07. Endocrine and Gastrointestinal

07.001

Protective effect of epiisopiloturine hydrochloride, a semisynthetic imidazole alkaloid isolated from *Pilocarpus microphyllus* leaves, on naproxen-induced gastrointestinal damage in rats. Nicolau LAD[1], Carvalho NS[1], Pacífico DM[1], Quaresma MP[1], Lucetti LT[2], Aragão KS[2], Leite JRA[1], Souza MHLP[2], Medeiros JVR[1] [1]UFPI, [2]UFC

Introduction: Naproxen (NAP), a representative of the NSAIDs family is often recommended clinically. However, this drug injures the gastrointestinal tract through various processes including generation of reactive oxygen species, inhibition of prostaglandin synthesis and lipid peroxidation (Yoshikawa, T., *Gut*, v.34, p.732, 1993). Thus, the aim of this study was to investigate the protective effect of the epiisopiloturine hydrochloride (EPI) on NAP-induced gastrointestinal damage in rats. **Methods:** This study was approved by the local ethics committee (protocol Nº 008/2012). Male Wistar rats were pretreated with 0.5% carboxymethylcellulose (vehicle) or EPI (3, 10 and 30 mg/kg, *p.o.* or *i.p.*) twice daily, for 2 days. After 1 h, NAP (80 mg/kg, *p.o.*) was given. The rats were euthanized on 2nd day, 4h after NAP treatment. Stomachs were removed and lesions measured using digital caliper. Furthermore, a portion of small intestine was used for macroscopic scores evaluation. Stomach and small intestine samples were used for histological evaluation and assayed glutathione (GSH) levels, malonyldialdehyde (MDA) concentration, and myeloperoxidase (MPO) activity. Moreover, it was measured gastric acid secretion, amount of mucus adhered to the gastric wall and evaluated the gastric mucosal blood flow (GMBF) by Laser-Doppler flowmetry. **Results and discussion:** EPI pretreatment prevented NAP-induced macroscopic gastric damage with maximal effect at a dose 10 mg/kg *i.p.* (68% lesion inhibition). In addition, EPI had significant protective alterations only at 10 mg/kg *i.p.* on NAP-induced gut injury. Histological analysis revealed that NAP increased hemorrhagic damage, edema, epithelial cell loss and inflammatory cell infiltration. In contrast, pretreatment with EPI decreased the infiltration of inflammatory cells, the formation of edema and the loss of epithelial cells. NAP increased MPO and MDA levels (MPO: 10.9 ± 1.8 U/mg and 18.3 ± 1.5 U/mg of gastric and gut tissue, respectively; MDA: 157.3 ± 18.1 nmol/g and 313.8 ± 33.3 nmol/g of gastric and gut tissue, respectively) and reduced GSH levels (76.79 ± 11.7 mg/kg and 93.1 ± 20 mg/g of gastric and gut tissue, respectively). However, EPI changed gastric biochemical parameters, reduced MPO (3.4 ± 0.3 U/mg of tissue), MDA (70.4 ± 8.3 mg/g of tissue) and GSH (246.2 ± 26.4 mg/g of tissue), while changed on gut tissue only GSH and MPO levels (189.5 ± 27.2 mg/g and 11.39 ± 2.6 U/mg of tissue, respectively). NAP decreased the amount of gastric adherent mucus (0.0224 ± 0.0057) when compared to the control group. Likewise, EPI pretreatment did not modify this effect of NAP (0.0262 ± 0.0061, *i.p.* and 0.0258 ± 0.0041, *p.o.*). On gastric acid secretion, EPI values showed no change in volume, pH or total acidity. NAP increased TNF-α levels (988.2 ± 52.01 pg/ml) while EPI pretreatment reduced (700.5 ± 59.95 pg/ml). Finally, on GMBF, the EPI *i.p.* increased blood flow in 15% suggesting an important gastroprotection factor. Our results suggest that EPI *i.p.* plays mainly a gastroprotective role against NAP-induced damage through mechanisms antioxidant, reducing pro-inflammatory cytokine, and increasing of GMBF rate. **Financial Support:** CNPq and FAPEPI.

07.002

Phytochemical screening and gastroprotective effect OF *Maytenus erythroxylon* Reissek (Celastraceae) against cold restrain stress induced ulcers in mice. Formiga RO[1], Sousa CGBL[1], Silva AKM[1], Souza SS[1], Silva Filho RN[2], Quirino ZGM[3], Batista LM[1] [1]CCS-DCF-UFPB, [2]UFPB, [3]CCAE-DEMA-UFPB

Introduction: Some medicinal plants belonging to the genus *Maytenus* have presented promising results in the context of peptic ulcers, being mostly constituted of phenolic compounds, especially flavonoids, glycosides, terpenes, steroids and alkaloids, already referenced in the literature as antiulcerogenic (Niero R, *Curr. Pharm. Des*., 17, 1851, 2011). The species *Maytenus erythroxylon* Reissek was selected for the present study based on chemotaxonomic criteria that aimed to provide a preliminary phytochemical determination and evaluate the gastroprotective activity of its ethanol extract (EEtOH-*Me*) obtained from the aerial parts of the plant against cold restrain stress induced ulcer model. **Methods:** The phytochemical screening was performed to evaluate and trace the major groups of chemical constituents, using for that standardized methods that rely on chemical reactions from 10 g of EEtOH-*Me* (Agra MF, *Ver. Bras. Farm*., 71, 72, 1990 – with modifications). For the cold restrain stress induced ulcer protocol, male Swiss mice were pretreated with vehicle (NaCl 0.9% p.o. – negative control), cimetidine 100 mg/kg (positive control) and EEtOH-*Me* (62.5, 125, 250 and 500 mg/kg p.o.). Posteriorly, they were subjected to the harmful agent (Levine R, Munksg., 92, 1971 – with modifications). The results were analyzed using ANOVA, followed by Dunnett's test. The experimental protocols were approved by the Ethics Committee on Animal Use (CEUA/CBIOTEC/UFPB) with number 2205/13. **Results and discussion:** According to the results, it was possible to detect the presence of steroids, triterpenoids, tannins, saponins and flavonoids in the EEtOH-*Me*. Concerning the gastric ulcer model, the oral doses 125, 250 and 500 mg/kg of the EEtOH-*Me* displayed a protective effect in gastric mucosa with ulcerative index of 53.83 ± 9.131 and 49% of injury inhibition ($p<0,0001$), 49.50 ± 15,28, 53% ($p<0,0001$) and 41.33 ± 7.763, 61% ($p<0,0001$) respectively, when compared to the negative control group (126.7 ± 29.08). Thus, the results of the present study demonstrate that ethanol extract of *Maytenus erythroxylon* has gastroprotective activity, as demonstrated by the significant inhibition of ulcer formation, being possibly related to the presence of the bioactive molecules evidenced in phytochemical tests. However, future studies are still necessary to evaluate the gastroprotective activity in other ulcer models, as well as the participation of those secondary metabolites in gastroprotection. **Acknowledgments:** CNPq/Capes/UFPB.

07.003

Does hydrogen peroxide (H_2O_2) have a dual effect on the C57Bl/6 isolated ileum?

