08. Respiratory and Gastrointestinal Pharmacology

08.001 Role of the TRPV1 receptor in plasma extravasation induced by captopril in rat airways. Matias-Oliveira JRJ[1], Otuki MF[1], Cabrini DA[1], Brusco I[2], Oliveira SM[2], Ferreira J[3], André E[1] [1]UFPR- Farmacologia, [2]UFSM – Bioquímica, [3]UFSC – Farmacologia

Angiotensin-converting enzyme inhibitors (ACEIs) are widely used in the treatment of hypertension, congestive heart failure and renal disease, and are considered relatively safe and generally well-tolerated drugs. However, adverse effects of ACEIs have been reported, including non-productive cough and angioedema, which can lead to poor adherence to therapy. The mechanisms by which ACEIs promote adverse effects are not fully elucidated, although increased bradykinin plasma levels following ACEI therapy seem to play an important role. Since bradykinin can sensitise the transient potential vanilloid receptor 1 (TRPV1), we investigated the role of TRPV1 in plasma extravasation in the trachea and bronchi of rats treated with the ACEI captopril. We observed that intravenous (i.v.) administration of captopril did not cause plasma extravasation in the trachea or bronchi of spontaneously breathing rats, but induced plasma extravasation in the trachea and bronchi of artificially ventilated rats. The intratracheal (i.t.) instillation of capsaicin or bradykinin also induced an increase in plasma extravasation in the trachea and bronchi of artificially ventilated rats. As expected, capsaicin-induced plasma extravasation was inhibited by i.t. pretreatment with the TRPV1 selective antagonist capsazepine (CPZ) while bradykinin-induced plasma extravasation was reduced by i.t. pretreatment with the selective B2 receptor antagonist Icatibant, originally known as HOE 140 (HOE). Interestingly, bradykinin-induced plasma extravasation was also inhibited by CPZ. The pretreatment with HOE and CPZ, singly or in combination and at doses which do not cause inhibitory effects *per se*, significantly inhibited the plasma extravasation induced by captopril treatment in artificially ventilated rats. In addition, treatment with a high dose of capsaicin in newborn rats, which induces degeneration of TRPV1-expressing sensory neurons, abolished both capsaicin and captopril-induced plasma extravasation in artificially ventilated rats. In conclusion, our study identified that captopril treatment promoted sensitization of TRPV1, via B2 receptor activation, inducing plasma extravasation in the airways of mechanically ventilated rats. The present findings add a new view about the role of TRPV1 in the plasma extravasation induced by captopril and could to contribute to the elucidation of mechanisms by which ACEI induces adverse effects on airways. This study was supported by grants from CAPES and CNPq. Experimental procedures were performed after approval of the protocols by the local Ethics Committee of Animal Experimentation of the Federal University of Paraná (Protocol n° 800/2014).

08.002 Functional evaluation of guinea-pig tracheal contractile reactivity in a model of chronic allergic asthma. Silva MCC, Vasconcelos LHC, Costa AC, Oliveira GA, Cavalcante FA, Silva BA DCF-UFPB

Introduction: Asthma is a heterogeneous disease, usually characterized by chronic inflammation associated with bronchial hyperresponsiveness of the airways, which triggers respiratory symptoms such as wheezing, breathlessness, chest tightness, cough and airflow expiratory limitation. It is a disease considered a world order problem that affects 300 million people (Cruz, J. Bras. Pneumol., v. 38, p. S1, 2012). Therefore, this study aimed to evaluate the contractile response of guinea-pig trachea to pharmaco- and electromechanical couplings in a model chronic allergic asthma. **Methods**: In vivo sensitization was performed in guinea-pig (Cavia porcellus, 300-350 g initially) with ovalbumin (OVA), employing the method adapted (Tibério, Am. J. Respir. Crit. Care Med., v. 155, p. 1739, 1997). Then, in vitro, segments of trachea were suspended in organ baths under appropriate conditions and isometric tensions were registered by force transducer. To verify the tracheal epithelium integrity, relaxation response to arachidonic acid 10^{-4} M were evaluated in pre-contracted trachea induced by carbachol (CCh) 10^{-6} M. The preparations were considered with functional epithelium when the relaxation was ≥ 50% and denuded in relaxation absence or less than 10% (Tschirhart, J. Pharmacol. Exp. Ther., v. 243, p. 310, 1987). Contractile reactivity of trachea was evaluated by fitting cumulative concentration-response curves to agonists CCh and histamine and to depolarizing agent KCl. The values were expressed as the mean and standard error of the mean and statistically analyzed by the Student's t-test or one-way ANOVA followed by Bonferroni's test ($p < 0.05$), $n = 5$ for each experimental protocol. **Results**: Guinea-pig trachea from asthmatic group (ASMG) presented increase in tensile strength ($t = 2.02 \pm 0.25$ gf) in response to stimulation by OVA 10 µg/mL compared to control group (CG) ($t = 0.04 \pm 0.02$ gf), indicating that allergic asthma model was induced successfully. Then, compared to CG, guinea-pig trachea from ASMG presented increased efficacy, but not altered potency to CCh in both the presence (E_{max} = 100 and 185.3 ± 16.1%; EC_{50} = 2.6 ± 0.5 and 1.8 ± 0.1 x 10^{-7} M, respectively) and absence (E_{max} = 100 and 144.0 ± 2.7%; EC_{50} = 2.6 ± 0.4 and 2.8 ± 0.5 x 10^{-7} M, respectively) of functional epithelium. Similarly for histamine, ASMG presented higher efficacy compared to CG without change on potency, in both the presence (E_{max} = 134.8 ± 4.1 and 100%; EC_{50} = 1.0 ± 0.1 x 10^{-5} and 9.0 ± 0.9 x 10^{-6} M, respectively) and absence (E_{max} = 139.0 ± 7.3 and 100%; EC_{50} = 2.1 ± 0.5 and 1.6 ± 0.3 x 10^{-6} M, respectively) of functional epithelium. However, for KCl, there was no difference in contractile response between CG and ASMG, in both the presence (E_{max} = 100 and 119.0 ± 14.2%; EC_{50} = 2.5 ± 0.1 and 2.8 ± 0.2 x 10^{-2} M, respectively) and absence (E_{max} = 100 and 107.6 ± 11.5%; EC_{50} = 1.4 ± 0.2 and 1.9 ± 0.2 x 10^{-2} M, respectively) of functional epithelium. **Conclusions**: These results indicate that the guinea-pig asthma model promotes pharmacomechanical-dependent changes in smooth muscle contractile machinery and the efficacy increase to agonists may be associated to hypertrophy of smooth muscle cells. **Financial support**: CAPES, CNPq, PPgPNSB/UFPB. Research approval: Ethical Committee on Animal Use/UFPB (0410/13).

08.003 Evaluation of gastric healing activity of *Baccharis dracunculifolia* **hidroalcoholic extract and the contribution of its isolated compounds.** Costa P[1], da Silva LM[1], Boeing T[1], Somensi LB[1], Bastos JK[2], Andrade SF[1] [1]Univali – Ciências Farmacêuticas, [2]FCFRP-USP

Introduction: *Baccharis dracunculifolia*, popularly knew as "vassourinha" or "alecrim-do-campo", is used in folk medicine to treat gastric diseases, inflammation and hepatic disorders. Despite gastroprotective effect of the hydroalcoholic extract of *B. dracunculifolia* (HEBD) have already been described, its effects on installed gastric ulcer and on the gastric healing process has not yet been clarified. Thus, this study was designed to clarify these issues. **Methods**: The 80% acetic acid- induced chronic gastric ulcer model was performed in anesthetized rats. In the second day after the surgical procedure, the rats were divided in groups (n=6) and orally treated by seven days, twice a day, with HEBD (30 - 300 mg/kg), omeprazole (20 mg/kg) or vehicle (10 mL/kg, water plus 0.5% DMSO). At the final of the treatment period, the stomachs were removed and ulcer area measured. Site of ulcer were collected and processed for histological, histochemical and biochemical analyses. In vitro trials were performed to evaluate the inhibitory effect of HEBD on the H^+/K^+- ATPase activity and their scavenger effect was in 2,2-diphenyl-1-picrylhydrazyl assay. Phytochemical analyses in HEBD identified, isolated and quantified the main compounds: cummaric acid, ferulic acid, caffeic acid, artepelin C, baccharin and aromadrendin; which were administered in mice exposed to 10% acetic acid to induce chronic gastric ulcers at the dose calculated by its yield in the HEBD. **Results**: The HEBD (300 mg/kg, p.o) accelerate the healing gastric ulcer area in 49.5%, when compared to ulcerated group treated with vehicle (108.8 ± 8.5 mm^2).The healing effect was confirmed in the histological evaluation and by an intense increase in mucin content on the periodic acid–Schiff staining, suggesting an expansion of the mucus layer. In addition, at ulcerated tissue superoxide dismutase and glutathione-S-transferase activity were normalized, the levels of glutathione reduced were increased, whereas the myeloperoxidase activity was decreased by the treatment with the extract compared to ulcerated vehicle group. These findings confirm that HEBD improves the inflammatory and oxidative status during the healing gastric process. In vitro assay also confirm an intense scavenging potential of HEBD up to 10 µg/mL. Besides, HEBD at concentrations of 100 and 1000 µg/mL reduced the H^+/K^+- ATPase activity in 23.7 and 35.2 %, when compared to vehicle group (1.6 ± 0.1 µMPi/mg protein/min). Then, the healing activity of the isolated compounds were verified and only cumaric acid (15 mg/kg) accelerate the healing gastric ulcer, promoting a reduction in the ulcer area by 66.3%, compared to vehicle group (34.7 ± 3.5 mm^2). Conclusion: The HEBD accelerate the healing gastric process and this effect is favored by an intense increase in mucus layer, enzymatic and non- enzymatic antioxidant mechanism, reduction in gastric inflammatory process and by inhibition of H^+/K^+- ATPase activity. Furthermore, the cumaric acid is an important constituent to the HEBD healing gastric effect. At this time, experiments are being conducted to evaluate the effect of each compound on the H^+/K^+- ATPase and on the COX-1 and -2 activity. **Financial support**: CNPQ, CAPES, FAPESC. Approval number CEUA: 10/2015.

