore, the oral treatment with HMC could be used to reduce LPS-induced acute lung inflammatory injury. **References:** [1] Boyle P et al. Int Angiol, v.22 (3), p.250. 2003. [2]Sahu et al. Curr Med Chem, v.19, p.209, 2012. **Financial Agencies and Acknowledgments:** CNPq, CAPES, MCTI, SETI/Fundação Araucária and Parana State Government.

**09.015** ***In vitro*** **antioxidant activity of ethanol extract of pods from** ***Samanea tubulosa*** **(Benth)**. Sales PAB, Oliveira JMG, Nogueira Neto JD, Oliveira MS, Sousa MRSC, Moura ER, Costa APR NPPM-UFPI

**Introduction:** The species *S. tubulosa* (Benth.) is known as bordão-de-velho in Piauí, in Alagoas, Maranhão, Paraíba, Pernambuco and Sergipe. The fruits are of type pod, sessile, 10-18 cm long, with 20 - 30 seeds (LORENZI, 2002; CARVALHO, 2007). This study aimed at evaluating the *in vitro* antioxidant activity of the ethanol extract of pods from *Samanea tubulosa* (St-EtOH). **Methods:** O óxido nítrico foi gerado a partir da decomposição espontânea de nitroprussiato de sódio em tampão fosfato (20 mM, pH 7,4). Uma vez gerado esse NO interage com o oxigênio para produzir íons nitrito, foram medidos pela reação de Griess (BASU; HAZRA, 2006). A mistura de reação (1 mL) contendo 10 mM nitroprussiato de sódio (NPS) em tampão fosfato e o *cis- e trans*-nerolidol em diferentes concentrações do St-OH (10, 20, 40, 60 E 80 µg/ml) foram incubados a 37°C por 1 h e depois homogeneizada com reagente de Griess. A absorbância foi mensurada ao comprimento de onda de 540 nm. A formação de OH-(radical hidroxilo), pela reação de Fenton foi quantificada utilizando a degradação oxidativa de 2-desoxirribose (LOPES; SCHULMAN; Hermes-LIMA, 1999). Para determinar a atividade antioxidante do *cis- e trans*-nerolidol contra o radical hidroxila, diferentes concentrações das amostras foram adicionadas ao sistema. . A absorbância foi medida em 532 nm e os resultados foram expressos como equivalentes do malondialdeído (MDA) formado por $Fe^{2+}$ e $H_2O_2$. O ensaio TBARS foi utilizado para quantificar a peroxidação lipídica e um método adaptado do de TBARS foi utilizado para medir a capacidade antioxidante homogeneizado utilizando gema de ovo como um substrato rico em lípidos. A gema de ovo foi homogeneizada (1% p/v) em 20 mM tampão fosfato (pH 7,4), 1 mL do homogenato foi sonicado e, em seguida, homogeneizado com 0,1 mL de *cis* e *trans*-nerolidol nas diferentes concentrações do St-EtOH. Após o resfriamento, a absorbância das amostras foi medida usando um espectrofotômetro a 532 nm. **Results and discussion:** St-EtOH (10, 20, 40, 60 E 80 µg/ml) presenting antioxidant potential, with decreased, respectively, of 16.74, 18.94, 22.08, 25.40 and 28.11% in relation to SNP (sodium nitroprusside) and 15.83, 24.65, 28.05, 34.12, and 38.79%, respectively, when compared the formation of hydroxyl radical. The reaction of the St-EtOH with thiobarbituric acid reactive species production (TBARS) at the same concentrations, was able to decrease 18.31, 21.75, 24.75, 28.34 and 29.91%, respectively, in relation to AAPH (100% of TBARS production). Our results demonstrate the antioxidant activity of ethanol extract of pods from *Samanea tubulosa* against different free radicals. **References:** LORENZI, H. Árvores Brasileiras: manual de identificação e cultivo de plantas arbóreas nativas do Brasil. Editora Plantarum,Odessa, p.201, 2002. CARVALHO, P.E.R. Embrapa Florestas. Circular técnica 132, 2007. LOPES, G.K.; SCHULMAN, H.M.; HERMES-LIMA, M. Polyphenol tannic acid inhibits hydroxyl radical formation from Fenton reaction by complexing ferrous ions. **Biochim.Biophys**.Acta, v. 1472, p.142-152, 1999. **Financial Support:** This work was supported by UFPI/CAPES

**09.016 Possible involvement of calmodulin and PI3K on endothelium-dependent relaxation evoked by butanolic fraction of *Caryocar brasiliense* Camb. leaves in rat thoracic aorta**. Oliveira LM, Oliveira TS, Costa EA, Filgueira FP, Ghedini PC UFG – Ciências Fisiológicas

**Introduction:***Caryocar brasiliense* Camb., known as "pequi," is a tree that belongs to the Caryocaraceae family and is widely distributed in the Cerrado region of Brazil. We have previously demonstrated that the vasorelaxant effect of the butanolic fraction of *C. brasiliense* leaves (BF) is endothelium-dependent and involves stimulation of the nitric oxide/cyclic GMP pathway (Oliveira et. al., Evid. Based Complement. Alternat. Med. 934142: 1, 2012). In the present study, we sought to further characterize the underlying mechanism involved in the vascular effects of BF. **Methods:** The vasorelaxant effect of BF was evaluated in the thoracic aorta rings from female Wistar rats (200-300 g; n = 5-7). Concentration-response curves to BF (0.1 to 30 µg/mL) were constructed in endothelium-intact rings pre-contracted with phenylephrine (0.1µM) in the presence or in the absence of a variety of inhibitors, as follows: the phosphatidylinositol 3-kinase (PI3K) inhibitor (Wortmannin - 1nM), the calmodulin inhibitor (Calmidazolium - 10µM), the $Ca^{2+}$/calmodulin-dependent protein kinase II (CaMKII) inhibitor (KN-93 - 10µM) and the Src kinase inhibitor (PP2 - 10µM). All experiments were conducted in accordance with the Sociedade Brasileira de Ciência em Animais de Laboratório (SBCAL) and were approved by the local Ethics in Research Committee (Protocol CEP/UFG 22/2011). Data are presented as mean±SEM of 5-7 experiments and compared by Student's t-test or one-way ANOVA when appropriated. P values less than 0.05 were considered significant. **Results and Discussion:** BF evoked concentration-dependent relaxation in aortic rings (Emax = 94,4 ± 2,5%). Incubation with calmidazolium or wortmannin significantly reduced BF-induced relaxation (Emax = 18.1 ± 2,3% and 37.2 ± 2.1% respectively). On the other hand, incubation with KN-93 and PP2 did not change BF-induced effects (Emax = 89.4 ± 2.8% and 85.9 ± 1.9% respectively). The results of the present study suggest that the BF-induced endothelium-dependent relaxation rat thoracic aorta occurs by activation of calmodulin and PI3K- dependent pathways. These results contribute to our understanding of the mechanism of action involved in the vasodilatation promoted by *C. brasiliense.* **Financial Support:** CAPES, FAPEG, CNPq.

**09.017 The inhibitory effect of crotoxin on the functionality of bone marrow neutrophils contributes to its long-lasting anti-inflammatory properties**. Lima TS[1,2], Oliveira RBB[1], Neves CL[1], Sampaio SC[1], Cirillo MC[1] [1]IBu – Pathophysiology, [2]IB-USP – Physiology

**Introduction:** Previous studies demonstrated that crotoxin (CTX), a toxin isolated from *Crotalus durissus terrificus* venom**,** has long-lasting anti-inflammatory properties. A single administration of CTX inhibited paw edema and cell migration to the peritoneal cavity for 7 and 21 days, respectively (Nunes FP, Toxicon, v55, p1100, 2010). Furthermore, CTX has a long-lasting inhibitory effect on the phagocytic activity of peritoneal neutrophils; a single subcutaneous injection inhibited this activity for 14 days (Lima TS, Exp Biol Med, v237, p1219, 2012). Considering the short life of neutrophils and the rapid removal of CTX after its administration, it is difficult to explain this long-lasting inhibitory effect on neutrophils. A potential hypothesis to explain this effect is the fact that this toxin could alter the functionality of neutrophils during its process of maturation. Therefore, the aim of this study was to investigate the effect of CTX on the phagocytic activity of bone marrow neutrophils. **Methods:** C57black/6 mice (Institutional Animal Care Committee of Butantan Institute, protocol number 880/12) were pretreated with CTX (44 µg/kg, subcutaneously) or saline 14 days before cells were isolated. Bone marrow cells were collected from both femurs and tibias and neutrophils were isolated through discontinuous Percoll gradients and a gradient of Histopaque 1119. In vitro, neutrophils ($1x10^6$/mL) were stimulated or not with fMLP (N-Formyl-Met-Leu-Phe) 10 µM for 30 min, at 37°C; washed and then incubated with C3bi-opsonized zymosan particles for 20 min, at 37°C. Phagocytic activity was determined in smears stained with a panchromatic dye. A total of 100 cells were counted by light microscopy. Different scores were given to the number of neutrophils that had phagocytized no zymosan particles (x0), one particle (x1), two particles (x2) or three or more particles (x3). The index of phagocytic activity was calculated by the sum of the scores obtained per sample. **Results:** The results demonstrated that CTX inhibits the process of phagocytosis of opsonized zymosan particles by bone marrow neutrophils stimulated with fMLP in 38% (group saline + fMLP: 108 ± 9.43, group CTX + fMLP: 67 ± 4.39). On the other hand, there is no difference between the phagocytic activity of unstimulated neutrophils from animals pretreated with CTX or saline (group saline: 69.12 ± 7.22, group CTX: 63 ± 5.05). **Discussion:** These results evidenced that CTX has a long-lasting inhibitory effect on bone marrow neutrophils, since a single administration of this toxin, 14 days before obtainment of cells, inhibits the process of phagocytosis by neutrophils. These results indicate that CTX probably interfere on the process of maturation of neutrophils and consequently on the functionality of these cells. Therefore, these results contribute to explain the long-lasting inhibitory effect of CTX on the inflammatory response, particularly on the functionality of neutrophils. **Financial Support:** CAPES and INCTTOX.

**09.018 Oxidative stress markers after acute treatment with fumonisin B1 and pentylenetetrazol in liver of mice**. Poersch AB, Lima CO, Trombetta F, Souto NS, Ribeiro LR, Furian AF UFSM – Physiology and Pharmacology

**Introduction**: Fumonisin $B_1$ ($FB_1$) is reported as potential cause of liver cancer in rats (Haschek et. al., 2007) and neurotoxicity in neuronal primary culture (Domijan et al, 2012). It mechanism of toxicity are related to inhibition of ceramida sintase causing inhibition of complex I of electron transport chain and consecutively elevates cytosol calcium levels increasing the excitability and developing oxidative stress (Domijan et. al, 2012). Pentylenetetrazole (PTZ) was used to induce an acute seizure model and oxidative stress. Therefore the aim of this study was to determine if there is a potentiating effect of $FB_1$ on hepatic oxidative damage in mice after PTZ administration. **Methods**: 33 C57BL/6J mice, males, 90 day of age received Vehicle (DMSO 1,6%+ NaCl 0.9% i.p) or FB1 (8 mg/kg i.p.) and 30 min after PTZ (30 mg/kg i.p.) or NaCl 0.9% i.p. At the end of 15 min, mice were euthanized and liver were collected, weighted and homogenate in Tris-HCl (50mM, pH7.4) buffer for the analysis of the activity of catalase (CAT) and glutathione-S-tranferase (GST), Vitamin C (Vit C), non-protein thiols (NPSH), thiobarbituric acid-reactive species *(*TBARS) and hemoglobin (Hb) content (Boeira et. al, 2012). Data were analyzed by using a two-way analysis of variance (ANOVA), followed by Bonferroni's Multiple Range Test when appropriate. Animal Ethics Committee License number 106/2012 (CEUA-UFSM). **Results**: PTZ reduced the liver weight and increases TBARS and Hb content. Moreover, this compound did not alter GST activity, Vit C, NPSH. On the other hand, the treatment with FB1 only reduces GST activity. It was also observed interaction in the treatment with FB1 and PTZ, resulting in decreased activity of catalase. **Discussion**: Studies have demonstrated that $FB_1$ induces liver damage in rats (Haschek et. al., 2007). In this work we demonstrated that acute treatment with $FB_1$ to mice doesn't modify Vit C, NPSH and TBARS content in liver. In addition, a decreased GST activity was observed in FB1+NaCl 0.9% group. PTZ induced oxidative stress since increases TBARS content. Thus such findings suggests that oxidative stress induced by $FB_1$ and PTZ could induce liver damage, the combination of these treatments only decreased activity catalase, demonstrating small potentiation in liver injure, and additional studies are necessary to evaluate these hypothesis. **References**: Boeira, S.P. et al., Toxicon, v.60, p.358, 2012. Haschek, W. M. et. al. Animal. Feed Sci. Technol., v. 37, p. 299, 2007 Domijan, A. M. et al., Neuroscience, v.202, p.10, 2012 **Financial Support:** CNPq, FAPERGS, CAPES. **Acknowledgments:** Neurotoxicity and Psychopharmacology Laboratory, Undergraduate Pharmacology Program-UFSM

**09.019 Effect of *Ocimum americanum* L essential oil effect on the leukocyte behavior evaluated by *in vivo* microcirculation technique**. Bastos RL, Yamada AN, Grespan R, Bersani-Amado CA, Cuman RKN UEM – Pharmacology and Therapeutic

**Introduction:** Plant essential oils and their constituents, products from secondary metabolism of plants, have many applications in ethno-medicine. These oils have been widely used in the pharmaceutical, cosmetic, food and beverage industries. Different properties, such as antioxidant, antiviral, antibacterial, antidiabetic, anticancer, analgesic, sedatives and anti-inflammatory have been reported for essential oils. *Ocimum americanun* L, family Lamiaceae, is an aromatic plant in which many species are used to treat insomnia, constipation, cough and microbial infections. The objective of this study was to evaluate the effect of *Ocimum americanun* L essential oil (OEO) on leukocyte behavior (rolling and adhesion) using an *in vivo* microcirculation model. **Methods:** The essential oil was extracted from fresh leaves by conventional steam distillation using a Clevenger-type apparatus, during 3 hours at temperature of 70ºC. The essential oil was kept at 4$^{o}$C in dark vials, and then used in the experiment. Essential oil analysis and chemical identification were performed by Gas Chromatography-Mass Spectrometry (GC/MS) and Nuclear Magnetic Resonance (NMR). *In vivo* Microcirculation Assay – This assay was performed in the mesentery. Male balb/c mice were treated orally with OEO (100, 200 or 400 mg/kg), vehicle (1%Tween 80 solution) as a negative control, or indomethacin (5 mg/kg) as a reference drug, *60* minutes before carrageenan intraperitoneal injection (500µg/cavity). Two hours after the injection the mice were anesthetized with an intramuscular injection of ketamine/xylazine (1:1 10+10µl/10g body weight) solution and the mesentery was exposed. The number of leukocytes rolling and adhered to the endothelium was determined at 10 minutes count. The protocol was approved by the Ethic Committee for Animal Experimentation of the State University of Maringá (CAEA/UEM 066/2010). The results were statistically analyzed using ANOVA followed by Turkey's test. Statistical significance was set at $P<0.05$. **Results:** The carrageenan injection significantly increased leukocytes rolling and leukocytes adhesion to the vascular endothelium 2h after the stimulation, when compared to that of mice pretreated only with an i.p. injection of saline. The treatment with OEO at doses of 100, 200 and 400 mg/kg led to a significant reduction of leukocytes rolling. However, only the treatment at doses 100 and 200 mg/kg decreased leukocyte adhesion. **Discussion:** OEO had an inhibitory effect on the initial stages of leukocyte migration, evaluated by the rolling behavior and adhesion. Our data suggest an anti-inflammatory effect of OEO by inhibition of leukocytes chemotaxis. **Financial Support:** CNPQ; CAPES; Fundação Araucária;

**09.020 Chemical composition and *in vitro* antimicrobial activity of the essential oil of *Nectandra grandiflora***. Murari AL[1], Heinzmann BM[2], Beutinger D[3], Peres MM[3], Gressler LT[4], Vargas APC[4], Silva DT[5], Longhi SJ[5] [1]UFSM – Farmacologia, [2]UFSM – Farmacologia / Engenharia Florestal, [3]UFSM – Farmácia, [4]UFSM – Medicina Veterinária, [5]UFSM – Engenharia Florestal

**Introduction:** In the last decades, aquatic farming has been considered the fastest growing food production industry, powered by governmental and technological impulsion (GRIGORAKIS et al., 2011). Intensification of aquaculture has resulted in an increase of fish stressors, favoring the emergence of infections by *Aeromonas hydrophila*, the main pathogen of freshwater fish (MAHANTY et al., 2013). The indiscriminate use of antibiotics in aquaculture has given rise to strains which are resistant to multiple drugs (BARCELLOS et al., 2008). In this context, essential oils are a potential tool for controlling fish infections. Plants of the genus *Nectandra* (Lauraceae), commonly known in Brazil as "cinnamons" (canelas), are traditionally used in folk medicine for treating several diseases. *Nectandra grandiflora* Nees & Mart. ex Ness is native to Brazil, and its essential oil (EO) can be an alternative for the treatment of *Aeromonas* in fish farming. **Methods:** Plant material of *N. grandiflora* was collected in Jaguari, RS, Brazil (voucher specimen nº SMDB 13.162). The EO was obtained from the aerial parts by hydrodistillation in Clevenger type apparatus for 3 h (British Pharmacopoeia, 2007) and subsequently analyzed by GC-MS. The evaluation of the antibacterial activity against *Aeromonas hydrophila* ATCC7966 was based on the document M31-A3 (CLSI, 2008). The concentrations tested ranged from 1.600 to 3.125 µg/mL. **Results:** A total of 40 compounds were identified in the EO. The major components were dehydrofukinone (17 %), bicyclogermacrene (11.5%), α-pinene (5 %), β-*E*-ocimene (4.6 %), valencene (4.4%) and kaurene (4.2%). The EO did not inhibit bacterial growth at the concentrations tested. **Discussion and Conclusion:** Literature reports a low susceptibility of Gram-negative bacteria to the antibacterial activity of plant extracts, including EO constituents. The greatest strength of these bacteria lies in the outcome of the interaction between several factors, including differences in their interface and a greater physicochemical complexity of the glycoprotein in their cell wall (HOLLEY et al., 2005). Additionally, the EO of *N. grandiflora* is a complex blend, and some of its constituents may have antibacterial activity, while others might antagonize this effect. Nervertheless the EO of this species did not inhibit the *in vitro* growth of *A. hydrophilla* up to concentration of 3.125 µg/mL. BARCELLOS, L. J. G. et al. Boletim do Instituto de Pesca, 34, 355, 2008. British Pharmacopoeia.Her Majesty's Stationery Office, London, 2007. Clinical and Laboratory Standards Institute (CLSI). Antimicrobial disk and dilution susceptibility tests for bacteria isolated from animals; Approved Standard. 3.ed. Wayne, PA, 2008. (CLSI document M31-A3 Clinical and Laboratory Standards Institute). HOLLEY, R. A. et al. Food Microbiol, 22, 273, 2005. Grigorakis, K. et al. Chemosphere, 85, 899, 2011. Mahanty, A. et al. Indian J Microbiol, in press, 2013. **Financial Agencies**: CAPES, FAPERGS

**09.021 Myocardial protective effects induced by the ethanol extract of leaves of *Alpinia speciosa* (Zingiberaceae) in infarcted rats with isoproterenol**. Tenório EP[1], Ferreira AKB[1], Barbosa DP[2], Brandão RAB[3], Smaniotto S[3], Araújo-Júnior JX[4], Ribeiro EAN[1] [1]UFAL – Enfermagem e Farmácia, [2]UFAL – Química e Biotecnologia, [3]UFAL – Ciências Biológicas e da Saúde, [4]UFAL – Enfermagem e Farmácia / Instituto de Química e Biotecnologia