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Introduction: Hydrogen peroxide (H_2O_2) is a ROS that are produced by normal and pathological cellular metabolism being either deleterious, due its ability to oxidize biological macromolecules, or an important redox signaling molecule. As these features on the intestine are not yet fully known, we thus explored the H_2O_2 effects on morphology, oxidation markers, and antioxidant defense in murine intestine. **Methods**: C57BL/6 male mice, 3-months, were provided by CEDEME, Unifesp, Ethics Committees # 0253/12. Different concentrations of H_2O_2 effects for 20 min on the isolated ileum were evaluated by histomorphometric analysis in HE-stained ileum sections (4 µM), by quantifying smooth muscle layer thickness (LT), microvilosities (MV) width and height, and crypts (CRT) depth; whole ileum lipid peroxidation (ILP) level, by measuring malondialdehyde concentration through TBARS technique, and spectrophotometric analysis (commercial acquired kits) of the activity of the antioxidant enzymes superoxide dismutase (SOD) and catalase (CAT). **Financial support**: Capes and Fapesp (2012/ 15716-9). **Results**: Morphological effects were concentration dependent. Thus, 100 nM H_2O_2 increased both longitudinal (43 ± 0,6 *x* 19,1 ± 0,4 µm; n = 5) and circular LT (55,1 ± 0,9 *x* 44 ± 1µm; n = 5), the CRT depth (143 ± 3 *x* 110 ± 2 µm; n = 5), but decreased the MV height (103 ± 2 *x* 213 ± 3 µm; n = 5); while 100 µM caused a significant reduction only in the circular LT (33 ± 2 *x* 44 ± 1 µm; n = 5), and dramatically destroyed MV width, (0,8 ± 0,6 *x* 63 ± 1 µm; n = 5) and height (2,31 ± 1,6 *x* 213 ± 3 µm; n = 5), without changing CRT depth or longitudinal LT; finally, 1 mM caused a full disintegration of the whole tissue (n = 5). ILP levels were not dependent on concentration, being similar for 100 nM (780 *x* 330,3 ± 8 $nmol.ml^{-1}/g$ dry tissue, n = 1 – pool 5 animals), 100 µM (514 ± 8,6 *x* 330 ± 8 $nmol.ml^{-1}/g$ dry tissue, n = 5) and 1 mM H_2O_2 (647 ± 47 *x* 330 ± 8 $nmol.ml^{-1}/g$ dry tissue, n = 5). In contrast, CAT activity decreased only for 1 mM H_2O_2 (5,7 ± 0,8 x 8,6 ± 0,4 UI/mg protein; n = 9), while SOD activity did not change (control: 3,06 ± 0,08;100 nM: 3,1 ± 0,1; 100 µM: 3,2 ± 0,2; 1 mM: 2,3 ± 0,2 UI/mg protein; n = 9). **Discussion:** These results are arguing in favor of a dual activity of H_2O_2 in C57Bl/6 intestine morphology and a trend for lipid peroxidation, which, however, did not seem to be related to strong alterations of the intestine antioxidant defense.

07.004

Molecular analysis of the effects of roscovitine on hepatic stellate cells of murine.

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Introduction: Hepatic stellate cells (HSC) play a crucial role in liver fibrogenesis (RIPPE, 1998). Roscovitine inhibits the cyclin-dependent kinases activity and fibrogenesis in some tissues (MEIJER, 1997; STARKEL, 2005). We aimed to investigate the effects of Roscovitine on the progression of hepatic fibrogenesis in mice. **Methods:** Hepatic fibrosis was induced by chronic CCl4 administration (20% v/v) intraperitoneally (i.p.), in Swiss mice, twice weekly for a period of 8 weeks. The animals were treated with Roscovitine (3 mg/kg) or vehicle i.p., from the sixth week, on alternate days for a period of 2 weeks. Collagen deposition was measured as the percentage of Sirius Red-positive staining (red). Assessment of apoptosis and proliferation of HSC was performed by double labeling immunohistochemistry (TUNEL + α-SMA) e (PCNA+ α-SMA), respectively. The gene expression of Procollagen α1 and TGF-β1 was evaluated by PCR-RT. The protein levels of Cyclin D1, TRAIL and p65 NFκB were quantified by Western blotting. **Results:** We observed a significant decrease in the collagen deposition (roscovitine 2.36 ± 0.14; control 3.83 ± 0.60, $p<0.01$), a diminution of proliferating α-SMA-positive cells (roscovitine 0.06 ± 0.01; control 0.12 ± 0.01, $p<0.01$), a higher apoptotic index of α-SMA-positive cells (roscovitine 0.59 ± 0.09; control 0.20 ± 0.02, $p<0.01$) and a reduction in the Procollagen α1 (I) gene expression (roscovitine 6.63 ± 3.09; control 33.94 ± 8.14, $p<0.05$) in all animals treated with Roscovitine. These data were related to the decrease in the TGFβ1 by Roscovitine treatment in the fibrosis period (roscovitine 0.50 ± 0.17; control 10.96 ± 5.15, $p<0.05$). The levels of TRAIL and NFkB protein were also augmented in all animals treated with Roscovitine (roscovitine + 0.41 -fold and + 0.91 –fold; control + 0.29 –fold and + 0.01 –fold), while Cyclin D1 was reduced (roscovitine + 1.35 –fold; control + 1.92 –fold). **Discussion**: The exposition of the animals to CCl4 as a model of hepatic fibrosis is widely employed, which results in a HSC activation, increased amount of collagen and inflammation (LEE, 2011). Roscovitine can inhibit the activity of CDK1, and thus decrease the expression of cyclin D1 (STEINMAN, 2012). The lower production of Cyclin D1, one of the main promoters of the cell cycle, implicates in diminution of cellular proliferation (PIPPIN, 1997). The data show a decrease in the levels of cyclin D1 protein and consequently, reduced the PCNA/αSMA-positive cells in animals treated. The TGF-β1 gene primarily responsible for the activation and proliferation of HSC, also had its decreased expression. The increased p65 NFκB protein amount may occurred as a consequence of the higher number of TUNEL/α-SMA-positive cells induced by Roscovitine. The activation of NFκB survival signaling may be related to the induction of cellular apoptosis by TRAIL (GIBSON, 2000). In the fibrosis, we observed an increase of TRAIL levels by Roscovitine treatment. In conclusion, the HSC apoptosis may be considered as an additional anti-fibrogenic event. Roscovitine promotes the reduction of Cyclin D1 and the increased of TRAIL protein levels, resulting in diminution of proliferation and increased of HSC apoptosis, culminating with the regression of liver fibrosis in treated mice. **Financial Agencies and Acknowledgment:** We would like to thank Fapesp (nº2010/20895-4), CNPq (nº479276/2007-2) and FAEPA. Ethics Committee approval (nº 163/2009).

07.005

Polysaccharide extracted from *Caesalpinia ferrea* prevents alendronate-induced gastric damage in rats. Pacífico DM[1], Silva OR[2], Pereira MG[2], Araújo S[1], Quaresma MP[1], Nicolau LAD[3], Araújo TSL[1], Medeiros JVR[1], Soares PMG[2] [1]LAFFEX-UFPI, [2]LAFICA-UFC, [3]NPPM-UFPI

