

07 Endocrine, Reproductive and Urinary Pharmacology

07.001 Immune and Functional Effects of Uvaol Treatment in Trophoblast cells and its Implication on Placental Dysfunctions Botelho RM¹, Silva ALM¹, Tenório LPG¹, Gonçalves CM¹, Pires KSN¹, Santos JC¹, Tanabe ELL¹, Bergeron J², Sébire G², Borbely AU¹, Borbely KSC¹ ¹UFAL – Ciências Biológicas e da Saúde, ²McGill University – Neurosciences

Introduction: The group B streptococcus (GBS) is the main bacteria to infect pregnant women and can cause inflammation of the amniotic membrane and placenta, resulting in chorioamnionitis, which can lead to abortion and prematurity. Increased production of pro-inflammatory cytokines can trigger preterm birth and it is also linked to preeclampsia, due to the decreased trophoblast invasion triggered by the inflammatory response. Olive oil consumption during pregnancy has been linked to various health benefits, including preterm birth reduction. One of its components, the triterpene uvaol, is described as a potent anti-inflammatory molecule and we analyzed if it would exert beneficial effects to pregnancy. As such, we aimed to analyze functional and immune effects of uvaol treatment on trophoblast cells incubated with inactivated GBS. **Methods:** HTR-8/SVneo cells were used to represent early-pregnancy trophoblast cells. They were pre-treated with uvaol and incubated with inactivated GBS. All groups were analyzed by MTT and wound healing assay, and for cell death, proliferation, migration and Th1/Th2 cytokines and NO production, as well as NFκB translocation immunoassay. **Results:** GBS at 10x8 CFU reduced cell viability in MTT assay, whereas GBS at 10x6 CFU unchanged viability. Uvaol pretreatment in different concentrations (1μM, 10μM, 50μM and 100μM) was able to improve the viability loss caused by GBS at 10x8 CFU. It was confirmed by annexin V and propidium iodide staining that uvaol has indeed a cytoprotective effect. *In vitro* wound healing closure was delayed in GBS 10x8 CFU group and uvaol prevented this effect. GBS also decreased IL-4 secretion and increased TNF-α, IL-6, IFN-γ and IL-2, while uvaol utterly decreased their secretion. NO production was also increased by GBS 10x8 CFU, but uvaol pretreatment had no effects. Moreover, NFκB translocation immunoassay performed after different time points of GBS 10x8 CFU incubation after uvaol pretreatment showed that NFκB translocation is greatly delayed. **Conclusion:** Inflammation caused by inactivated-GBS support its deleterious effects on pregnancy. Uvaol protected trophoblast cells from death and reduced inflammatory cytokines production, possibly by acting upstream NFκB activation. Therefore, it could be thought to be an interesting pharmacological compound to be taken during pregnancy in order to prevent placental dysfunctions and prematurity.

07.002 Perinatal exposure to the ibuprofen: repercussions on the reproductive development in male rats. Leite ARR, Balin PS, Jorge BC, Arena AC IBB-Unesp – Morfologia