**Introduction:** The *Alpinia speciosa (Pers.) B.L.Burtt. & R.M. Smith* = *Alpinia zerumbet* is an aromatic plant, belonging to family Zingiberaceae, in our country is popularly known as "colônia" and is widely used in Brazilian folk medicine. Many pharmacological activities have been reported for this plant, such: antihypertensive (LAHLOU, S, Fund. & Clinic. Pharmacol. V.17. p. 323, 2003) antioxidant (TAWATA, S. Food chem. p.486,2006), reducing the levels of LDL cholesterol type, reducing visceral adiposity (LIN, L, J. Agric. Food Chem. V.58. p.4435, 2008) and antiplatelet therapy (TENG, C. M. Chin J Physiol.p.41,1990) based on these assumptions the objective of this study was to investigate the cardioprotective effects of extract from leaves of *Alpinia speciosa* in wistar rats in the infarcted induction with isoprotenerol. **Methods:** Male Wistar rats (200-260g) were divided into 3 groups (n = 5), (G1 = 0.5 mL Saline P.O for 26 days) / (G2 = infarction by isoproterenol 85 mg/kg s.c on 2 consecutive days), (G3 = Treaties with ASEE 300 mg/kg, orally 26 days and underwent infarction with isoproterenol 85 mg/kg s.c in 25 and 26 days of treatment). On the 27th day the animals were euthanized, serum was collected and incubated in biochemical kits for the evaluation of CK-NAC, CK-MB and LDH markers of tissue damage. For morphometric analysis of hearts were measured the thickness ventricular of left, right and reason cardiac weight by body weight (TLV, TRV and WC/WB). For *postmortem* analysis the hearts were sectioned yet submitted to colorimetric test TTC1% and histopathological myocardial analyze qualitative and quantitative, analyzing: Edema, infiltration of leukocytes (myocarditis focus and Total Leukocyte Count (TLC), myonecrosis and deposition of collagen interfibrillar. The study was approved by the ethics committee of animal research (No. 010852/2009-01).The results were expressed as mean ± SEM, and analyzed statistically by ANOVA one-way followed by Dunnet's test. Considered significant when * p <0.01 (G3 vs G2) ***p<0.001 (G3 vs G2). **Results and discussions:** WC (G1 = 1.2 ± 0.1; G2 = 1.6 ± 0.1; G3=1,3±0,1*; respectively), TLV (4.8 ± 0.2; 6.2 ± 0.3; 4,6±0,3* mm) TRV (4.0 ± 0.3; 4.8 ± 0.2; 3,8±0,4 mm) WC/WB (3,98±0,1; 5,20±0,12; 4,36±7,07***) (CK-NAC = 326.3, ± 37.3; 862.3 ± 203.9; 115,4±25,9**U/L) (CK-MB = 452.7 ± 11.5; 765.2 ± 54.3; 209,6±39,9**##; U/L) (LDH = 208.0 ± 22.9; 233.9 ± 38.4; 233,9±38, U/L) (TLC=413± 0,7; 3.517±4,5; 1.376±2,6***cells/field) the results indicate that treatment with ASEE was able to prevent hypertrophy concentric cardiac it is observed that there is a decrease in TLV and WC/WB. In the biochemical analysis observed a reduction in counting enzyme CK-NAC and CK-MB fraction after treatment with ASEE. The colorimetric test revealed there wasn´t development necrotic areas in the heart. Histopathological analysis we observe reveals less intensity and low distribution of focal myocarditis and lymphocytic infiltrations, low amount of collagen deposition indicating no formation of cardiac remodeling, weren´t found focus of myonecrosis. **Conclusions:** The results indicate that treatment with ASEE was able to promote protective activity in myocardial infarction. **Financial Support and Acknowledgment**: CNPq, Fapeal and PPSUS-MS

**09.022 Effect of acute exposition to Fumonisin B1 on oxidative stress markers in liver of mice**. Lima C, Poersch AB, Trombetta F, Naieli S, Furian AF UFSM – Physiology and Pharmacology

**Introduction:** Fumonisin B1 (FB1) is a mycotoxin produced by *Fusarium* species and is mainly produced on corn. FB1 is of health concern due to its hepatotoxic and carcinogenic effects (HARRER et. al., 2012). Due to its structural similarity with sphingosine, FB1 inhibits ceramide synthase leading to intracellular accumulation of sphingoid bases and results in development of oxidative stress (HASSAN et al., 2010). The objective of this study was to determine the acute toxic action of FB1 in liver of mice by oxidative stress markers. **Methods:** 15 mice C57BL/6J, males, ninety days of age were randomly divided in two groups, group I received vehicle (DMSO 1,6% + NaCl 0.9%, i.p.) and group II received FB1 (8 mg/kg, i.p.). The animals were euthanized 45 minutes after administration of vehicle or FB1, and liver were collected and homogenate in Tris-HCl (50mM, pH7.4) buffer for the analysis of Catalase (CAT) and Glutathione-S-Transferase (GST), Hemoglobin (Hb), Ascorbic Acid (AA), Non-Protein Thiols (NPSH) and Thiobarbituric Acid Reactive Substances (TBARS) (BOEIRA et. al., 2012). Data were analyzed by a t Test. Animal Ethics Committee License number 106/2012 (CEUA-UFSM). **Results:** There was no significant difference in analyzed parameters of oxidative stress in liver of mice exposed to acute administration of FB1. **Discussion:** In laboratory animals, most studies of FB1 toxicity are performed in mice exposed to contaminated food sub chronically or chronically (DOMIJAN et. al., 2008). However, in this work, we demonstrated that acute exposition to fumonisin B1 had no significant toxic effect in the liver of mice. It could be explained by the single administration of FB1 or animal species or the time used to evaluate these parameters, since the effect of FB1 depends on route, concentration/dose and duration of exposure (DOMIJAN, 2012). Moreover, animal species and tissues may also be factors that differ among toxic effects caused by FB1 in different experimental protocols. Further studies with other doses, species, tissues and times of exposition should be performed to detect a possible acute toxicity induced by FB1. **References:** Boeira, S.P. et al., Toxicon, v.60, p.358, 2012. Domijan, A.M., Arh. Hig. Rada Torsikol, v.63, p.531, 2012. Domijan, A.M . et. al., Hum. Exp. Toxicol., v.27, p.895, 2008. Hassan, A.M. et al., Toxicon, v.56, p.8, 2010. Harrer, H. et. al., Mol. Nutr. Food Res., v.00, p.1, 2012. **Financial Support:** CNPq, FAPERGS, CAPES. **Acknowledgments:** Neurotoxicity and Psychopharmacology Laboratory and Federal University of Santa Maria.

**09.023 Phytochemical and anti-inflammatory analysis of *Agave sisalana* extracts**. Palacios JL, Da Quinta ARM, Kuruiwa D, Santos L UNESP-Assis – Ciências Biológicas

**Introduction:** In living organisms, many times the inflammatory response is presented in an improper and exacerbated way requiring the use of drugs that relieve its symptoms, as the non-steroid anti-inflammatory and the glucocorticoids. However, for the fact these drugs promote harmful effects to the organism, the medicinal plants bioprospection has led to the search for vegetal active compounds that present anti-inflammatory activity and fewer side effects. This way, it is known that the Agave sisalana (sisal), largely found in the interior of Bahia, presents five different steroidal saponins, a secondary metabolite that reduces the synthesis of lipoxygenases, similarly to glucocorticoids. But there are few studies that evidence the pharmacological actions of such plant. Towards it, this project aims to phytochemically analyze sisal juice, which is the liquid portion resulting from shredding of its leaves, to develop extracts from such juice and to evaluate the anti-inflammatory potential of them. **Methods:** Phytochemical analyze was performed through chemical reactions that resulted in coloration and/or precipitation. Three extracts were prepared from sisal, two aqueous ones: the wet precipitate (WP) resulting from centrifugation of the juice, and the DM obtained from the sun dried mucilage; and an extract obtained from the acid hydrolysis of the juice, the AH. These extracts were orally administered, in single dose, at doses of 50, 100 and 200 mg/kg. The anti-inflammatory effect was evaluated in male Wistar rats (n=6), after approval by the ethics committee - process 004/2012, through the model of paw edema induced by carrageenan (PEC). To analyze the results one-way analysis of variance (ANOVA) and Duncan post-hoc test were used. **Results:** The phytochemical analyze of sisal juice revealed the presence of saponins. The main results obtained from PEC are presented as Mean ± SEM, and they correspond to edema value in ml. The anti-inflammatory activity of AH, when compared to the control group (0.51 ± 0.06) was evidenced. The AH significantly inhibited the edema ($p<0.05$) at all used doses, at dose of 50 mg/kg it promoted 64.26% edema inhibition (0.18 ± 0.04); at dose of 100 mg/kg, inhibition of 53.47% (0.23 ± 0.02); and at dose of 200 mg/kg inhibition of 45.20% (0.28 ± 0.07). O WP presented antiedematogenic activity only at dose of 50 mg/kg, when compared to control group (0.34 ± 0.04), reducing edema in 52.35% (0.16 ± 0.01). Indomethacin 10 mg/kg, used as a standard, inhibited 61.51% of edema (0.19 ± 0.02). **Discussion:** Comparing the aims proposed in introduction to the results obtained we may conclude that the extracts from sisal present powerful anti-inflammatory activity. Especially, the result obtained with the AH, that presented at a dose of 50 mg/kg an antiedematogenic activity greater than the indometacina, what makes possible the economic exploitation of the sisal residue currently being discarded. The phytochemical study suggests that the antiedematogenic action may be related to presence of saponins. However, new studies will be carried out for a better comprehension of the anti-inflammatory activity observed by us. **Acknowledgments** – Programa Primeiros Projetos – PROPE - UNESP

**09.024 Antinociceptive and anti-inflammatory effects of β-glucan isolated from the *Kluyveromyces marxianus***. Oliveira RFA[1], Valasques Jr GL[1], Assis AS[1], Villarreal CF[2], Lima FO[1] [1]UEFS – Saúde, [2]UFBA – Farmácia

**Introduction:** The yeasts are an important source of diverse chemical compounds which can exhibit biological activity. *Kluyveromyces marxianus* is a species of yeast with biotechnological potential because present high metabolic diversity and qualities, such as a thermotolerance, high growth rates, ease handling, and broad substrate spectrum (1). The aim of this study was to determine whether β-glucan isolated from the *Kluyveromyces marxianus* yeast has antinociceptive and anti-inflammatory effects. **Methods:** The antinociceptive and anti-inflammatory effects of the β-glucan were assessed using acetic acid-induced writhing test (2), formalin test (3), tail immersion test (4) and carrageenan-induced paw edema test (5). The tests were conducted on male swiss mice (20-30g, n=7). All assays were carried out in mice pretreated intraperitoneally with β-glucan isolated from the *Kluyveromyces marxianus* dissolved in salina or saline solution (negative control), 30 min before noxious stimulation. Morphine (5 mg/kg, s.c.) and Indomethacin (10 mg/kg, i.p.) were used as standard drugs. This work was submitted and approved by the Animal Experimentation Ethics Committee of UEFS (004/2012). **Results and Discussion:** Intraperitoneal administration of β-glucan (3, 10 and 30 mg/kg) dose-dependently inhibited the acetic acid-induced writhing (28.17%, 48.25% and 74.54%, respectively). In the formalin test, the pretreatment with β-glucan (3, 10 and 30 mg/kg) reduced only the late phase (57.35%, 71.25% and 80.88%, respectively), suggesting that antinociceptive effect is due, at least in part, to anti-inflammatory activity. However, the pretreatment with β-glucan (30 and 90 mg/kg) did not show significant increase in tail immersion latency time, indicating that the β-glucan has peripheral antinociceptive effect. In addition, β-glucan (30 and 90 mg/kg) significantly reduced the paw edema induced by carrageenan (56.36% and 64.93%, respectively), confirming the anti-inflammatory action of β-glucan. Therefore, these findings demonstrate that the β-glucan isolated from the *Kluyveromyces marxianus* has antinociceptive and anti-inflammatory effects. **Financial Agencies**: This work was supported by CAPES. **References:** 1. Fonseca, GG et al. Microbiol Biotechnol, 79:339–354, 2008. 2. Collier, HO et al. Br J Pharmacol Chemother. 32: 295-310, 1968. 3. Hunskaar, S, Hole K. Pain. 30: 103-14, 1987. 4. D'amour FE; Smith DL. J Pharmacol Exp Ther. 72: 74-79, 1941. 5. Winter, C. et al. Soc. Exp. Biol. Med., 111: 544–547, 1962.

**09.025 Synergic effect of Brazilian nut ingestion and superoxide dismutase (MnSOD) polymorphism on blood oxidative stress biomarkers**. Barbisan F, de Rosso Motta J, Frescura Duarte MMM, Duarte T, Dal Berto M, Jung IEC, CRUZ IBM UFSM

**Introduction**: Under normal circumstances, reactive oxygen species (ROS) are neutralized by an antioxidant defense system consisting of enzymes as manganese superoxide dismutase (MnSOD). Humans present a Val9Ala gene polymorphism in MnSOD that produces AA, VV and AV genotypes that affect the oxidative metabolism homeostasis: VV genotypes present higher superoxide levels whereas AA present higher $H_2O_2$ levels. Both genotypes increase the risk of different chronic diseases. Previous studies described that environmental factors can modulate differentially the oxidative metabolism of subjects with homozygous genotypes. However, studies of fruit ingestion that present higher content of molecules that can affect the $H_2O_2$ levels such as the Brazilian Nut are incipient. **Methods**: A prospective experimental protocol approved by the Ethics Committee of the Universidade Federal de Santa Maria, by the number 23081.015838/2011-10, was performed to analyze the acute effect of 10g Brazilian nut (BN) ingestion on blood oxidative stress biomarkers in healthy adults. Initially, a blood collection in fasting conditions (8 h) was performed. After that, 9 volunteers with different MnSOD-genotypes ingested 10g of Brazilian nut. New blood collection was performed after 2 hours. Several oxidative stress biomarkers were analyzed and compared between subjects with different genotypes. **Results:** the effect of BN ingestion was MnSOD polymorphism-dependent considering three variables analyzed. After 2 hours of BN ingestion the cell-free DNA that is a biomarker of cytotoxicity decreased 78.7 ±1% when compared to fasting levels ($p<0.001$) just in AA-subjects. The V carriers did not alter the cell-free DNA level after BN ingestion. Thiols increased about 23-3% in A allele carriers (AA and AV) after BN ingestion (< 0.01). On the other hand, after BN ingestion a small but significant decrease in ROS levels was observed in V allele carriers (94.1 ± 1.2% of fasting analysis, $p< 0.05$). **Discussion and Conclusion:** Previous studies suggested that BN consumption improves the antioxidant status. However, the results described here suggest the occurrence of a differential BN effect on oxidative metabolism stress dependent of genetic variation on MnSOD2. Complementary analysis need to be performed to confirm the findings described in this study. **Financial Support: Fapergs / CAPES** **References:** Lemire M. No evidence of selenosis from a selenium-rich diet in the Brazilian Amazon. Environment International 2012 (40) 128–136. Célia C. Strunz.Brazil nut ingestion increased plasma selenium but had minimal effects on lipids, apolipoproteins, and high-density lipoprotein function in human subjects. Nutrition Research 2008 (28) 151–155. Brenneisen P. Selenium, oxidative stress, and health aspects. Mol Aspects Med 2005 (26)256-267. Cominetti C.Brazilian nut consumption improves selenium status andglutathione peroxidase activity and reduces atherogenic risk in obese women.Nutrition Research 2012 (32) 403-407.

**09.026 Evaluation of cytoprotective and healing gastric ulcers activity of bark extract from *Himatanthus sucuuba***. Lobato AMV[1], Batista LS[1], Marcondes HC[2], Silva MN[3], Sena CBC[1], Silva MCF[1], Hamoy M[1], Jóia VM[1] [1]ICB-UFPA, [2]Dequi-ICEB-UFOP, [3]ICEN-UFPA

**Introduction:** *Himatanthus sucuuba* is known for its important therapeutic applications and its popular ethnopharmacological usage in treating gastrointestinal disorders. Previous Phytochemical screening of the plant has showed the presence major of depsideos, terpenes, iridoids and flavonoids (Endo, Y. Chem, Pharm Bull, 42, 1198, 1994). The pathophysiology of gastric ulcer has generally focused on imbalance between aggressive and protective factors in the stomach, such as acid–pepsin secretion, mucosal barrier, mucus secretion, blood flow, cellular regeneration, prostaglandins (Lima, Z.P, J. Ethnopharmacol, 106, 29, 2006). The reactive oxygen species especially hydroxyl radical plays a major role in causing oxidative damage of mucosa in all types of ulcers. Herbal drugs obtained from the plant source are relatively less expensive, safe, and possess good tolerability even in higher doses (Goel, R.K., Indian J Pharmacol.34, 100, 2002). **Objective:** To evaluate the cytoprotective activity and gastric healing properties of extracts of bark *Himatantus sucuuba.* **Methods**: Bark extract of was prepared by percolation with ethanol 70% and subsequently analyses by High Performance Liquid Chromatography to obtain and verify the biological activity of subsequent fractions. Evaluation of gastric cytoprotective effect: Gastric lesions were induced in Wistar rats with ethanol (Ahmad M. J. Ethnopharmacol, 60 189, 1998) and indomethacin (Arun, M. J. Ethnopharmacol, 118, 460, 2008). Evaluation of gastric healing effect: The chronic gastric lesions in Wistar rats were developed surgically by acetic acid (Tsukimi, Y., J Gastroenterol Hepatol 9, S60, 1994). The area of ulcers (AU) was measured using special software - Image J® to determine the rate of gastric lesions (RGL) upon induction by indomethacin or ethanol. As positive control, reference drug sulcralfate were used. All protocols described herein were approved by our local ethical committee (CEPAE/UFPA-BIO057-12). **Results**: The treatments with extracts at doses of 40 mg/kg e 400 mg/kg expressed significant reductions in the AU and RGL, as compared to control in both models of cytoprotection. The 40 and 400 mg/kg) were efficient for the reduction of UA 59.52% and 96.52%, in ethanol induction, respectively (ANOVA, Dunnett $p > 0.05$). Different Extracts from young and mature bark were evaluated did not show statistically different results as their biological activities in this model. In indomethacin model the 40mg/kg reduced RGL in 72.93% (ANOVA, Dunnett $p > 0.05$). The cicatrizing activity of extract of Bark (400 mg/kg), in 5 and 10% acetic acid lesions, showed considerable UA reduction equal to 56.22% and 45.28% (ANOVA, Dunnett $p > 0.05$), respectively. The results in both models were followed by histological evaluation of each treatment, revealing compatible parameters with the results presented. **Discussion:** Phytochemicals previous study revealed the presence of compounds with high antioxidant activity that can associated these effects (data that are being evaluated, not show) the bark extract of *Himatanthus sucuuba* exhibited gastroprotective activity and healing in the models described, thus confirming the basis of chemotaxonomic and ethnopharmacological information used for selection of the species tested. Financial support: PADRC-UFPA

**09.027 Effect of methanol extract of *Baccharis dracunculifolia* in pancreatic islets of obese mice**. Hocayen PAS[1], Grassiolli S[2], Pochapski MT[3], Silva LA[4], Malfatti CRM[4] [1]UFPR – Farmacologia, [2]UEPG – Biologia, [3]UEPG – Odontologia, [4]Unicentro – Educação Física

**Introduction:** The model monosodium glutamate (MSG) promotes obesity resultant in a degeneration of hypothalamus arched nucleus, leading to obesity, grow deficit (low levels of Grow Hormonal – GH) and behavioral and sexual dysfunction in rodents (Morris et al., Regul Peptide., v.25, p. 441, 1998; Voltera et al., Arq Bras Endrocrinol Metab., v. 52, p. 47, 2007). The damage induced by MSG promotes denominated hypothalamic obesity, with different neuroendocrine and metabolic alterations, including insulin resistance, hyperinsulinemic and hyperleptinemic, due of minor activity of glucose protein translocation (GLUT-4) (Pereira, . Arq Bras Endocrinol Metab., v. 47, p. 111, 2003; Hirata, Braz J Med Biol Res, v. 30, p. 671, 1997). Since the primary effects of obesity can promote insulin resistance,induce diabetes , b-cell dysfunction, insulin secretion and insulin action. The objective was to identify whether chronic administration the extract metanolic *Baccharis dracunculifolia* stimulates insulin secretion in rat pancreatic islets obese. **Methods:** The study was conducted at the Universidade Estadual do Centro-Oeste with the approval of the local Ethics Committee (no. 016/2011).The Wistar rats were divided into 4 groups consisting of 8 animals. Newborn animals weighing about 7- 8g received intradermal monosodium glutamate (MSG) injections at a dose of 4g/kg body weight to induce obesity, during the first five days of life. Control group received the vehicle (distilled water and Tween 80), treated group received the extract of *Baccharis dracunculifolia* (400mg/kg). Isolation of islets from rat pancreas was performed by collagenase technique (Lacy & Kostianovsky, Diabetes, v. 16, p. 35, 1967) with adaptations. After a pre-incubation period, islets underwent further 60 min incubation in different glucose concentrations 5.6; 8.3 and 16.7mM in Krebs solution. Samples of incubation media were taken and stored frozen until they were assayed to measure secreted insulin by radioimmunoassay (RIE). **Results and Discussion**: The secretion of insulin from pancreatic β cells is the activation of the same by glucose (Lopes, Trat. Clín. Méd., 2009). The animal pancreatic islets were stimulated with increasing concentrations of glucose. The data presented show that islets of obese animals (MSG) secret more insulin as compared to control animals (CS), significant concentrations of 5.6 mM glucose (63%) and 8.3 mm (107%). The results of the comparison between groups of obese animals (MSG), there is a high level of insulin secretion in pancreatic islets of obese animals treated with the extract in relation to untreated obese animals, being Significant at concentrations of 8.3 mM (58%) and 16.7 mM (99.5%), with emphasis on the Latter. It was concluded that increased insulin secretion by islets in the obese animals treated with the extract could refer to a possible improvement of oxidative stress due to the antioxidant effect of the extract of *Baccharis dracunculifolia*. **Financial Support**: CAPES.

