07. **Endocrine and Gastrointestinal**

07.001 Diabetic neuropathy is ameliorated in streptozotocin-injected rats after treatment with sulfonylhydrazone derivative. Pereira SL, Souza BJ, Trachez MM, Monteiro CES, Costa FP, Romeiro NC, Lima LM, Barreiro EJ, Sudo RT, Zapata-Sudo G ICB-UFRJ

Introduction: Neuropathic pain is a significant cause of impairment among diabetic patients. This study describes the beneficial effects of a novel sulfonylhydrazone derivative (LASSBio-1473) in a model of diabetes-induced neuropathic pain in rats. **Methods:** Male Wistar rats (180 – 220 g) received a single intravenous injection of streptozotocin (STZ, 60 mg/kg) to induce diabetes. STZ-treated rats were randomly divided into two groups (n = 5 per group) treated with vehicle (dimethyl sulfoxide, DMSO) or LASSBio-1473 (20 mg/kg, i.p.). These groups were compared with a control group of non-diabetic rats. Plasma glucose levels were examined in blood samples collected by tail-vein puncture, using the Accu-Check®Performa monitoring system. Blood glucose, mechanical allodynia and thermal hyperalgesia were evaluated before and weekly after the STZ injection during 6 weeks. Six weeks after the induction of diabetes, rats with glucose levels >350 mg/dL were treated with either vehicle or LASSBio-1473 for 14 days. After the first administration of vehicle or LASSBio-1473, mechanical allodynia and thermal hyperalgesia were measured 30, 60, 120, 180 and 240 min after injection. Mechanical allodynia and thermal hyperalgesia were examined before and 1, 7, 10 and 15 days after treatment. All data were expressed as mean ± standard error of the mean (SEM). For the comparison of groups, two-way ANOVA was used and differences were considered significant when P was <0.05. The protocols used were approved by Animal Care and Use Committee at Universidade Federal do Rio de Janeiro under DFBCICB 041. **Results and discussion:** The blood glucose levels of diabetic rats were increased from 126.0 ± 3.4 mg/dL before STZ injection to 555.9 ± 16.9 mg/dL (P< 0.05) at 6 weeks after the induction. Paw withdrawal threshold of diabetic rats was decreased from 41.1 ± 0.3 g before STZ injection to 17.6 ± 1.1 g (P< 0.05) at 6 weeks after the induction. Paw withdrawal latency of diabetic rats was decreased from 10.5 ± 0.6 s before STZ injection to 7.1 ± 0.5 s (P< 0.05) at 6 weeks after the induction. Both alterations indicated the diabetic neuropathy. Sixty minutes after LASSBio-1473 administration, the paw withdrawal threshold increased from 17.1 ± 1.4 g (before injection) to 36.4 ± 1.1 g (P< 0.05). Reduced threshold was observed again after 240 minutes of LASSBio-1473 administration, when this parameter decreased to 21.6 ± 1.2 g. Also, the paw withdrawal latency increased from 7.3 ± 0.5 s (before injection) to 11.4 ± 0.4 s (P< 0.05) and reduced after 240 minutes of LASSBio-1473 administration, when the paw withdrawal latency decreased to 7.6 ± 0.2 s. Threshold of LASSBio-1473-treated diabetic rats was 17.1 ± 1.4 g before treatment and 34.0 ± 3.1 g after 15 days of treatment (P< 0.05). The paw withdrawal latency of LASSBio-1473-treated diabetic rats was 7.3 ± 0.5 s before treatment and 10.3 ± 0.4 s after 15 days of treatment (P< 0.05). Vehicle had no effect on mechanical allodynia and thermal hyperalgesia of diabetic rats. The novel sulfonylhydrazone derivative ameliorated mechanical allodynia and thermal hyperalgesia in rats with STZ-induced diabetes. **Financial Support:** CNPq, FAPERJ, CAPES, INCT, PRONEX.