Introduction: Non-steroidal anti-inflammatory drugs (NSAID), including Ibuprofen, are widely used in the treatment of pain and inflammatory processes, and are one of the most commonly classes of drugs used by pregnant women. By inhibiting the cyclooxygenase enzyme (COX), NSAID inhibit the prostaglandins synthesis, eicosanoids compounds that act not only as mediators and inflammatory modulators, but also in various physiological processes of the organism, such as the mechanism of sexual hypothalamic differentiation. The hypothalamus masculinization process is testosterone dependent, which by action of the aromatase cytochrome P450 enzyme is metabolized to estradiol. This hormone upregulates the expression of COX enzyme in the hypothalamus, increasing the production of prostaglandin E₂, which acts by increasing the formation of dendritic spines in the neurons of the sexually dimorphic nucleus of the preoptic area in males (SDN-POA). Due to the importance of prostaglandin E₂ in the process of hypothalamic sexual differentiation, the use of anti-inflammatory drugs during pregnancy is of concern. Thus, the aim of this study was to evaluate the possible effects resulting from *in utero* and lactation exposure to non-steroidal anti-inflammatory ibuprofen and its late repercussions on male reproductive parameters in male rats. **Methods:** Pregnant rats were exposed to three doses of ibuprofen (10; 30; 60 mg / kg) between the last week of pregnancy (Gestational Days 15-21) until the end of lactation (Postnatal Days 20) by gavage. During treatment, water consumption, food intake and body weight of the dams were monitored. After birth, male offspring were evaluated through the following parameters: body weight, anogenital distance and ages of testicular descent and preputial separation. In the adult life, these same animals were investigated in relation to behavioral parameters (male and female sexual behavior and sexual preference), sperm parameters (sperm count and sperm morphology), reproductive organ weights, hormonal levels and histology of testis and epididymis. **Results:** The treatment did not affect any of the maternal parameters evaluated. Male offspring presented reduction in body weight and anogenital distance, as well as delay in the ages of testicular descent and preputial separation. In adulthood, these animals showed reduced serum testosterone levels and the volume of Leydig cell nucleus. Exposure to ibuprofen did not alter reproductive organ weights, sperm count or the number of Sertoli cells; however it resulted in a decrease in the number of normal sperm. Regarding the behavioral parameters, the animals exposed to ibuprofen presented both male and female sexual behavior, but there was no change in relation to the pattern of sexual preference. **Conclusion:** Ibuprofen, under these experimental conditions, was able to disturb the hypothalamic-pituitary-gonadal axis programming and affected sexual maturation and male reproductive functions. Approved by ethics committee, nº830/2016. **Financial support:** CAPES/FAPESP(2017/03997-7).

07.003 Impacts of paraquat exposure to male reproductive function. Silva NGM¹, Parisotto EB¹, Wajima CS¹, Rahn B¹, Domingue JT¹, Cesconetto PA¹, Cattani D¹, Rieg CEH¹, Hellbrugge A¹, Felipe KB², Pedrosa RC¹, Zamoner A¹ ¹UFSC – Bioquímica, ²UFPR – Análises Clínicas

Introduction: The consumption of agrochemicals has been associated with health problems worldwide. Paraquat (PQ), a non-selective herbicide of broad spectrum, is considered extremely toxic and can cause fatal poisonings in humans and animals, if ingested. The present study investigated the effects of PQ exposure to male fertility in 60-day-old rats. **Methods:** Male Wistar rats aged 60 days received PQ (10 mg/kg body weight) or saline (control group) via intraperitoneal for 5 consecutive days. Rats (n=8/group) were euthanized and the testis and epididymis were dissected. The cauda epididymidis was quickly removed and the sperm were released by cutting the cauda epididymidis longitudinally. The sperm suspension was centrifuged and a part of the sperm suspension of the epididymis was used for the evaluation of total sperm count (SPTZ), sperm viability, sperm motility and teratospermia rate. The other part was used to perform the immunodetection for p53 protein. The testis was fractionated for evaluation of markers of oxidative damage (lipid peroxidation and protein carbonyl-PC levels), activity of antioxidant enzymes (superoxide dismutase-SOD, catalase-CAT and glutathione-S-transferase-GST), myeloperoxidase activity (MPO) as well as testicular p53 expression. The concentration of reduced glutathione (GSH) in the testis was also measured. **Results:** The results showed that PQ exposure decreases the fertile capacity, as demonstrated by decrease in the total number of viable SPTZ. In addition, we did not observe any motile SPTZ in PQ treated animals. The results regarding teratospermia rate showed significant changes in the SPTZ morphology of the group treated with PQ, compared to the control group. PQ exposure decreased GSH levels as well as MPO and SOD activity, while CAT and GST activities were not altered by herbicide treatment. Moreover, results showed that p53 expression was increased in the testis and sperm from PQ-treated group. **Conclusion:** In the present study, it has been shown that exposure to PQ induces oxidative stress and compromises male fertility. The pro-oxidant effect of PQ and the modulation of p53 levels may be associated with the mechanisms involved in the toxicity of this herbicide in the male reproductive system. **License number of ethics committee:** 8510150517 **Financial support:** CNPq; Fapesc; CAPES

07.005 Effects of contraceptive anti-EPPIN S21C antibody on mouse sperm motility and hyperactivation. Silva AAS¹, Mariani NAP¹, Raimundo TRF², Kushima H¹, Silva EJR¹ ¹Unesp – Farmacologia, ²IFSULDEMINAS-Inconfidentes - Biociências