**09.028 Investigation of the activity of *Maytenus obtusifolia* (Celastraceae) on gastrointestinal motility**. Machado FDF, Sales IRP, Sousa TM, Gomes IF, Tavares JF, Batista LM UFPB

**Introduction:** The species *Maytenus obtusifolia* is a small tree, distributed in many states of Northeastern Brazil where is popularly known as “Bom nome”. In phytochemicals studies performed with *Maytenus obtusifolia* were isolated secondary metabolites, especially celastróides, pentacyclic triterpenes, alkaloids and flavonoids. Pharmacological studies showed that the ethanolic extract and the ethyl acetate phase (FAcOEt-Mo) obtained from this plant have analgesic and antiulcer activity. Thus, the study aimed to evaluate the activity of the FAcOEt-Mo on changes in gastric emptying and intestinal transit. **Methods:** To measure gastric emptying, Swiss albino mice (25-30 g with n = 5-7), fasting 12 h, were treated orally with vehicle (0.9 % saline/10mL/kg), loperamide (5 mg/kg) or FAcOEt-Mo (62,5; 125; 250 e 500 mg/kg). After 1 hour the animals received a suspension of phenol red 0.05% in 1.5% carboxymethylcellulose (10 mL/kg). The animals were euthanized 30 minutes after marker administration. The gastric contents were collected into tubes, solubilized in distilled water and centrifuged (3000 rpm - 15 min). After a series of reactions, 150 µL were pipetted into microplate and the spectrophotometric reading was taken at a wavelength of 560 nm. The results were expressed as the percentage of gastric emptying (SCARPIGNAT S., Arch. Int. Pharmacodyn, 246, 286, 1980). The animals used in the experimental model described above, had their small intestines removed and connected with dental floss at the pylorus and the ileocecal junction. With a ruler, the total length of the small intestine (pylorus to the ileocecal valve) and the distance traveled by phenol red were measured to calculate the percentage of red route depending on the total length of the intestine (STICKNEY J.C., NORTHUP D.W., Proc Soc Exp Biol Med, 101, 582, 1959). Data were analyzed by ANOVA followed by Dunnet's test with significance set at $p<0.05$ *. The results were expressed as mean ± standard deviation (SD) of the mean analyzed with GraphPad Prism software 5.0. The experimental protocols were approved by the Ethics Committee on Animal Research (CEUA / UFPB) with number 0411/11. **Results and discussion:** The results showed that FAcOEt-Mo promoted changes in gastric emptying in the dose of 500 mg/kg having 80% (79,56 ± 7,72) of gastric emptying when compared to the negative control 93% (92,85 ± 2,96). Also were observed changes in the intestinal transit in the dose of 500 mg/kg with 47% (47,42 ± 9,54) when compared to the negative control 63% (62,54 ± 3,31). With these results we concluded that FAcOEt-Mo promotes changes in gastrointestinal motility. **Financial Support:** CAPES / UFPB

**09.029 Antibacterial activity of the ethanol extracts from *Terminalia fagifolia* Mart & Zucc (Combretaceae)**. Araujo AR[1], Quelemes PV[2], Perfeito MLG[2], Nunes PHM[3], Soares MJS[4], Leite JRSA[1] [1]UFPI – Medicinal Plants [2]UFPI – Biodiversity and Biotechnology, [3]UFPI – Physiology and Biophysics, [4]UFPI – Veterinary Morphophysiology, Teresina

**Introduction:** Most of microorganisms have been acquiring resistance to traditional antibiotics thus, the search for new antimicrobials agents, especially from plants, has been intensified. The Combretaceae family comprises 18 genera, among them, *Combretum* and *Terminalia* are the most abundant. Several *Terminalia* species and its isolated compounds have been the subject of research for many pharmacological activities. In this study we evaluated the antibacterial activity of the ethanol extract (EET) from the *Terminalia fagifolia* stem bark and its aqueous (AQ), hydroalcoholic (HA) and hexane (HE) fractions. **Methods:** For tests were used five bacterial strains such as three Gram-positive bacteria: *Staphylococcus aureus*ATCC 29213; *Staphylococcus aureus* - Col (methicillin-resistant); *Staphylococcus epidermidis* ATCC 12228 and two Gram-negative bacteria: *Escherichia coli* ATCC 25922 e *Pseudomonas aeruginosa* ATCC 27853. MIC (minimum inhibitory concentration) was determined according adapted CLSI using 96-well microdilution plate where the strains (concentration of $5 \times 10^5$ CFU/mL) were exposed to two-fold dilution series of EET and its fractions. Sterile Mueller-Hinton broth was used as negative control and inoculated broth was used as the positive control. Standard antibiotics effective against the bacterial strains were also tested. MIC was defined as the lowest concentration of agent that restricted the bacterial visible growth in the inoculated broth. **Results and Discussion**: Results demonstrated that EET and its AQ and HA fractions have been active against Gram-positive bacteria. Ethanol extract (EET) was the most active against *S. epidermidis* with a MIC at 50 µg/mL, AQ fraction showed most activity against *S.aureus*-Col and *S. epidermidis* with MIC at 25 µg/mL, HA fraction also showed most active against *S. epidermidis* with MIC at 25 µg/mL. Only HE fraction not showed antimicrobial activity. The results obtained for these plant extract and its fractions exhibit an antibacterial potential effect on Gram-positive bacteria. **Financial support**: UFPI/CAPES/CNPQ. **References:** ALMEIDA, S.P.; PROENÇA, C.E.B.; SANO, S.M.; RIBEIRO, J.F. Embrapa: Planatina, 1998. CLSI - Clinical Laboratory Standards Institute. Approved standard M07–A9. 32, 2012. MANNA, P.; SINHA, M.; SIL, P.C. Complement Alternative Medicine. 30, 33, 2006.

**09.030 Gastroprotective effect of essential oil of *Croton argyrophylloides* Muell Arg**. Gama CS, Silva TFS, Araújo SA, Estevam CS, Batista JS UFS – Fisiologia

**Introduction**: *Croton argyrophylloides* is a plant of the semi-arid of the Brazil Northeast known popularly as sacatinga and marmeleiro prateado. It is used by traditional popular medicine in the treatment of pain, heartburn and indigestion. The essential oil of this plant contains α-pineno (14,23%), 1,8-cineol (8,15%) and espatilenol (9,8%) as major constituents and possess antioxidant properties, which suggest a correlation with gastroprotective activity. Therefore, the aim of this study is to evaluate the antiulcer activity of the essential oil of Croton argyrophylloides (EOCA) on ethanol- and indomethacin-induced ulcers. **Methods**: the experimental protocols were approved by the Ethics Committee for Animal Research of the Federal University of Sergipe (protocol 56/12). In the gastroprotective activity tests, rats w ere orally treated with EOCA (25, 50 and 100 mg/kg), ranitidine (50 mg/kg) and 5% Tw een 80 (Control). One hour after the above treatments, the animals received oral treatment with ethanol (0.4 mL/100 g) or indomethacin (100 mg/kg). One half h and 6 h after administration of ethanol and indomethacin, respectively, the animals were sacrificed, their stomachs were removed and ulcers were quantified. Evaluation of EOCA gastric antisecretory activity was performed by pylorus ligation test. The rats were anesthetized with ether and the pylorus was ligated. Afterward, EOCA (25, 50 and 100 mg/kg), ranitidine (50 mg/kg), and 5% tween 80 were intraduodenally administered. Four hours after the above treatments, the rats were anesthetized with ether and the gastric content was collected and centrifuged. The gastric volume, pH, proton concentration of the supernatant were determined. **Results**: the EOCA presented gastroprotective effect against ethanol- and indomethacin-induced ulcers at all doses tested. The percentages of gastric lesions induced by ethanol (m ± epm) were 12.9 ± 1.5, 4.6 ± 1.2 and 0.07 ± 0.03% in the animals treated with EOCA at the doses of 25, 50, and 100 mg/kg, respectively, and 21.7 ± 4.2 and 0.3± 0.1% in the animals treated with 5% tween 80 and ranitidine, respectively. The percentage of indomethacin-induced gastric ulcers were 1.4 ± 0.3, 1.9 ± 0.4 e 1,1 ± 0,3% in the animals treated with EOCA at the doses of 25, 50, and 100 mg/kg, respectively, and 4.5 ± 0.9 and 0.8 ± 0.3% in the animals treated with 5% tween 80 and ranitidine, respectively. Volume gastric, pH and proton concentration values were not significantly modified by EOCA. **Discussion**: The present results indicate that EOCA presents antiulcer effect against ulcer induced either by ethanol or by indomethacin and does not involve antisecretory activity. In addition, ethanol-induced ulcers inhibition by EOCA suggests that antiulcer effect of EOCA is related to its antioxidant property. **Support financial**: CNPq and FAPITEC.

**09.031 Study of the cytotoxic effect of *Bothrops jararacussu* and *Apis mellifera* venom in renal tubular cells (LLC-Pk1) and antagonism by polyanions**. Teixeira-Cruz JM, da Silva Amaral L, da Silva Gonçalves T, Monteiro-Machado M, Amorim-Tomaz M, Melo PA, Quintas LEM ICB-CCS-UFRJ – Farmacologia e Química Medicinal

**Introduction:** Venoms of *Bothrops* are involved in most snake bites in Brazil and they consist of complex mixtures of substances, mostly proteins with different enzymatic activities. Once inoculated in tissues they cause both local and systemic actions, which may lead to severe dysfunction in highly vascularized organs such as kidney, a process that may lead to acute renal failure. Another group of medical importance venom that is being investigated is the venom of bee *Apis mellifera*. This venom is responsible for several medical complications. Poisoning by bites of *A. mellifera* induces local inflammatory response and also systemic including acute renal failure. Although renal dysfunction has been described in the literature, little is known about cellular and molecular mechanisms involved in this disorder. We evaluated the cytotoxic effects of *Bothrops jararacussu* and *A. mellifera* crude venom on the LLC-PK1 cell line and its antagonism by heparin. **Methods and Results:** The direct action of crude venom of *B. jararacussu* and *A. mellifera* and different concentrations of heparin on the renal LLC-PK1 cell line were studied in vitro. The lesion was characterized quantitatively by LDH release and viability by staining with trypan blue and the count of living cells in a Neubauer hemocytometer. Incubation of LLC-PK1 cells with 50 µg/mL of *B. jararacussu* venom for 3 h and 25 µg/mL of *A. mellifera* venom for 15 minutes and 1 h increased LDH release up to 1130,7 ± 134,8 U/L (n=12), 558,8 ± 32,5 U/L and 875,9 ± 38,8 U/L (n=6), respectively, compared to their controls (122,9 ± 22,9, 25,8 ± 08 and 5,3 ± 5,3 U/L, respectively, $p < 0.01$). Increasing concentrations of heparin pre-incubated with these poisons in the concentrations and times described were able to antagonize the increased LDH release, with a maximal reduction of approximately 75% and 65% and 45%, respectively. Heparin was also able to inhibit cell death caused by these poisons. **Conclusion:** Our study demonstrates that the venom of *B. jararacussu* and *Apis mellifera* has a cytotoxic action in these kidney cells and that heparin, a polyanionic molecule, has an important protective effect, probably due to its interaction with positive aminoacid residues present in venom's proteins. **Financial Support:** CAPES, CNPq, PRONEX and FAPERJ

**09.032** ***Piper spp***. **Amazon**: **antimicrobial activity of extracts and essential oils**. Soares-Mota MR[1], Batista AC[1], Cunha ALB[1], Santos SM[2], Souza DJF[2], Pohlit AM[3], Fernandes OCCF[4], Chaves CMC[1] [1]EMBRAPA – Medicinal Plants, [2]Literatus, [3]INCA – Natural Products Research, [4]Fiocruz – Biodiversity

**Introduction:** The Family Piperaceae is one of the most represented in the flora of the Amazon biome. Some species of *Piper* are used in folk medicine for the treatment of various diseases. The present work aims to study pharmacological *in vitro* antimicrobial extracts and essential oil of *Piper* species against species of bacteria and fungi commonly associated with human diseases. **Methods:** The leaves of *Piper hispidum* (**Ph**), *Piper tuberculatum* (**Pt**) and *Piper marginatum* (**Pm**) were collected and the leaf powder were exhaustively extracted with $H_2O$/EtOH (1:1), concentrated entirely and dried to provide the hydroalcoholic extract, designated $\mathbf{EEA_{Ph}}$, $\mathbf{EEA_{Pt}}$ and $\mathbf{EEA_{Pm}}$. In a water bath at a temperature of about 120 °C, the powder of the leaves of **Ph**, **Pm** and **Pt** in distilled water under manual shaking, filtered and lyophilized to obtain the aqueous extract termed $\mathbf{EA_{Ph}}$, $\mathbf{EA_{Pt}}$ and $\mathbf{EA_{Pm}}$. The extraction of essential oils was conducted in *Clevenger* type system by hydrodistillation and was coded $\mathbf{O_{Ph}}$, $\mathbf{O_{Pt}}$ and $\mathbf{O_{Pm}}$. The extracts and essential oils were analyzed the minimum inhibitory concentration test (MIC) in sterile microplates of 96 holes were added 100 µL of liquid culture medium (broth) in all holes. The line in the plate samples were added (100 µL) of the extracts and essential oils to be analyzed at a concentration of 100 µg/mL solubilized in alcohol. The MIC was determined as the lowest concentration of active compound capable of inhibiting cell growth. **Results:** The minimum inhibitory concentration against *Staphylococcus aureus* through with extracts $\mathbf{EEA_{Ph}}$ (25 µg/mL), $\mathbf{EEA_{Pt}}$(1,5 µg/mL), $\mathbf{EEA_{Pm}}$(1,5 µg/mL),$\mathbf{EA_{Ph}}$(25 µg/mL), $\mathbf{EA_{Pt}}$ (1,5 µg/mL), $\mathbf{EA_{Pm}}$(6,2 µg/mL) and essential oils $\mathbf{O_{Ph}}$ (12,5 µg/mL), $\mathbf{O_{Pt}}$ (3,1 µg/mL), $\mathbf{O_{Pm}}$ (1,5 µg/mL); against *Escherichia coli* through with extracts $\mathbf{EEA_{Ph}}$ (25 µg/mL), $\mathbf{EEA_{Pt}}$(12,5 µg/mL), $\mathbf{EEA_{Pm}}$(12,5 µg/mL),$\mathbf{EA_{Ph}}$(50 µg/mL), $\mathbf{EA_{Pt}}$ (12,5 µg/mL), $\mathbf{EA_{Pm}}$(6,2 µg/mL) and essential oils $\mathbf{O_{Ph}}$ (12,5 µg/mL), $\mathbf{O_{Pt}}$ (12,5 µg/mL), $\mathbf{O_{Pm}}$ (1,5 µg/mL); against *Pseudomonas aeruginosa* through with extracts $\mathbf{EEA_{Ph}}$ (25 µg/mL), $\mathbf{EEA_{Pt}}$(12,5 µg/mL), $\mathbf{EEA_{Pm}}$(12,5 µg/mL),$\mathbf{EA_{Ph}}$(50 µg/mL), $\mathbf{EA_{Pt}}$ (3,1 µg/mL), $\mathbf{EA_{Pm}}$(1,5 µg/mL) and essential oils $\mathbf{O_{Ph}}$ (12,5 µg/mL), $\mathbf{O_{Pt}}$ (1,5 µg/mL), $\mathbf{O_{Pm}}$ (1,5 µg/mL). The results of antifungal activity were confirmed for the extracts $\mathbf{EEA_{Ph}}$(50 µg/mL), $\mathbf{EEA_{Pt}}$ (50 µg/mL), $\mathbf{EEA_{Pm}}$ (50 µg/mL),$\mathbf{EA_{Ph}}$(50 µg/mL), $\mathbf{EA_{Pt}}$ (50 µg/mL), $\mathbf{EA_{Pm}}$ (50 µg/mL) and essential oils $\mathbf{O_{Ph}}$ (50 µg/mL), $\mathbf{O_{Pm}}$ (50 µg/mL), $\mathbf{O_{Pm}}$ (50 µg/mL) against yeast *Candida albicans*. Results were negative in tests using *Penicillium sp.* and *Aspergilus sp.* **Discussion:** The study so far is proving the potential therapeutic antimicrobial activity of extracts and essential oils from the leaves of *Piper spp.* Such activity is probably related to the presence of compounds of the class of terpenes, alkaloids and amide already described with similar activity in the Family Piperaceae species. The group aims to identify the active chemicals compounds of the species of *Piperspp*. The study as prototypes certainly contributes to obtaining herbal effective. **Acknowledgements:** This research was supported by grants from CAPES (Coordination of Improvement of Higher Education Personnel).