07.002 Acute toxicity and gastroprotective activity of *Cissampelos sympodialis* Eichl.(Menispermaceae). Sales IRP, Formiga RO, do Nascimento RF, Lúcio ASSC, Barbosa-Filho JM, Batista LM UFPB

Introduction: *Cissampelos sympodialis* Eichl. (Menispermaceae), popularly known as “milona”, “orelha-de-onça” or “abuteira”, is endemic in Brazil, found in the Northeast and Southeast. Our choice was based on chemotaxonomic criteria because this species is rich in alkaloids (such as warifteine, metilwarifteine and milonine) and showed gastroprotective activity in previous studies. The aim of this study was to evaluate the acute toxicity and gastroprotective activity of total alkaloid fraction obtained from the aerial parts of *Cissampelos sympodialis* (FAT-*Cs*). **Methods:** At trial evaluation of acute toxicity according to OECD 423, female Swiss mices (*Mus musculus*) (25-35 g, n=3-7) were treated orally (p.o.) with vehicle Tween solution 80 (12%) (negative control), and FAT-*Cs* (300 or 2000 mg/kg) carried out a behavioral assessment (ALMEIDA, R. N. Rev Bras Far, 80, 72, 1999) and monitoring of animals during a period of 14 days. In the evaluation of the gastroprotective activity male Swiss mices were treated (p.o.) with vehicle Tween solution 80 (12%) (negative control), cimetidine 100 mg/kg (positive control) and FAT-*Cs* (62.5 125, 250 and 500 mg/kg) and subjected to non-steroidal anti-inflammatory drugs (NSAIDs)-induced ulcer protocol (PUSCAS, I. Arzneimittelforschung, 47, 568, 1997). The data were analyzed using ANOVA, followed by Dunmett’s test. The experimental protocols were approved by the Ethics Committee on Animal Use (CEUA / CBIOTEC / UFPB) with number 0408/12. **Results and Discussion:** The study of acute toxicity and behavioral assessment the mice treated with 2000 mg/kg of the FAT-*Cs* showed the presence of analgesia and Straub tail. No death was observed for animals treated with 300 mg / kg of the FAT-*Cs*, although at a dose of 2000 mg / kg two animals died. Referring to the flowchart values, the estimated lethal dose 50% (LD 50) around 1000 mg / kg according to OECD 423. Treatment with the FAT-*Cs* (300 mg/kg) did not alter the weight gain, organ weights and water consumption or feed when compared with the negative control group. In ulcer model induced by NSAIDs, the FAT-*Cs* (62.5 125, 250 and 500 mg/kg) showed protective effect in gastric mucosa with ulcerative index (UI) of 42,71 ± 9,36 , 32,57 ± 9,48, 20,71 ± 8,81 and 18,43 ± 5,53 mm², respectively, when compared to the negative control group (UI: 84,86 ± 19,16 mm²). Thus, the gastroprotective activity already observed earlier may be related to the alkaloids of this species and other studies will elucidate the mechanism of action of the FAT-*Cs*. **Acknowledgments:** CNPq/CAPES/PgPNSB /UFPB.

07.003 Acute toxicity and protective effect of *Maytenus erythroxylon* Reissek (Celastraceae) against ethanol/HCl-induced gastric ulcers in mice. Formiga RO, Caldas Filho MRD, Paulo LL, Quirino ZGM, Batista LM UFPB