Introduction: Male contraceptive drugs development requires the characterization of a target with crucial role in fertility and druggable properties. The sperm surface protein EPPIN (Epididymal protease inhibitor) regulates the acquisition of sperm motility upon ejaculation, thus playing an essential role on sperm function. Contraceptive anti-EPPIN antibodies mapping EPPIN C-terminus are able to inhibit human sperm motility *in vitro*. Our laboratory is focused on the establishment of a mouse model to further study EPPIN's functions and to foster its development as a contraceptive drug target. Although EPPIN is immunolocalized on the surface of mouse spermatozoa, its role on mouse sperm function remains unknown. To gain insights into the physiological roles of EPPIN we evaluated the effects of the contraceptive anti-EPPIN S21C antibody on mouse sperm motility. **Methods:** Adult (90-110 days old) male C57BL/6 mice (n=3) were euthanized and their cauda epididymis were dissected, placed in HTF medium supplemented with 0.75% BSA (37°C, 5%/95% CO₂/air), and cut with scissors to release spermatozoa. Sperm suspension (2.5 x 10⁵ sperm/ml final concentration) was then incubated in HTF medium containing 0.4 mg/ml pre-immune serum (PIS, control) or anti-EPPIN S21C antibody, which recognizes EPPIN of mouse origin. Sperm motility was assessed after 30, 60, 90 and 120 min of incubation by computer-assisted sperm analysis (CASA) using a CEROS II system. Sperm tracks were classified as motile, progressive, and static. The following sperm kinematic parameters were analyzed: average path velocity (VAP; µm/s), straight line velocity (VSL; µm/s), curvilinear velocity (VCL; µm/s), lateral head displacement (AHL; µm), straightness (STR). Hyperactivated spermatozoa were determined from kinematics parameters using CASAnova Software. Data were analyzed by Student's t-test; p<0.05 was considered significant. **Results:** Anti-EPPIN S21C antibody significantly reduced sperm motility and progressive motility in comparison to control after 60 min (control vs S21C; %motile: 78.3 ± 4.9 vs 60.5 ± 4.0; %progressive: 48.3 ± 5.3 vs 30.3 ± 3.9). At this time-point, anti-EPPIN S21C antibody significantly decreased sperm kinematic parameters that described progressive (VAP: 102.7 ± 4.5 vs 66.8 ± 5.4; and VSL: 66.3 ± 7.2 vs 39.9 ± 4.2) and vigour (VCL: 218.1 ± 8.7 vs 144.9 ± 5.1 and ALH: 17.6 ± 0.8 vs 11.8 ± 0.2) movements. In addition, anti-EPPIN S21C antibody decreased hyperactivated motility in comparison to control (11.6 ± 1.6 vs 2.6 ± 1.4). Similar results were observed after 90 and 120 min of incubation. **Conclusions:** Our results indicate that EPPIN is involved in the regulation of mouse sperm motility, highlighting its conservation as a modulator of sperm motility between mice and humans and its crucial role in male fertility. The effects of anti-EPPIN antibody on hyperactivated sperm motility suggest that EPPIN is involved in the process of hyperactivation, which is critical to fertilization. The mouse is a suitable experimental model for translational studies on EPPIN's functions and mechanism of action. **License number of ethics committee:** 703-CEUA. **Financial support:** Fapesp (2015/08227-0 and 2017/20499-0).

07.006 Inhibitory effects of PYR6 (an Orai channels blocker) on agonists-induced contractions in the rat uterus. Sousa IA¹, Meneses GMS¹, Cardoso JVM¹, Cavalcanti PMS², Cavalcanti SMG³, Alves Filho FC¹ ¹UFPI – Biofísica e Fisiologia, ²UFPB – Ciências Farmacêuticas, ³UESPI – Ciências Médicas