08.004 Effect of pyridostigmine on respiratory dysfunction in mdx mouse Amancio GCS[1], Silva-Barcelos MN[1], Cazorla O[2], Grabe-Guimarães A[1] [1]UFOP – Ciências Farmacêuticas, [2]Université de Montpellier

Introduction: Piridostigmine (PYR) is a reversibible inhibitor of acetylcholinesterase, and clinically employed to treat Miastenia gravis. PYR promotes an increase of endogenous acetylcholine that, besides increasing muscular strength, also plays an important role in inflammatory processes modulation. The Duchenne Muscular Dystrophy (DMD) is a recessive hereditary disorder linked to the X chromosome, resulting from lack of dystrophin expression in skeletal muscle. The absence of dystrophin causes chronic inflammation and muscles degeneration and consequently leads to muscle strength loss. Patients with this dystrophy gradually develop cardiac and respiratory failure. The focus of the current work was to verify the effect of PYR on respiratory dysfunction in the mdx mouse model of DMD. **Methods:** We evaluated the effect of PYR on respiratory function in vivo by whole body plethysmography in 17 month-old mdx mice and C57BL10 (control group). Baseline ventilatory parameters (VT: tidal volume, MV: minute ventilation, and RR: respiratory rate) of the animals were recorded during ambient air flow and hypercapnia conditions with airflow containing 8% CO2. The plethysmography was performed before (baseline) and after single dose treatment with PYR (0.01 mg/kg. 0.1 mg/kg and 1 mg/kg, S.C.). **Results:** The respiratory parameters are altered in mdx mice. In basal conditions, there was a reduction of VT (0.24 ± 0.01 vs. 0.35 ± 0.03 µl) and VM (39.85 ± 3.1 vs. 51.4 ± 5.1 ml/min) and increased RR (178 ± 6 vs. 148 ± 8 bpm) compared to C57BL10. During hypercapnia, the mdx showed significant reduction of VT (0.46 ± 0.03 vs. 0.63 ± 0.03 µl), VM (131.9 ± 7.6 vs. 172.9 ± 10.6 ml/min), and RR (259 ± 3 vs. 276 ± 7 bpm) compared to C57BL10 mice. The treatment with PYR 0.01 didn't alter the ventilatory parameters in mdx. During ambient airflow and hypercapnia, there was no difference in the VT (0.23 ± 0.02 and 0.45 ± 0.03 µl), VM (35.5 ± 3.7 and 121 ± 8.4 ml/min) and RR (172 ± 3.3 and 272 ± 5.4 bpm), respectively. The dose PYR 0.1 mg/kg also didn't change the parameters, VT (0.21 ± 0.02 and 0.47 ± 0.04 µl), VM (34.7 ± 3.2 and 122 ± 10.5 ml/min) and RR (171 ± 8.6 and 259 ± 4.7 bpm). On the other hand, PYR 1 mg/kg was toxic and animals died about 1 hour after subcutaneous administration, probably due to marked bradycardia. This dose was not toxic for C57BL10 mice. Thus, mdx mice seems to be more responsive to acethylcholine acumulation. **Conclusion:** Treatment with PYR did not show any beneficial effect on respiratory function in mdx mice. Despite the result on the plethysmography, the effect of PYR on muscle inflammation should be evaluated. **Keywords:** Pyridostigmine, Duchenne Muscular Dystrophy, Respiratory function, Pletysmography. **Financial Support:** FAPEMIG (Rede NanobioMG, PPM 2013); CNPq (205897/2014-2), CAPES, UFOP, INSERM U1046. **Process number Animal Research Ethical Committee**: nº 2014/12.

08.005 Gastroprotective xanthones isolated from *Garcinia achachairu*: Study on mucosal defensive factors and H^+, K^+-ATPase activity Mariano LNB, da Silva LM[1], de Souza P[1], Boeing T[1], Somensi LB[1], Bonomini TJ[1], Cechinel-Filho V[1], de Andrade[1], Niero R[1] [1]Univali

Introduction: In the last years several studies have shown a wide variety of natural compounds with potential gastroprotective effect, including alkaloids, saponins, tannins, triterpenoids and xanthones. In this context, some species of the genus Garcinia are of great interest, given the presence of chemicals such as benzophenones and xanthones with relevant biological effects. The present study was designed to investigate the gastroprotective effect of xanthones isolated from Garcinia achachairu in ethanol-induced gastric ulcer model in mice. **Methods**: The four xanthones have been isolated of branches from G. achachairu through column chromatography silica-gel and eluted with mix solvents of polarity increasing and were identified through nuclear magnetic resonance (NMR) proton and carbon, 13C-NMR spectrum using polarization transfer (Dept) and Heteronuclear Multiple Bond Correlation (HMBC), in comparison with data reported previously. The xanthones were tested against gastric ulcer 60%/HCl 0.3 N-induced in female swiss mice (25-30 g). The mice were divided in groups of six animals each orally pretreated with vehicle (VEH; water plus 1% tween, 1 ml/kg), carbenoxolone (CBX; 200 mg/kg; a positive control) or xanthones at dose of 10 mg/kg. One hour later, all the groups received 0.2 ml of ethanol 60%/HCl 0.3 N to induce gastric ulcer. After one hour, the animals were euthanized, the stomachs removed, opened along the greater curvature and the area of lesion (mm^2) was measured using EARP® software. The stomachs were also used to analysis of mucin content, oxidative stress, inflammatory parameters, as well as, the determination of H^+K^+-ATPase activity was performed. **Results**: The oral treatment with xanthones 7-preniljacareubin (PJB) and 1,3,5,6-tetrahydroxy xanthone (THX), but not 3-demethyl-2-geranyl-4-prenylbellidypholine (DGP) and 1,5,8-trihidroxy-4', 5'-dimethyl-2H-pyrane (2,3:3,2)-4-(3-methylbut-2-enyl) xanthone (TDP), displayed protective effect against gastric ulcer ethanol 60%/HCl 0.3 N- induced. Both PJB and THX have promoted gastroprotection by oral route at 10 mg/kg, in parallel to the augmentation in the antioxidative capacity of tissue by an increase in glutathione levels, as well as, were able to prevent an increase in myeloperoxidase activity and tumor necrosis factor level. The minimum effective dose of PJB was 1 mg/kg (p.o) and of THX was 10 mg/kg (p.o). Furthermore, only PJB avoided mucus depletion on gastric mucosa, which was not associated with an increase in mucin production at glandular level. Besides, the four xanthones promoted gastroprotection against ethanol acidified, when administered intraperitoneally at the dose of 1 mg/kg. In addition, PJB and THX inhibited the in vitro H^+K^+-ATPase activity at similar range as omeprazole. Conclusion: Together, these results demonstrate the gastroprotective efficacy of xanthones isolated from G. achachairu, which can contribute for future development of effective drugs to treat gastric diseases. **Financial support**: CNPQ, CAPES. Process number: CEUA 034/15.

08.006 Eucalyptol attenuates oxidative stress and inflammation on mouse lung. Kennedy-Feitosa E[1], Cattani-Cavalieri I[2], Valente M[3], Romana-de-Souza B[2], Lanzetti M[1], Gitirana LB[1], Valença SS[1] [1]UFRJ – Ciências Biomédicas, [2]UERJ, [3]UFRJ – Microbiologia

Introduction: Eucalyptol (EUC) is a monoterpene known for its mucolytic and spasmolytic action on the respiratory tract, with proven clinical efficacy (Juergens, Drug Res; 64: 638–646, 2014). Our aim was to investigate the EUC activity against acute and chronic lung inflammation induced by cigarette smoke (CS) in C75BL/6 mice. **Methods**: Mice were grouped in CS and sham-smoked groups. CS group was exposed for 5 days (acute phase) or 60 days (chronic phase) to CS and treated with EUC (1, 3 or 10 mg/mL by nebulization) or vehicle. During the acute phase the EUC was given during the same 5 days of CS exposed, however, in the chronic phase the animals were treated during 60 days post emphysema condition. Twenty-four hours after BAL was performed and lungs were removed for histological analysis and homogenized for biochemical analyses and molecular biology. **Results** were considered statistically significant when $p<0.05$. **Results**: In acute phase, histological analysis shows reduce of inflammatory cells especially in EUC 10 mg/mL group. EUC reduced leukocyte numbers (3 and 10 mg/mL). Macrophage was lower at all doses. EUC also reduced TNF-α (10 mg/mL), IL-1β (3 and 10 mg/mL) IL-6 (10 mg/mL) and KC (10 mg/mL) levels. EUC reduced NF-κB expression in all the doses. EUC was able to reduce ROS (3 and 10 mg/mL), SOD (all the doses) and CAT (3 and 10 mg/mL). MDA also was reduced (3 and 10 mg/mL), and recovered the GSH levels (3 and 10 mg/mL). In chronic phase, histological analysis shows that EUC 10 mg/mL reduced mean linear intercept (Lm) and septum alveolar density (Vv septum). MPO levels were reduced in the dose of 10 mg/mL. Elastin/Neutrophil elastase expression ratio was recovered (10 mg/mL) while TIMP-1/MMP-12 expression ratio was not recovered. EUC 10mg/mL also reduced TNF-α, IL-1β, IL-6, TGF-β1 and KC levels. EUC 1 and 10 mg/mL reduced MDA levels. SOD activity was recovered with EUC (10 mg/mL), without any difference in Nrf2 expression. **Conclusion**: Eucalyptol is able to reduce inflammation and oxidative stress induced by cigarette smoke on mouse lung. **Financial support**: CNPq CEUA: DFBCICB067

08.007 Assessment of gastroprotective components of the *Dalbergia brasiliensis*. Dalarmi L, Burci LM[1], Silva CB, Boeing T, Bordignon L, dos Santos SCS, da Silva LM, de Andrade SF[2], Miguel MD [1]UFPR- Ciências Farmacêuticas, [2]Univali – Ciências Farmacêuticas

Introduction: The stem barks from Dalbergia monetaria L. are popularly used in Brazil for the treatment of gastric ulcer; while Dalbergia sissoo Roxb. stem barks are used to treat the same disease in the Indian system of medicine. In addition, preclinical studies have already confirmed the antiulcer potential of preparations from stem barks of these species (Khan and Khan, Osong *Public Health Res Perspect.* 4(5):271-277, 2013; Cota et al., J Pharm Pharmacol. 51(6):735-740, 1999). Dalbergia brasiliensis (Fabaceae), popularly known as "jacarandá" is a Brazilian native plant found in the Midwest, Southwest and South of Brazil. Aim: Taking into account the gastroprotective potential of Dalbergia genus and that D. brasiliensis is endemic on the Brazilian Cerrado and Atlantic Forest, this study was conducted to evaluate the presence of antiulcer compounds in D. *brasiliensis* stem bark methanol extract (DBME) in ethanol- and indomethacin-induced gastric ulcer in rodents. **Methods**: Firstly, the gastroprotective effects of DBME (1 – 100 mg/kg, p.o) were investigated in acute gastric ulcer induced by ethanol/HCl in mice and after against indomethacin-induced ulcer in rats at the minimum effective dose displayed in acidified ethanol model. In parallel, phytochemical trials were performed to identify and to obtain isolated compounds from DBME. Further, the antiulcer potential of isolated constituents was tested against acidified ethanol-induced ulcer in doses based in their yield and the minimum effective dose of the DBME. Carbenoxolone (200 mg/kg, p.o) was employed as positive control in the ulcer experiments. The ulcerated tissues were collected to biochemical analysis. The experiments were conducted in accordance with the Ethical and Practical Principles of the Use of Laboratory Animal Guidelines, and the experimental procedures were previously approved by the Institutional Ethics Committee of the Federal University of Paraná (CEUA/UFPR; approval number 917). **Results**: Oral administration of DBME at doses of 10, 30 and 100 mg/kg reduced the ulcer area induced by ethanol/HCl in mice by 68, 62 and 61%, respectively, compared to the vehicle group (24.8 ± 1.8 mm^2). In addition, DBME (10 mg/kg, p.o) was able to decrease the ulcer area by 98% in the indomethacin-induced gastric ulcer in rats (vehicle group: 9.7 ± 2.0 mm^2). Three semi-purified fractions were obtained from DBME, namely: 1, 2 and 3. Only the semi-purified fraction 1 was able to reduce the HCl/ethanol- induced gastric ulcer by 70%; and this effect was accompanied by the prevention of the mucus depletion, the decrease in myeloperoxidase activity and lipoperoxides content, as well as, the increase in the gluthatione reduced levels at ulcer site. Finally, the isoflavonoids afrormosin and fujikinetin were identified in bioactive semi-purified fraction. Conclusion: Together, these results point out that the gastroprotective effect of stem barks from D. *brasiliensis* is due to the presence of the isoflavonoids and is mediated by the increase in the mucus protective barrier in parallel to the reduction in oxidative damage. **Financial support**: CAPES, EMBRAPA, FAPESC.