Introduction: *Maytenus erythroxylon*Reissek is rich in bioactive metabolites from the class of terpenes, anteriorly referenced in the literature as antiulcerogenic (GUTIERREZ, F., J. Nat. Prod., 70, 1049, 2007). This species was selected for this study based on chemotaxonomic criteria that aimed to evaluate the acute toxicity (behavioral assay and Lethal Dose 50%), as well as the gastroprotective property of ethanolic extract obtained from the aerial parts of *Maytenus erythroxylon* (EEtOH-*Me*) against gastric ulcers induced by ethanol/HCl. **Methods:** In the evaluation of acute toxicity (ALMEIDA R.N., Rev. Bras. Farm., 80, 72, 1999) was used male and female Swiss mice (*Mus musculus*) weighting between 25-35 g (n=3-7) which were divided into 4 groups (2 groups of male animals and 2 groups of female animals) and treated orally (p.o.) with the vehicle NaCl 0.9% (control group) or EEtOH-*Me* (2000 mg/kg). Then, it was carried out a behavioral assessment and a monitoring of the animals during a period of 14 days, where parameters such as death and water and feed consumption were measured. For the ethanol/HCl-induced gastric ulcers protocol, male Swiss mice were pretreated with vehicle (NaCl 0.9% p.o. - negative control), lansoprazole 30 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 (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 0701/13. **Results and Discussion:** The EEtOH-*Me* administered in the single dose of 2000 mg/kg, p.o., induced no apparent changes in the central nervous system and autonomic when compared to the respective control group (saline solution 0.9%). The assessment of water and feed intake showed that the extract did not cause significant increase or decrease of these parameters. There was no death during the experiment and it was also observed no significant changes in animals' weight or in their organs (heart, kidneys, liver and spleen), as well as the macroscopic characteristics of the animals which received EEtOH-*Me*, when compared to the control group. In the ethanol/HCl-induced gastric ulcers model the oral doses 250 and 500 mg/kg of the EEtOH-*Me* presented protective effect in gastric mucosa with ulcerative index of 85.67 ± 10.56 with 32% of injury inhibition ($p < 0.01$) and 61.80 ± 8.643, 49% ($p < 0.001$), respectively, when compared to the negative control group (126.7 ± 29.08). Thus, the results of the present study show that ethanolic extract of *Maytenus erythroxylon* has low toxicity being its LD_{50} over 2000 mg/kg and it displays gastroprotective activity, as demonstrated by the significant inhibition of ulcer formation. However, future studies are still necessary to evaluate the gastroprotective activity in other induced gastric ulcers models. **Acknowlegments:** CNPq/CAPES/UFPB.

07.004 Protective effect of *Nanuza plicata* (Mart.) L. B. Smith & Ayensu (Velloziaceae) against NSAID and stress-induced gastric ulcers in mice. Sousa TM, Lima GRM, Tavares JF, Batista LM UFPB

Introduction: The species *Nanuza plicata* (Mart.) L. B. Smith & Ayensu (Velloziaceae) is popularly known as "canela d'ema". The criteria of selection were the chemotaxonomic because this species is rich in flavonoids, substances previously reported in the literature as antiulcerogenic. The objective of this study was to evaluate the gastroprotective activity of the ethanolic extract obtained from aerial parts of *N. plicata* (EEtOH-*Np*) in two models of induced acute ulcer: stress (immobilization and cold) and non-steroidal anti-inflammatory drug (NSAID). **Methods:** The animals used were male mice *Mus musculus*, Swiss strain (n = 5-7) weighing 25-35 g, fasted for 24 hours and pre-treated with the negative control (Tween 80 solution - 12%, 10 mg/kg), positive control (cimetidine 100 mg/kg) and EEtOH-*Np* (62.5, 125, 250 and 500 mg/kg). Subsequently it was performed the induction of ulcers by immobilization and cold stress (LEVINE, R. J. Munksgaard, Copenhagen, p. 92, 1971) and administration of NSAID (piroxicam 30 mg/kg) subcutaneously (PUSCAS, I. Arzneimittelforschung, v. 47, p. 568, 1997). The results were analyzed using ANOVA, followed by Dunmett's test. The experimental protocols were approved by the Ethics Committee on Animal Use (CEUA / CBIOTEC / UFPB) with number 0507/12.**Results and Discussion:** In NSAID-induced gastric ulcer the results show a reduction in the ulcer index (UI) at all doses evaluated of EEtOH-*Np* (62.5, 125, 250 and 500 mg/kg) at 41, 50, 64 and 64% ($p < 0.001$), respectively, when compared to the negative control. According the stress model, the doses evaluated of EEtOH-*Np* (62.5, 125, 250 and 500 mg/kg) decreased the UI to 24, 25, 49 and 49% ($p < 0.001$), respectively, when compared to the negative control group. Analyzing these results it can be inferred gastroprotective activity to EEtOH-*Np* in two models of acute ulcer induction evaluated, however, more studies are needed to elucidate the mechanisms of this protective activity in the gastric mucosa. **Acknowledgments:** CNPq/CAPES/PgPNSB /UFPB.