Introduction: Several drugs are available for treatment of osteoporosis and bisphosphonates have become the mainstay. The efficacy of these agents to reduce the risk of fracture has been repeatedly demonstrated (Cummings SR; *JAMA*, 250, 2077, 1998). Among the most usually used bisphosphonates are the alendronate (ALD). The most common adverse effects of the ALD, which limits its prolonged use, are gastrointestinal disturbances such as abdominal discomfort and ulcers involving the esophagus and stomach (de Groen PC; *N Engl J Med*, 335, 1016, 1996).The present study was carried out in order to evaluate the gastroprotective effect of the polysaccharide fraction from *C. ferrea* (PLS) on ALD induced gastric damage in rats. **Methods:** This study was approved by the Ethics Committee in Animal Research of the UFPI (protocol Nº 0067/10). Female Wistar rats (100-140g) were received saline or PLS (1, 5, and 15 mg/kg, *p.o.*). After 30 min ALD (30 mg/kg, pH 7.0, *p.o.*) was administered. All substances were administered once daily for 4 days (Costa NR, *Eur J Pharmacol*, 700: 51-59, 2013). On the last day of treatment, 4 h after ALD administration, the animals were killed and their stomachs removed. Gastric damage was measured using Image J® software. Other samples were retired for histopathological analysis dosage of the glutathione (GSH) levels, malondialdehyde (MDA) concentration (Mihara M, *Anal Biochem*, 86, 271, 1978), myeloperoxidase (MPO) activity and cytokine (TNF-α and IL-1β) levels. **Results and discussion:** ALD (30 mg/kg, *p.o.*) administration by 4 days induced mucosal gastric damage (50.1 ± 4.3 mm^2). However, PLS (1, 5, and 15 mg/kg, *p.o.*) significantly ($p<0.05$) prevents alendronate-induced lesions in a dose-dependent manner, with maximal inhibitory effect observed at dose of 15 mg/kg PLS (11.0 ± 2.7 mm^2). Thus, this dose of PLS was used to study the possible mechanisms involved in these experimental model. Histopathological analysis showed that ALD induced gastric damage by epithelial cell loss intense cellular infiltration and edema. On the other hand, PLS (15 mg/kg, *p.o.*) reverted these alterations. Moreover, PLS (15 mg/kg) reverted the effect of the ALD increasing GSH (390.8 ± 16.1 µg/g of tissue) levels, resulting in values similar to the control. PLS (15 mg/kg) reduces MDA concentration (55.2 ± 7.7 nmol/g of tissue) in the gastric tissue. PLS (15 mg/kg) (17.8 ± 1.9 U/mg of tissue) significantly attenuated the increase in MPO activity. Compared to treatment with ALD group, PLS (15 mg/kg) produced significant inhibitory effect on TNF-α (986.3 ± 305.6 pg/ml), but had no impact on IL-1β levels (1936.0 ± 322.2 pg/ml). PLS prevented ALD-induced gastric damage by inhibiting neutrophil infiltration, decreasing pro-inflammatory cytokine (TNF-α and IL-1β) levels and elevations in oxidative stress. **Financial Support:** CNPq, FUNCAP and FAPEPI.

07.006

Antidiarrheal activity of cashew gum, a complex heteropolysaccharide of *Anacardium occidentale* L., in rats. Araújo TSL, Sousa NA, Pacífico DM, Carvalho NS, Araújo S, Sousa FBM, Quaresma MP, Barbosa AL, Medeiros JVR LAFFEX-UFPI

Introduction: Diarrhea is a condition where there is an increase in defecation. Diarrhea affects many people in developed and developing countries and millions of people die each year due to this disease. Keeping this in mind World Health Organization encourages studies on diarrhea which include research on traditional herbal medicine (KUNA, *IRJP*, 8, 289, 2012). The aim of the present study was to investigate the antidiarrheal activity of cashew gum (CG), a complex heteropolysaccharide of *Anacardium occidentale* L. tree. **Methods:** This study was approved by UFC ethics committee (nº 11/2013). Initially, the antidiarrheal activity of CG was evaluated for castor oil-induced diarrhea and *enteropooling*. Albino (Wistar) rats (150-200g) were pretreated with CG (30, 60, and 90 mg/kg, *p.o.*), and after 1 h, was administered castor oil (10 ml/kg, *p.o.*). Loperamide (5 mg/kg, *p.o.*), was used as a standard drug for diarrhea. Animals were placed in cages lined with filter paper and observed for 3 h for the presence of diarrhea defined as watery (wet), unformed stool. Moreover, they were sacrificed and the small intestine from the pylorus to the caecum was isolated and the volume of intestinal contents was measured by graduated tube. In PGE_2-induced *enteropooling*, rats were pretreated with CG (60 mg/kg, *p.o*) and immediately after the administration PGE_2 was administered (100 µg/kg, *p.o*). After 30 min they were sacrificed and the volume of intestinal contents was measured by graduated tube. Cashew gum was evaluated for intestinal motility using charcoal meal. The rats received castor oil to produce diarrhea and 1h later they were treated with CG (60 mg/kg, *p.o*). After 1 h, all animals were received 1 mL of charcoal meal (10% charcoal suspension in 5% gum acacia) orally. One hour later, animals were sacrificed, and the distance covered by the charcoal meal in the intestine from the pylorus to the caecum was measured. **Results and discussion:** Cashew gum (30, 60, and 90 mg/kg) was reduced significantly ($P<0.05$) the diarrheal severity (24.02%, 52.20% and 45.52%, respectively). Cashew gum also decreased the frequency of defecation and the total number of wet feces produced upon administration of castor oil. However, CG was not able to reduce significantly the intestinal volume in castor oil induced *enteropooling*. On the other hand, CG (60 mg/kg) significantly inhibited PGE_2-induced *enteropooling* (32.14%) and the activity was similar to that of loperamide (31.42%). The gastrointestinal distance traveled by the charcoal meal in the rats was significantly ($P<0.05$) lessened by CG (60 mg/kg) compared with the control group, producing a decrease (31.91%) in the propulsion of charcoal meal through gastrointestinal tract. These observations suggest that the CG reduced diarrhea by inhibiting gastrointestinal motility and PGE_2 induced *enteropooling* in rats. **Financial Support:** CNPq and FAPEPI.

07.007

Antidiarrheal activity of *Cissampelos sympodialis* Eichl. (Menispermaceae). Sales IRP[1], Sousa CGBL[2], Formiga RO[2], Nascimento RF[1], Lúcio ASSC[1], Barbosa-Filho JM[2], Batista LM[2] [1]UFPB – Produtos Naturais e Sintéticos Bioativos, [2]UFPB – Ciências Farmacêuticas

Introduction: *Cissampelos sympodialis* Eichl. (Menispermaceae), popularly known as "Milona", "orelha-de-onça" or "abuteira", is endemic in Brazil and is found in the Northeast and Southeast. Their choice was based on ethnopharmacological criteria, considering that this species is used in folk medicine for the treatment of diarrhea and respiratory problems. *C. sympodialis* is rich in alkaloids, substances that have the most diverse pharmacological activities, among them the antidiarrheal activity. The study aimed to evaluate the activity of the total alkaloid fraction obtained from aerial parts of *Cissampelos sympodialis* (TAF-*Cs*) in gastrointestinal motility and castor oil-induced diarrhea. **Methods:** Male mice, *Mus musculus*, Swiss (25-35 g) (n = 5-7), fasting for 12 hours or 24 hours were pre-treated with the negative control (Tween 80 solution at 12%), positive control (metoclopramide 30 mg/kg or loperamide 5 mg/kg) and TAF-*Cs* at doses of 62.5; 125; 250 and 500 mg/kg. After pretreatment the animals were subjected to the same protocols of gastric emptying (Scarpignato, *Arch Pharmacodyn Ther*, 246, 286, 1980), normal intestinal transit (STICKNEY, PSEBM, 101, 582, 1959) and by castor oil-induced diarrhea (Awouters, *J Pharm Pharmacol*, 30, 41 1978). Data were analyzed using ANOVA followed by Dunnett's test or Kruskal-Wallis test followed by Dunn's test. The experimental protocols were approved by the Comitê de Ética em Uso Animal (CEUA/CBIOTEC/UFPB) with number 2205/13. **Results and discussion:** In the model for evaluation of the TAF-*Cs* on gastric emptying, doses of 250 and 500 mg/kg reduced the percentage of gastric emptying in 46.91 % ± 6.76 and 44.07 ± 13.38% ($p<0.01$), respectively, when compared with the negative control group (70.08 ± 8.03) and the other doses did not alter gastric emptying. In the intestinal transit doses of 250 and 500 mg/kg of the TAF-Cs reduced the percentage of intestinal transit: 28.13 ± 12.00% and 25.89 ± 13.20% ($p<0.01$), respectively, when compared with the negative control group (47.06 ± 9.82). The TAF-*Cs* also showed antidiarrheal activity at the doses of 250 and 500 mg/kg with a reduction in diarrheal score of 1.43 ± 1.81 and 1.00 ± 0.89 ($p<0.01$), respectively, when compared with the negative control group (12.17 ± 4.21). Thus, the antidiarrheal activity observed here corroborates the popular use of this species and this activity may be related to the presence of alkaloids that act by reducing gastrointestinal motility. Further studies should be conducted to elucidate the mechanisms involved in the antidiarrheal activity of TAF-*Cs*. **Acknowledgements:** CNPq/Capes/PgPNSB/UFPB .