**09.033 Gastroprotective effect of hydroalcoholic extracts of croton *Argyrophylloides* Muell Arg**. Silva TFS, Gama CS, Araújo SA, Estevam CS, Batista JS UFS – Fisiologia

**Introduction**: *Croton argyrophylloides* is a plant of the semi-arid of the Brazil Northeast and popularly known as “sacatinga” and “marmeleiro prateado”. It is used by traditional popular medicine in the treatment of pain, heartburn and indigestion. The hydroalcoholic extract of *Croton argyrophylloides* (HECA) contains flavonoids, steroids, alkaloids, saponins and diterpenoids. In addition, HECA presents antioxidant properties, which suggest a correlation with gastroprotective activity. Therefore, the aim of this study is to evaluate the antiulcer activity of HECA on ethanol- and indomethacin-induced ulcers. **Methods**: the experimental protocols were approved by the Ethics Committee for Animal Research of the Federal University of Sergipe (protocol 56/12). In the gastroprotective activity tests, rats were orally treated with HECA (50, 100 and 200 mg/kg), ranitidine (50 mg/kg) and 5% Tween 80 (Control). One hour after the above treatments, the animals received oral treatment with ethanol (0.4 mL/100 g) or indomethacin (100 mg/kg). One half h and 6 h after administration of ethanol and indomethacin, respectively, the animals were sacrificed, their stomachs were removed and ulcers were quantified. Evaluation of gastric antisecretory activity HECA was performed by pylorus ligation test. The rats were anesthetized with ether and the pylorus was ligated. Afterward, HECA (50, 100 and 200 mg/kg), ranitidine (50 mg/kg), and 5% tween 80 were intraduodenally administered. Four hours after the above treatments, the rats were anesthetized with ether and the gastric content was collected and centrifuged. The gastric volume, pH, proton concentration of the supernatant were determined. Results: the HECA presented gastroprotective effect against ethanol- and indomethacin-induced ulcers at all doses tested. The percentages of gastric lesions induced by ethanol (m ± epm) were 8.3 ± 1.1, 3.4 ± 0.7 and 0.08 ± 0.03% in the animals treated with HECA at the doses of 50, 100, and 200 mg/kg, respectively, and 21.7 ± 4.2 and 0.3 ± 0.1% in the animals treated with 5% tween 80 and ranitidine, respectively. The percentage of indomethacin-induced gastric ulcers were 1.0 ± 0.2, 0.6 ± 0.2 e 0.13 ± 0,05% in the animals treated with HECA at the doses of 50, 100, and 200 mg/kg, respectively, and 4.5 ± 0.9 and 0.8 ± 0.3% in the animals treated with 5% tween 80 and ranitidine, respectively. Volume gastric, pH and proton concentration values were not significantly modified by HECA. **Discussion**: The present results indicate that HECA presents antiulcer effect against ulcer induced by either ethanol or indomethacin and does not involve antisecretory activity. In addition, ethanol-induced ulcers inhibition by HECA suggests that antiulcer effect of HECA is related to its antioxidant property. **Support financial**: CNPq and FAPITEC.

**09.034 Anti-allergic activity of *Stephanolepis hispidus* skin aqueous extract in an allergic pleurisy model in mice**. Ferraris FK[1], Costa TEMMC[2], Penido C[2], Fernandes LDA[3], Amendoeira FC[1] [1]INCQS-Fiocruz – Farmacologia, [2]Farmanguinhos-Fiocruz – Farmacologia Aplicada, [3]IEAPM – Oceanografia

**Introduction**: *Stephanolepis hispidus* is one of the most common filefish species in Brazil and is popularly known as “peixe-porco”, “peroá” or “cangulo”. Although some people living in the northern coast of Rio de Janeiro, Southeast of Brazil, usually consume *S.hispidus* and others filefishesas the main source of protein, meanwhile the *S. hispidus* skin is discarded. Its skin is traditionally used as a complementary treatment for inflammatory disorders. Many traditional fishermen in those areas consume water infusion of dried and powdered skin of filefishes as a complementary treatment for inflammatory disorders of the respiratory system. This study was undertaken in order to investigate the effect of aqueous crude extract of *S. hispidus* skin (SAE) in a model of allergic pleurisy. **Objective**: In the current study we investigated the antiallergic effects of aqueous crude extract of *S. hispidus* skin (SAE) in a model of allergic pleurisy. **Methods:** *Animals*: BALBc mice (20–25 g) provided by Oswaldo Cruz Foundation breeding unit (Rio de Janeiro, Brazil) were used (CEUA, Fiocruz; license n. L-0004/08). *Induction of pleurisy*: Presensitezed mice were challenged with an intrapleural (i.pl.) injection of OVA (12.5 µg/cavity) diluted in sterile PBS. Twenty-four hours after the stimulus, the mice were euthanized and their thoracic cavities were rinsed with 1 ml of saline containing EDTA (10 mM), pH 7.4. Total and differential cell counts from pleural washes were determined using a Neubauer chamber, under an optical microscope, after dilution in Turk fluid (2% acetic acid). Alternatively, total protein levels were measured by Bradford protein assay. *Preparation of extract*: The aqueous crude extract of *S.hispidus* skin (SAE) were obtained by infusion with 1 liter of boiling distilled water of triturated skin, followed by filtration and lyophilization. At the time of use, extract was reconstituted in 0.9% sterile saline at the required doses. *Treatments*: mice received an intraperitoneal (i.p.) injection of SAE (1–100 mg/kg) diluted in sterile PBS or of dexamethasone (1 mg/kg) 1 h prior to OVA stimulation. **Results:** The intra-peritoneal (i.p.) pretreatment with SAE (100 mg/kg) in previously sensitized BALBc mice impaired total leukocyte (sal 11.0 ± 1.4; ova 35.9 ± 5.9; dexa 20.6 ± 0.6; SAE 23.4 ± 1.8 x $10^5$ cells, n=6) and eosinophil influx (sal 0.4 ± 0.0; ova 8.9 ± 0.8; dexa 2.1 ± 0.6; SAE 3.5 ± 0.8 x $10^5$ cells, n=6) into pleural cavities triggered by the i.pl. challenge with ovalbumin. In accordance with such results, Bradford protein assay showed decreased levels of total protein in the pleural cavities of SAE pretreated mice 24 h after OVA i.t. stimulation (sal 240.0 ± 3.5; ova 623 ± 5.8; dexa 340.6 ± 6.6; SAE 355.1 ± 2.8 µg/ml, n=6). **Conclusion**: Our results provide evidence that aqueous crude extract of *S. hispidus* skin might decrease allergic inflammatory response. **Supported by** FIOCRUZ**.**

**09.035 Antioxidant and vasodilatory activities and chemical evaluation of the ethanolic extract of aerial parts of *Stachytarpheta schottiana* (Verbenaceae)**. Moreira AP, Leal MCR, Ferreira LLDM, Zanetti GD, Leal ICR, Guimarães DO, Muzitano MF, Carmo PL, Raimundo JM
UFRJ

**Introduction:** The Restinga of Jurubatiba National Park, located in the northern Rio de Janeiro state, protects a coastal region of great biodiversity where we can find *Stachytarpheta schottiana*. Other species of the *Stachytarpheta* genus, as *S. jamaicensis* and *S. cayennensis*, are popularly used for the treatment of hypertension[1,2]. Therefore, the objective of this study was to evaluate the antioxidant and vasodilatoy activities of the ethanolic extract of *S. Schottiana* (EES), as well as, its chemical profile. **Methods:** Aerial parts of *S. schottiana*were dried, pulverized and subjected to a maceration process with EtOH: $H_20$ (70:30). The solution obtained was concentrated in rota-evaporator and the crude extract assessed by TLC and revealed with different specific reagents. EES was also assessed by analytical HPLC-DAD using a gradient system comprising different proportions of acetonitrile and water. Liquid–liquid fractionation of EES yielded an ethyl acetate fraction (EAFS). DPPH assay was used for investigate the antioxidant activity of EES. The vasodilatory activity was evaluated by using isolated aorta from male Wistar rats (220-280g) prepared for isometric tension recording. Aortic rings were placed in vertical chambers filled with Krebs-Henseilet solution continuously oxygenated with carbogen gas (95% $O_2$/ 5% $CO_2$), at 37°C. Vascular smooth muscle contraction was induced with phenylephrine (10 µM) and then cumulative concentrations of EES or EAFS were tested (1–300µg/ml). It were used aortas with and without endothelium, which was considered intact if the relaxation induced by acetylcholine (10µM) was greater than 80%. All protocols were approved by the Animal Care and Use Committee under license Macaé01. **Results:** EES analysis by TLC indicated the presence of phenolic substances when used under UV-PEG NP as specific reagent. HPLC-DAD analysis showed the presence of 5 majority peaks with retention times between 20 and 25 minutes. The UV spectra of two peaks in the chromatogram showed the following maximum absorbance: 210, 217 and 331nm. In the DPPH assay, the half maximal effective concentration of EES was 96.01 µg/ml. EES and EAFS caused a concentration-dependent relaxation in aortas with endothelium. At 300µg/ml, EES and EAFS produced a relaxation of 60.02 ± 3.15% and 47,18 ± 3,12%, respectively (n= 4-7, $P<0.05$). Removal of endothelium partially inhibited EES-induced vasodilation. Relaxation was reduced to 22.47 ± 0.75% at 300 µg/ml ($P<0.05$). **Discussion:** These data suggest the presence of a skeleton compatible with a phenylpropanoid[3]. Verbascoside stands out in this chemical group and has already been isolated in species of the genus *Stachytarpheta*[4]. The other three peaks exhibit maximum absorbance at 254 and 365 nm, consistent with the class of flavonoids. The mechanism of action of EES vasodilatory activity seems to involve the release of endothelial factors and a direct effect on vascular smooth muscle. EAFS appears to be partially responsible for EES vasodilation. **References:**[1]Garcia-Gonzales M. Rev Cubana Plant Med 7:100, 2002; [2]Idu M. Int J Pharmacol 2:163, 2006; [3]Santos PML. Rev Bras Farmacogn 20:147, 2010; [4]Okokon JE. Indian J Pharmacol 40:111, 2008. **Financial support:** FAPERJ, FUNEMAC, UFRJ.

**09.036 Participation of the TRP channels in vasorelaxant effect induced by carvacrol in vascular tissue from spontaneously hypertensive rats**. Ramos-Reis M[1], Almeida MM[2], Alves QL[1], Ferreira JM[1], Albuquerque JM[1], Simões LO[1], Silva DF[1] [1]UFBA – Biorregulação, [2]UFPB – Biotecnologia

**Introduction:** Carvacrol, a monoterpenoid phenol, is a natural product isolated of essential oils of various plants used in popular medicine. The aim of our study was to investigate the vasorelaxant effect induced by carvacrol in spontaneously hypertensive rats (SHR) and the involvement of potential receptor transient channels (TRP) in mediating this response. **Methods:** Isolated SHR superior mesenteric artery rings (1-2 mm) were suspended by cotton threads for isometric tension recordings in a Tyrode's solution at 37 ºC, gassed with a 95% $O_2$ and 5% $CO_2$, under a resting tension of 0.75g. (CEUA/UFBA Nº 012/2011). **Results and Discussion:** In phenylephrine (Phe, 1µM)-precontracted mesenteric artery rings, carvacrol ($10^{-8}$ - $10^{-3}$ M) induced a concentration-dependent relaxation ($pD_2$ = 5.2 ± 0.05; Maximum Response (MR) = 115.1 ± 5.5%, N=8). After removal of the vascular endothelium, carvacrol promoted a concentration-dependent rightward shift of the response-curve, with no changes in the MR ($pD_2$ = 4.9 ± 0.05; MR = 112.8 ± 5.4%, N=9, $p < 0.01$), suggesting that vasorelaxantion induced by carvacrol appears to be mediated by vascular endothelium and smooth muscle. Based on the preliminary results, the subsequent experiments were performed to investigate the endothelium-independent relaxation induced by carvacrol. Then, to investigate the involvement of TRP channels in the vasorelaxant effect induced by carvacrol, rings were pre-incubated with non-selective distinct inhibitors these channels. In presence of ruthenium red ($10^{-5}$ M), N-(4-t-Butylphenyl)-4-(3-Chloropyridin-2-yl)tetrahydropyrazine-1(2H)-carboxamide (BCTC) ($2x10^{-6}$ M), gadolinium ($10^{-4}$ M), lantanium ($10^{-4}$ M) and magnesium ion (2.25 mM), no significant changes in potency or efficacy of carvacrol were observed ($pD_2$ = 5.2 ± 0.08; N=9; $pD_2$ = 5.05 ± 0.29; N=5; $pD_2$ = 4.8 ± 0.12; N=9; $pD_2$ = 4.8 ± 0.05; N=8; $pD_2$ = 5.02 ± 0.02; N=7; respectively). However, in the presence of capsaicine ($10^{-5}$ M, desensitizing TRPV1) the potency of carvacrol was significantly reduced ($pD_2$ = 4.5 ± 0.15; N=5; $p<0.05$), suggesting that TRPV1 participates in the vasorelaxation mediated by monoterpenoid. In conclusion, these results suggest that carvacrol induced vasorelaxant effect in superior mesenteric artery isolated from SHR might act, at least in part, through TRPV1 channels. **Sources of research support:** FAPESB; CNPq

**09.037 Carvacrol induces vasorelaxant effect by inhibiting calcium influx in vascular tissue from spontaneously hypertensive rats**. Ferreira JM, Ramos-Reis M, Alves QL, Albuquerque JM, Silva DF UFBA – Biorregulação

**Introduction:** L-type voltage-dependent calcium channels ($Ca_v$), receptor-operated channels (ROC) and store-operated channels (SOC) play a putative role in vascular contraction. Carvacrol, a monoterpenoid isolated from essential oils of various plants, is known to act through different ionic channels. The aim of this study was to investigate the contribution of calcium channels on the vasorelaxant effects induced by carvacrol in isolated mesenteric artery from spontaneously hypertensive rats (SHR). **Methods:** Isolated rat superior mesenteric artery rings (1-2 mm) were suspended by cotton threads for isometric tension recordings in a Tyrode's solution at 37 ºC, gassed with a 95% $O_2$ and 5% $CO_2$, under a resting tension of 0.75g (CEUA/UFBA nº 012/2011). **Results and Discussion:** In phenylephrine (Phe, 1µM)-precontracted mesenteric artery rings from hypertensive rats, carvacrol ($10^{-8}$ - $10^{-3}$ M) induced a concentration-dependent relaxation ($pD_2$ = 5.2 ± 0.05; Maximum Response (MR) = 115.1 ± 5.5%, N=8), which was not observed after vehicle solution administration (data not shown). After removal of vascular endothelium, carvacrol promoted a discrete rightward shift of the response-curve, with no changes in the MR ($pD_2$ = 4.9 ± 0.05; MR = 112.8 ± 5.4%, N=9, $p < 0,01$). These data suggest that vasorelaxantion response induced by carvacrol appears to involve direct participation of vascular smooth muscle. Based on the preliminary results, the following experiments were performed to investigate the endothelium-independent relaxation induced by carvacrol. Under nominally $Ca^{2+}$-free conditions, isolated concentrations of carvacrol ($10^{-5}$, $10^{-4}$ or $10^{-3}$ M) significantly attenuated extracellular $Ca^{2+}$-induced contractions in Phe (1 µM) pre-incubated vessels, in the presence of nifedipine and cyclopiazonic acid, suggesting a possible inhibition of calcium influx through store operated channels (SOC) and receptor operated channels (ROC). Furthermore, carvacrol ($10^{-4}$ M) significantly inhibited the contractile response to the re-introduction of $Ca^{2+}$ in artery rings incubated in $Ca^{2+}$-free high-$K^+$ buffer.Our results suggest that carvacrol induced-vasorelaxation on SHR isolated superior mesenteric artery, might act by inhibiting $Ca^{2+}$influx through $Ca_v$, SOC and ROC. **Sources of research support:** FAPESB; CNPq.

**09.038** ***Yerba mate*** **extract increase** ***in vitro*** **biomineralization in osteogenic differentiation model of rat bone marrow-derived mesenchymal stromal cell**. Brito VGB, Barros TL, Nakamune ACMS, Chaves Neto AH, Oliveira SHP FOA-Unesp – Ciências Básicas

**Introduction:** The aim of this study was to investigate the effect of yerba mate (*Ilex paraguariensis*) extract in rat bone marrow-derived mesenchymal stromal cells (BmMSCs) during osteogenic differentiation. **Methods:** BmMSCs culture was obtained from Wistar male rats (about 4 weeks old). The experimental protocol was approved by the Institutional Animal Welfare Committee at the School of Dentistry of Araçatuba (Process 00716-2012). BmMSCs were harvested by flushing out bone marrow from femurs with proliferation medium (PM), supplemented with 10% fetal bovine serum. Culture flasks were maintained at 37 °C in humidified atmosphere of 5% $CO_2$and culture medium was replaced every 4 days. When culture reached about 80% confluence, cells were seeded in 24-well plate at 75000 cells/well, which were used for all subsequent experiments. For cytotoxicity experiments, BmMSCs were treated with PM or osteogenic medium (OM - proliferation medium plus 50 µg/mL ascorbic acid, 10 mM β-glicerophosphate and 10 nM dexamethasone) plus different yerba mate extract concentrations (1, 10, 20, 50, 75, 100 and 200 µg/mL) for 7 days and cell viability was determined by MTT assay. For differentiation experiments, groups were divided into PM and OM treated or not with 10, 20 and 50 µg/mL of yerba mate extract. From the beginning of treatment, proliferation rate, alkaline phosphate (ALP) activity and total protein content were evaluated by colorimetric methods, at $0^{th}$, $7^{th}$ and $10^{th}$ day and extracellular matrix mineralization was determined by alizarin stain at $10^{th}$ day. **Results:** *In vitro* cytotoxicity assay, the half maximal inhibitory concentration ($IC_{50}$) values were not reached when BmMSCs were treated with yerba mate extract in different concentrations in PM, however when treated in the same concentrations using OM, the $IC_{50}$ value has been found between 100 and 200 µg/mL. In the differentiation experiments, only 50 µg/mL yerba mate extract concentration showed significant cytotoxic effect at $10^{th}$ day of treatment, exhibiting 36.60% reduction in proliferation rate, similar results are seen in protein content data, with a reduction of 40% relative to OM. ALP activity showed no significant change except at the $10^{th}$ day, when OM showed an increase of 320% when compared to PM and the group treated with 10 µg/mL of extract exhibited 12% higher ALP activity to OM. Analysis of the extracted alizarin showed an extracellular matrix calcification 290% higher in the group treated with 10 µg/mL of extract relative to the OM. **Discussion:** The positive role of yerba mate has been associated with protective effect, mainly related with its phenolic compounds and their antioxidant properties, however our results suggest a direct stimulatory effect in biomeralization, independent of the analyzed parameters in this study. An extracellular matrix proteins qualitative analysis may provide an explanation for this direct stimulatory effect, elucidating the genic expression profile of proteins directly involved or not with mineral deposition. **Financial agency:** FAPESP (Grant # 2012/20547-1; 2011/06070-5 and 2011/19458-1).