08.008 Relaxant activity of flavonoid galetin 3,6-dimethyl ether on non-asthmatic and asthmatic Guinea-pig trachea Vasconcelos LHC, Martins IRR, Silva MCC, Souza ILL, Oliveira GA, Santos BVO, Cavalcante FA, Silva BA UFPB

Introduction: Galetin 3,6-dimethyl ether (FGAL) was obtained from aerial parts of Piptadenia stipulacea (Benth.) Ducke (Fabaceae), a Caatinga tree from Brazilian northeast[1]. Previously, we demonstrated a relaxant effect of FGAL on trachea from non-asthmatic guinea-pigs pre-contracted by carbachol (CCh)[2]. Thus, we aimed to characterize a possible relaxant action of FGAL and its mechanism on asthmatic guinea-pig trachea as well as on non-asthmatic, using different contractile agent. **Methods**: Sensitization of guinea-pig (350-400 g) was performed with ovalbumin (OVA)[3]. Then, segments of guinea-pig trachea were suspended in organ baths under appropriate conditions, and force transducer registered isometric contractions. **Results** were expressed as mean and standard error of mean and analyzed by Student's t-test or one-way ANOVA followed by Bonferroni's post-test (n=3-5). **Results**: As expected, while non-asthmatic guinea-pig trachea did not present contractile effect in response to stimulation by OVA 10 µg/mL, asthmatic guinea-pig developed tension of 2.41 ± 0.15 gf. FGAL (10^{-8}-10^{-4} M) relaxed tracheal segments from asthmatics pre-contracted by CCh 10^{-6} M in both the presence (pD_2 = 5.04 ± 0.04) and absence (pD_2 = 4.98 ± 0.09) of functional epithelium, not differing on pD_2 values of those from non-asthmatic animal. The flavonoid also presented equipotent relaxation on non-asthmatic and asthmatic guinea-pig trachea pre-contracted by histamine 3 x 10^{-5} M in both the presence (pD_2 = not determined and 5.29 ± 0.08, respectively) and absence (pD_2 = 5.58 ± 0.06 and 5.45 ± 0.04, respectively) of functional epithelium. The relaxant potency of FGAL was greater front histamine than CCh in both non-asthmatic and asthmatics. Additionally, FGAL inhibited the tracheal basal tone (pD_2 = 5.53 ± 0.05 and 5.09 ± 0.03, respectively) being more potent in asthmatics. In the presence of propranolol 10^{-6} and 3 x 10^{-6} M (pD_2 = 5.01 ± 0.07 and 5.43 ± 0.17, respectively), the relaxant potency of FGAL (pD_2 = 5.04 ± 0.04) in asthmatics was not altered. However, in the presence of propranolol 10^{-5} M, it was approximately 3-fold reduced (pD_2 = 4.65 ± 0.08), indicating a possible involvement of β_2 receptors. Nonetheless, neither the adenylate cyclase nor the PKA are involved, since the relaxant effect of forskolin (pD_2 = 7.20 ± 0.07) was not altered in the presence of FGAL (pD_2 = 7.01 ± 0.06), and the relaxant potency of FGAL (pD_2 = 5.04 ± 0.04) was not modified in the presence of H-89 10^{-7}, 3 x 10^{-7} or 10^{-6} M (pD_2 = 5.14 ± 0.13; 4.84 ± 0.06 and 4.89 ± 0.03, respectively). Conclusion: Therefore, FGAL presents more potent effect to reduce the basal tone of asthmatic than non-asthmatic guinea-pig trachea, and its relaxant effect in pre-contracted organ appears to involve blockade of histaminergic and activation of β_2 receptors, with no involvement of the downstream AC-cAMP-PKA pathway. **Financial support**: CNPq, CAPES, PPgPNSB/UFPB. Research approval: Ethical Committee on Animal Use of UFPB (0410/13). References: [1]Queiroz, J. Ethnopharmacol., v. 128, p. 377, 2010; [2]Macedo, Z. Naturforsch. C., v. 69, p. 434, 2014; [3]Espinoza, J. Steroid Biochem. Mol. Biol., v. 138, p. 174, 2013.

08.009 Is it possible to treat GERD with natural products? Novel approach of a versatile biopolymer obtained from *Anacardium occidentale* **L.** Nicolau LAD[1,2], Batista-Lima FJ[2], Santana APM[2], Medeiros JV[3], Silva DA[3], Santos AA[2], Sifrim D[1], Souza MHL[2] [1]Queen Mary University of London – Barts and the London School of Medicine and Dentistry, [2]UFC – Fisiologia e Farmacologia, [3]UFPI – Biotechnology and Biodiversity

Introduction: Gastroesophageal reflux disease (GERD) can be defined as symptoms or mucosal damage produced by the abnormal reflux of gastric contents into the esophagus (DeVault KR. Am J Gastroenterol.1:190, 2005). Alternative ways of treatment have to be considered, and in this context, natural products appear as new pharmacological tools. We aimed to develop the first review related to natural products vs GERD and to assess the mucosal protection effect of the biopolymer cashew gum (BCG), a natural product obtained from bark of Brazilian northeastern tree (*Anacardium occidentale* L.), in human esophageal biopsies. The present biopolymer has previously shown gastro-protective effect in animal models of NSAID-induced inflammation (Carvalho NS. Drug Dev Res.3:143, 2015). Impairment of esophageal mucosal integrity is important in the pathophysiology of GERD. Previous studies showed esophageal topical protective effect by alginates (Woodland P. Am J Physiol Gastrointest Liver Physiol.12:G975, 2015). **Methods**: The review was done under an extensive search to access in the last 30 years on databases (PUBMED, LILACS and SCIELO) including strategies such combinations of keywords. The experimental studies were performed on distal esophageal biopsies from patients; Eighteen patients with heartburn (nine with NERD). Biopsies were mounted in specially adapted Ussing chambers to measure transepithelial electrical resistance (TER). After a 30 minutes period of stabilization, the chambers were opened for a short exposure of the biopsies' mucosal side to a protectant solution (BCG 2.5, 5 and 10% w/v). Negative control biopsies were not exposed to "protectants". Positive control biopsies were exposed to a commercial alginate based product. **Results**: We had found around 25 natural products with different mechanisms of action and targets in the esophagoprotection both in experimental models and in clinical trials, this is an original compilation in gastroenterology. Moreover, our experimental data show that the acid-pepsin-BA solution provoked a TER drop in the "unprotected" biopsies (negative control) of -20.02±2.4%. In biopsies protected by alginates (positive control), the TER change was of +3.5±0.7% ($P<0.05$). The BCG at 2.5% did not prevent a drop of TER. In contrast, BCG at 5% and 10%, majorly, had a significant ($P<0.05$) protective effect (TER drop of -1.69±2.4% and change of +4.4±1.0% respectively). **Conclusion**. The compilation review opens avenues to GERD research. Our experimental data show that the BCG solution (5% and 10%) produced "in vitro" topical esophageal mucosal protection. This effect was probably due to its mucoadhesiveness properties provided by complex polysaccharides. In vivo long-lasting effect of this muco-protective product will be further explored as add-on therapy for GERD. **Financial Support**: CNPq. **Approval by the Human Research Ethical Committee**: Federal University of Ceará - 39538814.6.0000.5045.

08.010 Pharmacological effects of β-Phenylethylamine (β-PEA) on the contractility of stomach fundus and ileum isolated strips of rats. Oliveira TL, Rodrigues FMS, Batista-Lima FJ, Brito TS, Magalhães PJC UFC – Farmacologia e Fisiologia

Introduction: β-Phenylethylamine (β-PEA) is a trace biogenic amine present in low concentrations in the body, and naturally found as constituent in foods such as chocolate and cheese. It was previously shown that β-PEA has direct pharmacological effects in isolated ileum and mesenteric vessels (Br J Nutr. 101, 2009). The present study aimed a further characterization of the effects of β-PEA in gastrointestinal tissues, with emphasis on the mechanism of action. **Methods**: Strips of stomach fundus and ileum were carefully isolated from male *Wistar* rats and transferred to a tissue bath (5 ml) filled with Tyrode's solution (pH 7.4) continuously aerated at 37 °C with 5% CO_2 in O_2. Tissues were stretched with a passive tension of 1 g and tension was recorded using isometric force transducer connected to a data acquisition system. Equilibration period was 60 min. Afterwards, repeated stimuli with KCl (60 mM) were applied until obtain two consecutive similar responses. **Results**: Cumulative addition of β-PEA (0.1 – 1000 μM) contracted fundic strips in a concentration-dependent manner ($n = 8$; $p < 0.05$, ANOVA Holm Sidak) reaching magnitude of 73.1 ± 6.4% of a reference contraction (60 mM KCl) at the highest β-PEA concentration. Pretreatment with the muscarinic antagonist atropine (1 μM) did not significantly modify the contractile effect as the highest concentration of β-PEA elicited a contraction corresponding to 69.8±10.9% ($n = 5$; $p > 0.05$, ANOVA). However, when the preparation was maintained in Ca^{2+}-free medium, the contraction caused by β-PEA was abolished ($n = 5$; $p < 0.05$, Holm Sidak). Restoration of extracellular Ca^{2+} by adding $CaCl_2$ (0.1 – 10 mM) in a Ca^{2+}-free medium containing β-PEA (300 μM) induced a maximum effect of 42.8 ± 11.6% ($n = 7$) of the reference contraction. In the presence of the voltage-dependent Ca^{2+}channel (VOCC) blocker verapamil (10 μM) this effect was significantly reduced to 14.9 ± 9% ($n = 7$; $p < 0.05$, Holm Sidak). When acetylcholine (ACh, 3 μM) was used in place of β-PEA, cumulative addition of $CaCl_2$ (0.1 – 10 mM) produced maximum effect of 53.0 ± 12.7% ($n = 7$). Verapamil (10 μM) reduced the $CaCl_2$ response in presence of ACh to 22.2 ± 4.7% ($n = 8$; $p < 0.05$, Holm Sidak). In Ca^{2+}-free medium containing β-PEA (300 μM), cumulative addition of $BaCl_2$ (0.1 – 10 mM) in place of $CaCl_2$, the maximum contraction was 90.8% ± 12.8% ($n = 7$) and verapamil (10 μM) abolished this effect ($n = 6$; $p < 0.05$, ANOVA). In strips of ileum, β-PEA (0.1 – 1000 μM) did not change values of basal tonus and spontaneous activity parameters, as rate and amplitude of contractions ($p > 0.05$, ANOVA). Used as positive control, ACh (0.01 – 100 μM) effectivelly stimulated contractile behavior on ileum strips. Conclusion: The contractile effect of β-PEA in isolated strips of gastric fundus does not involve cholinergic muscarinic receptors to produce contractions. In part, β-PEA recruited VOCC opening to promote Ca^{2+} influx and force development. Financial Support: CNPq. Ethics committee approval # 22/2014.