07.008

Gastroprotective effect of 1,4-cineole in ethanol-induced gastric lesions by macroscopic and microscopic analysis. Chaves Filho AJM, Feitosa ML, Venâncio ET, Lima CNC, Fonteles MMF, Florenço FC UFC – Physiology and Pharmacology

Introduction: In Brazil, a large number of medicinal plant extracts are used in folk medicine to treat various digestive disorders and many different substances obtained from these plants promote gastroprotective effects. Among the major classes of compounds related to this effect, the terpenes, mainly monoterpenes, have been shown to have higher inhibitory activity on ulceration induced by different agents. So this study aim to demonstrate the gastroprotective effect of natural monoterpene 1,4-cineole in well-established model of gastric lesions utilizing absolute ethanol by macroscopic and microscopic analysis. **Methods:** Absolute ethanol (0.2 mL/animal, p.o) was administrated to mice treated 1 h previously with vehicle (3% tween 80 in distilled water;p.o, controls) or 1,4-cineole [100 mg/kg;p.o.(CIN100) and 200 mg/kg;p.o.(CIN200)], while cyproheptadine [10 mg/kg; p.o.(CYPRO)] was used as reference drug. Thirty minutes after ethanol administration, mice were sacrificed and their stomachs were removed. The injured stomach areas were measured by *Image J*. For histological evaluation, tissue samples were processed for routine paraffin block preparation and stained with hematoxylin and eosin. The mucosal injury evaluation was performed under light microscopy and followed the criteria described by Laine and Weinstein (1988): (1) edema (score 0–4), (2) hemorrhagic damage (score 0–4), (3) inflammatory infiltration (score 0–3), and (4) epithelial cell loss (score 0–3). Data were analyzed by ANOVA followed by Student-Newman-Keuls *post* hoc test, with significance of $p<0,05$. This study was realized under the consent of the Committee of Ethics in Animal Research,Federal University of Ceará(Protocol 64/09). **Results**: The administration of absolute ethanol produced lesions in the gastric mucosa (18.61 ± 2.92 %), which were reduced in the animals pretreated with CIN200 (4.45 ± 1.06 %; $p<0.001$) and CYPRO(4.11 ± 0.61 %; $p<0.001$). CIN100 did not alter significantly the gastric damage (21.82 ± 3.62 %). As expected, the group treated only with saline did not present gastric damage. In histopathological analysis, animals pretreated with CIN200 showed significantly less microscopic mucosal damage [(1):0 (0-1)*; (2):0 (0-0)**; (3):0(0-0)**; (4):1(1-1)**] when compared with the ethanol control group[(1):2(2-4)$^{\#}$; (2):3,5(3-4)$^{\#}$; (3):2(2-2)$^{\#}$; (4):3(3-3)$^{\#}$]. The saline group did not present gastric damage [(1):0(0-0); (2):0(0-0); (3):0(0-0); (4):0(0-1)]. The results are presented as mean ± SEM (n = 5), with $^{\#}$ $p<0.01$ vs Saline; and *$p<0.05$, **$p<0.01$ vs. ethanol. **Discussion:** In the macroscopic analysis, CIN200 showed the capacity to protect the gastric mucosa of damage induced by ethanol through the high percentage of reduction on the gastric area damage (76.09%) when compared to vehicle control group. Accordingly, the microscopic analysis also shows us the deleterious effects of ethanol and the capacity of CIN200 to block significantly these effects. Thus these results suggest the gastroprotective activity from 1,4-cineole at the highest tested dose and its potential to be a new useful natural tool for gastric protection. However more studies need to be performed to confirm this property. **Financial support**: CNPq; Capes. **References:** Laine L. *Gastroenterol.* 94: 1254, 1988.

07.009

Intestinal anti-inflammatory effect of *Combretum duarteanum* Cambess (Combretaceae) leaves in TNBS colitis model (Acute Model). Lima GRM, Machado FDF, Nascimento RF, Silva AKM, Tavares JF, Batista LM UFPB – Ciências Farmacêuticas

Introduction: *Combretum duarteanum* Cambess. is found in South America, particularly in Bolivia, Paraguay, and Brazil. In Paraiba state (Brazil), the species usually occurs in the Caatinga biome. It is popularly known as mufumbo, cipiúba, or cipaúba. This work aims to evaluate the anti-inflammatory intestinal effect of the ethanolic extract (Cd-EtOHE) and hexane phase (Cd-HexP) obtained from the leaves of *C. duarteanum*. **Methods:** The animals were treated 48, 24 and 1h prior to the induction of colitis and 24h after with Cd-EtOH or Cd-HexP (31.25, 62.5, 125, 250 mg/kg p.o.) or tween 80 solution 12% (negative control) (n=5-7). The ulcerative colitis was induced by intracolonic injection of 2,4,6 trinitrobenzene sulfonic acid (TNBS) (10 mg dissolved in 0.25mL 50% ethanol). Colonic damage was scored according to a previously described scale (Morris *et al.*, 1989) and lesion area was determined using an image analyser, Bioview4AvSoft program. The results were expressed in mean ± S.D and were compared using ANOVA followed by Dunnetťs test. Nonparametric data (score) were expressed as the median (range) and analyzed with the Kruskal–Wallis test. Differences between proportions were analyzed with the Fisher's test. Statistical significance was set at $p<0.05$. The experimental protocols were approved by the Institutional Committee for Ethics in Animal Research of LTF/UFPB registered under 0211/09. **Results and discussion:** Rats with colitis developed macroscopic colonic lesions (colonic damage escore and lesion area) accompanied by diarrhea and significant rise in colonic weight/ length ($p<0.001$) when compared to sham group. Cd-EtOH (62.5 and 125 mg/kg) and Cd-HexP (31.25 and 62.5 mg/kg) significantly reduced the score ($p<0.05$) and lesion area ($p<0.05$, $p<0.001$) in comparison with Tween 80 12% group. The diarrhea also was reduced after of the treatment with Cd-EtOH (125 mg/kg, $p<0.01$) and Cd-HexP (62.5 mg/kg, $p<0.05$) when compared with theirs respectives control groups. These results suggest that the Cd-EtOH and Cd-HexP obtained from leaves of *Combretum duarteanum* displays anti-inflammatory effect against TNBS induced colitis model in rats. **Financial Support:** Capes/PgPNSB/UFPB