Introduction: The Ca²⁺ influx is the key event in the smooth muscle contraction. In uterine smooth muscle cells, there is evidence of the presence of ORAI and TRPCs channels on plasma membrane, which are Ca²⁺ channels activated by intracellular Ca²⁺ release from sarcoplasmic reticulum. It is also described agonist selectivity to activate different types of ORAIs and TRPCs channels. The aim of this study was to investigate the effects of Pyr6 compound, described as an inhibitor of ORAI-mediated Ca²⁺ currents, in the agonists-induced contractions in rat uterus. **Methods:** All experimental protocols were approved by the Committee Animal Research and Ethics/UFPI (408/2017). Wistar rats (0.3 kg) were pretreated with diethylstilbestrol (100 µg/kg, subcutaneously, 48 hrs). Subsequently, the rats were euthanized by decapitation after the injection of pentobarbital (50 mg/kg, intraperitoneally). The abdominal cavity was opened and longitudinal uterine horns segments (1.0 cm) were removed and placed in organ baths containing Tyrode's solution modified [(g/L): NaCl: 8; KCl: 0.2; MgCl₂: 0.1; CaCl₂: 0.2; Na₂HPO₄: 0.1; NaHCO₃: 1.0 and glucose 1.0] at 30° C, bubbled with air and under a resting pressure of 1 g for recordings of isotonic or isometric contractions. After one-hour stabilization, the preparation viability was tested by potassium chloride (KCl, 80 mM) addition, thereafter the carbachol (CCh, 100 µM), oxytocin (OT 5 mU/ml) or cyclopiazonic acid (CPA, 10 µM) were tested. Pyr6 (3 µM) was added to the plateau or before contractions induced by CCh, KCl or CPA. In Tyrode Ca²⁺ free, CCh or OT were added, and after 5-10 min, the contractions were induced by Ca²⁺ (1 mM) in the absence or presence of Pyr6. **Results:** The Pyr6 addition on the CCh-induced contractions plateau reduced these contractions to 14.18 ± 2.68% (n=4) after 10-15 min. No effect was observed when the Pyr6 was added on the KCl-induced contraction plateau, but the verapamil addition (1 µM) completely abolished this contraction (n=2). The Pyr6 preincubation (5 min) reduced CCh-induced phasic and tonic contractions respectively to 87.59 ± 3.45% (n=3) [control of 101.75 ± 1.55% (n=4)] and 25.29 ± 9.51% (n=3, p <0.005, t-test) [control of 95.17 ± 4.57% (n=4)]. In Tyrode without Ca²⁺, the area under the curve (AUC) of the Ca²⁺-induced contraction after CCh was reduced by Pyr6 to 24.11 ± 5.052% (n=7) [control of 64.32 ± 10.35% (n=4, p <0.005, t-test)]. Pyr6 also reduced the Ca²⁺-induced first transient contraction, contraction frequency and tonic contraction after CCh addition, respectively, to 48.18 ± 9.71% (n=9); 81.76 ± 6.07% (n=8) and 1.75 ± 1.175% (n=8). In the Pyr6 presence, AUC of the Ca²⁺-induced contractions after OT addition were reduced to 86.97 ± 3.57% (n=6) [control of 94.39 ± 6.19% (n=2)]. The CPA addition in Tyrode modified (0.2 mM of Ca²⁺) did not promote contraction (10 min). However, after Ca²⁺ addition (1mM) was observed transient contractions, which was completely abolished after the Pyr6 addition (5 min, n=3). **Conclusion:** Considering that the Pyr6 selectivity, we suggest that CCh and CPA-induced contractions in the rat uterus are mainly dependent on the Ca²⁺-entry by ORAI channels, whereas OT-induced contractions appear to involve other channels. **License number of ethics committee:** 408/2017