08.011 Evaluation of antioxidant and gastroprotective activities of ethanolic extract of *Avicennia schaue*riana Stapf & Leechman. Rios ACM[1], Barbosa JAP[1], Melo MCS[1], Santana MAN[1], Oliveira TB[1], Bastos IVGA[1], Correa AJC[2], Souza MVB[3], Neto PPM[1], Vieira JRC[4], Silva TG[1] [1]UFPE – Antibióticos, [2]UFPE – Ciências Farmacêuticas, [3]UFPE – Química, [4]UFPE – Ciências Biológicas

Introduction: Brazilian flora plants found in different ecosystems, present a great diversity and are explored in folk medicine (Cechinel Filho, 2000). *Avicennia schaueriana*, popularly known as black mangrove, is an endemic species of mangrove vegetation belonging to the family Acanthaceae. The species of the genus Avicennia are widely used by traditional communities for the treatment of tumors, rheumatism, ulcers and wound healing (Bandaranayake, 1998). Thus, the aim of this study was to evaluate the antioxidant and gastroprotective property of the ethanolic extract of *A. schaueriana*. **Methodology:** The ethanolic extract of the leaves of *A. schaueriana* (As-EtOH) was obtained by maceration, followed by the determination of total phenolic contents, flavonoids, tannins and coumarin. The antioxidant potential of As-EtOH was evaluated by DPPH radical scavenging activity. In acute toxicity were observed physiological, hematological and biochemical parameters. The gastroprotective activity was evaluated by ethanol-induced ulcer in rats, also was determinate the levels of myeloperoxidase (MPO) and histological analysis of the stomach. **Results:** As-EtOH presented a high content of phenolic and total tannins (TEA 216.86 and 199.5 mg/g, respectively), as well as significant antioxidant activity (42.99 ± 0.77 µg/mL). No toxic signs, mortality or changes in the physiological, hematological and biochemical parameters were observed after oral administration of As-EtOH at a dose of 2000 mg/kg. In the model of the ethanol-induced ulcer, As-EtOH (100 mg/kg) reduced the ulcerative lesion by 88.5% and MPO levels, indicating an inhibition in neutrophil migration to the gastric mucous (65.2 %). As-EtOH, also preserved the gastric pits and parietal cells. **Conclusion:** This study showed that the ethanol extract of the leaves of *Avicennia schaueriana* has gastroprotective property, most likely associated with antioxidant capacity of phenolic compounds present in the extract, making it a promising therapeutic alternative for the treatment of gastric ulcer. **Keyword:** antioxidant; gastroprotective; *Avicennia schaueriana.* References: Cechinel F.V. Quím. Nova, v. 23, p 680, 2000. Bandaranayake W.M. Mangroves Salt Marsh, v.2, p. 133, 1998. **Financial Support:** Propesq; CNPq; FACEPE; Universidade Federal de Pernambuco. The experimental protocols were approved by the Ethics Committee on Animal Experimentation (CEEA) / UFPE, process nº **23076.018743/2015-42).**

08.012 Study of gastroprotective activity *Wissadula periplocifolia* **L. (Malvaceae) Mice.** Barros MEFX, Teles YCF, Formiga RO, Pessoa MMB, Souza MFV, Batista LM UFPB – Ciências da Saúde

Introduction: *Wissadula periplocifolia* (L.) C. Presl (Malvaceae) was selected for this study considering the chemotaxonomic criteria, since it is rich in terpenes, fatty acids and flavonoids (VENKATESH, S. J Ethnopharmacol, 67, 1999.), and due to ethnopharmacological criteria, given that the population frequently use it for treating gastric ulcers (SARTORI et al., Rev. Bras Pharmacog, 13, 2003). Some species from this family have already been referenced in the literature as anti-ulcer (LIMA, I.; Rev. Bras Pharmacog, 19, 2009). This study aimed to evaluate the gastroprotective activity of the ethanol extract obtained from the aerial parts of Wissadula periplocifolia (EtOHE-Wp) in the non-steroidal anti-inflammatory drugs (NSAIDs) and stress (immobilization and submission to cold) gastric ulcer protocols. **Methods**: To evaluate the gastroprotective activity in the gastric ulcer model induced by NSAIDs (PUSCAS et al., Arzneimitt. 47, 568, 1997), male Swiss mice (n=7) were pretreated orally with vehicle (Tween 80 solution 8% - negative control) cimetidine 100 mg/kg (positive control) and EtOHE-Wp (62.5, 125, 250 and 500 mg/kg). Thirty minutes after, it was administered the harmful agent, Piroxicam 30 mg/kg. In gastric ulcer model induced by stress (LEVINE, R., Munksg., 92, 1971 – with modifications), male Swiss mice (n=7) were pretreated orally with vehicle (Tween 80 solution 8% - negative control), cimetidine 100 mg/kg (positive control) and EtOHE-Wp (62.5, 125, 250 and 500 mg/kg). After 30 minutes, the animals were immobilized and submitted to the cold of 4 °C. The results were expressed as mean ± standard deviation and analyzed by ANOVA followed by Dunnett's test and Tukey's post test. **Results**: In the model of gastric ulcers induced by NSAIDs, the oral doses of 62.5, 125, 250 and 500 mg/kg from EtOHE-Wp showed gastroprotective effect with ulcerative lesion index of 82.4 ± 11.1 and ($p< 0.01$), 68.3 ± 6.13 and ($p<0.001$), 67.6 ± 10.8 and ($p<0.001$) and 65.4 ± 7.85 and ($p<0.001$), respectively, compared with the negative control group (99.1 ± 20.0) and a lesion inhibition of 17%, 31%, 32%, 34%, respectively. In the model of gastric ulcers induced by stress, oral doses of 62.5, 125, 250 and 500 mg/kg EtOHE-Wp showed gastroprotective effect with ulcerative lesion index of 191 ± 10.6 and ($p<0.01$), 103 ± 4.68 and ($p<0.001$), 97.2 ± 8.59 and ($p <0.001$) and 69.7 ± 4.32 and ($p<0.001$), respectively, when compared with the negative control group (160 ± 16.7) and a lesion inhibition of 19%, 36%, 39%, 56% respectively. Conclusion: Thus, the results of this study show that EtOHE-Wp presented gastroprotective activity to inhibit the formation of mucosal lesions significantly in evaluated models. Acknowledgments: CNPq / CAPES / UFPB. Ethics Committee on Animal Use (UFPB) number 046/2015.

08.013 Evaluation of the antidiarrheal activity and effects in the gastrointestinal motility of p-cymene in mice. Pessoa MMB, Formiga RO, Barros MEFX, Sobral MV, Batista LM UFPB – Ciências da Saúde

Introduction: *p*-cymene (*p*-isopropiltoluene) is an aromatic organic compound from *Potrium* genus essential oils, being more than 80% of these species found in the Amazon region (SANTANA, Rev. Bras. Farmacog., 21, 2011). It is classified as a hydrocarbon belonging to the monoterpene class, carvacrol precursor and its selection for this study was based on chemotaxonomic criteria.The aim of this study was to evaluate the antidiarrheal activity and the effects in gastrointestinal motility of *p*-cymene in animal models. **Methods**: For the experimental protocols, male Swiss mice were used (n=7) weighing 25-35 g and they were pre-treated orally with vehicle, Tween 80 5% (10 mL/kg) (negative control), loperamide 5 mg/kg (positive control) and *p*-cimene (25, 50, 100 and 200 mg/kg – p.o.). The antidiarrheal activity was evaluated using the diarrhea induced by castor oil model (AWOUTERS, F., J. pharmacol., 30, 1978) and the assessment of possible effects on gastrointestinal motility determined by the gastric emptying and intestinal transit protocols (SCARPIGNATO, S., Pharmacodyn., 246, 1980 and STICKNEY, J. Exp. Biol. Med., 101, 1959). The results were analyzed using Kruskal-Wallis test followed by Dunn's (median, minimum and maximum - non-parametric data) and ANOVA followed by Dunnett's test (mean ± standard deviation - parametric data). **Results**: The castor oil-induced acute diarrhea model showed that *p*-cimeno (100 mg/kg and 200 mg/kg) showed antidiarrheal activity with a percentage of diarrhea inhibition of 85% and 100% ($p < 0.001$), respectively, when compared to the negative control group. In the evaluation of gastric emptying, *p*-cymene showed no activity in the different tested doses, when compared to the negative control group. Although, in the intestinal transit model, all doses tested (25, 50, 100 and 200 mg/kg) showed activity reducing the intestinal transit, when compared to the negative control, with percent of transit inhibition of 49%, 47%, 42% and 29% ($p < 0.001$), respectively. **Conclusions**: It is possible to conclude that *p*-cymene has antidiarrheal activity that can be related to antimotility effects. **Acknowledgment**: PIBIC/CNPq/CCS/UFPB. Ethics Committee on Animal Use (UFPB) number 046/2015.