07.010

Enteric neuropathy induces changes in enteric nervous system and in nNOS expression in female diabetic rats. Da Silva LM[1], Maria-Ferreira D[1], Da Silva RCMVAF[1], Crestani S[2], Vicentino-Vieira SL[3], Da Silva Santos JE[2], Sant'Ana DMG[3], Baggio CH[1], Werner MFP[1]
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Introduction: Gastroparesis is a common gastrointestinal complication observed in patients with *Diabetes mellitus* that predominantly affects women. The mechanisms involved are not fully understood, but impairment of the nitrergic system is one of the main factors responsible for this disease. In this study we investigated some adaptive changes that occur in enteric nervous plexus, targeting the nitrergic system. **Methods:** Diabetes was induced with a single injection of streptozotocin (55 mg/kg, ip) in female Wistar rats and experiments were performed on week 8, in animals daily treated with vehicle (water, 0.1 ml/100g, p.o.), insulin (6 UI/day, s.c, starded 3days after diabetic induction) or ascorbic acid (300 mg/kg, p.o, started 2 weeks after diabetic induction) treatment. Gastric emptying was accessed by stomach phenol red content, functional studies were performed in organ bath, gastric reactive oxygen species (ROS) levels were detected by 2',7'-dichlorodihydrofluorescein diacetate (DCFH-DA) reaction. Furthermore, nicotinamide adenine dinucleotide phosphate diaphorase (NADPH-d) histochemistry was performed for study gastric nitrergic neurons and changes in gastric neuronal nitric oxide synthase (nNOS) protein levels were analyzed by Western blotting (CEUA/UFPR, 674). **Results:** As expected, at 8 weeks, diabetes promoted hyperglycemia, hemoglobin glication, weight loss and delayed gastric emptying (diabetic vehicle-rats: 43 % ± 10 versus normoglicemic controls: 76 % ± 6). Furthermore, vehicle-diabetic rats showed significant ($p<0.05$) impairment in sodium nitroprusside (10^{-9}-10^{-3}M) evoked relaxation and also after electric field (8-64 Hz) stimulation in NANC conditions, accompanied by increase in ROS levels in gastric tissues. Interestingly, the number and the size of cell body of gastric NADPH-d positive neurons and the gastric nNOS protein expression were highest in diabetic rats when compared to normoglicemic controls. Only insulin treatment prevented hyperglycemia, hemoglobin glication and weight loss induced by diabetes. However, both insulin and ascorbic acid treatments normalized all others changes induced by diabetes in female rats. **Discussion:** For the first time, our data provide evidences of an increase in gastric nitrergic neurons density and in gastric nNOS expression in the stomach of female rats. To better correlate our results, new experiments are performed to evaluated gastric nitrite levels. In fact, these changes may be a response to the impairment of gastric nitrergic system in attempt to increase the availability of nitric oxide in gastric tissues. Although diabetes gastroparesis remains even in the presence of these changes, these adaptations needs to be further explored to better understand potential therapeutic targets and improve the treatment of this disorder. Moreover, insulin and ascorbic acid treatments reversed delayed gastric emptying in diabetic conditions, suggesting that hyperglycemia and oxidative stress are key factors in these alterations.

07.011

Gastroprotective properties of cashew gum, a complex heteropolysaccharide of *Anacardium occidentale*, in naproxen-induced gastrointestinal damage in rats. Carvalho NS[1], Silva MM[1], Nicolau LAD[2], Silva RO[3], Soares PMG[3], Silva DA[1], Leite JRSA[1], Medeiros RJV[1] [1]UFPI – Biotechnology, [2]UFPI – Pharmacology, [3]UFC – Pharmacology

Introduction: Long-term use nonsteroidal anti-inflammatory drug (NSAIDs) is associated with gastrointestinal lesion formation (Wallace J.L, *J Gastroenterol*, 119, 706, 2000). There is an increasing body of evidence to support the use of cashew gum (CG) to treat pathophysiological conditions. The aim of this study was to investigate the protective activity of CG, a PLS complex extracted from *Anacardium occidentale* on naproxen-induced gastrointestinal damage. **Methods**: Experiment approved by the local ethics committee (Protocol No. 0066/10). Male Wistar rats were pretreated with carboxymethylcellulose (CMC, control group) or CG (1, 3, 10 and 30 mg/kg, *p.o.*) twice daily for 2 days. After 1 h, naproxen (80 mg/kg, *p.o.*) was administered. Rats were euthanized on day two. Stomachs were rapidly excised, opened and measured using digital calipers. The intestines were removed and a portion of the medial intestine was used to the evaluation of macroscopic scores. Samples of the stomach and the medial intestine were used for histological evaluation, morphometric analysis, and assays for glutathione (GSH), malonyldialdehyde (MDA), and myeloperoxidase (MPO). Additional rats were used to measure gastric mucus and secretion. **Results and discussion:** CG treatment reduced the macroscopic and microscopic naproxen-induced gastrointestinal damage in a dose-dependent manner, with maximal effect at dose of 10 mg/kg. Pretreatment with CG significantly decreased the infiltration of inflammatory cells, the formation of edema and the loss of epithelial cells induced by naproxen in the stomach. In the small intestine, the treatment with naproxen provoked significant villi shortening, increased crypt depth, and a decreased villus/crypt ratio were seen. However, when the animals were pretreated with CG, we observed a complete reversal of the intestinal morphometry alterations. In the evaluation of myeloperoxidase activity CG significantly reduced the MPO activity in both stomach (4.90 ± 0.34 U/mg of tissue) and intestine (4.52 ± 1.01 U/mg of tissue) as compared to naproxen group in the stomach (12.34 ± 2.42 U/mg of tissue) and the intestine (24.89 ± 5.84 U/mg of tissue). The administration of naproxen induced an increase MDA in stomach (157.3 ± 18.10 nmol/g tissue) and in medial intestine (292.7 ± 34.51 nmol/g tissue) and decreased GSH levels in stomach 76.79 ± 11.70 mg/g tissue and in medial intestine 93.13 ± 20.04 mg/g tissue. However, pre-treatment with CG significantly reduced MDA and increased GSH levels (80.80 ± 5.374 nmol/g and 189.5 ± 8.170 mg/g, respectively) in stomach and in the medial intestine (162.5 ± 2.681 nmol/g and 217.7 ± 32.97 mg/g, respectively). Furthermore, CG returned adherent mucus levels to control values. Our results suggest that CG has a protective effect against gastrointestinal damage through mechanisms that involve the inhibition of inflammatory cell infiltration and increasing the amount of adherent mucus in mucosa. **Financial support:** CNPq and FAPEPI

07.012

Actions of nitric oxide (NO) or hydrogen sulfide (H_2S) donors and possible interactions between the two systems in gastric functions in rodents. Lucetti LT[1], Medeiros JVR[2], Santana APM[1], Tavares BM[1], Soares PMG[3], Vale ML[1], Ribeiro RA[1], Souza MHLP[1] – [1]UFC – Fisiologia e Farmacologia, [2]UFPI – Biologia, [3]UFC – Morfologia