**09.039 Cardiovascular responses to *Lachesis muta* (South American bushmaster) snake venom in anesthetized rats**: **No cholinergic involvement**. Dias L[1], Rodrigues MAP[1], Soubhia PC[2], Brunieri LVP[1], Brunieri LVP[1], Rennó AL[1], Melgarejo AR[3], Hyslop S[1] [1]FCM-Unicamp – Farmacologia, [2]Unicamp – Controle de Intoxicações, [3]IVB – Zoologia Médica

**Introduction**: Systemic envenoming by *Lachesis muta* (South American bushmaster) in humans results in coagulopathy, bradycardia, hypotension and activation of the autonomic nervous system, with manifestations such as abdominal pain, diarrhea and vomiting. In this work, we examined the cardiovascular responses to Peruvian *L. muta* venom in rats. **Methods and Results:** Male Wistar rats (300-400 g) were anesthetized with isoflurane (2% in 98% air); the left carotid artery was cannulated for blood pressure measurement and a femoral vein was cannulated for venom injection (1.5 mg/kg) and arterial blood sampling. Heart rate and ECG were monitored electronically and respiratory rate was determined manually. Changes in cardiovascular parameters were monitored for 240 min after which the rats were killed with an overdose of anesthetic. Heart, lung, liver and kidney samples were processed for histological analysis. The experiments were approved by an institutional Committee for Ethics in Animal Use (CEUA/UNICAMP, protocol no. 2182-1). The results (mean±SEM) were analyzed with ANOVA followed by the Tukey-Kramer test, with $p<0.05$ indicating significance. All rats injected with venom survived until the end of the experiment. Venom caused immediate hypotension that was maximal after 5 min [mean arterial blood pressure fell from 95±7 to 44±2 mmHg; n=5; $p<0.05$] but gradually returned to baseline over 60 min, decreasing again at 120 and 240 min. There were no significant changes in heart rate or respiratory rate. In the ECG, the QRS interval and amplitude tended to increase, as did the P and T wave amplitudes. Pretreating the rats with atropine (2 mg/kg, i.v., 20 min before) did not attenuate the venom-induced hemodynamic alterations and plasma cholinesterase activity was not significantly altered. Treatment with L-NG-monomethyl-L-arginine (L-NMMA; 30 mg/kg, i.v., 20 min before), an inhibitor of nitric oxide synthase (NOS), had no significant effect on hemodynamic parameters. In contrast, Nw-nitro-L-arginine methyl ester (L-NAME; 20 mg/kg, i.v., 20 min before) potentiated the hypotension and lethality of the venom. Creatine kinase-MB was significantly ($p<0.05$) elevated at 120 and 240 min compared to baseline values (from 44±14 to 91±25 and 69±16 IU/L, respectively; n=5), whereas LDH and glucose levels were unaltered. Macroscopically, there was marked but well-delimited hemorrhage in the ileum. Histological analysis showed discrete hemorrhage and a small infiltration of inflammatory cells in the kidney and liver; hemorrhage was more marked in the lungs. **Conclusion**: In rats, *L. muta* venom causes hypotension predominantly by affecting the vasculature, with little cardiac involvement. There is no significant cholinergic involvement in the hemodynamic responses to venom. The cause of the divergent effects of L-NAME and L-NMMA is unclear, but could reflect differences in the susceptibility of NOS isoforms to inhibition. **Financial support:** CAPES, CNPq, FAPESP.

**09.040 Anxiolytic-like effects of acute and repeated treatment with *Cissussicyoides* (Vitaceae) extract**. Souza TS[1], Froza MG[1], Silva JD[1], Duarte RP[2], Scarpelim OJ[3], Baretta IP[4]
[1]Unipar – Biomedicine, [2]Unipar, [3]Unipar – Nursing, [4]Unipar – Pharmacology

**Introduction**: The genus Cissus is the largest family Vitaceae, with about 350 species distributed between the Americas, Asia and Australia. The *Cissussicyoides* V. is a woody vine, vine-called miraculous, indigo-climbing and popularly called plant insulin, being a native plant of Brazil (Beltrame et al., 2001). With the increasing demand for drugs, the search for alternative sources and implementation of studies and validation of the use of medicinal plants that seem more justifiable (Biavatti et al., 2007), so the aim of this study was to evaluate the possible central action of the crude *extract Cissussicyoides* in mice. **Methodology**: We used adult male Swiss mice. A temperature of 20 ± 2 ° C and the cycle of light/dark 12h (6h to 18h of light) were controlled automatically. The animals had free access to food and water except during the experiments. The experimental and control groups (n = 8/group) were randomized and received orally crude extract of *Cissussicyoides* (EB) at doses of 0, 25, 50, 250, 500 mg / kg and diazepam (0.75 mg / kg), respectively twenty-five consecutive days. Animals subjected to the elevated plus-maze (EPM), hind-limb splay, hole-board, marble-burying, tail suspension and forced swimming tests. All experiments were conducted between 8:00 and 13:00, after approval by the Ethics Committee (Protocol No 22232/12). On the day of the experiments the animals were habituated to the experimental conditions for at least 1 hour before. **Results and Discussion**: EB significantly reduced dose dependent, the number of marble buring and significant increase in the length of stay and number of entries in the open arms in the EPM. In tests hind-limb splay and hole-board, the chronic treatment of EB no significant changes in exploratory activity and muscle relaxation. These results demonstrate that the anxiolytic action occurred without modification of exploratory activity and motor, which may be a good indicator of the effect on the reduction of muscular activity even after chronic administration. These results indicate that the EB Cissus sicyoides repeatedly administered orally presents a possible anxiolytic effect without changing the motor activity. This plant has potential for the search of a herbal medicine with anxiolytic action. Experiments are being conducted with different fractions of the plant, to complement these results. BELTRAME FL. et al. Phytochemical study and evaluation of the potential antidiabetic Cissus sicyoides L. (Vitaceae). Quim Nov, vol 24, p 783, 2001. BIAVATTI MW.et al. (2007) Ethnopharmacognostic survey on botanical compendia for potential cosmeceutic species from Atlantic Forest. Rev Bras Farmacogn, vol 17, p 640, 2007. Financial Agencies: Fundação Araucária and UNIPAR.

**09.041 Antiedematogenic effect of Carvacrol in histamine-, dextran- and substance P-induced edema in mice**. Silva FV[1], Sousa-Neto BP[1], Arcanjo DDR[1], Machado FDF[1], Quintans-Júnior LJ[2], Guimarães AG[2], Oliveira FA[1], Oliveira RCM[1] [1]UFPI – Medicinal Plants Research, [2]UFS – Physiology

**Introduction:** Essential oils are volatile mixtures, natural and complex and characterized by pungent odor produced by aromatic plants. Many essential oils have pharmacological properties including analgesic, anti-inflammatory and spasmolytic. Carvacrol is a monoterpene constituent of the essential oil produced by many herbs and spices. The aim of this study was to investigate the activity of carvacrol antiedematogenic models of paw edema induced by histamine, dextran and substance P in mice. **Methods:** Swiss mice (30-35 g), male and female (n=7/group). All experimental protocols were approved by Ethics Committee for Animal Research of the Federal University of Piaui, Brazil (n° 044/10). In the paw edema induced by histamine or dextran, the animals were orally treated with vehicle (NaCl 0.9%), carvacrol (25, 50 and 100 mg/kg) or cyproheptadine (10 mg/kg). After 1 h of treatment, animals received 0.05 mL of application/paw (i.pl.) of histamine (10 mg/kg) or dextran (150 mg/kg) into the right paw and the paw of vehicle left. After 1 hour of histamine induced edema and after 2 h of induction of dextran edema and the animals were euthanized with an overdose of anesthesia and the hind legs were cut at the level of the tibio-tarsal joint and weighed. The swelling was recorded as the weight difference between right and left paws of each animal and was expressed in milligrams (mg). Edema induced by substance P, animals received 20 µL of substance P (30 nmol, i.pl.) in the right hind paw and the same volume of vehicle contralateral paw. The animals were treated orally with vehicle, carvacrol (25, 50 and 100 mg/kg) or ruthenium red (3 mg/kg) 1 hour before edema substance. 1 hour after edema induction, the animals were euthanized and edema measured as previously mentioned in the model of paw edema induced by histamine and dextran. Data were expressed as mean ± E.P.M. and considered significant at * $p < 0.05$ (One-way ANOVA followed by Tukey post- test). **Results and Discussion:** In models of paw edema induced by histamine and dextran, carvacrol was effective only at a dose of 50 mg/kg reduced the edema formation by 46% (40.23 ± 6.80* mg) and 35% (36.42 ± 2.01* mg) respectively in the two models, cyproheptadine reduced the edema by 61% (28.90 ± 2.98* mg) and 43% (32.28 ± 3.91* mg) compared to vehicle group (75.75 ± 5.99 mg e 56.71 ± 4.75 mg) respectively in the two models. Edema induced by substance P, carvacrol (100 mg/kg) and ruthenium red (3 mg/kg) reduced the edema formation by 46% (26.62 ± 6.05* mg) and 40% (29.78 ± 5.69* mg), respectively, compared to vehicle group (49.66 ± 4.42 mg). These results suggest antiedematogenic action of carvacrol, which seems to interfere with the synthesis or release of prostanoids involved in the inflammatory process. **Financial Support:** UFPI/UFS/CAPES.

**09.042 Gastroprotective effect of (-)-myrtenol against gastric ulcer induced by ibuprofen and cold restraint-stress, in rodents**. Viana AFSC[1], Carvalho EF[1], Lima GS[1], Oliveira IS[1], Silva FV[1], Reis Filho AC[1], Sousa DP[2], Oliveira RCM[1] [1]UFPI – Medicinal Plants, [2]UFPB

**Introduction**: The (-)-myrtenol is a natural monoterpene used in the manufactured of detergents, fine fragrances, shampoos, toilet soaps and other toiletries (Bhatia, Food Chem. Toxicol. 46:S237, 2008). This monoterpene is present in several plant species, such as the *Rhodiola rosea* L. (Crassulaceae) possess antioxidant, neuroprotective and anticancer activities. Previous studies revealed gastroprotective effect of (-)-myrtenol against ethanol-induced gastric ulcer. The present study aimed to analyze the gastroprotective activity of (-)-myrtenol in models of gastric ulcer induced by ibuprofen and cold restraint-stress in mice and rats respectively. **Methods:** For this study, female Swiss mice (25-30 g) and Wistar rats (200-250 g) with two months of age, kept under controlled conditions (24 ± 1°C, 12-h dark/light cycle) and access to food and water *ad libitum* were used. The animals were fasted for 18h, prior to all assays. The gastroprotective activity was evaluated against gastric lesions induced by ibuprofen, nonsteroidal antiinflammatory drug. In this model, mices were orally treated with control (saline 10 mL/kg), cimetidine (100 mg/kg) or (-)-myrtenol (25, 50 and 100 mg/kg). After 1 h, the animals orally received ibuprofen (400 mg/kg). After six additional hours, the rats were anesthetized and their stomachs were removed, opened along the greater curvature and scanned; the ulcer area ($mm^2$) was determined by planimetry. In the model of cold restraint stress-induced gastric ulcers, the rats were orally treated with control (saline 10 mL/kg), (-)-myrtenol (25, 50 and 100 mg/kg, p.o.) or cimetidine (100 m/kg, p.o.). One hour after, rats were individually restrained and placed inside the cages were kept at 4±1 °C for 3 h. After this time, the animals were anesthetized and the stomachs removed and opened along the greater curvature to determine the lesion volume. All experimental protocols were approved by Ethics Committee for Animal Research of the Federal University of Piaui, Brazil (nº 008/12). 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 and Discussion:** Ibuprofen is among the most commonly utilized experimental model for the evaluation of gastroprotective activity in mice. In this model, the (-)-myrtenol presented gastroprotective action at a dose of 100 mg/kg (2,25 ± 0,19* $mm^2$, n=6) and cimetidine 100 mg/g (3,82 ± 0,36* $mm^2$ , n=6) compared with control group (9,02 ± 1,61 $mm^2$, n=7). The volume of erosions of gastric injury induced by cold restraint-stress decreased after oral treatment with (-)-myrtenol at dose of 50 and 100 mg/kg (3,27 ± 0,39* and 1,15 ± 0,45* $mm^2$, respectively, n=5) and cimetidine 100 mg/kg (3,26 ± 0,99* $mm^2$, n=6) when compared with the control group (12, 74 ± 1,05 $mm^2$, n=6). Through these results, we concluded that the (-)-myrtenol promotes gastroprotection against gastric lesions induced by ibuprofen and cold restraint-stress, suggesting a possible involvement of prostaglandins and antioxidant properties in its gastroprotective effect. Further investigations are needed to elucidate additional mechanisms involved in this effect. **Apoio Financeiro**: UFPI/FAPEPI/CAPES/CNPq

**09.043 Gastroprotective and healing activity of the hydroalcoholic fraction from leaves of *Cenostigma macrophyllum* Tul. var. Acuminata Teles Freire**. Viana AFSC[1], Fernandes HB[1], Reis Filho AC[1], Lima GS[1], Santos MO[1], Chaves MH[2], Oliveira RCM[1] [1]UFPI – Medicinal Plants, [2]UFPI – Chemistry

**Introduction**: *Cenostigma macrophyllum* Tul.var. *acuminata* Teles Freire (Leguminosae) is, popularly known as "canela-de-velho", "maraximbé" and "fava-do-campo" in Brazilian Northeastern Region. The hydroalcoholic fraction of *C. macrophyllum* var. *acuminata* leaves (Cm-FHA) exihibit gastroprotective activity in ethanol, ethanol/HCl and ischemia/reperfusion induced gastric lesions. This study evaluated the effect of Cm-FHA in models of gastric lesions induced by cold restraint-stress, as well as the healing effect against gastric ulcers induced by acetic acid after 7 or 14 days of treatment. **Methods**: For, Female Wistar rats (200-250 g, n=6-7) maintened under controlled conditions (24 ± 1°C, 12-h dark/light cycle) and *ad libitum* access to food and water were used. The animals were fasted for 18h, prior to all assays. For the cold restraint stress-induced gastric ulcers model the rats were orally treated with saline (1 ml/100g), Cm-FHA (50, 100, 200 mg/kg) or cimetidine (100 mg/kg). After one hour, rats were individually restrained and placed inside the cages were maintened at 3±1 °C for 3 h. After wards, the animals were euthanized, their stomachs removed and the ulcer area was determined by planimetry ($mm^2$). In acetic acid-induced gastric ulcers model the animals were anaesthetized (Ketamine 30 mg/kg and xylazine 0.3 mg/kg, i.m) and the abdominal wall was opened by laparatomy, gastric ulcers were induced for 70 µl of 80% acetic acid solution applied to the serosal surface of the stomach for 1 min, and then washed with sterile saline. One day after the surgery, the rats were treated orally with saline, Cm-FHA (100 mg/kg) or cimetidine (100 mg/kg) for 7 or 14 days. The seventh day after or fourteenth of treatment the animals were euthanized, the stomachs were removed and the lesion was assessed. All experimental protocols were approved by Ethics Committee for Animal Research of the Federal University of Piaui (nº 008/12). 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 significant**. Results and Discussion**: The Cm-FHA presented gastroprotective action at dose of 100 and 200 mg/kg (3,9 ± 1,2* and 2,5 ± 1,4* $mm^2$, respectively) and cimetidine 100 mg/kg (1,0 ± 0,3* $mm^2$) compared with saline group (10,5 ± 0,9 $mm^2$) against cold restraint-stress-induced gastric lesions. The volume of gastric lesion induced by acetic acid decreased (16,6 ± 3,1* and 4,4 ± 1,8* $mm^3$) after 7 days of the oral treatment with Cm-FHA 100 mg/kg or cimetidine 100 mg/kg respectively, compared with saline group (37 ± 4,5 $mm^3$ ). The Cm-FHA 100 mg/kg and cimetidine 100 mg/kg reduced the volume of gastric ulceration induced by acetic acid in 8,4 ± 3,2* and 6,1 ± 2,1* $mm^3$ respectively, compared with saline group (45,5 ± 4,8 $mm^3$), after 14 days of the oral treatment. These results suggest the Cm-FHA is effective in preventing and healing gastric lesions induced by cold restraint-stress and acetic acid respectively. Considering these data, the Cm-FHA may provide an important contribution to the treatment of gastric ulcers. Further investigations are needed to elucidate the mechanisms involved in these effects. **Financial Support:** UFPI/CAPES/CNPq.

**09.044 A carvacrol synthetic derivative attenuates inflammatory and nociceptive responses**. Bonfim RR[1], Paiva-Souza IO[1], Pereira DS[1], Moraes JP[1], Sousa DP[2], Barreto EO[3], Camargo EA[1] [1]UFS – Physiology, [2]UFS – Pharmacy, [3]UFAL – Cellular Biology

**Introduction**: Monoterpenes, compounds mainly presented in essential oils, have important pharmacological actions. Isopropoxycarvacrol (IPC) is a new derivative of the monoterpene carvacrol and its pharmacological properties have not yet been investigated. The aim of this study was to analyze the anti-inflammatory and antinociceptive proprieties of IPC. **Methods**: This study was approved by the Institution's Animal Ethic Committee (protocol 09/11). We used male Swiss mice (25-30 g) and Wistar rats (150-230 g), which received i.p. injection of IPC at 10, 30 or 100 mg/kg or vehicle (Tween 80, 0.5%), 30 min before the experiments, or at 0.3-3 mg/ear, applied topically during the induction (in the case of mice ear edema test). The nociceptive parameters evaluated were the licking/biting time induced by formalin and the hyperalgesia induced by carrageenan, both injected in the mice paw. We also assessed the locomotor activity of mice in the open field. The inflammatory parameters evaluated were the rat paw edema induced by carrageenan and the mice ear edema induced by TPA (accompanied by the myeloperoxidase activity measurement in the ears). **Results and Discussion**: We observed that the pre-treatment with IPC (100 mg/kg) reduced the licking/biting time of paws, both in the first (34±4 s, $p<0.05$, 100 mg/kg) and second (56±22 and 13±8 s, $p<0.05$, for 30 and 100 mg/kg, respectively) phases of the formalin test, when compared with the vehicle-treated group (63±6 s for first phase and 141±26 s for second phase). Pre-treatment with aspirin or morphine inhibited licking/biting time in the first phase (7±4 s and 5±2 s, respectively $p<0.05$) as well as morphine inhibited this time in second phase (3±1 s, $p<0.01$). Injection of carrageenan (CAR, 3%, 20 uL) in mice paw reduced the threshold of intensity of stimulus of a magnitude of 6.6±0.3 g after 1 h and 6.7±0.3 g after 3 h. This was significantly impaired by 100 mg/kg of IPC (4.4±0.4 and 4.9±0.6 g, for 1 and 3 h respectively, $p<0.05$) and by 15 mg/kg of indomethacin (2.8±0.2 and 3.6±0.6 g for 1 and 3 h respectively, $p<0.05$). No alteration of the locomotor activity was observed in mice in the open field test. In rats, the administration of IPC (100 mg/kg) diminished the area under curve of the paw edema (1.63±0.34 mL.h, $p<0.05$) induced by carrageenan, when compared with the vehicle group (2.86±0.35 mL.h), which was also found by pre-treating rats with dexamethasone (1.40±0.10 mL.h, $p<0.05$). No antiedematogenic effect was observed by the local administration of IPC in the TPA-induced mice ear inflammation, however, the myeloperoxidase activity was decreased in the ears by the simultaneous application of IPC (119±12, 70±6 and 118±14 UMPO/site for 0.3, 1 and 3.0 mg/ear, respectively, $p<0.001$ for all doses), when compared with the vehicle group (229±12 UMPO/site), which was also observed for 0.05 mg/ear of dexamethasone (35±9 UMPO/site, $p<0.001$). These results demonstrate that IPC has anti-inflammatory and antinociceptive activities and suggests that this compound may be of value for the development of monoterpene-derived synthetic compounds as a future strategy to treat acute inflammation. **Financial Support**: FAPITEC/SE.

**09.045 Influence of the route of administration on the cardiovascular responses to *Bothrops atrox* snake venom in anesthetized rats**.