08.014 Evaluation of tracheal relaxant reactivity from chronic allergic asthmatic Guinea-pig. Costa AC, Vasconcelos LHC, Silva MCC, Oliveira GA, Cavalcante FA, Silva BA UFPB

Introduction: Asthma is a chronic inflammatory disease that causes reversible airflow obstruction, leading to bronchial smooth muscle remodeling, increase in mucus production and recruitment of leukocyte cells (Franova, J. Pharm. Pharmacol., p. 1, 2016). Guinea-pig is an animal model easily sensitized to ovabulmin (OVA) developing an asthmatic profile involving eosinophilia and increased airways responsiveness, similar to human (Tibério, Am. J. Respir. Crit. Care Med., v. 155, p. 1739, 1997). Thus, we aimed to evaluate the in vivo inhalation time and in vitro tracheal relaxant response in a model of chronic allergic asthma on guinea-pig.
Methods: *In vivo* sensitization was performed in guinea-pig (Cavia porcellus, 300-350 g initially) with OVA, adapting standardized method (Tibério, Am. J. Respir. Crit. Care Med., v. 155, p. 1739, 1997). Then, isometric contractions of tracheal segments were recorded by force transducer. To verify the tracheal epithelium integrity, relaxation response to arachidonic acid 10^{-4} M was evaluated on carbachol (CCh) 10^{-6} M-induced pre-contracted trachea. Preparations were considered with functional epithelium when relaxation was ≥ 50% and denuded in relaxation less than 10% (Tschirhart, J. Pharmacol. Exp. Ther., v. 243, p. 310, 1987). Relaxing activity was assessed by cumulative addition of isoprenaline (10^{-12}-10^{-5} M) or nifedipine (10^{-11}-10^{-3} M) over CCh-induced tonic contraction. The values were expressed as mean and standard error of mean and statistically analyzed by Student's t-test or one-way ANOVA followed by Bonferroni's test (n = 5-6). **Results**: In the first four nebulizations (1 mg/mL), no difference was observed in the inhalation time between the control group (CG), which was exposed to saline, and the asthmatic group (ASMG) (time = 900 s). Similarly, in the fifth inhalation (OVA 2.5 mg/mL) there was no difference between groups (time = 900 and 878.7 ± 21.3 s, respectively). However, in the sixth (OVA 2.5 mg/mL; time = 506.2 ± 98.7 s) and seventh (OVA 5 mg/mL; time = 285.0 ± 33.7 s) challenge, there was reduction in the inhalation time, compared to CG (time = 900 s), interrupted by sneezing and coughing episodes and/or writhing, characterizing the induction of asthma on guinea-pig. Furthermore, in vitro assessments revealed that relaxing potency of isoprenaline on ASMG trachea was attenuated without change on efficacy compared to CG, in the presence (E_{max} = 124.4 ± 6.6 and 135.7 ± 9.1%; EC_{50} = 6.3 ± 1.4 and 1.8 ± 0.4 x 10^{-8} M, respectively), but not in the absence of functional epithelium (E_{max} = 116.7 ± 12.0 and 121.6 ± 9.2%; EC_{50} = 1.5 ± 0.3 and 1.7 ± 0.3 x 10^{-8} M, respectively). Conversely, there was not any change in relaxing potency and efficacy of nifedipine in both the presence (E_{max} = 122.8 ± 8.8 and 138.2 ± 8,3%; EC_{50} = 5.0 ± 0.2 and 3.6 ± 1.0 x 10^{-5} M, respectively) and absence (E_{max} = 114.7 ± 6.1 and 132.9 ± 7.2%; EC_{50} = 2.9 ± 1.0 and 2.1 ± 0.5 x 10^{-5} M, respectively) of functional epithelium. **Conclusions**: We suggest that the sensitization OVA-induced on guinea-pig may be promoting changes in pharmacomechanical coupling of smooth muscle relaxation in an epithelium-dependent manner. **Financial support**: CAPES, CNPq, PPgPNSB/UFPB. Ethical Committee on Animal Use/UFPB: 0410/13.

08.015 Extract polysaccharide from *Ximenia americana* **Barks prevents indomethacin-induced gastric damage via inibition of neutrophil migration.** Pantoja PS[1], Silva RO, França FV, Matos VEA[2], Pereira MG[1], Soares PMG[2] [1]UECE, [2]UFC – Fisiofarmacologia do Aparelho Gastrintestinal

Gastritis is an inflammation of the stomach, being in many cases synonymous for erosive gastritis or ulcer. The imbalance between aggressive and protective mucous factors contributes to the formation of gastric ulcer. Several factors can destabilize the gastric mucosal barrier, producing damage to the gastrointestinal tract, such as drugs (antineoplasic, bisphosphonates and non-steroidal anti-inflammatory drugs - NSAIDs) or irritants (alcohol and free radicals). Chronic use of NSAIDs causes erosion, ulceration, perforation and hemorrhage in the gastric mucosa. Natural products derived from plants have been the focus of studies to the discovered of new molecules of pharmacological and biomedical interest. Ximenia americana barks are used by the population for medicinal purposes, such as stomach pain, cancer, mouth infections, scarring, gastrointestinal disease and mucous inflammation. Pharmacological studies have demonstrated several biological effects of the aqueous extract of X. americana barks, such as anticancer, antinoceptive and anti-inflammatory. Previous studies by our group with extract polysaccharide and fractions decreased inflammatory pain in formalin, carrageenan and acetic acid model. In this study aimed to evaluate the anti-inflammatory and anti-ulcer effects of the extract polysaccharide of X. americana barks (TPL-Xa) in mice model of gastric damage induced by indomethacin. Polysaccharides were obtained by a combination of extraction with NaOH and ethanol precipitation. Female Swiss mice (20 - 25 g), were obtained from Federal University of Ceará. Animals were housed in a temperature-controlled room, receiving water and food ad libitum and were deprived of food for 18-24 h before the experimentation and approved by the UFC ethics committee (Protocol No. 118/14). received p.o. saline (0.9% NaCl), saline + indomethacin (control groups) or TPL-Xa (1, 3, 10, 30 or 90 mg/kg) 1 h before indomethacin (20 mg/kg, p.o.). Animals were sacrificed 7 h after indomethacin-treatment. Stomach lesions were measured using digital calipers and samples fixed in 10% formalin for histological evaluation (inflammatory cell infiltrate and the loss of epithelial cells). Other samples from stomach were weighed, frozen and stored at -80 °C for determination of myeloperoxidase (MPO) activity. Leukocyte adhesion and rolling were also evaluated by intravital method. TPL-Xa, containing 43% of carbohydrate, reduced macroscopic (54%) and microscopic (85%) damage, MPO activity (59%), rolling (86%) and adhesion (84%) of leukocyte compared to indomethacin. In conclusion, our results suggested that the TPL-Xa ameliorate the gastric injury induced by indomethacin, an effect that was dependent of the reduction of neutrophil infiltration. These findings indicate that TPL-Xa can form the basis for discovery and development of new compounds for the treatment gastrointestinal diseases.

08.016 Effect of a hyperlipidic diet in the contractile reactivity and morphology of rats ileum. Oliveira GA, Souza ILL, Barros BC, Ferreira ES, Vasconcelos LHC, Queiroga FR, Silva PM, Andrade LFLI, Cavalcante FA, Silva BA UFPB

Introduction: Obesity is a chronic and multifactorial disease characterized by body fat excess, leading to damage in human health (BOUCHARD, C. Atividade física e obesidade. São Paulo: Manole, 2000; DAMASO, A. Etiologia da obesidade. Rio de Janeiro: Medsi, 2003). In addition, high fat diet promotes molecular alterations in the small intestine associated with lipid metabolism, inflammatory immune response and increase fatty acids oxidation (NOBREGA, F.J. Distúrbios da nutrição. Rio de Janeiro: Revinter, 1998). However, it is unclear whether obesity alters the intestinal reactivity. Thus, we aimed to investigate a possible alteration in the reactivity and morphological structure of ileum from obese rats. **Methods**: Wistar rats (8 weeks of age) were randomly divided into control group (CG), that received a standard diet, and obese group (OG), fed with a hyperlipidic diet during 8 weeks (ESTADELLA. Nutrition, v. 20, p. 218, 2005). After treatment, animals were euthanized and ileum segments were suspended in organ baths containing physiological solution under appropriate conditions. Then, isotonic contractions were monitored by a quimograph and the thickness of the intestinal muscle layers were analyzed by histological staining with hematoxylineosin. The values were expressed as the mean and the standard error of the mean and compared by the Student's t-test ($p < 0.05$, $n = 5$). **Results**: Cumulative concentration-response curves to KCl 10^{-3}-1 M, an electro-mechanical contractile agent, were not displaced in the OG ($pD_2 = 1.8 \pm 0.8$) comparing to CG ($pD_2 = 1.8 \pm 0.2$). However, was observed a reduction in the E_{max} values of OG compared to CG ($E_{max} = 42.7 \pm 3.1$ and 100%, respectively), indicating a decrease in efficiency without alteration in contractile potency of KCl. Meanwhile, cumulative concentration-response curves to carbachol (CCh) 10^{-9}-3x10^{-5} M, a pharmacomechanical contractile agonist, were shifted to the right in the OG ($pD_2 = 6.6 \pm 0.1$) compared to CG ($pD_2 = 6.3 \pm 0, 05$) with reduction of E_{max} values on OG related to CG ($E_{max} = 32.7 \pm 7.5$ and 100%, respectively), changing both potency as efficiency of CCh. Regarding the circular and longitudinal smooth muscle layers, there was no significant difference in the thickness of these layers in the OG (48.3 ± 4.0 and 36.53 ± 4.6 µm, respectively) compared to CG (47.0 ± 1 8 and 29.0 ± 1.9 µm, respectively), showing that an increased calorie intake does not interfere in the structure of intestinal layers, despite the change in contractile reactivity of ileum rat. **Conclusion**: Obesity causes a decrease in contractile reactivity of rat ileum in response to different contractile agents and seems not to promote alteration in the thickness of the circular and longitudinal smooth muscle layers. **Financial support**: CNPq, CAPES, PPgPNSB/UFPB. Research approval: Ethical Committee on Animal Use/UFPB (0201/14)

08.017 Activity antiulcer extract of nebulized *Spondias mombin* (Anacardiaceae) Araruna MEC[1], Santos VL[2], Medeiros ACD[2], Silva PR[1], Rego RIA[1], Albuquerque HCP[1], Cabral ILO[1], Dantas RS[1], Medeiros FD[2], Ribeiro AP[1] [1]UEPB, [2]UEPB – Ciências Farmacêuticas

Introduction: Gastric ulcer is a complex disease of uncertain etiology. It is known that can be triggered by an imbalance between the factors that impair the mucosa and those who protect and indiscriminate use of anti-inflammatory drugs (NSAIDs) and alcohol favor its development. The conventional treatment aims to solve the final problem and not the cause, but the relapse rate and the cost is high. Therefore, the search for natural products with anti-ulcer activity has deserved highlight. The *Spondias* genus has worldwide distribution, and *Spondias mombin* species, popularly known as cajazeiras, it is widely grown in tropical regions. Its leaves, flowers and bark are used in folk medicine for the treatment of digestive tract diseases, back pain, rheumatism, angina, sore throat, fever, congestion, malaria, diarrhea, urethritis and as a contraceptive. **Objective**: The goal of this study was to investigate the antiulcer potential of nebulized extract of *Spondias mombin*. **Methods**: The leaf extract was obtained by exhaustion extraction in an ultrasound bath with water: ethanol (30:70, v / v), and subjected to drying by a spray dryer, using as glidant colloidal silicon dioxide. Swiss male and female mice were used, weighing 25-30g, using ulcer model induced by ethanol and by NSAIDs. To verify the involvement of prostaglandin and sensitive potassium channels to ATP the animals were pretreated with indomethacin 30 mg/kg or glibenclamide 10mg/kg. In addition, it evaluated the volume gastric and pH through the pylorus ligature. **Results**: In the induction by ethanol , the extract at doses of 250 and 500 mg/kg and lansoprazole inhibited ulcer formation by 42, 60 and 57%, respectively; In induction by NSAIDS the extract was used at a dose of 250mg/kg and inhibited 74.7%, while cimetidine 62.7%, when compared to the control. In the assessment of mechanism of action, we found that the effect does not involve maintaining of prostaglandins levels, but has participation of potassium channels sensitive to ATP. When administered intraduodenally, the extract reduced the volume, but did not change the gastric pH. **Conclusion**: The extract in the used doses and models, significantly inhibits the formation of ulcers without participation of prostaglandins, but involves potassium channels, shown to be a promising alternative for the treatment of gastric ulcer, however it will require complementary studies to better characterize this activity and reach the development an appropriate formulation constituted by the extract under study. Support: CNPq and UEPB. Research approved by the Ethics in Animal Research Committee (FACISA- FCM): 6101032016. Key words: Gastric ulcer. *Spondias mombin*. Phytotherapy.