07.007 Gestational Rat Parameters (Wistar) under moderate or severe hypoglycemia. Castro WCS¹, Justina VD², Lima VV³, Giachini FRC^{3,2}, David FL⁴
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Objectives: To characterize and compare gestational and variable parameters in model rats with mild hyperglycemia (MH) and severe hyperglycemia (SH), evaluated at glycemic and placental levels. **Methodology:** SH was induced by the administration of streptozotocin (STZ, Sigma Chemical Co St. Louis, Missouri; 40 mg/kg body weight, i.p.), dissolved in citrate buffer (0.1 M, pH 6.5) in Wistar female rats (13-15 weeks-old). The respective control group (C) received vehicle (citrate buffer) injections. Severe hyperglycemia (> 300 mg/dL; n= 5) or normoglycemia (< 120 mg/dL; n= 6) was confirmed 3 days after STZ administration. MH was induced by the administration of STZ 100 mg/kg body weight, s.c., in new-born Wistar female rats, on the first day of life. The respective control group received vehicle in a similar way. Between the 90-100th day of life, animals were submitted to the oral glucose tolerance test (OGTT). For the normoglycemia group, the rats should present normal OGTT, with all points displaying glycemic levels lower than 140 mg/dL. For the mild hyperglycemic group, rats should present abnormal OGTT, with at least two or more points with glycemic levels higher than 140 mg/dL, with a maximum limit of 300 mg/dL. OGTT was conducted after 6 hours fasting, by determining glycemia in a blood drop collected by tail vein puncture (time point 0). A D-glucose solution (2.0 g/kg body weight) was administered by gavage. Thereafter, blood glucose levels were measured at 30, 60 and 120 minutes. These measurements were used to estimate the total area under curve, using the trapezoidal mathematical method proposed by Tai. Mating period: Female Wistar rats from both control groups, as well as from severe and mild hyperglycemic groups were mated in a proportion of 4 females for each male. In the morning of the 21st gestational day, rats were anesthetized with sodium pentobarbital 3% (50 mg/Kg body weight, i.p.) and subsequently submitted to laparotomy for removal the uterus. Rats were killed by pneumothorax. The fetus and placentas were quickly removed and weighted. The placental index was defined by the ratio between placental weight and fetal weight. **Results:** Rats with SH presented very high glucose levels (480 ± 500 mg / dL), and there was no statistical difference when compared to the MH group (80 ± 110 mg / dL) and control group (40 ± 106 mg / dL and 70 ± 102 mg / dL), respectively (p <0.05) among 21 days of gestation. There was evidence of placental enlargement (SH 0.66g vs. C 0.52g, p <0.05) and fetal size reduction (4 g SH vs 5 ± 5.5 g C), we did not observe statistical difference between MH and control group for placental index (MH 0.90 vs. C 0.91), placental increase MH 0.7 g vs. C 0.8 g) and fetal size (MH 5.2 g vs. C 5.1 g). **Conclusion:** As to the glycemic levels MH rats did not present significant differences to the control group. In addition, MH placental index did not present statistical difference to the control group. On the other hand, the SH rats presented higher values when compared to C. where we observed an increase in plasma glucose, allowing an increase in the placental index, directly influencing the size of the fetus and the placenta. **Keywords:** Hyperglycemia; Placental dysfunction; Gestation **License number of ethics committee:** 23108.902445/2018-61 (CEUA-UFMT) **Financial support:** Capes

07.008 *In utero* and lactational exposure to anti-inflammatory ibuprofen: Late repercussion on female reproductive parameters in rats. Gazoli MB, Balin PS, Jorge BC, Carneiro GB, Zanatta FC, Inocencio LCL, Arena AC IBB-Unesp – Morfologia

Introduction: Non-steroidal anti-inflammatory drugs (NSAID) act through inhibition of the cyclooxygenase (COX) enzyme, leading to prostaglandin E2 (PGE2) reduction. The PGE2 is closely related with the process of sexual hypothalamic differentiation in males, however it is not yet known what the contribution of this prostanoid pathway to the same process in females. Thus, it is important to investigate the use of NSAID during the perinatal period also in the female offspring in order to evaluate their effects. Our objective was the evaluating of the effect of *in utero* and lactational exposure to ibuprofen and its late repercussions on female reproductive parameters. **Methods:** 40 pregnant rats were treated by gavage from the last week of pregnancy to the end of lactation: the control group received corn oil and the other groups were treated with different doses of ibuprofen (10, 30 or 60 mg/kg). After birth, the following parameters were evaluated in the female offspring: body weight, anogenital distance (AGD), nipple count, vaginal opening and first estrous. In adult life, these same animals were investigated for estrous cyclicity, sexual behavior, fertility test, reproductive organ weights and histopathological analysis (processing). **Results:** Female offspring exposed to ibuprofen had a reduction in body mass and AGD at birth when compared to control. In adulthood, females exposed to a dose of 10mg/kg showed a significant reduction in female sexual behavior (acceptance of mating). There was no significant difference in the other parameters analyzed. **Conclusion:** The results suggest that ibuprofen was able to modify the process of hypothalamic sexual differentiation of females, through the alteration of the hypothalamic-pituitary-gonadal axis, affecting the reproductive parameters in adulthood. **License number of ethics committee:** 958/2017 **Financial support:** CAPES