**Introduction:** Envenoming by *Bothrops atrox* can result in systemic effects. In this work, we investigated the influence of the route of *B. atrox* venom administration on blood pressure, heart rate, electrocardiogram (ECG), respiratory rate, marker enzymes (creatine kinase-MB – CK-MB; creatine kinase – CK; lactate dehydrogenase – LDH), glucose and venom kinetics in rats. We also examined the histological alterations caused by venom in selected organs. **Methods:** Male Wistar rats (300-400 g) were anesthetized with isoflurane (2% in 98% air; 1 l/min) and a carotid artery was catheterized for continuous blood pressure measurement. The left femoral vein was catheterized for i.v. venom administration (0.4 mg/kg; n=6; injected in 100 µl and washed in 100 µl of 0.9% NaCl) while for i.m. administration the rats received venom (4 mg/kg in 100 µl; n = 6) in the left gastrocnemius muscle. Changes in cardiovascular parameters were monitored for 120 min. Blood samples were obtained for quantification of CK, CK-MB, LDH and glucose with commercial kits. After 120 min, the rats received an overdose of anesthetic and samples of heart, lung, liver, kidney and gastrocnemius muscle were processed for histological analysis. Urine samples were also collected. Venom was quantified in serum and urine by ELISA. The results (mean±SEM) were analyzed with ANOVA followed by the Tukey-Kramer test, with $p<0.05$ indicating significance. The experiments were approved by an institutional Committee for Ethics in Animal Use (CEUA/UNICAMP, protocol 2181-1). **Results:** Venom injected i.v. caused immediate hypotension that was maximal after 5 min (mean blood pressure decreased from 110±6 to 54±4 mmHg) and gradually returned to baseline over 60 min. The hemodynamic responses to i.m. administration were not significantly different from those seen with i.v. injection. There were no significant changes in heart rate, ECG parameters or respiratory rate after injection by either route. Venom given i.v. caused a progressive increase in LDH and CK was elevated at 120 min with both routes; there were no changes in CK-MB or blood glucose. Circulating venom decreased rapidly after i.v. injection but increased progressively with i.m. administration (indicating absorption from the injection site). At 5 min post-injection, i.e., the maximum decrease in blood pressure, circulating venom concentrations were 963±132 ng/ml (i.v., n=4) and 51±15 ng/ml (i.m., n=4). Venom was detected in urine 2 h after administration (368±147 ng/ml i.v. and 186±66 ng/ml i.m.). There was hemorrhage in the lungs and deposition of proteinaceous material in renal cortex tubules and Bowman's capsular space, but no alterations in heart or liver (for i.v. and i.m.). The gastrocnemius muscle showed hemorrhage only with i.m. administration. **Conclusion:** The route of administration did not significantly influence the pattern and extent of venom-induced cardiovascular changes. There was no correlation between circulating venom concentrations and extent of hypotension. The detection of venom in urine indicated a renal route of elimination. **Financial support:** CAPES, CNPq, FAPESP.

**09.046 Resveratrol reduces maximum contractile response under alpha1-adrenoceptor stimulation in non-vascular smooth muscle**. Vieira DFA[1], Domingos AO[2], Restini CBA[2] – [1]Unaerp – Ciências Farmacêuticas, [2]Unaerp – Medicina

**Introduction**: Stimuli on alpha1-adreneceptor trigger the production/activation of reactive oxygen species (ROS), which are involved in regulating mechanisms of contraction and relaxation in vascular smooth muscle cells (TSAI, J Biomed Sci., 17:67, 2010). Resveratrol (RESV), a polyphenol with widely accepted antioxidant activity (LEONARD, Biochem Biophys Res Commun., 21:269, 2005) has been used to evaluate role of ROS on those mechanisms. We hypothesized that RESV may alter contractile responses stimulated by alpha-1-adrenergic agonist, phenylephrine (PE), in non-vascular smooth muscle. **Aim**: Evaluate the effect of RESV on the contractile response to PE and on its transduction mechanism on the rat anococcygeus smooth muscle. **Methods**: Male Wistar rats (180-200 g, n=5-7) were killed by cervical dislocation (Ethics Committee of Animal Experiments of UNAERP - CEP/UNAERP: 019/2012), the anococcygeus muscle was isolated and suspended in a organ chamber bath containing Krebs solution to measure isometric contractions. Muscle preparations were set at a resting tension of 0.5 g and allowed to equilibrate for 1 h, then they were stimulated with increasing concentrations of PE (1 nmol/L to 100 mmol/L) before and after 20 min incubation with just RESV or RESV plus different drugs: prazosin (Pz: $10^{-8}$ mol/L); 2-APB ($10^{-4}$ mol/L); GF109203X ($0.5x10^{-5}$mol/L) or atorvastatin (ATV: $10^{-4}$mol/L). Statistical analysis: Student paired t-test or one-way ANOVA, Bonferroni post-test. Significance: $p<0.05$. **Results:** Higher concentrations of RESV ($10^{-4}$ or $10^{-3}$mol/L) reduced maximum contraction (MC) stimulated with PE (RESV $10^{-4}$ mol/L: 101.7±1.3% to 69.3±1.1%, n=7; RESV $10^{-3}$ mol/L: 100.3±0.7% to 8.92±4.9%, n=5). $10^{-4}$ mol/L RESV was used to all subsequent protocols. Pz (alpha1-adrenoceptor antagonist) was not effective on reducing MC stimulated with PE, but RESV+Pz reduced this MC (100.6±0.7% to 55.8±4.7%, $p<0.0001$). 2-APB ($IP_3$ receptor antagonist) was effective on reducing MC stimulated with PE (101.8±0.73% to 28.8±1.19, $p<0,001$), RESV+2-APB also reduced ME (99.3±0.5% to 5.3±1.4%, $p<0.0001$). $pD_2$ values were reduced under RESV+2-APB incubation (6.2±0.09 to 4.47±0.22, $p<0.0001$). Incubation with GF109203X (PKC inhibitor) was effective on reducing MC stimulated by PE (100.2±0.8% to 40.5±7.3%, $p<0.0001$). $pD_2$ values were also altered after GF109203X incubation (6.2±0.09 to 5.7±0.08, $p<0.0001$). ATV (NADPH oxidase inhibitor) was not effective on reducing MC stimulated with PE, but ATV+RESV reduced it (90.5±4.3% to 56.9±7.7%, $p<0.0001$). **Discussion**: According to the literature RESV is an antioxidant compound. In this regard, it was concluded that the steps triggered through PE stimulation on the alpha 1-adrenoceptors are involved in the production of free radicals (FR), which were sensitive to RESV. That is, these FR must be produced during the steps involved in the intracellular signaling pathways involving $IP_3$ ,PKC and NADPH oxidase.The sensitivity to the RESV is shown by decreased contractile response stimulated by PE and its intracellular pathways of signaling. If, in considering that RESV is capable to scavenge FR, the reduction of induced PE contraction, may be due to reducing the FR levels. **Financial support**: CNPq/PIBIC, UNAERP.

**09.047 Vasodilator effect of extract of *Cecropia glaziovi* in normotensive and hypertensive rats**. Lobo KL[1], Carioletti GH[1], Santos TC[2], Campos AM[2], Linder AE[1] [1]UFSC – Pharmacology, [2]UFSC – Pharmaceutical Sciences

**Introduction:** The genus Cecropia is distributed throughout Latin America, especially in Brazil. Commonly it is used to treat heart failure, high blood pressure, inflammation, cough, asthma, bronchitis, and it is also used as diuretics[1]. Unpublished data from our laboratory indicates that the standardized extract of *C. glaziovi* [18% of the plant ethanol 27% (v / v), homogenized for 3 days] induces relaxation of vascular vessels from normotensive rats. Our goal is to verify whether this extract is capable to induce relaxation and/or to modulate contractile responses of vessels from hypertensive rats. **Methods**: Female and male normotensive and spontaneous hypertensive rats (SHR) were anesthetized with a mixture of ketamine and xylazine and the aorta was isolated, cut into rings (~4 mm) and mounted in isolated organ chambers containing physiological salt solution for isometric tension recording under 3.0 g of passive tension (CEUA PP00706). The presence of functional endothelium was assessed by the ability of acetylcholine (ACh, 1 µM) to induce relaxation of phenylephrine (PE, 1 µM) induced- contraction. Aortic rings from hypertensive and normotensive rats were contracted with PE (1 µM) followed by the addition of increasing concentrations of *C. glaziovi* (0.1 to 100 µg / ml) given in a 5 min-interval. Concentration-effect curves (CEC) to PE (1 nM to 1 µM) in the absence and in the presence of *C. glaziovi* (100 µg / ml) were performed. *C. glaziovi* or vehicle was added 30 min prior to PE. The responses were measure as percentage (%) of relaxation of PE-induced contraction or as grams (g) of contraction. Data were expressed as mean +/- SEM and analyzed by two way ANOVA followed by Bonferroni post test or by Student's t test when appropriate. * represents $P< 0.05$. **Results and Discussion:** As expected, the relaxation to ACh 1 µM was impaired in aortic rings from hypertensive (50.29 % ± 5.769*, N=5) rats compared to normotensive (76.03 % ± 4.566, N=8) rats. The maximal relaxation induced by the extract of *C. glaziovi* (100 µg / ml) was also impaired in aortic rings from hypertensive (51.60 % ± 10.40*, N=5) rats compared with vessels from normotensive (92.59 % ± 2.368, N=8) rats. The concentration effect curves to PE in the presence of the extract were significantly impaired in aortic rings from normotensive and hypertensive rats, when compared to those curves obtained in the presence of vehicle. These data show that the extract of *C. glaziovi* relaxes aortic rings from hypertensive rats and normotensive rats and that this relaxation is impaired in vessels from hypertensive animals probably due to endothelial dysfunction seen in this pathology. These data corroborate previous findings indicating that vasoactivity of *C. glaziovi* is dependent on endothelium derived relaxing factors. Moreover, the extract of *C. glaziovi* impairs the contraction of vessels from both groups. The vasoactivity of *C. glaziovi* will be tested for a potential hypotensive effect in future experiments. **References**: 1) COSTA, G. M. et al.. *Nat. Prod.Commun,* 6, 913, 2011. **Financial Support:** CNPq/FAPESC, PPG-FMC-UFSC

**09.048 Capsaicin or eugenol treatment protects mice against some activities of *Apis mellifera* bee venom**. Tavares-Henriques MS, Gonçalves TS, Monteiro-Machado M, Amorim-Tomaz M, El-Kik CZ, Passos-Guimarães, Melo PA ICB-CCS-UFRJ – Farmacologia e Química Medicinal

**Introduction:** The spread of Africanized honeybee in the American continent, especially in Brazil, led to the rise in the incidence of accidents making up a public health problem, with estimated 600 cases in the state of Rio de Janeiro every year. **Material and Methods:** In this study we assessed the participation of TRPV1 receptors (through capsaicin-induced desensitization) in different actions of *Apis mellifera* venom in adult Swiss mice, as well as the posttreatment with eugenol. **Results:** The capsaicin-induced desensitization (50 mg/kg) abolished the paw edema induced in mice by *A. mellifera* venom (1 µg/paw), reduced in 80% the changes in vascular permeability (intradermal 1 mg/kg), reduced lethality from 100% down to 50% and inhibited in 40% the rise in hematocrit in mice that received lethal dose of the venom (10 mg/kg). However, there were no changes in neither myeloperoxidase nor myotoxic activities. Posttreatment with eugenol (100 mg/kg) reduced lethality down to 50%, edema in 53% and vascular permeability in 75%, but did not alter myeloperoxidase, myotoxic, phospholipase nor hyaluronidase activities of *A. mellifera* venom. On the other hand, eugenol inhibited in 55% the rise in hematocrit in mice that received lethal dose of the venom. **Conclusion:** We conclude that TRPV1-mediated neurogenic inflammation plays an important role in the cytotoxicity of *A. mellifera* venom, so that it could be a possible therapeutic target. Additionally, we demonstrated the ability of eugenol in counteracting some activities of *A. mellifera* venom. **Financial Support:** CAPES, CNPq, PRONEX and FAPERJ. Animal Care Commission CEUA-UFRJ # Aproved DFBCICB072-04/16

**09.049 Rat isolated right atrial responses to *Vitalius dubius* (Araneae, Theraphosidae) venom and a purified polypeptide**. Tamascia ML[1], Rennó AL[1], Zelanis A[2], Serrano SMT[2], Hyslop S[1] [1]Unicamp – Farmacologia, [2]CAT-CEPID-IBu – Toxinologia Aplicada

**Introduction:** The venom of *Vitalius dubius*, a theraphosid spider from southeastern Brazil, contains a variety of toxins. In this work, we examined the action of *V. dubius* venom and a purified polypeptide on rat isolated right atrial function. **Methods:** Right atria obtained from isoflurane-anesthetized male Wistar rats (300-400 g) were mounted (resting tension: 1 g) in warm (37 °C), aerated (5%$CO_2$-95%$O_2$) modified Krebs-Henseleit solution (composition, mM: NaCl 118, KCl 4.7, $CaCl_2$ 2.5, $MgSO_4$ 0.45, $NaHCO_3$ 25, $KH_2PO_4$ 1.03, D-glucose 11.1, ascorbic acid 0.14; pH 7.4) for measurement of contractile force and atrial rate. Creatine kinase MB (CK-MB) activity was measured before and 60 min after venom addition. Venom was fractionated on Superdex 75, SP-Sepharose and RP-HPLC. A tryptic digest of Peak IV-3 was used for protein identification by mass spectrometry. The results (mean±SD) were analyzed using ANOVA for repeated measures followed by the Tukey test, with $p<0.05$ indicating significance. The animal experiments were approved by an institutional Committee for Ethics in Animal Use (CEUA/UNICAMP, protocol no. 2166-1). **Results:** Venom caused a progressive decrease in atrial contractile force during a 60 min incubation (maximum decrease of 25±8%, 33±17% and 59±22%* for 25, 50 and 100 µg/ml, respectively; n=5-8; *$p<0.05$ vs. pre-venom values). Atrial rate also decreased (maximum of 5.5±6.0%, 4.8±4.2% and 20.2±12.0%* for 25, 50 and 100 µg/ml, respectively; n=5-8; *$p<0.05$ vs. pre-venom values). A higher venom concentration (200 µg/ml) caused atrial arrest after 49±10 min, at which point contractile force and atrial rate had decreased by 82±8% and 25±11%, respectively (n=6). CK-MB release increased after a 60 min incubation (control: 0.76±0.40 U/ml, n=6, vs. 2.14±0.40 U/ml and 2.71±0.30 U/ml for 100 µg/ml and 200 µg/ml of venom, respectively, n=5 each; $p<0.05$). The two highest venom concentrations caused discrete muscle fiber disorganization and pyknotic nuclei. Of six gel filtration peaks, only Peak IV (10 µg/ml) affected atrial function (baseline tension increased from 0.65±0.1 g to 0.79±0.1 g; 22.4±11.5%; $p<0.05$; CK-MB release increased from 0.48±0.4 U/ml vs. 2.89±1.8 U/ml 60 min post-venom; n=5; $p<0.05$). Fractionation of Peak IV yielded three peaks, with Peak IV-3 (major peak) causing progressive negative inotropism (maximum decrease for 10 µg/ml: 64±24%, n=5; $p<0.05$ vs. pre-venom values); atrial rate decreased by 14±6% ($p<0.05$) after 60 min but there was no increase in CK-MB release. Incubation with 300 µM $N^w$-nitro-L-arginine methyl ester (L-NAME) significantly attenuated (by ~58%) the negative inotropism (maximum decrease: 27±2%) and abolished the decrease in atrial frequency. Mass spectrometry of Peak IV-3 indicated a molecular mass of 5859 Da and sequencing identified two peptides (FFECTFECDIKK; LKLCLK) identical to TXL1_LASPA, a calcium channel-blocking toxin from *Lasiodora parahybana* spider venom. **Conclusion:** *Vitalius dubius* venom attenuated atrial contractile activity partly by modulating nitric oxide production and calcium-channel activity. **Financial support:** CAPES, CNPq, FAPESP.

**09.050** ***Polygala cyparissias*** **induces vasorelaxation by inhibition calcium influx in rat isolated mesenteric artery**. Albuquerque JM[1], Alves QL[1], Simões LO[1], Ramos-Reis M[1], Cechinel-Filho V[2], Silva DF[1] [1]UFBA – Biorregulação, [2]NIQFAR-CCS-UNIVALI

**Introduction:** *Polygala cyparissias* (PCT-1) is a plant species known in folk medicine as "pinheiro da praia" or "gelol". We have previously described that PCT-1 promotes vasorelaxant effects in normotensive rats, however the mechanism of action involved in vasodilator activity remains unclear. The aim of this study was to investigate the mechanisms underlying the vasorelaxant effects induced by PCT-1 in rat mesenteric artery. **Methods:** Isolated rat superior mesenteric artery rings (1-2 mm) were suspended by cotton threads for isometric tension recordings in a Tyrode's solution at 37 ºC, gassed with a 95% $O_2$ and 5% $CO_2$, under a resting tension of 0.75g. All surgical and experimental procedures were approved by the local Animal use and care ethics committee – CEUA/ICS/ UFBA. **Results and Discussion:** In phenylephrine (Phe, 1µM)-pre-contracted mesenteric artery rings, PCT-1 (0,01 – 300 µg/mL) caused a concentration-dependent relaxation [Maximum Response (MR) = 98.22 ± 8.52%, $EC_{50}$ = 85.24 (68.22 – 106.05) µg/mL, n=7]. The endothelium removal not altered relaxation induced by PCT-1 [MR = 85.78 ± 5.65%, $EC_{50}$ = 66.71 (53.08 – 83.83) µg/mL, n=7], suggesting that endothelium-derived factors do not seem to participate of vasorelaxant effect induced by PCT-1, therefore the subsequent experiments were performed with rings in the absence of functional endothelium. In contractions induced by $K^+$-high Tyrode's modified solution (KCl 60 mM), the potency and efficacy of PCT-1 were not significantly altered (MR = 61.91 ± 11.15%, $EC_{50}$ = 69.28 (48.78 – 98.39) µg/mL). Similar results were observed in pre-contracted vessels with L-type $Ca^{2+}$ channel agonist (Bay K 8644, 200 nM) [MR = 75.76 ± 14.93%, $EC_{50}$ = 57.72 (28.42 – 117.20) µg/mL]. Furthermore, PCT-1 inhibited the vasoconstriction induced by $CaCl_2$ in depolarizing nominally $Ca^{2+}$-free medium in two different concentrations (100 and 300 µg/mL), suggesting that the vasodilatation induced by PCT-1 involved, at least in part, inhibition of $Ca^{2+}$ influx probably through L-type voltage-dependent calcium channels ($Ca_v$ type-L). Taken together, these results show that PCT-1 induces endothelium-independent vasodilatation which involves inhibition of $Ca^{2+}$ influx through of L-type voltage-operated calcium channels in vascular smooth muscle. **Sources of research support:** FAPESB; CNPq

**09.051 A role for adenosine in the hypotension caused by *Bothrops alternatus* snake venom in rats**. Pereira EM, Tamascia ML, Hyslop S Unicamp – Farmacologia

**Introduction**: Purines present in snake venoms or released endogenously by venom enzymes such as 5'-nucleotidase may play a role in the hemodynamic responses to snake venoms. We have previously shown that adenosine contributes to edema caused by *Bothrops* snake venoms. In this work, we examined the involvement of adenosine in the hypotension caused by *Bothrops alternatus* snake venom. **Methods:** Male Wistar rats (300-400 g) were anesthetized with urethane (1 g/kg i.p.) and a carotid artery was catheterized for continuous blood pressure measurements (PowerLab, ADInstruments); a femoral vein was catheterized for administration of venom (0.5 mg/kg) and other test agents [**adenosine (600 mg/kg; n=5), theophylline – a non-selective adenosine receptor antagonist (**20 mg/kg, n=6**), CSC –** 8-(3-chlorostyryl) caffeine, an $A_{2A}$ adenosine receptor antagonist (6 mg/kg, 30 min before venom; n=5), DMPX – 3,7-dimethyl-1-proparglyxanthine, an $A_{2B}$ adenosine receptor antagonist, and vanillic acid – a 5'-nucleotidase inhibitor (1 mg/kg; n=3) that was pre-incubated for 30 min at 37 $^{o}$C prior to co-injection with venom]. Only one venom dose was tested per rat; all agents were injected in 100 µl and washed in with a further 100 µl of 0.9% NaCl. The changes in blood pressure were monitored for 120 min. The results (mean ± SEM) were analyzed statistically with ANOVA followed by the Tukey-Kramer test, with $p<0.05$ indicating significance. This work was approved by an institutional Committee for Ethics in Animal Research (CEEA/UNICAMP, protocol no. 1318-1). **Results:** Venom caused a significant decrease in blood pressure that was maximal within 10 min (from 97±3 to 55±5 mmHg, $p<0.05$; 43% decrease), followed by a gradual recovery to basal values. Theophylline significantly attenuated (by ~49%) the venom-induced hypotension (from 97±3 to 76±5 mmHg; ~22% decrease vs. 43% with venom alone). The $A_{2A}$ receptor antagonist CSC significantly attenuated (by ~38%) the venom-induced hypotension (from 98±1 to 72±3 mmHg; 27% decrease vs. 43% with venom alone), as did DMPX, an $A_{2B}$ receptor antagonist (~50% attenuation, with blood pressure decreasing from 98±4 to 78±5 mmHg; ~20% decrease vs. 43% with venom alone). At the concentrations tested, both of these antagonists significantly ($p<0.05$) inhibited the decrease in arterial blood pressure caused by the $A_{2A/2B}$ receptor-selective agonist 5´-N-ethylcarboxyamidoadenosina (NECA; 3 mg/kg, i.v.; n=5) by 54% in the case of CSC and 62% in the case of DMPX (n=4 each). Vanillic acid attenuated venom-induced hypotension by ~70% (from 116±5.31 to 101±9.8 mmHg; ~13% decrease vs. 43% with venom alone). Adenosine caused a 40% decrease in blood pressure (from 105±7 to 63±1 mmHg; $p<0.05$) that was significantly ($p<0.05$) attenuated by theophylline (~71%; n=5). There were no significant changes in heart rate or respiratory rate in any of the experimental groups. **Discussion:** These results indicate that adenosine generated by venom 5´-nucleotidase or formed by endogenous ecto-5´-nucleotidase contributes to *B. alternatus* venom-induced hypotension. **Financial support:** CAPES, CNPq, FAEPEX-UNICAMP, FAPESP.