07.005 Evaluation of participation of sulfhydryl compounds and nitric oxide in the gastroprotective effect of *Maytenus distichophylla* mart. ex Reissek (Celastraceae). Caldas Filho MRD, Jesus NZT, Machado FDF, Duarte MC, Silva MS, Tavares JF, Batista LM
UFPB

Introduction: The genus Maytenus is the one with greater prominence within the family Celastraceae, comprising about 80 species, which are distributed throughout the Brazilian territory and adapted to different vegetation, such as rainforest, altitude, and especially in the "caatinga" (BAGGIO, C.H., J Ethnopharmacol, 113, 433, 2007). The specie *Maytenus distichophylla* Mart. ex Reissek, popularly known as "casca amarela" or "pau-colher" (CARTAXO, S.L., J Ethnopharmacol, 131, 326, 2010), was selected by chemotaxonomic criteria, due to the presence of triterpenes of the class friedelano, such as the compound "Maytensifolona" and in previous studies, demonstrated potent gastroprotective activity in models of acute ulcer induction. Thus, this study aimed to evaluate the possible involvement of sulfhydryl compounds and nitric oxide in the gastroprotective mechanism of action checked to the methanolic extract (*Md*-MeOHE) and the ethyl acetate phase (*Md*-EtOAcP), obtained from the leaves of *M. distichophylla*. **Methods:** Male Wistar rats (*Rattus norvegicus*) weighing between 180-250g fasted for 24 hours were divided into 12 groups (n = 5-7). Intraperitoneally (i.p.), 4 groups received 0.9% saline (vehicle), 4 with N-ethylmaleimide (NEM, a blocker of sulfhydryl compounds) (MATSUDA, H., Life Sci, 65, 27, 1999), and to the remaining 4 were given L-NAME, a blocker of oxide nitric synthase enzyme (SIKIRIC, P., Eur J Pharmacol, 332, 23, 1997). After 30 min, each of 4 groups were treated orally (p.o.) with 0.9% saline (negative control), carbenoxolone (100 mg/kg), *Md*-MeOHE (500 mg/kg) or *Md*-EtOAcP (500 mg/kg). The following lesions were induced by absolute ethanol (p.o.). The animals were killed, the stomachs photographed and Ulcerative Lesion Area (ULA) determined using the program AVSoft Bioview Spectra 4.0®. Data were analyzed using ANOVA followed by Dunnett's post-test or Student's "t" test. The protocols were approved by the Ethics Committee on Animal Research (CEPA/UFPB - nº 0508/11). **Results and Discussion:** In animals pretreated (i.p.) with 0.9% saline and that received (p.o.) *Md*-MeOHE, *Md*-EtOAcP or carbenoxolone were observed a significant reduction in the ULA, respectively, 5.58±2.16 (96%), 6.32±1.86 (96%) and 15.54±3.32 (89%) inhibition of the gastric lesions caused by ethanol as compared to negative control group (143.1±52.04). However, when evaluated animals pre-treated (i.p.) with NEM, there was an exacerbation of the ULA, with consequent reduction in the percentage of protection of the gastric mucosa to 215±57.92 (34%), 179.3±41.89 (45%) and 115.3±31.77 (64%), respectively, for the treated groups (p.o.) with *Md*-MeOHE, *Md*-EtOAcP or carbenoxolone, as compared to negative control group (323.9±31.31). Lastly, for the animals pre-treated (i.p.) with L-NAME was seen an exacerbation of ULA only for the group that received carbenoxolone, while the animals that received (p.o.) *Md*-MeOHE or *Md*-EtOAcP maintained the ability to protect in 6.99±1.42 (96%) and 6.46±1.54 (97%), respectively. These results suggest the involvement of sulfhydryl compounds in the gastroprotective mechanism promoted by both the *Md*-MeOHE and the *Md*-EtOAcP, while nitric oxide has no role in this activity. **Financial Agencies and Acknowledgments:** CNPq/PgPNSB/UFPB.