07.009 *In utero* and lactational exposure to Diisopentyl Phthalate (DiPeP) induces maternal toxicity and antiandrogenic effects in rats. Curi TZ¹, Silva GN¹, Meldola HG¹, Sari Hey GB¹, Grechi N¹, Tolouei SEL¹, Passoni MT¹, Martino Andrade AJ², Dalsenter PR¹ ¹UFPR – Farmacologia, ²UFPR – Farmacologia e Fisiologia

Introduction: Phthalates are industrial chemicals found in a variety of consumer products including polyvinyl chloride plastics, cosmetics, personal care products, food packaging, toys, solvents and formulations of pesticides and medicines. The toxicity of these compounds is a concern for human health since many phthalates are potentially toxic to male reproductive system, especially during critical prenatal windows of androgen-dependent sexual differentiation. In a pilot pregnancy cohort study conducted by our laboratory in Curitiba, we observed high exposure of Brazilian pregnant women to several phthalates, and in particular to diisopentyl phthalate (DiPeP), which is in contrast to any other study population worldwide. In a prior animal study, we also demonstrated that DiPeP can reduce fetal rat testosterone production in a dose-responsive manner. Based on these data, the aim of this study was to investigate whether *in utero* and lactational exposure to DiPeP is capable of causing behavioral and reproductive changes in rats. **Methods:** Pregnant Wistar rats (n = 9-11/group) were exposed by oral gavage to vehicle (canola oil) and four doses (1,10,100 and 300 mg/kg/day) of DiPeP between gestation day (GD) 10 and post-natal day (PND) 21. Male offspring was evaluated for some sexual development and differentiation markers, such as anogenital distance, nipple retention, and age at puberty (preputial separation). **Results:** Signs of maternal toxicity, such as reduced weight gain during gestation and reduced number of litters with live offspring, were observed at the highest dose. The anogenital distance, marker of prenatal androgenization, was reduced in male offspring exposed to DiPeP 300 mg/kg/day. In addition, dose-dependent increase in nipple retention was observed in males, but without statistical significance. The age at preputial separation, a marker of puberty onset in males, did not differ between groups. Currently, we are investigating additional reproductive and behavioral endpoints in male offspring. **Conclusion:** Our results indicate that DiPeP, a phthalate relevant for the Brazilian human exposure scenario, induces maternal toxicity and has antiandrogenic effects in rats, especially at the highest dose tested. **License number of ethics committee:** CEUA UFPR 1024 **Financial support:** CNPq e CAPES

07.010 N-Acetylcysteine and lipoic acid improve oxidative and inflammatory alterations in ovariectomized rats in an estrogen-independent manner. Delgobo M, Agnes JP, Gonçalves RM, Santos VW, Zanotto-Filho A UFSC – Farmacologia