Aim: We evaluated the effects of Nitric Oxide (NO) and Hydrogen Sulfide (H_2S) donors and possible interactions between their systems in gastric functions of secretion, in mucosal defense mechanism and gastric motility. **Methods:** Saline, NPS (donor of NO) and NaHS (donor of H_2S) were administered in groups of Swiss mice and after 1 h were sacrificed for analysis of expression of CSE / CBS (enzymes involved in H_2S synthesis) and eNOS (enzyme involved in NO synthesis) in the respective groups. For gastric blood flow, Wistar rats were used, in groups of NPS, PAG (inhibitor of CSE), NaHS and L-Name (inhibitor of NOS). For other analyzes, the Swiss mice were divided in groups saline, PAG, NPS, PAG + NPS, L-Name, NaHS, LAW (donor of H_2S), L-Name + NaHS and L -Name + LAW. The PAG and L -Name inhibitors, were administered 30 min before NPS, NaHS and LAW donors. Secretion analyzes were performed after 4 h of pylorus ligation, mucus secretion by determination of soluble mucopolysaccharides, ethanol injury were determined as parameters determining the area of injury, microscopic analysis and assay of glutathione and malondialdehyde and the assessment of gastric emptying awake 20 min after test meal with phenol red in mice. To study the contractility of gastric fundus and pylorus NPS (0.3-100μM), PAG (1 mM), NaHS (10-1000μM) and L-Name (300μM) were added to the cub containing the tyrode solution and tissues. Data were analyzed using One-Way ANOVA and Newman- Keuls test. All animal treatments and surgical procedures were approved by the local ethics committee (protocol No 63/07). **Results:** Treatment with NPS (19.01 ± 1.62 %) increases expression of CSE when we compared with saline (7.49 ± 1.14%) and treatment with NaHS (9.92 ± 0.77%) increases eNOS expression when we compared with saline (2.49 ± 0.81%) in gastric tissue. NPS, NaHS and LAW do not alter gastric acid secretion but NPS (0.0862 ± 0.0042) and LAW (0.0634 ± 0.0024) increases mucus production when we compared with saline (0.0338 ± 0.0042) and these effects are reversed by PAG (0.0653 ± 0.0106) and L-Name (0.0481 ± 0.0062) respectively (mg/g of tissue). NPS (122.8 ± 2.87%) and NaHS (125.4 ± 1.56%) increase gastric blood flow when we compared with PBS (100.0 ± 0.40%) being reversed by PAG (107.0 ± 1.47%) and L-Name (104.0 ± 1.03%) respectively. NPS (14.62 ± 4.82%) protects the gastric mucosa against ethanol injury (94.27 ± 11.87%) and PAG (46.90 ± 5.62%) reverses this effect. NaHS (22.33 ± 7.05%) protect the gastric mucosa against ethanol injury and L-Name (88.99 ± 16.96%) reversed this effect of NaHS. NPS (62.24 ± 5.53%) delay gastric emptying when compared with saline (19.18 ± 3.59%) and PAG (44.58 ± 7.10%) reversed this effect. NaHS (20.60 ± 1.11%) accelerate gastric emptying when compared with saline (29.36 ± 2.95%) and L-Name (31.17 ± 2.55%) reversed this effect. NPS and NaHS cause relaxation of gastric fundus and pylorus and PAG and L-Name, reverted the effect on gastric pylorus but not in gastric fundus respectively. **Conclusion:** NO and H_2S are involved in the regulation and protection of various gastric functions and can act in association effects on mucus secretion, in the defense mechanism, and gastric motility. **Financial Support:** Capes

07.013

Regulation of nodal, Cripto and Smad 4 expression during decidualization and by steroid hormones in human endometrial stromal cells. Dela Cruz C[1,2], Kaya HS[2], Taylor RN[3], Reis FM[1], Bagchi MK[2] [1]UFMG – Obstetricia e Ginecologia, [2]UI – Molecular and Integrative Physiology, [3]WFBMC

Introduction: Nodal is a member of TGF-beta superfamily and initiate its actions through activation of type I and II activin receptors by the co-receptor Cripto, and subsequent activation of intracellular Smad proteins 2 and 3. These proteins interact with a common Smad 4 and this complex is translocated to the nucleus where it combines with DNA-binding proteins at the promoter regions of target genes (Park and Dufort, 2013). Currently, there are no reports about the regulation of these proteins by steroid hormones in human endometrial stromal cells. In this study, the effects of estrogen and/or progesterone on the expression of Nodal, Cripto and Smad 4 were evaluated as well as the expression of Nodal and Cripto during the process of decidualization *in vitro.* **Materials/Method:** Endometrial samples from 4 healthy women with regular cycles were obtained at the proliferative phase and isolated stromal cells were cultured for 24 hours in the presence of estradiol, progesterone, or estradiol plus progesterone. Cells cultured in the absence of steroid hormones served as a control. Using quantitative real-time PCR we evaluated gene expression of Nodal, Cripto and Smad 4 and using Western Blot we assessed the protein expression levels of Nodal. For decidualization study, the cells were cultured in the presence of a decidualization cocktail consisting of 10nM estradiol, 1uM progesterone and 0.5mM cyclic AMP. After 8 days of treatment, the morphology of the cells was assessed. Total RNA was isolated and cDNA synthesized, followed by quantitative real-time PCR to evaluate the gene expression of Nodal and Cripto. Using Western Blot we assessed the protein levels of Nodal. Prolactin and IGFBP-1 gene expression were also measured, as standard markers of decidualization. **Results:** For the treatment during 24h, we found an increase of Cripto gene expression when cells were treated with estradiol plus progesterone ($p<0.05$) and an increase of Smad 4 gene expression ($p<0.04$) when cells were treated with progesterone alone. Nodal protein expression was significantly higher when cells were cultured with estradiol plus progesterone ($p<0.01$). In the other hand, our results showed that the decidualization cocktail was able to induce a significant and persistent decrease in the gene expression of Cripto mRNA ($p<0.05$), whereas no changes were found in the expression levels of Nodal mRNA or protein. **Conclusions**: These preliminary results suggest that proteins involved in Nodal signaling pathway are expressed by human endometrial stromal cells, and this pathway is regulated by ovarian steroid hormones. In addition, in relation to the decidualization process, further studies should evaluate if Cripto inhibition is maintained post-transcriptionally and extends to the endometrial tissue as a whole, in order to shed more light on the role of this signaling system in the mechanisms of endometrial decidualization. This study was supported by Brazilian National Institute of Hormones and Women's Health and CNPq. Reference: Park, CB. *Reproduction*. 24;145(2):R55-R64

07.014

Inhibition of intestinal transit induced by clozapine in mice: Role of cholinergic, serotonergic and endocannabinoid systems. Marques AC, Viana AFC, Arruda BR, Rao VS, Santos FA UFC – Fisiologia e Farmacologia

Introduction: Clozapine (CLZ), the first second generation antipsychotic drug developed, is still the drug of choice for treating refractory and severe cases of schizophrenia. Constipation can be the most frequent side effect affecting one out of three patients treated with clozapine. **Objective:** The aim of this study was to investigate the involvement of ACh, 5-HT and CB1-receptors in clozapine induced intestinal transit delay in mice. **Methods**: Male Swiss mice (25-30g, n=8/group) were treated orally with saline (10 mL/kg, control vehicle) or CLZ (5, 10 and 20 mg/kg) 45min before the oral administration of 0.2 mL of charcoal meal (5% activated charcoal suspended in 10% aqueous gum Arabic) (Camass *et al.*, 1976). The animals were sacrificed 20 min later, the extent of charcoal propulsion in the small intestine was measured and the gastrointestinal transit (GIT) was expressed as the percentage (%) charcoal marker traversed in relation to total length of small intestine. In order to evaluate the role of ACh, 5-HT and CB1 receptors on CLZ effect, groups of animals were pretreated with neostigmine (1 mg/kg, i.p.), ketanserin (5 mg/kg, p.o.) or AM251 (1 mg/kg, i.p.) 15 min before the administration of CLZ (10 mg/kg, p.o.). The Institutional Ethics Committee approved the experimental protocol (CEUA-UFC NS-33). Statistical analysis was performed by ANOVA followed by Student Newman Keul's test. The data were expressed as mean ± SEM. Differences were considered to be statistically significant when $p<0.05$. **Results**: CLZ significantly ($p<0.05$) reduced GIT at oral doses of 10 and 20 mg/kg by 27.41 ± 5,533 % and 21,87 ± 3,846 % respectively, as compared to vehicle-treated control group (51,31 ± 8,637%). While the delayed transit induced by CLZ was not ameliorated in mice pretreated with neostigmine or ketanserin, AM251, a cannabinoid receptor antagonist significantly ($p<0.05$) reversed the CLZ induced inhibition of GIT. **Discussion:** Activation of presynaptic CB1 receptors expressed in intrinsic enteric neurons may result in reduced cholinergic and serotonergic outputs and consequently an impaired peristalsis. The results of this study indicate that CB1 receptor activation is involved in CLZ-induced inhibition of GIT, since AM251, a CB1 receptor antagonist effectively ameliorates it. **Conclusion:** The study suggests that the enteric CB1 receptor blocking pathway is likely a possible target for treating clozapine-induced constipation. **Financial Support:** CNPq, Capes.