08.018 Anti-motility pathways involved in the antidiarrheal mechanisms of action of *Maytenus erythroxylon* Reissek (Celastraceae) ethanol extract in mice. Formiga RO, Machado FDF, Barros MEFX, Pessoa MMB, Quirino ZGM, Tavares JF, Batista LM UFPB

Introduction: *Maytenus erythroxylon* Reissek, popularly known as “casca grossa” and “bom-nome”, is a species with folk indication to treat gastrointestinal disorders. Previous studies with its ethanol extract has presented low acute toxicity, gastroprotective effect and antidiarrheal activity, being this last one attributed to a decrease of secretory and gastrointestinal motility. Thus, this study aimed to evaluate the anti-motility pathways involved in the mechanisms of action of the ethanol extract obtained from the aerial parts of *M. erythroxylon* (EtOHE-*Me*). **Methods**: Male mice (n=7) were fasted for 24 hours and treated orally with 0.9% saline solution (10 mL/kg), EtOHE-*Me* (500 mg/kg – selected dose), and to obtain information about the mechanism of actions it was used different drugs, such as glibenclamide (1 mg/kg i.p) to evaluate the K_{ATP} channels, L-NAME (1 mg/kg i.p.), to determine the participation of nitric oxide, yohimbine (1 mg/kg i.p.) to evaluate α_2-adrenergic receptors and propranolol (1 mg/kg i.p.) to see the involvement of β-adrenergic receptors. These drugs were given 30 min before extract administration. After 60 minutes it was administered 10 mL/kg (p.o.) of the black marker (5% charcoal suspension in 5% arabic gum) and 30 minutes later, the animals were euthanized to calculate the percentage of intestinal transit (IZZO, R., Curr. Pharm. Des., 17, 1851, 1999). The results were analyzed using ANOVA followed by Dunnett's test and Tukey’s post-test. **Results**: The results showed that the distance travelled by charcoal meal was about 80% in the NaCl 0.9% control groups. The treatment with EtOHE-*Me* in its best dose (500 mg/kg) produced significant ($p<0.001$) reduction in the percentage of intestinal transit (36%), when compared to control group. Although, when EtOHE-*Me* was associated with standard drugs glibenclamide, L-NAME and yohimbine it was observed an increase of the intestinal transit in 70%, 78% and 74%, respectively. Furthermore, when the extract was administered with yohimbine, the decrease in the intestinal transit was maintained, with no significant difference ($p>0.05$) to the group treated only with EtOHE-*Me*. **Conclusions**: Those results suggest the participation of nitric oxide, K_{ATP} channels and β-adrenergic receptors in the anti-motility activity of EtOHE-*Me*, due to reversal of the effect when the extract was administered along with the respective blockers. Acknowledgment: CNPq/UFPB. Ethics Committee on Animal Use (UFPB) number 0105/14.

08.019 Constituents of aerial parts from *Bauhinia curvula* exert gastroprotective activity in rodents by favoring defensive factors of gastric mucosa. Beber AP[1], da Silva LM[1], Boeing T[1], Somensi LB[1], Cury BJ[1], da Silva CB[2], Simionatto E[3], Andrade SF[1] [1]Univali – Ciências Farmacêuticas, [2]UFPR- Ciências Farmacêuticas, [3]UFMS – Química

Introduction: The Bauhinia genus is known as "Pata-de-Vaca" and many of these plants are used in Brazilian folk medicine. This study was based in gastroprotective potential of Bauhinia sp. and motivated by the absence of studies exploring the therapeutic potential of Bauhinia curvula on this area. Aim: To evaluate the gastroprotective activity of the ethanolic extract from the aerial parts of B. curvula (EEBC) and the contribution of phytochemicals constituents in this effect. **Methods**: Ethanol/HCl- and indomethacin- induced ulcer was performed in rodents to evaluate gastroprotective effects of EEBC (3-100 mg/kg). Ulcerated tissues were processed for histological, histochemical and biochemical analysis. The antisecretory effect of EEBC was assessed in vivo and in vitro. The role of nitric oxide (NO), sulfhydryl non-proteic groups (NPSH), prostaglandins (PGs)and alpha-2 adrenergic receptor in gastroprotective effects of EEBC also was studied. The main compounds were obtained in a semi-purified fraction and after were isolated, identified, quantified and its gastroprotective properties were investigated. **Results**: The oral administration of EEBC (10, 30, 100 mg/kg) reduced the gastric ulcer induced by ethanol/HCl in mice by 57.59%, 73.10% e 69.29%, respectively (vehicle group: 35.99 ± 5.34 mm²). Similarly, EEBC (1 mg/kg) by intraperitoneal (i.p) route also decreased 77.97% of the injured area. The administration of indomethacin (80 mg/kg, p.o) induced gastric lesion in an extension of 37.38 ± 7.85mm² in rats and the treatment with EEBC (100 mg/kg) reduced this lesion by 70.75%. The EEBC increased the mucin content (verified by periodic acid-Schiff stain) and normalized the superoxide dismutase, catalase and myeloperoxidase activity to basal levels in parallel to reduction in lipoperoxides contents at site of the ulcer. However, EEBC (100 mg/kg, intraduodenally. and 10 mg/kg, i.p) does not promote changes in volume, pH, total acidity or pepsin activity of acid gastric secretion in rats, and also does not inhibited the in vitro H^+, K^+ATPase activity up to 100ug/ml. Furthermore, the gastroprotective effect of EEBC (100 mg/kg) was abolished in mice pretreated with Nω-Nitro-*L*-arginine methyl ester (70 mg/kg, i.p), N-Ethylmaleimide (10 mg/kg, i.p) or indomethacin (10 mg/kg, i.p). The yeld of semipurified fraction of EEBC was 2% and this fraction displayed gastroprotective effects at 1 and 3 mg/kg (p.o) in a similar extension to extract. The compounds identified in semipurified fraction were the flavonoids quercitrin (65%) and kaempferol (35%). Kaempferol (1mg/kg, p.o) reduced the area of the gastric ulcer induced by ethanol/HCl in mice by 69.32% compared to vehicle group (29.59 ± 8.07 mm²), while gastroprotective effect of quercitrin has been described by our research group (de Barros et al. Naunyn Schmiedebergs Arch Pharmacol. 389:403-417, 2016). **Conclusions**: These findings confirm that B.curvula it has a clear gastroprotective potential, mainly explained by the presence of flavonoids quercetrin and kaempeferol, favoring defensive factors of gastric mucosa and through of NO, NPSH and PGs pathways. **Financial support**: CNPQ, CAPES, FAPESC. Approval number CEUA: 917/2015.

08.020 Investigation of spasmolytic and antitussive activities of essential oil from *Lippia origanoides***.** Menezes PMN[1], Brito MC[2], Paiva GO[2], Lucchese AM[3], Ribeiro LAA[2], Silva FS[2] [1]UNIVASF – Recursos Naturais do Semiárido, [2]UNIVASF – Ciências Farmacêuticas, [3]UEFS – Ciências Exatas

Introduction: Essential oils are natural complex systems composed mainly by terpenes and phenylpropanoid, being responsible for pharmacological activity of medicinal plants used to treat various respiratory diseases, as asthma. **Objetives:** Aim this work was to investigate the mechanism of spasmolytic activity in guinea-pig isolated trachea and antitussive activity in mice of essential oil from *L. origanoides* (OLO). **Materials and Methods:** Experimental protocols were established in accordance with CEUA/UNIVASF (protocol # 0006/021014). Guinea-pig isolated trachea (n= 3 to 9) was incubated in 10 ml chambers of tissue organ bath system filled with a Krebs solution at 37°C and constant oxygenation by 1h and tension of 1g. Airway smooth muscle was contracted with carbachol or histamine 1 µM and when contractions had reached a plateau, cumulative concentrations of OLO (1-729 µg/mL) was added. To elucidate the relaxant mechanism of OLO*,* set of experiments were performed in the presence or absence of 4-aminopyridine (4-AP, 2mM), tetraethylammonium (TEA, 5mM), glibenclamide (GLIB, 3µM), cesium chloride (CsCl - 5mM). In antitussive activity, mice (n=5) were treated with OLO (30, 100 and 300 mg/kg, via i.p.), morphine (5 mg/kg) or vehicle and 30 min after exposed to citric acid (0,4 M) via inhalation, being cough accounted. Data are presented as means ± standard error of the mean (SEM) and was analyzed using GraphPad Prism Software (v.5). Concentration that caused 50% of the relaxation (EC_{50}) in guinea-pig isolated trachea was calculated by non-linear curve fitting. Statistically significant differences were calculated using non-parametric test t or one-way ANOVA and the post-hoc Tukey's multiple comparison test. **Results:** OLO had as major constituent carvacrol (53.89%), linalool (5.84%) and E-caryophyllene (5.54%). In guinea-pig isolated trachea, OLO was more potent in to relax airway smooth muscle contracted with histamine (EC_{50} = 5,76±1.29 µg/mL) than carbachol (EC_{50} = 49.39±0.77 µg/mL). Relaxation induced by OLO after contractions induced by histamine in the presence of potassium channel blockers 4-AP, GLIB, CsCl and TEA had not change when compared with relaxation in the absence of OLO. However, EC_{50} of OLO in the presence of 4-AP (30.07±8.44 µg/mL) showed significant increase in comparison with EC_{50} in the absence (6.71±1.68 µg/mL). Relative to antitussive activity, OLO reduced cough of mice treated with doses 100 and 300 mg/kg when compared to negative control, while there was increasing in the latency to the first cough with 300 mg/kg of OLO in comparison to negative control. **Conclusions:** The essential oil from *L. origanoides* present spasmolytic and antitussive activities in animal models of respiratory diseases. Spasmolytic effect, possibly involving the opening of voltage-gated potassium channel (K_v), while the antitussive effect can be involved to promote tachyphylaxis to $TRPA_1$ in inhibiting cough, probably to major component carvacrol present in OLO.