**09.052 Gestational toxicological evaluation of *Nepeta cataria* (Catnip) in rats by behavioral tests**. Pereira MS, Mataqueiro MI, Moranza HG, Rizzo LF, Ferraz GC, Queiroz-Neto A FCAV-Unesp-Jaboticabal – Morfologia e Fisiologia Animal

**Introduction:** Catnip (*Nepeta cataria* – Lamiaceae) has a pseudo-narcotic drug effect, related to the presence of various active principles, like nepetalactone (Bernardi *et* al., 2010). This plant attracts and calms down most of the cats and for this reason it is commonly used in toys for pets (Marchei *et* al., 2010). There are studies on the effects of the catnip but we believe that additional information about this plant is necessary since it has central and toxic actions associated with its use as a repellent. We evaluate the effects of exposure to the plant, in the form of diet supplied to female Wistar rats during the gestation, as a possible source of physical and reflexological development changes in pups. **Methodology:** Litters consisted of 4 male and 4 female pups per dam; pregnant female rats (n=11) were fed a dried catnip diet (10% v.v.) and the control group (n=10) was fed common ration until the end of the gestation. In order to determine whether catnip added to the diet affected pup behavior or not, the following tests were performed: Open Field (21 days), Elevated Plus Maze (22 days), Equilibrium in rotating drum or "Rota Rod" (32 days) and Morris Water Maze (35 days). Statistical analysis was performed using the *t* Student test for both groups. The significance level was set at $p<0.05$. **Results and Discussion:** The adults dams did not show any signis of intoxication. The result of the open field, elevated plus maze and rota rod tests were not significantly different for pups whose mothers were fed Catnip during de pregnancy compared to ration diet. However, the results in the Morris Water Maze showed that males and females whose mothers were fed catnip took 3 and 2 repetitions respectively to learn the location of the platform, while males and females of the control mothers that took 5 and 3 repetitions respectively. Thus, the offspring of treated mothers took less time to learn the platform location ($p<0,05$). This result suggested that Catnip can promote better development of the pup hippocampus, area that is related to learning (D'Hooge & Deyn, 2001). It is concluded that the active principle of *Nepeta cataria* is able to pass to the pups through the placenta, thus promoting significant changes in offspring development. **Bibliography:** D'Hooge, R. Brain Res. Rev., v. 36, p. 60, 2001. Bernardi, M. M. J. Ethnopharmac., v. 137, p. 1318, 2011. Marchei, P. J. Vet. Behav.: Clinic. App. and Res., v. 5, p. 50, 2010. **Footnote:** Supported by CNPq/PIBIC and approved by the ethics committee (protocol number 007177/11).

**09.053 Antihypertensive potential of extract from *Solanum sisymbriifolium* in spontaneously hypertensive rats – ethnopharmacological study**. Simões LO[1], Silva AQG[2], Cechinel-Filho V[3], Silva DF[2] [1]UFBA – Ciências Farmacêuticas, [2]ICS – Biorregulação, [3]Univali

**Introduction:**Natural products research is a successful tool to reveal novel candidates for targeting treatment of prevalent human diseases. *Solanum sisymbriifolium* is used in folk medicine in many South American countries as antihypertensive and diuretic. Previously, we showed that *Solanum sisymbriifolium* promotes vasorelaxation in normotensive rats, however the hemodynamic effect and mechanism of action involved remains unclear. Our aim was to investigate vasodilator properties of *Solanum sisymbriifolium* (extract and fractions) on mesenteric arteries from spontaneously hypertensive rats (SHR). Additionally, the effects of venous administration of *solanum sisymbriifolium* on arterial blood pressure (BP) and heart rate (HR) were evaluated. **Methods**: Male SHR (250-300 g) were euthanized and the superior mesenteric artery was isolated, sectioned in rings (1-2 mm) and treated with *Solanum sisymbriifolium* methanolic extract, chloroform, ethyl acetate or n-hexane fractions. Isometric tension recordings of suspended arterial rings in a Tyrode's solution at 37 ºC, gassed with a 95% O2 and 5% CO2, were performed at a resting tension of 0.75g. In another set of experiments, animals were implanted with catheters in the femoral artery and vein to record BP, HR and drug administration respectively. *Solanum sisymbriifolium* extract was intravenously administered at 1, 5, 10, 20 and 40 mg/kg. All surgical and experimental procedures were approved by the local Animal use and care ethics committee – CEUA/ICS/ UFBA (030/2012). **Results and Discussion**: Methanol extract of *Solanum sisymbriifolium* aerial parts (0.01 – 300 µg/mL) relaxed phenylephrine-induced contractions in a concentration-dependent manner (Maximum Response (MR) = -78.5 ± 9.2%, EC50 =9.2±2.6 µg/ml; n=5) in endothelium intact vessels. Endothelium removal did not alter extract induced relaxation (MR= -69.5 ± 2.8%, EC50=11.4 ±4.2 µg/mL; n=7). Methanol extract of *Solanumsisymbriifolium* was fractioned by solvent-solvent partitioning, where the chloroform fraction (MR= -74.2 ± 1.9 %, EC50=123.3 ±2.0 µg/ml; n=4) and ethyl acetate (MR=-79.4± 5.4%, EC50= 98.6±5.5 µg/ml; n=5) exhibited similar relaxation effects. Contrarily, the n-hexane fraction induced vasorelaxation was significantly lower when compared to other evaluated fractions (MR =-19.3 ± 1.3 %, EC50 = 185.5 ± 5.5 µg/ml, n=5). Endothelial removal did not alter the relaxing effect of any tested fractions, suggesting that endothelium-derived factors do not participate in *Solanum sisymbriifolium* induced vasorelaxation. Posteriorly, the preparations were pre-contracted with $K^+$-high Tyrode's modified solution and the relaxation response was not altered (MR=-75.9 ±1.9, EC50= 21.5 ±7.5 µg/ml; n=6) when compared to rings pre-contracted with PHE. In vivo assays using different extract doses (1, 5, 10, 20 and 40 mg/kg) were effective in lowering BP (MR=-10.2 ±2.9; -13.2 ±1.9, -15.5±4.7; -18.2± 1.3, -39.8± 1.7, respectively). Results suggest that the vasorelaxant response induced by methanol extract and fractions of *Solanum sisymbriifolium* might contribute to hypotensive effect observed in SHR. These findings might explain, at least in part, the medicinal use of *Solanum sisymbriifolium* in cardiovascular disorders. **Financial support**: CNPq and FAPESB.**References**: Koehn, F.E. The evolving role of natural products in drug discovery.N.R.D.D, vol. 4, pp. 206. 2005. Gonzales Torrez, D.M.Catalogo de Plantas Medicinales (y Alimenticias y Utiles) Usadas en el Paraguay. E.P, Asuncio´n, pp. 312 and 452. 1992.

**09.054 Investigation of tocolytic effect of *Lippia microphylla* Cham. essential oil (Verbenaceae) and its major compounds, thymol and carvacrol, on rat uterus**. Silva MCC, Medeiros MAMB, Souza ILL, Ferreira PB, Sampaio RS, Martins IRR, Calvacante FA, Tavares JF, Silva BA UFPB

**Introduction:** *Lippia microphylla* Cham. (Verbenaceae) is popularly known as "alecrim-do-mato", "alecrim-de-tabuleiro" and "alecrim-pimenta" and it is used in folk medicine in the form of decoction or maceration as antiseptic and to treat respiratory diseases such as colds, bronchitis, cough and asthma (AGRA, Rev. Bras. de Farmacogn., v. 18, p. 472, 2008.). From aerial parts of *L. microphylla* was extracted the essential oil (LM-OE), which one has thymol as major compound (OLIVEIRA et al., 2013, IX Simpósio Brasileiro de Farmacognosia, Goiânia/GO). LM-OE presented vasorelaxant action on rat aorta and mesenteric artery (ARAÚJO, 2011, Thesis of doctorate CCS/UFPB), as well as spasmolytic activity on guinea-pig ileum by decrease in the cytosolic calcium concentration (OLIVEIRA et al., 2013, IX Simpósio Brasileiro de Farmacognosia, Goiânia/GO). Thymol showed spasmolytic effect on rat aorta and ileum (BEGROW et al., Planta Med. v. 76, p. 311, 2010). As well, carvacrol showed spasmolytic effect on rat aorta (PEIXOTO-NEVES et al., Fundam. Clin. Pharmacol. v. 24, p. 341-350, 2010). Based on these premises we decided to investigate a possible spasmolytic effect of LM-OE, thymol and carvacrol on rat uterus. **Methods:** Rat uterus was suspended in organ baths containing Locke-Ringer solution in appropriate conditions. Isotonic and isometric contractions were monitored and recorded. All experimental protocols were approved by Ethical Committee in Animal Use of CBiotec/UFPB (Protocol 1005/13). **Results:** LM-OE antagonized, in a significant and concentration-dependent manner, CCh-(1-81 µg/mL) ($IC_{50}$ = 7.8 ± 1.3 µg/mL) and oxytocin-(3-243 µg/mL) ($IC_{50}$ = 35.1 ± 4.9 µg/mL) induced phasic contractions, being significantly more potent to CCh. It is suggestive that LM-OE can be acting as an antagonist of CCh receptors, but more experiments are required to confirm this hypothesis. On the other hand, thymol and carvacrol did not antagonized CCh-($E_{max}$ = 10.7 ± 5.0 and 41.4 ± 10.3%, respectively) or oxytocin-($E_{max}$ = 29.3 ± 11.6 and 9.2 ± 5.2%, respectively) induced phasic contractions. LM-OE (0,003-81 and 0,003-27 µg/mL, respectively) relaxed in a significant and concentration dependent manner the rat uterus pre-contracted by KCl 60 mM ($E_{max}$ = 98.8 ± 0.8% and $EC_{50}$ = 5.0 ± 0.8 µg/mL) and oxytocin $10^{-2}$ UI/mL ($E_{max}$ = 100% and $EC_{50}$ = 2.7 ± 0.8 µg/mL). **Discussion:** Brazil has a prominent place in the worldwide essential oils production (BIZZO et al., Química Nova, v. 32, p. 588, 2009) and it seems evident the potential of these natural products in the development of pharmaceuticals. LM-OE both inhibited the contractions and relaxed the rat uterus, but thymol and carvacrol were not able to antagonize the phasic contractions in this organ. The major compounds of the essential oils are frequently pointed as the responsible by their biological effects (BAKKALI et al., Food Chem. Toxicol. v. 46, p. 446, 2008). However, thymol and carvacrol, as isolated compounds, seemed not participate in the LM-OE tocolytic effect on rat uterus, but its synergic effect with the other components of the essential oil is not discarded. Thus, LM-OE showed to be a promising essential oil with tocolytic effect on rat uterus. **Financial support:** CNPq, CAPES, PgPNSB/UFPB.

**09.055 Gastroprotective properties of hydroalcoholic extracts and fractions from leaves of *Camellia sinensis* in rats**. Borato DG[1], Ferreira DM[1], da Silva LM[1], Galuppo LF[1], Scoparo CT[2], Iacomini M[2], Werner MFP[1], Baggio CH[1] [1]UFPR – Pharmacology, [2]UFPR – Biochemistry and Molecular Biology

**Introduction:**The leaves of *Camellia sinensis* (L.) Kuntze (Theaceae) are widely used in infusions and popularly known as "tea". Based on the process of auto-oxidation catalyzed by enzymes, they are classified in non-oxidized (green and white tea), semi-oxidized (oolong tea), oxidized (black tea) and post-fermented (pu-erh tea). Besides, their popular uses are associated with weight loss, reduction of cholesterol levels and treatment of degenerative diseases. Considering the therapeutic benefits of *Camellia sinensis* and preliminary results obtained by our group, which demonstrated the gastroprotective action of hydroalcoholic extract from leaves of *Camellia sinensis* (black and green teas), the present study aimed to find the compounds involved in this activity and the possible mechanisms of action. **Methods:** Fasted Wistar rats (female adults) were orally treated with vehicle (water, 1 ml/kg), omeprazole (40 mg/kg), hydroalcoholic extract of black tea (HEBT, 1-30 mg/kg) or hydroalcoholic extract of green tea (HEGT, 1-30 mg/kg), one hour before the induction of gastric lesions with P.A. ethanol (0.5 ml/200 g). After that, gastric mucus and GSH levels were measured in ethanol-induced lesions. In another set of experiments, the fractions of both extracts were also evaluated. Chloroform (ClF), ethyl acetate (EAF), buthanolic (ButF) and aqueous (AqF) fractions (from black tea: 3.2, 2, 3.2 and 1 mg/kg and from green tea: 1.2, 0.6, 1 and 0.4 mg/kg) were orally administered to animals and, one hour after, the gastric lesions were induced with ethanol. Gastric mucus and GSH levels were also measured (CEUA/BIO-UFPR approval number 689). **Results and Discussion:** Oral treatment of animals with HEBT and HEGT reduced the gastric lesions induced by ethanol with $DE_{50}$ values of 10.2 and 3.6 mg/kg, respectively. Besides, HEBT at doses of 10 and 30 mg/kg increased the GSH levels in 104 and 223%, respectively compared to lesionated group (C: 286.7 ± 52.1 µg/g of tissue) but only the dose of 10 mg/kg restored the gastric mucus to basal levels. However, HEGT (10 and 30 mg/kg) increased the GSH amounts in 110 and 112%, respectively, and at doses of 3 and 10 mg/kg also increased the mucus levels in 149 and 130%, respectively, compared to control group (C: 199.4 ± 20.5 µg/g of tissue and 240.1 ± 49.5 µg of Alcian Blue/g of tissue, respectively). Next, the extracts were partitioned with different solvents and EAF, ButF and AqF from HEBT inhibited the formation of lesions by 49, 63 and 55%, respectively, while ClF, EAF and ButF from HEGT inhibited by 45, 73 and 73%, respectively. Moreover, AqF from HEBT was able to increase the levels of mucus (113%) and GSH (71%) but ButF only increased the GSH levels (76%). However, ClF from HEGT increased the mucus levels in 72%. Altogether, our results demonstrate that the hydroalcoholic extracts and fractions from leaves of green and black teas protect the gastric mucosa against lesions induced by ethanol through maintenance of both protective factors, gastric mucus and GSH. **Financial support:** CAPES

**09.056 Antispasmodic effect of *Cardiospermum corindum* L. (Sapindaceae) on rat ileum**.
Silva VA[1], Andrade JR[1], Silva FL[2], Barbosa-Filho JM[3], Rigoni VLS[4,5], Nouailhetas VLA[4], Silva JLV[1] [1]Uninove – Farmácia-Bioquímica, [2]CCS-UFPB – Produtos Naturais e Sintéticos Bioativos, [3]CCS-UFPB – Ciências Farmacêuticas, [4]Unifesp – Biofísica, [5]Uninove – Medicina

**Introduction**: *Cardiospermum corindum* L. is known as "balãozinho" and has wide distribution in Brazil. There are not effects reported for species, thus the aim of this study was to investigate the effects of the ethanol crude extract obtained from the aerial parts of *C. corindum* (Cc-EtOH) on contractile response-induced rat ileum. **Methods**: the antispasmodic activity was investigated on ileum isolated from rats (250-300g) were fasting (24h) in glass baths containing Krebs modified solution, at 37°C, 1g resting tension and bubbled $O_2$. Tissue contractile response was recorded through acquisition and analogy system AQCD (AVS Projetos, Brazil). The contractions were accessed by addition of KCl (40mM), a depolarizing agent, or CCh (1μM), a muscarinic agonist, considerate as control and verified in presence of Cc-EtOH (27, 81, 243 or 500 μg/mL) expressed as maximum response ($E_{max}$) to contractile agents. These procedures were approved for ethics committee in research of Federal University of São Paulo (CEP 0038/10). The data were expressed as mean **±** SEM and analyzed by GraphPad Prism 5.0 software, it tested for significance by ANOVA one-way following Dunnett´s post-test, where results were regarded as significant when $p < 0.05$. Results and discussion: the extract Cc-EtOH (27-500 μg/mL) inhibited in a concentration-dependent manner and potentially ($p < 0.05$) the ileum rat (n=4) pre-contracted both KCl ($E_{max}$= 97.9±2.0; 55.2±5.3; 41.9±3.8 and 26.9±7.3 %, respectively) or CCh ($E_{max}$= 78.1±8.6; 75.4±5.8; 50.6±3.4 and 42.8±3.9 %, respectively). As Cc-EtOH promoted effect on different contractile agents, it is suggestive that extract presents non-selective antispasmodic effect. These results demonstrate that the aerial parts from *Cardiospermum corindum* have antispasmodic effect, probably due to contain active principles responsible. Support: CNPq/ CAPES

**09.057 Antimicrobial effect of the peppers *Capsicum baccatum var*. *Pendulum* and *Capsicum chinense* on *Staphylococus aureus* and *Pseudomonas aeruginosa* and its toxicity levels over *Artemia salina* Leach**. Gontijo LS, Lima EA Pitágoras – Medicina

**Introduction:** The peppers in their diversity are widely consumed in Brazilian cuisine and in view of their biological properties; several studies have been performed, especially regarding the antimicrobial activity and the toxicity. This paper aims to evaluate the Minimum Inhibitory Concentration (MIC) of the extracts of peppers *Capsicum baccatum var. pendulum* and *Capsicum Chinense* on *Staphylococus aureus* and *Pseudomonas aeruginosa* and verify its toxicity on the *Artemia salina*. **Methodology**: The crude extracts of peppers were obtained from 500g of *C. baccatum* and 500g of *C. chinense*. The final alcoholic extracts obtained were stored in plastic vial, protected from light at room temperature. To perform the REMA, cultures of *S. aureus* (ATCC 6538) and *P. aeruginosa* (ATCC 27853) were used. The strains were maintained in Müller-Hinton broth to the moment of use. It was used the clorofenicol stock solution at 10 mg/mL as a reference drug. The acute toxicity test in *A. salina* was performed according to Meyer et al. (1982), with some modifications. **Results and discussion:** The MIC varied according to the bacteria tested, whereas the extracts of *C. baccatum* (MIC ≤ 1.000 µg/mL) and *C. chinense* (MIC ≤ 1.000 µg/mL) showed weak antimicrobial power against *P. aeruginosa* and *S. aureus*, respectively, and the extracts of *C. chinense* (MIC ≤ 250 µg/mL) demonstrated a moderate activity against *P. aeruginosa*. According to Holetz et al. (2002), in plant extracts considered strong antimicrobial MIC must be lower than or equal to 100 µg/mL; for the moderate the value rises from 100 to 500 µg/mL, the weak to MIC between 500 and 1.000 µg/mL and over 1.000 µg/mL, the extract is considered inactive. In the work developed by Domingo; Lopes-Brea (2003), the toxicity of phenolic compounds against microorganisms, are directly related to the location and number of hydroxyl groups present on the aromatic ring, so that the higher the hydroxylation greater its poignancy and their toxicity. These mechanisms can be the probable reasons for the peppers of the species *C. chinense,* poignancy with approximately 50,000 units Scoville scale, presenting a better antimicrobial activity against the strains of *P. aeruginosa* and *S. aureus,* compared with the species *C.baccatum* with pungency ranging from 5 to 15 thousand units. In the acute toxicity tests, the results revealed that pepper extracts of *C. baccatum* and *C. chinense* promoted lethality in *A. salina* in all dilutions tested. The results indicate that the pungent pepper can present toxicity against *Artemia salina* eggs and may be a antimicrobial protective factor, therefore, the regular consumption of this spice, combined with a healthy diet can help in reducing the risk of emerging infectious diseases as well as in maintaining health. **Keywords:** Minimum Inhibitory Concentration; toxicity; *Capsicum baccatum var. pendulum*; *Capsicum chinense*. **Financial Support:** Without support.