07.006 The effects of a *Baccharis trimera* hydroethanolic extract in alcoholic hepatic steatosis in mice. Lívero FR[1], Alves de Souza CE[1], Oliveira LG[1], Diettrich RL[2], Werneck MC[1], Strapasson RLB[3], Stefanello MEA[3], Botelho EL[4], Acco A[1] [1]UFPR – Farmacologia, [2]UFPR – Medicina Veterinária, [3]UFPR – Química, [4]Unipar – Farmácia

Introduction: The liver is the main organ of the ethanol biotransformation. Therefore, it can suffer from oxidative stress and can develop steatosis after a long-term alcohol abuse. Oxidative mechanisms participate of the alcohol metabolization, contributing to liver damage by alcohol. The aim of this work is to investigate the influence of the *B. trimera* ('carqueja') hidroethanolic extract (BTHE) in an alcoholic hepatic steatosis (AHS) model in mice, focusing in the antioxidant activity. **Methods:** All the procedures were approved by the institutional committee for the animal care (CEUA # 619). The AHS was induced in mice fed to 10% ethanol and 6% hypoproteic chow for 6 weeks. In the last 15 days of this diet the mice were separated in groups (n = 6): (1) positive control (vehicle); (2) BTHE 90, treated with 90 mg/kg of BTHE once a day by gavage; (3) BTHE 270, treated with 270 mg/kg of BTHE once a day by gavage; and (4) BTHE 810, treated with 810 mg/kg of the same extract. The negative control group (5) was composed by mice fed to water and chow, and treated orally with vehicle (Tween 80 + water). After the treatment period, the animals were anesthetized (xylazine + cetamine) and liver and blood were collected and frozen for further analyses. The oxidative stress was checked by the measurements of the enzymes GST, Cat and SOD, and by the LPO and GSH levels. The liver function and toxicity were assessed by the ALT and AST plasmatic levels. The abdominal fat tissue was also collected and weighed, as the same of the liver and stomach. **Results:** The livers of the positive control (10% ethanol) mice were pale and fat, as expected for steatotic organ. Despite of this appearance any difference in the weight of liver, stomach and fat pad was observed comparing the 5 groups, although the evident tendency in reducing the fat present at the abdominal cavity in all groups treated with BTHE. The positive control group (10% ethanol) presented an increase of @64% and @122% in the plasmatic AST and ALT, respectively, when compared to the negative control group (water). However, the treatment with all doses of BTHE reversed this increase. The diet with ethanol increased the LPO level and the Cat activity, and reduced the SOD activity in the liver. However, the treatment with BTHE reduced the Cat activity (all doses), increased the SOD activity and reduced the LPO level (BTHE 90), while the higher doses of the BTHE increased the GST hepatic activity. **Discussion:** The results confirmed the hepatic oxidative conditions and the steatosis expected after the ethanol consumption, validating the AHS model. The treatment with BTHE controlled several parameters related with both steatosis and oxidative situations. Since the *B. trimera* has been used in the folk medicine for hepatic protection, as antioxidant and as hypotrygliceridemiant, our data suggest that it has potential to be used for AHS. However, more studies covering the mechanisms of action, the toxicity and the isolation of the active compounds from the BTHE are still necessary. **Financial support:** REUNI-CAPES, CAPES and Fundação Araucária