08.021 Antispasmodic effect of *Platonia insignis* **Mart. ethanolic extract on rat isolated trachea.** Almendra RB[1], Santos RS[1], Rodrigues TO[1], Vieira MM[1], Costa ICG[2], Lima GM[1], Chaves MH[2], Oliveira RCM[1], Santos RF[1] [1]NPPM-UFPI, [2]UFPI – Chemistry

Introduction: Over the years, nature has provided a number of natural products extracted from medicinal plants used for the treatment of various diseases such as respiratory diseases. Among these plants, we can highlight the *Platonia insignis* Mart. species, popularly known as 'bacurizeiro'. This species has been already shown in some studies its anti-ulcer, healing, antinociceptive and cardiovascular activities. This study aimed to evaluate the antispasmodic effect of the ethanol extract of *Platonia insignis* Mart. (Pi-EtOH) on isolated rat tracheal rings. **Methods:** Tracheal rings (2-4mm) from naive male Wistar rats were mounted in isolated organ baths and suspended by rods attached to a force transducer, connected to an amplifier and then to a computer. The tissue viability was determined by the contractile response after adding carbachol (3x10-6 M) (CCh) to the bath and epithelial integrity was verified by adding arachidonic acid (3x10-4 M) (AA) to the bath during the tonic contraction phase promoted by CCh. In the second contractile response, Pi-EtOH was added in different preparations and cumulative concentrations (0.1-1000 / ml). To verify the involvement of the oxide synthase (NOS), guanylate cyclase (GC) and cyclooxygenase (COX) enzymes and potassium channels in the relaxing effect of Pi-EtOH (0.1-1000 mg / mL), incubations with L-NAME, ODQ, indomethacin, tetraethylammonium (5 mM) or glibenclamide were prepared. **Results:** Pi-EtOH promotes relaxation on rat isolated trachea (logCE50 = 2.36 ± 0.17*) significantly (*P <0.05) in the presence of functional epithelium (Emax = 85.75 and 9.9% for rings with and without functional epithelium, respectively), suggesting a key role of epithelium-derived relaxing factors. In the presence of L-NAME (logCE50 = not calculated (NC), Emax = 44%), ODQ (logCE50 = CN, Emax = 48.22%), indomethacin (logCE50 = 2.73 ± 0.03 *, logCE50 = 2.36 ± 0.17) and tetraethylammonium (logCE50 = NC, Emax = 23.7%), the concentration-response curves of Pi-EtOH were significantly shifted to the right (*P<0.05), reducing the relaxation potency, suggesting a participation of NOS, GC, COX and potassium channels. To verify the involvement of K_{ATP} in Pi-EtOH-induced relaxation, preparations were preincubated with glibenclamide (logCE50 = 2.40 ± 0.09, 2.36 ± logCE50 = 0.17), and it was observed that the relaxation of trachea did not change significantly (P>0.05), indicating that probably this potassium channel subtype does not influence the relaxing action of Pi-EtOH. **Conclusion:** Thus, it was concluded that the Pi-EtOH extract is significantly (*P<0.05) endowed with relaxing activity on isolated trachea of rats, an effect dependent on the epithelium-derived relaxing factors, with participation of nitric oxide synthase, guanylate cyclase, cyclooxygenase and potassium channels, determinants for that purpose. **Financial Support**: CAPES and FAPEPI. Animal Experimentation Ethics Committee / Federal University of Piauí (CEEA/UFPI No. 008/2012)

08.022 Airway relaxant properties of JME-173, a mexiletine analogue planned to present limited inhibitory effect on the sodium channel. Carvalho KIM[1], Joca HC[2], Souza ET[1], Cruz JD[2], Silva ET[1], Costa JCS[1], Silva PMR[1], Martins MA[1] [1]Fiocruz, [2]UFMG

Introduction: Lidocaine analogues, screened for reduced local anesthetic (LA) activity, exhibited better antispasmodic, anti-inflammatory and safety profile as compared to the prototype lidocaine. Mexiletine is a LA antiarrhythmic agent whose chemical structure and electrophysiological properties closely resemble those of lidocaine although, unlike lidocaine, it is active following oral administration. **Aim:** The current study was undertaken to investigate the anti-asthmatic potential of JME-173, a structurally original mexiletine analogue designed to present the airway relaxant effects of mexiletine with limited sodium channel blockade activity. **Methods:** In vitro settings, the effect of JME-173 was assessed in GH3 cells, isolated rat tracheal rings, mouse cardiomyocytes, assessing changes in sodium current, contraction, proliferation and survival and calcium current, respectively. Bronchoconstriction was measured in unrestrained mice using non-invasive whole-body plethysmography. All animal experiments occurred under the CEUA FIOCRUZ license number LW-23/10. **Results:** The IC_{50} values for blockade of Na^+ currents after treatment with JME-173 was remarkably higher than that of mexiletine (183 *vs.* 0.28 mM), indicating an attenuated activity of this analogue on sodium channels. In contrast, JME-173 was more potent than mexiletine in inhibiting tracheal contraction. IC_{50s} reduced from 395.2 to 32.0 µM following carbachol, and from 440.2 to 8.3 µM after allergen challenge. Notably, the relaxing effect of JME-173 remained unaltered following epithelium removal or co-treatment with either nitric-oxide synthase inhibitor N -nitro- L-arginine methyl ester (L-NAME, 100 µM), beta adrenergic receptor antagonist (propranolol, 1 µM) or adenylate cyclase inhibitor (SQ22,536, 100 µM). Furthermore, JME-173 was quite effective in inhibiting contraction dependent on the addition of extracellular Ca^{2+} (under high K+ depolarization) (IC_{50s}= 10.0 µM and 380.8 µM, respectively). In another setting of experiments, JME-173 blocked L-type Ca^{2+} channels in cardiomyocytes (IC_{50}= 30 µM). Finally, JME-173 (30 mg/kg, oral) significantly inhibited methacholine-induced bronchoconstriction for at least 6 h, while theophylline (100 mg/kg, oral) inhibited it at 3 h but not at 6 h post-treatment. **Conclusion:** These findings suggest that the oral treatment of the analogue JME-173 is a way of achieving the bronchodilator effect of mexiletine without the anesthetic effect, which has been associated with airway irritant action. The beneficial effect of JME-173 seems to be, at least in part, related to the blockade of voltage-dependent Ca^{2+} channels. **Financial support:** FAPERJ and CNPq

08.023 Alcoholic fatty liver disease: a new promisor pharmacological treatment with *Baccharis trimera.* Lívero FAR[1], Telles JEQ[2], Franco CRC[3], Acco A[1] [1]UFPR- Farmacologia, [2]UFPR- Patologia, [3]UFPR- Biologia Celular e Molecular

Introduction: The harmful use of ethanol is associated with high morbidity, mortality, and disability worldwide and is either directly or indirectly responsible for 3.3 million deaths annually. Among the consequences of excessive ethanol use is alcoholic liver disease (ALD), one of the major chronic liver disease, which is in the top 20 causes of death worldwide. The spectrum of ALD comprises alcoholic fatty liver disease (AFLD; also called steatosis), which is the earliest response to excessive ethanol consumption, followed by more severe lesions that characterize steatohepatitis and cirrhosis. AFLD is an asymptomatic condition that is characterized by triglyceride (TG) accumulation in hepatocytes. The pathophysiological mechanisms that trigger ALFD include lipogenesis imbalance, oxidative stress, cytokine production, lower hepatic antioxidant defenses, and ethanol metabolism that is mediated by CYP2E1. Although benign, no drug treatments are available that can act on so many pathways to reverse the hepatocyte injury that is present in AFLD. *Baccharis trimera*, a plant with a wide distribution in South America, popularly known as “carqueja”, is used in folk medicine for the treatment of gastrointestinal and liver disease. **Methods**: We evaluated the effects of 15 days of treatment with hydroethanolic extract of *B. trimera* (HEBT; 30mg·kg^{-1}) on ethanol-related hepatotoxicity, steatosis, and oxidative stress in the liver of mice that were fed to 10% ethanol and a 6% low-protein diet, during 6 weeks. Mice fed with water and norm-protein diet, treated with vehicle, composed the basal group. In the end of the experiment, mice were anesthetized and liver and blood were collected for the following analyses: Catalase (Cat); superoxide dismutase (SOD); reduced, peroxidase and s-Transferase glutathione (GSH, GPx, GST); lipoperoxidation (LPO) and total reactive oxygen species (ROS) were measured as hepatic oxidative stress parameters; ALT and AST plasmatic levels were indicative of liver function; plasmatic and hepatic levels of TG, cholesterol (CHO), HDL (high density lipoprotein) and LDL (low density lipoprotein) were performed to demonstrate AFLD; gene expression of CYP2E1, Nrf2 and SCD1 were assessed to check pathways of ethanol metabolism, antioxidant system, and lipogenesis, respectively; and hepatic histology (HE) and transmission electron microscopy were performed to check hepatocyte damage. **Results**: HEBT reversed ethanol-induced oxidative stress, reducing LPO, normalizing GPx, GST, SOD and Cat activity, and GSH and total ROS levels. The reverser effect of HEBT was observed upon ethanol-induced increases in the levels of plasma ALT and AST; plasma and hepatic TG and LDL; and plasma CHO and HDL. Moreover, HEBT reduced the histological ethanol-induced lesions in the liver. HEBT also altered the expression of CYP2E1, Nrf2, and Scd1. Conclusion: We propose that HEBT may be a promising pharmacological treatment for AFLD since it acts at enzymatic, molecular and gene expression level. **Financial support:** REUNI-CAPES, CAPES and Fundação Araucária. **CEUA-UFPR:** The institutional committee for the animal care # 619 approved all the procedures.