**09.058** ***Bidens pilosa*** **L. Root (Asteraceae) protects stomach against ulcer gastric in rats**. Nascimento AJA[1], Nascimento PF[1], Santos JR[1], Costa DES[1], Silva FL[2], Barbosa-Filho JM[3], Silva JLV[1] [1]Uninove – Farmácia-Bioquímica/Saúde, [2]CCS-UFPB – Produtos Naturais e Sintéticos Bioativos, [3]UFPB – Ciências Farmacêuticas

**Introduction** and objective: *Bidens pilosa* L. (Asteraceae) is known as "picão-preto" and is widely found in Brazil. Its leaves are used to treat pain, diabetes, infection and inflammation, confirmed anti-ulcer activity in model animal, but there is not reported of the root for species. Thus, the aim of this study was to evaluate the effects of the ethanol crude extract obtained from the root of *B. pilosa* (Bpr-EtOH) on gastric ulcer ethanol-induced in rat and its toxicity on mice. **Methods**: to verify gastric protection Wistar rats (200-250 g), in fasted (24h), were divided in groups and treated with Bpr-EtOH (50, 150 or 500 mg/kg, o.r.), omeprazole (4 mg/kg, i.p.) or vehicle (TWEEN-20 0,1%) during 1 hour, following ethanol (1mL/kg, o.r.). After 1h, animals were euthanized on $CO_2$ camber, its stomachs isolated, washed with distilled water and opened. The ulcerative lesion area (ULA) of each stomach was visualized with stereoscopy and calculated ($mm^2$) (Kauffman, Gastroenterol, 75, 1099, 1978). Histological analyses were accessed in the tissues fixed in buffered formaldehyde (10%) and processed in paraffin, following slices (5µm) were prepared in plate and stained in HE, observed on microscopy optical (40x). The acute toxicity of Bpr-EtOH (2g/kg, o.r.) was evaluated on Swiss balb-c mice (25-30g). The locomotor and behavior activity were observed during 30 to 90 minutes after administration. During 3 days the animals were weighted, feed or consume of water were monitored. After the animals were euthanized in chamber $CO_2$, the hearts, lungs and livers were isolated and weighted. All procediments were approved for the Ethical Committee Animal Use of Nove de Julho University (AN 0002/11 and 0003/11). The data were expressed as mean **±** SEM and analyzed by GraphPad Prism 5.0 software, it tested for significance by Student test-t or ANOVA one-way following Dunnett´s post-test, where results were regarded as significant when $p < 0.05$. Results and discussion: the ethanol promoted damage gastric (ULA= 367.5±89.3 $mm^2$, n=4) that was reverted in a dose-dependent manner and significantly ($p < 0.05$) by Bpr-EtOH (ULA= 178.3±10.0; 67.40±9.5; 35.50±14.3 $mm^2$, respectively, n=5-4) as soon as omeprazole (ULA= 145.7±20 $mm^2$, n=6). These results were confirmed by not observation of inflammatory lesion in gastric mucosa treated with Bpr-EtOH (500 mg/kg). Nevertheless, Bpr-EtOH did not modified behavior in both locomotor activity of the animals (n=5) and emotionality in open field test after 30 - 90 min. of treatment. Bpr-EtOH did not altered either weight, feed or consume of water after 3 days, but induced one death. After animals were euthanized, we observed that extract did not increased ($p > 0.05$) isolated organs weight when compared to control. We conclude that *Bidens pilosa* roots also have antiulcer effect, probably due to contain protective principles, without potentially toxicity. **Support**: CNPq/ CAPES

**09.059 Evaluation of the antimicrobial activity of *Agave sisalana***. Santos L, Santos HZT, Oliva Neto P [1]Unesp-Assis – Ciências Biológicas

**Introduction:** The therapeutic agents currently used in the treatment of mycoses present several problems related to their activity spectrum, toxicity and microbial resistance, making fungal infections to increase in incidence and fatality. The medicinal plants bioprospection has led to the identification of powerful antimicrobial agents for controlling diseases caused by bacteria and fungi. Thus, the search for new plants that present antimicrobial activity has been the subject of intense research in recent years. In this direction, this study aimed to evaluate the antifungal effect of different aqueous extracts and fractions of *Agave sisalana* (sisal), a plant found in the Brazilian northeast, against the pathogenic yeast *Candida albicans*, as well to determine the minimum inhibitory concentration of growth (MIC) of this one. It also was determined the concentration of saponins in the fractions resulting from the extract that presented best antifungical activity. This project is a cooperation between UNESP and SECTI – Bahia, and it aims to find new utilizations for the sisal juice that has been despised and the sustainable development of the producing region of the sisal, one of the poorest in the country. **Methods:** The method, based on the *Candida albicans* CCT 0776, evaluated the antifungal action from sisal aqueous extracts obtained from the shredding of its leaves. The extracts were: wet precipitate (WP) resulting from the centrifuged juice; dried precipitate (DP) resulting from drying of the WP in greenhouse; dried mucilage (DM) obtained from the mucilage that was sun-dried for one week. The hexanic and alcoholic fractions were obtained from the extract that showed the best antifungical activity. All the extract and fractions were subsequent dissolved in distilled water, and their concentrations were obtained by fractionated dilution. The microbial growth was assessed using spectrophotometer readings at 600 nm, and their minimal inhibitory concentrations were then determined. Nystatin was used as antifungal reference. **Results:** The DP presented the best result, a MIC of 87 µg/ml against the yeast *Candida albicans*. From its fractions, the hexanic presented a MIC of 6.12 µg/ml,a result comparable to the nystatin MIC, that was of 3.1 µg/mL. The alcoholic fraction did not potentiate the DP effect. In the concentration of 350 µg/mL the hexanic and alcoholic fractions presented respectively proportional saponins concentration of 57% and 92%. **Discussion:** Comparing the aims proposed in introduction to the results obtained we may conclude that the different aqueous extracts and fractions of *Agave sisalana* (sisal) presented antifungal activity. The results obtained, specially from the hexanic fraction, make possible the economic exploitation of sisal residue. The phytochemical studies suggest that, besides the saponins, it is probable other metabolites are responsible for the powerful antifungal action found by us. Thus new studies will be carried out for a better comprehension of the antifungal activity observed by us. **Acknowledgments:** Secretaria de Ciência, Tecnologia e Inovação da Bahia; Fundação de Amparo à Pesquisa do Estado de São Paulo; Universidade Estadual Paulista “Júlio de Mesquita Filho”.

**09.060 Anticoagulant effect of chemically sulfated plant polysaccharides**. Castro RR[1], Silva RO[1], Madeira JC[1], Pereira MG[1], Almeida RR[2], Ricardo MNPS[2] [1]UECE, [2]UFC

**Introduction**: Heparin is widely used as anticoagulant and antithrombotic drug. However, several side effects have been reported, such as thrombocytopenia, osteoporosis, subcutaneous necrosis and immunological reactions provoked by remaining contaminants after its extraction from animal sources, leading to the research of alternative approaches for its use. Among them, there are the chemically-sulfated plant polysaccharides (PS). **Methods**: Seeds PS of *Caesalpinia ferrea* and *Adenanthera pavonina* were obtained from aqueous extraction. Native FT-IR spectra of *C. ferrea* and *A. pavonina* showed characteristic bands of the presence of polysaccharides relative to the glycosidic ether linkage and primary alcohol, respectively (1149 and 1045 $cm^{-1}$), C-O in C-O-H (993 $cm^{-1}$) of the galactomannans sugar composition, C-O-C group of 3,6-anhydro-α-L-galactopyranose (931 $cm^{-1}$). After the reaction with pyridine:formamide, the sulfation was confirmed by the presence of the band at 1255 $cm^{-1}$, that refers to the asymmetrical stretching vibration (S=O) of the ester sulfate groups. The PS were dissolved in sterile saline (0.9%), and the anticoagulant activity was evaluated through the activated partial thromboplastic time (aPTT) test. 90 µl of pooled blood plasma (3 individuals/pool) were incubated with 10 µl of sulfated PS solutions, at different concentrations (0.3 – 10 µg/µl). 100 µl of activated cephalin and 100 µl of $CaCl_2$ 0.25 M were added, and the time required for coagulation was measured. Unfractioned heparin and the vehicle were used as positive and negative controls, respectively. Data were expressed as means ± SD. Statistical analysis was perfomed using one-way ANOVA followed by Bonferroni's post hoc test. $P < 0.05$ was considered significant. The research followed the ethical guidelines expressed by the Resolution 196/96 (National Health Council- Brazil). Healthy volunteers have subscribed their agreement during the blood donation at the Center of Hematology and Hemotherapy Center of Ceará (HEMOCE). The blood samples were then provided by HEMOCE through a contract for mutual cooperation with the State University of Ceará (UECE). **Results**: As seen by aPTT, vehicle control group spent 37.5 ± 1.3 s until coagulate. Heparin 0.3 µg/µl increased the aPTT by 145% (92.0 ±7.5 s; $P < 0.05$). *C. ferrea* sulfated PS, at 0.3 and 1.0 µg/µl increased significantly the aPTT in 27% and 81%, respectively (47.9 ± 1.7 s; 68.0 ± 3.5 s). Using the same concentrations, *A. pavonina* sulfated PS also increased significantly the aPPT by 32% and 29%, respectively (49.6 ± 1.4; 48.6 ± 0.8 s). At 10 µg/µl, both sulfated PS elevated the aPTT for values > 300 s. **Discussion**: Heparin promotes anticoagulation indirectly, via antithrombin linkage, which inhibits some serine-proteases, such as the IXa, XIa and XIIa factors from the intrinsic via, and the Xa and IIa factors from the common via. Once aPTT test is clinically used to monitor the heparin therapy as well to access the intrinsic via functioning, it is possible that the anticoagulant effect displayed by the sulfated PS of *C. ferrea* and *A. pavonina* is due a heparin-like mechanism. Further studies are required to confirm this hypothesis. **Financial support**: FUNCAP.

**09.061 Antioxidant potential of extracts and fractions of *Agave sisalana***. Mazo GS, Zamaro HS, Santos L Unesp-Assis – Ciências Biológicas

**Introduction:** Brazil is possessor of the greatest biodiversity on the planet, but it presents an immense medicinal flora still unknown, little studied and explored. In this direction, one can observe through literature reviews that although Brazil is the largest producer of sisal, *Agave sisalana*, the number of scientific researches on the juice, resulting from shredding the leaves of this plant, is negligible. Very little is known about the pharmacological effects of sisal juice, as well as its chemical composition. Given this context, this project aimed to develop aqueous extracts and hexanic and alcoholic fractions from sisal juice and to evaluate the antioxidant activity of this plant through such extracts and fractions. This project is a cooperation between UNESP and SECTI – Bahia, and it aims to find new utilizations for the sisal juice that has been discarded and the sustainable development of the producing region of the sisal, one of the poorest in the country. **Methods:** Antioxidant activity of sisal juice, obtained from the shredding of its leaves, and the resulting aqueous extracts from such juice were evaluated; the extracts were: wet precipitate (WP) resulting from the centrifuged juice; dried precipitate (DP) resulting from drying of the WP in greenhouse; dried mucilage (DM) obtained from the mucilage that was sun-dried for one week. The hexanic and alcoholic fractions were obtained from the sisal juice. All the extracts and fractions were subsequently dissolved in distilled water. The test employed for evaluation of the antioxidant activity was the free radical DPPH (2,2-diphenyl-1-picrilidrazila). It was also determined the concentration of flavonoids and total phenols in sisal juice and, as well as in the different extracts and fractions. The concentration of saponins was determined in fraction that presented best antioxidant activity. **Results:** The best obtained antioxidant activities were with the sisal juice, an IC50 of 21604.54 µg/mL and with the alcoholic fraction of sisal juice, an IC50 of 975 µg /mL. IC50 represents the fraction amount necessary to neutralize 50% of the DPPH solution. The concentrations of flavonoids and total phenols were low in sisal juice and in all the extracts and fractions evaluated. At the concentration of 350 µg/ml, the alcoholic fraction showed a proportional concentration of saponins of 92%. **Discussion:** Comparing the aims proposed in introduction to the results obtained we may conclude that only the sisal juice and alcoholic fraction present powerful antioxidant activity. Especially, the results obtained from the alcoholic fraction, that presented an IC50 about 22 times lower than the one of the juice, what make possible the economic exploitation of the sisal residue. The phytochemical study shows that the alcoholic fraction has a high proportion of saponins. However, new studies will be carried out for a better comprehension of the antioxidant activity observed by us. **Acknowledgments –** SECTI - Secretaria de Ciência, Tecnologia e Inovação da Bahia; Fundação de Amparo à Pesquisa do Estado de São Paulo; Universidade Estadual Paulista “Júlio de Mesquita Filho”.

**09.062 Comparative toxinology of *Bothrops jararaca* and *Bothrops fonsecai* snake venoms**. Collaço RCO[1], Silva IRF[1], Tamascia ML[1], Cogo JC[2], Randazzo-Moura P[3], Rodrigues-Simioni L[1], Hyslop S[1] [1]FCM-Unicamp – Farmacologia, [2]Univap – Pesquisa e Desenvolvimento, [3]PUC-SP – Farmacologia

**Introduction:** *Bothrops jararaca* is a major cause of snakebite in southeastern Brazil and the composition and action of this species´ venom have been extensively studied. In contrast, *Bothrops fonsecai* has a very limited distribution in the Serra da Mantiqueira of southeastern Brazil and relatively little is known of the toxinology of this species. In this work, we compared the biological activities of *Bothrops jararaca* and *Bothrops fonsecai* venoms. **Methods:** Coagulant activity (clotting time) was assayed in citrated platelet-poor plasma, proteolytic activity was assayed using casein and esterase activity was quantified using tosyl-L-arginine methyl ester (TAME). Myotoxicity was assessed *in vivo* based on creatine kinase (CK) release and histological analysis 3, 6 and 12 h after venom (30 mg) injection in mouse gastrocnemius muscle. Neuromuscular activity was assayed in mouse *extensor digitorium longus* (EDL) preparations using standard myographic techniques. Hemorrhagic activity (3-30 mg for *B. fonsecai* and 4.5, 13.5 and 45 mg for *B. jararaca*) and edema formation (30 mg of venom) were determined in rat dorsal skin. The results were expressed as the mean±SD. These experiments were approved by an institutional Committee for Ethics in Animal Use (CEUA/UNICAMP, protocol no. 2648-1 and 2253–1). **Results:** *Bothrops fonsecai* venom caused a partial neuromuscular blockade at 30µg/ml and total at 100µg/mL (n=5-7) while *Bothrops jararaca* produces a parcial blockade at all tested concentrations (n=4). Both venoms (*Bothrops fonsecai* and *Bothrops jararaca*, 30 mg) demonstrated a myotoxicity by CK release, with activity peak 6 hours after the venom injection (1736.82±93.7 and 981.1± 279.6 U/L, respectively, mean±SD, n=5) as also showed muscle damage on histological analysis. *B. fonsecai* and *B. jararaca*, also show edema-forming action (330±23µl and 149.8±56.4µl respectively, mean±SD, n=5), rat plasma clotting activity (33±10.5 and 42.13±12.2s, respectively, mean±SD, n=5) and hemorrhagic activity (MHD: 69.2mg and 5.8mg, respectively). Both venoms were able to degrade casein (100ug) and show sterasic activities (*B. fonsecai*: 2.5±0.37 and 1.45±0.52U/min and *B. jararaca*: 15.3±0.5 and 6.2±0.68U/min, respectively; means±SD; n=3). **Discussion:** These results show that both venoms contained all of the activities investigated although there were variations in the potencies of the two venoms. **Financial support:** CAPES, CNPq, FAPESP, FAEPEX-UNICAMP

**09.063 Preliminary assessment of the bioactivity of ethanol extracts of parts of *Moringa oleifera* Lam**. Nascimento JA[1], Santos AM[2], Nascimento AA[2] [1]UFPB – Ciência e Tecnologia de Alimentos, [2]Unifap – Ciências da Saúde

*Moringa oleifera* Lamarck is a tree native to India (Bezerra, Hort. Bras.,v. 22, p.295, 2004) where it is traditionally used as a medicinal herb to treat and prevent numerous diseases, acting as antibiotic, antitripanossomal, hypotensive, anti-ulcer, antispasmodic, anti-inflammatory, hypocholesterolemic and hypoglycemic (Cáceres J. Ethnopharmacol., v.36, p. 233, 1992; Faizi J. Nat. Prod., v. 57, p. 1256, 1994; Haristoy, Planta Med., v.71, p.326, 2005; Karadi, J. Ethnopharmacol.,v. 105, p. 306, 2006; Chumark, J. Ethnopharmacol., v. 116, p.439, 2008; Jaiswal J. Ethnopharmacol., v. 123, p. 392, 2009; Oluduro, Folia Microbiol.,v. 55, p. 422, 2010; Bijina, SJBS. v. 18, p. 273, 2011; Debnath J. P. Phytopharmacol.,v. 18, p. 91, 2011; Abrogoua J. Ethnopharmacol., v.141, p. 840, 2012). Popularly known as “lírio-branco”, “quiabo de quina” or simply “moringa” (Santos, 2010) was introduced in Brazil by 1950, where it is cultivated as an ornamental and medicinal plant however still little explored in here. Given the rich constitution of compounds found in "moringa", it should also be emphasized the need to demonstrate the safe use of the plant, ie, the guarantee that it has no ability to produce toxic effects to the consumer. The aim of this study was to make a preliminary assessment of the toxicity of above the etanolic extracts from M. oleifera (leaves, flowers, seed pods and seeds) using the bioassay with Artemia salina to determine the LC50 (median lethal concentration). The metanauplius brine shrimp were exposed to different concentrations of the extract (1-1000 ug / ml) was performed 24 hours after the counting of live and dead larvae. The LC50 was determined according to the statistical method using the probit program Microcal Origin 6.0. The etanolic extracts from M. oleifera (leaves, flowers, seed pods and seeds) showed bioactivity against Artemia salina, according to determined LC50 (394.07, 349.82, 391.97 e 444.83, respectively).These results suggest that the extract has in its constitution bioactive compounds. Probably such activity is not related to toxic property, because according to Meyer (1992) the LC50 is less than 1000 mg / mL indicates bioactivity and the closer to zero toxicity. **Financial support:** CNPq/PIBIC/CAPES