07.007 Gastroprotective effect of ethanolic extracts of the roots and stem from *Pilosocereus gounellei* (Cactaceae). Sousa GA[1], Oliveira IS[1], Viana AFSC[1], Carvalho CS[1], Souza MFV[2], Oliveira RCM[1], Oliveira FA[1] [1]UFPI – Medicinal Plants, [2]UFPB – Pharmaceutical Technology

Introduction: *Pilosocereus gounellei* (A. Weber ex K. Schum.) Bly. Ex Rowl*,* popularly known as "xique-xique", is an endemic species of Northeast Brazil. Species of the genus *Pilosocereus* present various chemical constituents with antiulcer activity. Previous studies have shown that EERPG reduces gastric lesions induced by absolute ethanol**.** The present study aimed at investigating the gastroprotective activity of the ethanol extracts from the root (EERPG) and stem (EESPG) of *Pilosocereus gounellei*, by using ischemia/reperfusion-induced model of gastric lesions in rats, and to evaluate the participation of the nitric oxide in this action. **Methods:** In the model of gastric lesions induced by ischemia and reperfusion (I/R), Wistar rats (180-200 g, n = 7), females, fasted for 18 h were treated with vehicle (p.o.), N-acetylcysteine (NAC, 200 mg/kg, i.p.), EERPG or EESPG at doses of 100, 200 and 400 mg/kg (p.o.). After 60 min, under anesthesia with ketamine and xylazine (50 and 5.0 mg/kg i.m., respectively), the celiac artery blood flow was interrupted by a "clamp" microvascular. After 30 min of this procedure, the "clamp" was removed and reperfusion was established. The animals were euthanized 60 min after induction of reperfusion injury and the area calculated by planimetry (mm^2). To evaluate the role of nitric oxide, mice were pretreated with saline or nitro L-NG-Nitroarginine Methyl Ester (L-NAME, 20 mg/kg, i.p.). After 30 min received vehicle (p.o.), EERPG or EESPG (200 mg/kg, p.o.) and L-arginine (600 mg/kg, i.p.). After 60 min treatment with the extracts or vehicle and 30 min later administration of L-arginine, each animal was given orally 0.2 mL of absolute ethanol. They were euthanized 30 min later. All animal experiments protocols were approved by Ethics Committee on Animal Experiments of the Federal University of Piauí (CEEA/UFPI 077/11). Values $p<0.05$ were considered significant (data were expressed as a percentage). The significance level was evaluated for values of $*p < 0.05$. **Results and discussion:** The results of this study show that both extracts reduce the gastric damage induced by ischemia and reperfusion. EECPG (100, 200 and 400 mg/kg) and NAC (200 mg/kg) significantly decreased the area of gastric lesion (3.86 ± 0.59; 1.46 ± 0.14; 1.78 ± 0,38; 1.30 ± 0.29 mm^2, respectively) when compared to the control group (4.84 ± 0.65 mm^2). Similarly, EESPG (100, 200 and 400 mg/kg) and NAC (200 mg/kg) significantly reduced the area of gastric lesion (2.04 ± 0.25; 1.46 ± 0.13; 1.72 ± 0.29; 1.54 ± 0.55 mm^2, respectively) compared to the control group (11.14 ± 1.00 mm^2). L-NOARG, a blocker of the enzyme NO synthase, reversed the protection of gastric mucosa presented by EERPG 200 mg/kg (5.28 ± 2.08 to 23.4 ± 2.78), EESPG 200 mg/kg (5.95 ± 0.24 to 27.3 ± 2.47) and L-arginine (6.18 ± 1.14 to 28.1 ± 3.81) suggesting the involvement of nitric oxide in the gastroprotective effect produced by these extracts. However, new protocols are required to isolate the gastroprotective compounds and to elucidate their mechanisms. Through these results, we conclude that EERPG and EESPG present gastroprotective effect with possible participation of NO synthase pathway. **Financial Support: UFPI/CAPES/FAPEPI/CNPq**