08.024 Pre-clinical evaluation of antiulcerogenic activity of the crude ethanol extract of Spondias mombin (Anacardiaceae) in mice. Araruna MEC, Dantas RS, Albuquerque HCP, Cabral ILO, Rêgo RIA, Silva TD, Almeida MCF, Silva PR, Medeiros AC, Medeiros FD, Santos VL UEPB – Farmácia

Introduction: *Spondias mombim*, a fructiferous tree of the Anacardiaceae family and native to tropical America, is distributed in all regions of Brazil, and is known also by many popular names, such as cajazeiro, cajazeira, cajá, caja-Mirim, and cajazeiro-miúdo. In folk medicine, leaves of *S. mombin* have been used for induction of abortion, as anti-inflammatory, healing, antidiarrhetic and to relieve stomach ache. Extracts from its leaves have pharmacological activities recognized as antimicrobial, antiviral, leishmanicide, antioxidant, anticonvulsant, antipsychotic, anthelmintic, anti-inflammatory. Its phytochemical shows the presence of phenolic compounds, tannins, anthraquinones and flavonoids which may be responsible for the effects observed in the extracts. **Objective:** The aim of this study was to investigate the potential gastroprotective of crude ethanol extract of *S. mombin* (EEBSm) leaf and identify the possible mechanism of action. **Methods**: The leaf extract was obtained by extraction exhaustion with ethanol and then rotatory evaporator under reduced pressure. The acute gastric ulcer was induced by absolute ethanol and NSAIDs (piroxicam), in mice treated with vehicle (1ml / 100g p.o.) or EEBSm (250 and 500mg / kg). Lansoprazole (30mg / kg) or cimetidine (100 mg / kg) were used as positive control. To evaluate the involviment of prostaglandin and sensitive potassium channels ATP animals were pretreated with indomethacin 30mg / kg (blocker prostaglandin synthesis) or glibenclamide mg / kg (potassium channel blocker sensitive to ATP), respectively, prior EEBSm treatment. It was also evaluated if the EBSm would only have a physical effect using the barrier test in which the extract was administered intraperitoneally. **Results**: The SSBSm showed gastroprotective activity, which can be observed in both models of acute gastric ulcerIn. the model of ulcer ethanol, EEBSm inhibited by 41.7 and 60.2%, and ulcers induced by NSAIDs inhibition was 73.0 and 89.8% when compared to the control ($p < 0.01$). In physical barrier test EEBSm both administered orally and by intraperitoneally protected the mucosal action of ethanol in 71 and 61%, respectively, showing that the activity is not only the physical. In animals pretreated with indomethacin it was observed that the EEBSm protection was not reversed, giving evidence of non-participation of prostaglandins in cytoprotection. However, when animals were pretreated with inhibiting potassium channel (glibenclamide) protection was inhibited, indicating the involvement of these channels in EEBSm activity. **Conclusion:** The ethanol extract of S. mombim has gastroprotective activity and this effect involves the participation of potassium channels sensitive to ATP. **Financial support**: CNPq and UEPB. Research approved by the Animal Research Ethics Committee (FACISA- FCM): 6101032016.

08.025 The ruthenium complex nitric oxide donor presents higher relaxing effect than sodium nitroprusside in isolated trachea from asthmatic rats. Castro PFS[1,2], Batista AC[3], Silva RS[4], Rocha ML[1] [1]UFG – Farmácia, [2]Universo, [3]UFG – Faculdade de Odontologia, [4]FCF-USP

Introduction: Nitric oxide (NO) is a potent bronchodilator produced mainly by nerves and epithelial cells. It has been demonstrated as the primary agent in relaxing airways and established clinical interest in the treatment of obstructive airways diseases. In this work, we investigated the effects and action mechanisms of a new NO donor $[Ru(terpy)(bdq)NO^{+}]^{3+}$(TERPY) in isolated trachea of control and asthmatic rats (induced by ovalbumin) pre-contracted with carbachol (0.5µM) in an isolated organ bath. **Methods:** The relaxing effects of TERPY and sodium nitroprusside (SNP) (both 10nM to 100µM) were determined. Thus, we verified the contribution of sGC/cGMP pathway (using sGC inhibitor, ODQ) and the influence of the contraction produced by Ca^{2+} influx across membrane. Furthermore, we verified the inflammatory infiltration in tracheas of asthmatic animals and bronchoditation by TERPY in slices bronchioles of asthmatic animals. These analyses were performed under light microscopy. The protocols were approved by the Animal Research Ethics Committee of the UFG under protocol 029/2013. **Results:** The histological analysis has confirmed intense inflammation and mast cells inside the tracheal tissue of the asthmatic rats ($p<0.05$). The SNP led to relaxation the isolated pre-contracted rat trachea in a dependent-concentration way, producing maximum effect higher in control (68.3±3.1%,n=9) than asthmatic rats (48.3±2.7%,n=5;$p<0.001$). The relaxation effect of TERPY was similar in control or asthmatic both group (110.2±3.2%,n=9 vs 106.1±1.5%,n=9, respectively). In control group, the TERPY-induced relaxation was not altered after ODQ treatment (98.7±1.3%,n=5). However, TERPY significantly reduced ($p<0.001$) the contraction induced by Ca^{2+} influx stimulated by carbachol (before: 118.0±6.0%,n=5 and after TERPY 27.0±4.1%,n=4). In asthmatic rats, the potency values to TERPY (5.0±0.09,n=9) was reduced ($p<0.001$) after ODQ treatment (4.4±0.08,n=4). Likewise, the pD2 values to SNP (6.2±0.06,n=6) also was reduced ($p<0.05$) in asthmatic rat tracheas after sGC/cGMP blocking (5.9±0.04,n=4). In experimental group, the contraction induced by Ca^{2+} influx (123.7±7.6%,n=5) was reduced by SNP (84.1±7.4%,n=5) and completely inhibited by TERPY (-1.6±2.1%,n=4). Besides, the TERPY is able to reverse the contraction of carbachol in bronchioles from asthmatic rats. **Conclusion:** TERPY and SNP have their mechanisms of relaxation modified by the inflammatory process. However, these modifications were not able to alter the relaxation effect of TERPY. The relaxing effect to SNP was lesser than TERPY in asthmatic rat tracheas. These results make TERPY a promising drug to reverse the constriction of the airways. **Financial support:** FAPEG and CNPq.

08.026 Atorvastatin and simvastatin promoted mouse lung repair after cigarette smoke-induced emphysema. Pinho-Ribeiro V[1], Melo AC[1], Kennedy-Feitosa E[1], Graça-Reis A[1], Barroso MV[2], Cattani-Cavaliere I[3], Carvalho GMC[4], Zin WA[4], Porto LC[3], Gitirana LB[1], Lanzetti M[5], Valença SS[5,1] [1]ICB-UFRJ, [2]UFRJ – Microbiologia, [3]UERJ, [4]UFRJ – Biofísica, [5]UFRJ – Farmacologia e Química Medicinal

Introduction: Cigarette smoke (CS) induces pulmonary emphysema by inflammation, oxidative stress and metalloproteinase (MMP) activation. Pharmacological research studies have not focused on tissue repair after the establishment of emphysema but have instead focused on inflammatory response. The aim of our study was to analyze the effects of atorvastatin and simvastatin on mouse lung repair after emphysema caused by CS. **Methods:** Male mice (C57BL/6, n=45) were divided into the following groups: control (sham-exposed), CSr (emphysematous mice exposed to 12 cigarettes/day for 60 days and then treated for another 60 days with the vehicle), CSr+A (CSr emphysematous mice treated with atorvastatin for 60 days) and CSr+S (CSr emphysematous mice treated with simvastatin for 60 days). The treatment with atorvastatin and simvastatin was administered via inhalation (15 min with 1 mg/mL once a day). Mice were euthanized 24 h after the completion of the 120-day experimental procedure. Biochemical, morphological and physiological analyses were performed. **Results:** We observed decreased levels of leukocytes, cytokines and oxidative stress markers in statin treated mice. The CSr group had increased ($p<0.001$) number of leukocytes when compared to the control group. The CSr+A group exhibited fewer ($p<0.01$) leukocytes when compared to the CSr group, whereas the CSr+S group was not different from the CSr group neither to the control group. Macrophages was similar to total leukocytes but neutrophils was higher in the CSr group ($p<0.01$) when compared to the control group while atorvastatin ($p<0.05$) and simvastatin ($p<0.01$) were able to reduce neutrophils in comparison to the CSr group. KC levels were elevated ($p<0.01$) in the CSr group when compared to the control group, but CSr+A and CSr+S presented reduction on KC levels ($p<0.01$) when compared to the CSr group. ROS were elevated in CSr group ($p<0.001$) when compared to the control group, while both CSr+A and CSr+S groups showed a reduction in comparison to the CSr group ($p<0.001$). We also observed a morphological improvement in statin treated mice confirmed by mean linear intercept (Lm) and volume density of elastic fibers (Vvef) count. Lm was elevated in CSr group ($p<0.05$) and reduced ($p<0.05$) in both CSr+A and CSr+S groups when compared to the control group. The Vvef was lower in the CSr group ($p<0.01$) when compared to the control group and restored in CSr+A and CSr+S groups when compared to the CSr group ($p<0.01$). Finally, statins also ameliorated lung function parameters (lung maximum pressure -Pmax,L; viscoelastic elastance-DE,L; static elastance component, Est,L) when compared to CSr group. **Conclusion:** Inhalation of atorvastatin and simvastatin improved lung repair in mice after cigarette smoke-induced emphysema. **Financial support**: CAPES, FAPERJ, CNPq. Ethical committee approved number (CEUA 125/13).

08.027 Effect of the aqueous and ethanolic extracts of *Capsicum pubescens***, "Rocoto" on experimental gastric ulcers.** Castañeda B, Ibañez L, Taxa L II-FMH-USMP

Objective: To evaluate the effect of aqueous and ethanolic extract of *Capsicum pubescens* (ROCOTO) on the experimental gastric ulcer evolution.
Materials and Methods: This is a cross-sectional, analytic and quasi-experimental study. We worked with 50 holtzman male rats, between 250 – 300 g of weight, distributed into 7 groups: G1: received ROCOTO aqueous extract, 250 mg / kg; G2: received ROCOTO aqueous extract, 500 mg / kg; G3: received ROCOTO ethanolic extract 250 mg / kg; G4 received ROCOTO ethanolic extract 125 mg / kg; G5 received ROCOTO ethanolic extract, 500 mg / kg; G6 received Ranitidine, 10 mg/kg; G7 received distilled water. The substances were administered orally using an orogastric cannula, after fasting for 48 hours, one hour before to the indomethacin administration, 75 mg/kg. Three hours later the tested substances were being re-administered, at the same doses. Six hours after the indomethacin administration, the animals were sacrificed and necropsied. We perform the phytochemical screening according to the methodology of Ciulei modified by the ITTCUSMP. **Results**: In the groups that received aqueous extract of ROCOTO at doses of 250 and 500 mg/kg we observed, macroscopically, a significant reduction in gastric lesions caused by indomethacin (75 and 78 %, respectively). The ethanolic extract at 125/kg presented 79% of inhibition. At doses of 250 mg and 500 mg/kg, the grade of inhibition was 82 and 85 %, respectively, compared with 20% of protection with ranitidine. Phytochemical analysis revealed the presence of fats, oils, alkaloids, lactones, coumarins, triterpenes, steroids, catechins, resins, reducing sugars, phenols, tannins, among others. **Discussion and Conclusion**: Both, aqueous and ethanolic of rococo, showed dose-dependent gastroprotective effect, better than ranitidine and could be an effective and safe alternative in the prevention of gastric inflammatory lesions. **Financial Support**: This study was partially funded by the School of Medicine of the Universidad San Martin de Porres, and was performed according to the International Guiding Principles for Biomedical Research Involving Animals (December 2012) and the Universal Declaration of Animal Rights (UNESCO 1977, UNITED NATIONS 1978). It wasn't app roval byAnimal Research Ethical Commitee, becauso we don't have an Research Animal Ethical Commitee yet. **Keywords**: Gastric ulcer, *Capsicum pubescens*, Rocoto, aqueous extract, ethanolic extract