07.015

Intestinal anti-inflammatory effect of ethyl acetate phase of *Maytenus obtusifolia*.

MachadoFDF, Lima GRM, Paulo LL, Souza SS, Tavares JF, Batista LM UFPB

Introduction: *Maytenus obtusifolia* Mart. is distributed in many states in the Northeast and Southeast of Brazil. It is popularly known as "bom nome" or "carne-de-anta" or "carrancudo", being used in folk medicine to treat ulcers and general inflammation. Phytochemical studies with *M. obtusifolia* showed the presence of pentacyclic triterpenes of friedelane and lupane series, alkaloids and flavonoids. Pharmacological studies showed that the selected species has neuroleptic, analgesic and antiulcer activity. **Aim:** To evaluate the anti-inflammatory intestinal activity of ethyl acetate phase of *Maytenus obtusifolia* in experimental ulcerative colitis in rats. All experimental procedures were approved by the Ethics Committee on Animal Use (CEUA) with certificate number 0411/11. **Materials and Methods:** Wistar rats were treated with saline (10mL/kg) or FAcOEt -*Mo* (62.5, 125, 250, 500 mg/kg) 48, 24 and 1 hour prior to induction of colitis, that was performed with TNBS (10 mg – 0,25 mL), and 24 hours after the induction. After 48 h of induction of inflammation, the animals were euthanized and colonic segment was removed for assessment of damage score and relation colon weight/length. **Results and discussion:** The results were expressed as minimum and maximum median. FAcOEt-*Mo* significantly reduced the damage score at doses of 250 [5 (3-5; $p<0,01^{**}$)] and 500 [5 (4-6; $p<0,05^{*}$)] mg/kg, when compared to the ulcerative colitis control 7 (5-8). In the parameter weight/length FAcOEt-*Mo* not caused a significant change. **Conclusion:** Based on these results it is concluded that FAcOEt-*Mo* have intestinal anti-inflammatory activity in ulcerative colitis induction model. **Support:** Capes/PgPNSB/UFPB

07.016

Acute toxicity and gastroprotective effect of rosmarinic acid in gastric ulcer model induced by ethanol/HCl in mice. Nascimento RF, Sales RPS, Paulo LL, Machado DFM, Barbosa-Filho JM, Batista ML UFPB – Ciências Farmacêuticas

Introduction: Rosmarinic Acid (RA), a secondary metabolite of various plant species is chemically characterized as an ester of caffeic acid and lactic acid 3.4 dihydroxyphenyl. Its name is derived from *Rosmarinus officinalis*, the first plant from which it was isolated and has shown several activities as antioxidant, anti-inflammatory, antimicrobial, among others (DOMITROVIC, Food Chem. *Toxicol*, 66, 321, 2014). This study aimed to evaluate the acute toxicity as well as the gastroprotective activity of RA in gastric ulcer induced by ethanol/HCl. **Methods:** The available of acute toxicity was performed according to OECD 423, for both was used female Swiss mice (*Mus musculus*) (25-30 g, n = 3-6), which were treated orally (p.o.) with the vehicle NaCl 0,9% (control group) or RA (300 and 2000 mg/kg) and after was performed a behavioral assessment (Almeida, RN Far Bras, 80, 72, 1999). The animals were observed for a period of 14 days. For the ethanol/HCl-induced gastric ulcers protocol, male Swiss mice were pretreated with vehicle (NaCl 0.9% p.o.), carbenoxolone 100 mg/kg (positive control) and RA (25, 50, 100 and 200 mg/kg p.o.). Posteriorly, they were subjected to the harmful agent (MIZUI, T., *Jap J Pharmacol*, 33, 934, 1983 – with modifications). The results were analyzed using ANOVA, followed by Dunnett's test. The experimental protocols were approved by the Ethics Committee on Animal Use (CEUA/CBIOTEC/UFPB) with number 2205/13. **Results and discussion:** The RA administred in the single dose of 300 mg/kg induced constipation. There was not death of animals treated with RA in the doses of 300 mg/kg of RA during the experiment, however one animal treated with RA in the dose of 2000 mg/kg died. Thus the LD_{50} (lethal dose 50%) of RA was about 2500 mg/kg according to OECD 423. Treatment with RA (300 mg/kg and 2000 mg/kg) did not affect weight gain or weight of the organs when compared to the control group. In the ethanol/HCl-induced gastric ulcers model the oral doses 25, 50, 100 and 200 mg/kg of the RA presented protective effect in gastric mucosa with ulcerative index of 61,83 ± 11.41, 61.33 ± 9.44, 60.60 ± 4.39, 53.60 ± 7,40, respectively, when compared to the negative control (105,2 ± 9,74). Thus, the results of the present study show that the RA has low toxicity and it has gastroprotective activity, in experimental conditional evaluated. **Acknowlegments:** CNPq/UFPB.

07.017

Chronic aerobic exercise changes the contractile reactivity of rat ileum. Araujo LCC[1], Souza ILL[2], Vasconcelos LHC[2], Cavalcante FA[3,2], Silva BA[4,1,2] [1]UFPB – PPgBCM, [2]UFPB – PPgPNSB, [3]DFP-UFPB, [4]DCF-UFPB

Introduction: exercise is a multifactorial activity that affects all organs and tissues, resulting in many health benefits (Bherer, *J Aging Res*, v. 2013, p. 8, 2013). The execution of physical exercises has remarkable interferences on intestinal motility in general for positive stimulation. According to this fact, there are changes in plasma concentrations of hormones associated with gastrointestinal tract function of mice exercised on a treadmill (LIRA, *Eur J Appl Physiol*, v. 103, p. 215, 2008). Therefore, this study aimed to evaluate the influence of chronic aerobic exercise in the form of swimming on contractile reactivity of rat ileum. **Methods:** Wistar rats (*Rattus norvegicus*) from sedentary group (SED) stayed in contact with water for 2 min during the exercised rats training. Animals from exercised group were submitted to a swimming exercise for 1 h, with a metal ring attached to their chest corresponding to 3% of their body weight. Animals were randomly divided into groups which perform this procedure 5 days per week during 2 (EX2), 4 (EX4), 6 (EX6) or 8 (EX8) weeks. After the 5th day of training, the animals rested for 48 h (Davies, *Arch Biochem Biophys*, v. 299, p. 539, 1981). Then, animals were euthanized, ileum were removed and suspended in organ baths and isotonic contractions were registered. All experimental protocols were previously approved by Ethical Committee on Animal Use of CBiotec/UFPB (Protocol 0907/13). **Results:** KCl cumulative concentration-response curves for EX2 (E_{max} = 63.1 ± 3.9%), EX4 (E_{max} = 48.8 ± 3.8%), EX6 (E_{max} = 19.4 ± 1.8%) and EX8 (E_{max} = 59.4 ± 2.8%) were altered when compared to SED (E_{max} = 100%), decreasing the maximum effect (E_{max}), but had no significant difference on potency parameter. Similary, the carbachol (CCh) cumulative concentration-response curves for EX2 (E_{max} = 74.1 ± 5.4%), EX4 (E_{max} = 75.9 ± 5.2%) and EX6 (E_{max} = 62.9 ± 4.6%) were altered when compared to SED (E_{max} = 100%), decreasing the maximum effect, meanwhile the EX8 (E_{max} = 89.7 ± 3.4%) not presented difference to SED. However, CCh contractile potency was not altered when compared to SED group, but was altered between groups EX2 (CE_{50} = 1.5 ± 0.5 x 10^{-6} M) and EX8 (CE_{50} = 2.1 ± 0.4 x 10^{-7} M), EX6 (CE_{50} = 1.5 ± 0.3 x 10^{-6} M) and EX8. **Discussion:** increased intestinal contractility is one of the processes that characterize intestinal cramps, diarrhea and constipation (SATO, Biol. Pharm. Bull., v. 30, p. 145, 2007). According to the results, aerobic exercise altered the ileum response to KCl and CCh, decreasing the intestinal contraction amplitude. Additionally, in EX8, the contractile response to CCh had no difference to SED, showing an adaptive response that is characteristic of chronic exercise (YALCIN, J. *Appl. Physiol.*, v. 88, p. 2074, 2000). Thus, exercise has long been considered an important therapeutic tool in the prevention and treatment of various diseases such as cardiovascular, respiratory (SESSA, Circ. Res. v. 74, p. 349, 1994) and gastrointestinal diseases (PETERS, *Int. J Gastroenterol*, v. 48, p. 435, 2001). Finally, the obtained data indicate a direct relation between swimming exercise and intestinal smooth muscle reactivity that should be better studied and so clarify the involved mechanisms and possible therapeutic implications. **Support:** CNPq, Capes, PPgBCM/CCEN/UFPB, PPgPNSB/CCS/UFPB.

07.018

Gastroprotective activity of the geopropolis of *Melipona Fasciculata* Smith (Tiúba).

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Introduction: The peptic ulcer, a major gastrointestinal disease, is caused by multiple factors including stress, smoking, nutritional deficiencies, noxious agents such as alcohol, anti-inflammatory drugs (NSAIDs) and *Helicobacter pylori* infection, among others (BELAICHE *et al*., 2002). The geopropolis of the southeastern Maranhão region is rich in chemical classes of phenolic acids, triterpenes and tannins. The aim this study was to investigate the antiulcerogenic potential of the geopropolis extract produced by bee *Melipona fasciculata* Smith (tiúba) (DUTRA, 2012). **Methods:** *Gastric lesion* – After 16 h of fasting, animals (n = 6) were treated orally with saline, omeprazole (20 mg/kg) or hydroalcoholic extract of geopropolis (HEG). One hour after treatment, the gastric injury was induced by oral administration of 1 mL of ethanol 75% and indomethacin (30 mg/kg) subcutaneously. The animals are euthanized one or four hours after the induction of lesions. Stomachs were removed and photographed to determine the area of gastric lesions (mm²) through Software ImageJ®. *Ligation of the pylorus* – After 24 hours of fasting, through an incision in the epigastric region, was located the stomach and the pylorus was tied with suture string. Then the animals were treated with saline, omeprazole (40 mg/kg), HEG intraduodenal and the incisions were sutured. Four hours later the animals were euthanized, the gastric contents were collected and volume, pH and acidity of gastric secretion were determined. *Histological analysis* – The stomach samples submitted the by ethanol injury were undergoing staining eosin/hematoxylin for histological analysis. All tests were approved by the Ethics Committee on the use of animal-UFMA, 018302/2011-1. **Results:** The treatment of the animals with ulcer induced by ethanol 75% with HEG (50 or 100 mg/kg) reduced the ulcer area in 63% and 90%, respectively, compared to the control group. In injury by indomethacin induced, the treatment with HEG (100, 200, and 500 mg/kg) reduced the ulcer area in 61%, 80% and 52%, respectively, compared to the control group. The stomachs histological examination of the animals treated with HEG not showed no acute erosion and the epithelium, the surface layer of the mucous remained intact. The extract did not alter the volume, pH and acidity of gastric juice. **Discussion:** The effect of the HEG on the lesions by ethanol must be due to the antioxidant properties of geopropolis. The antioxidant activity is important, since free radicals are a determining factor in the formation of ulcer and erosive lesions of the gastrointestinal tract. The effect of the HEG on the injury by indomethacin may be due to interference in the production of prostaglandins due to the presence of phenols found in high concentration in the geopropolis, since some studies have shown its influence in producing these. In our results we observed that the extract of geopropolis no altered these parameters, keeping them similar to the negative control group, which received only saline. Thus, these results reinforce the idea that the action of the HEG to inhibit the ulcer does not involve the inhibition of gastric secretion. **Acknowledgments:** FAPEMA, Capes and CNPq. **References:** Belaiche, J. *et al.* Study Group of NSAID-GI Complications. Observational survey of NSAID-related upper gastro-intestinal adverse events in Belgium. Acta *Gast Belgian*, 65, 65–73, 2002. DUTRA, R. P. Bioprospecção da geoprópolis de *Melipona fasciculata* Smith como insumo na geração de produtos leishmanicidas. 2012. Tese de Doutorado- Programa de Pós-Graduação em Biotecnologia da Rede Nordeste de Biotecnologia. São Luís, 2012.

07.019

Gastroprotective effect of baicalein against ethanol/HCL-induced gastric damage in mice. Ribeiro ARS, Thomazzi SM UFS – Fisiologia

Introduction: Baicalein, a constituent of several medicinal plants with gastroprotective actions as *Scutellaria baicalensis*, (Li, J Chromatogr B, 812, 277, 2004) presents various biological activities including anti-inflammatory (CHEN, Biochem. Pharmacol., 61, 1417, 2001), anti-tumor (TANIGUCHI, Cancer Res. 68, 8918, 2008), and anti-apoptotic (LIU, J. *Neuroprotection*, 112, 1500, 2010). However, the gastroprotective properties of this compound have not yet been studied. The purpose of this study was to assess the gastroprotective property of baicalein (10, 30, and 100 mg/kg) and some of the mechanisms underlying its gastroprotective effect in mice using ethanol/HCl-induced ulcer model. **Methods**: To evaluate the gastroprotective effect of baicalein, Swiss mice (n = 6/group) were obtained from the Central Biotery of the UFS. All experimentals protocols were approved by the Ethics Committee on Animal Research of the UFS (CEPA/UFS 63/2010). After 24 h of fasting, the mice were pretreated with baicalein (10, 30, and 100 mg/kg, p.o.), omeprazole (30 mg/kg, p.o.), and water (10 mL/kg, p.o.), and 45 minutes later, the acute gastric ulcers were induced by the administration of 60% ethanol/0.3 M HCl (100 µL/10 g, p.o.) (MIZUI, *Jpn J Pharmacol*, 33, 939, 1989). One hour later, the animals were anesthetized and euthanized by cervical dislocation, and the stomachs were removed for analysis of the ulcer lesion index (ULI) using specific "EARP" software. To investigate the role of prostaglandins (PG), nitric oxide (NO), and sulfhydryl groups in the protective effects of bacalein, the animals were pretreated with an inhibitor of PG synthesis (indomethacin, 10 mg/kg, p.o.), an inhibitor of NO synthase (L-NAME, 75 mg/kg, i.p.), or an inhibitor of sulfhydryl group synthesis (NEM, 3 mg/kg, i.p.). After 45 minutes, the animals were treated as previously described in the ethanol/HCl-induced ulcer model. Results were expressed as mean ± SEM of ULI and statistically analyzed by analysis of variance (ANOVA) followed by Tukey's test, and considered significant p values <0.05. **Results**: The treatment with baicalein at 10, 30, and 100 mg/kg reduced significantly ($p<0.01$) the ulcer lesion index by 9.40 ± 0.81, 4.28 ± 0.64, and 3.80 ± 1.46 ULI, respectively, when compared with vehiche treatment (16.28 ± 1.52 ULI). The pretreatment with L-NAME or NEM was unable to reverse the gastroprotective effect of baicalein against ethanol/HCl-induced gastric damage, but indomethacin pretreatment abolished the gastroprotective effect of baicalein ($p<0.01$). **Discussion:** The present results suggest that baicalein, a flavonoid present in many medicinal plants, produces dose-related gastroprotective response on ethanol/HCl-induced ulcer in mice through mechanisms that involve prostaglandins. **Financial agency**: Capes/CNPq.