Introduction: Over the last decades, life expectancy has been growing in developed countries, so the number of menopausal and post-menopausal women has increased as well. The clinical manifestations of decreased levels of estrogen and progesterone in menopause result in disruption of endocrine signaling in both reproductive and non-reproductive systems, which are accompanied by aging-related alterations such as sub-chronic low-level oxidative stress, inflammation, dyslipidemia and decreased metabolism. These pro-oxidant and inflammatory conditions were demonstrated in previous studies with menopausal women as well as were validated in experiments with ovariectomized (OVX) rodents. Given that hormone replacement therapy is related to side effects and low adherence to treatment by women, there is increasing interest in novel and safe strategies to attenuate systemic impairments caused by estrogen deficiency. On the other hand, while some antioxidants have been associated with improvement in some menopause-associated parameters, the comparison between different molecules and doses in a long-term context upon different menopause-associated impairments is lacking. Thus, the aim of this study is to determine the effect of long-term supplementation with antioxidants on oxidative, inflammatory and metabolic alterations in OVX rats. **Methods:** Female Wistar rats (90 days), N=8/ group (CEUA number: 2231170317) were ovariectomized (OVX) or Sham-operated, and then treated with two antioxidants with differing mechanisms of action (N-acetylcysteine – NAC; and Lipoic acid – LA) at 10 to 50 mg/ Kg by gavage for 60 days. Liver, kidney and heart were collected and markers of i) oxidative stress (Thiobarbituric acid reactive substances (TBARS); protein carbonyl and sulfhydryl; and Glutathione (GSH), Superoxide dismutase (SOD); Catalase (CAT); Glutathione peroxidase (GPX); Glutathione reductase (GR) and Glutathione S-transferase (GST) activities), ii) Inflammation (Interleukin-6 (IL-6) and Tumor necrosis factor alpha (TNF- α) by ELISA) and iii) lipid metabolism (total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), and triglycerides) as well as changes in body weight; retroperitoneal fat and uterine weight were evaluated. **Results:** Antioxidants prevent neither uterine atrophy nor body weight gain induced by OVX; both NAC and LA decreased total and LDL cholesterol without affecting triglycerides or HDL cholesterol in OVX rats; NAC and LA decreased OVX-induced lipoperoxidation and protein carbonylation as well as impeded the decay of GPX and GR activities in OVX animals. Serum TNF- α and IL-6 levels were slightly increased in OVX but not in OVX treated with antioxidants. **Conclusion:** Although not exerting estrogenic-like activity, our data suggest that NAC and LA supplementation is a newsworthy alternative to attenuate oxidative stress, low-level chronic inflammation and lipid metabolism alterations associated with hormonal depletion in females. Extrapolation of our data to menopause context requires further testing in humans. **License number of ethics committee:** 2231170317

07.011 Evaluation of in utero and lactational exposure to diisopentyl phthalate (DiPeP) on sexually dimorphic behaviors in rats Silva GN¹, Curi TZ¹, Hey GBS¹, Grechi N¹, Meldola HG¹, Passoni MT¹, Tolouei SEL¹, Andrade AM², Dalsenter PR¹
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Introduction: Phthalates are high production volume chemicals used as plasticizers and additives in a wide variety of consumer products, including polyvinyl chloride plastics, cosmetics, and personal care products. Many of these compounds are considered antiandrogenic endocrine disruptors that are able to inhibit testicular testosterone production. The exposure to these chemicals during pregnancy is a concern, since it is known that there is a critical prenatal period when androgens are crucial to the sexual differentiation of reproductive organs and the brain. In a pilot pregnancy cohort study conducted by our laboratory, we observed high exposure of pregnant women from Curitiba/PR to different phthalates, including diisopentyl phthalate (DiPeP). A previous study has shown that this phthalate reduced fetal rat testosterone production better than others. Therefore, the aim of this study was to investigate whether pre- and post-natal exposure to DiPeP alters sexual and cerebral differentiation causing behavioral changes in male offspring rats. **Methods:** Pregnant Wistar rats (n = 9-11/group) were exposed to DiPeP (1, 10, 100 or 300 mg/kg/day) or vehicle (canola oil) by oral gavage between gestation day (GD) 10 and post-natal day (PND) 21. Male offspring was assessed for sexually dimorphic behavioral changes with a battery of tests including elevated plus maze task (EPM; PND 25-27), play behavior (PB; PND 40-45) and partner preference (PP; PND 82-88). **Results:** No differences were observed among groups tested in the EPM. This test will be repeated with the siblings on PND 70-73, the period in which the brain is fully differentiated. There were no differences in PB and PP either. However, animals will still be assessed for possible changes in mating behavior. **Conclusion:** Despite the reported inhibition of fetal testosterone production in rats, in utero and lactational exposure to DiPeP was not capable of altering sexually dimorphic behaviors investigated in pre-pubertal, pubertal and adult period. Additional behavioral tests will be performed in adult offspring, since some dimorphic behaviors may not be apparent before the attainment of sexual maturation. Also, at the end of the study, the testes and brains will be investigated for changes in histology and morphology to better understand and complement these results. **License number of ethics committee:** CEUA 1024 **Financial support:** CAPES, Cnpq

07.012 Differential expression and regulation by sexual maturation of EPPIN (Epididymal Protease Inhibitor) In the mouse reproductive tract. Mariani NAP¹, Camara AC¹, Andrade AD¹, Lupi LA², Chuffa LGA², Kushima H¹, Silva EJR¹ ¹IBB-Unesp – Farmacologia, ²IBB-Unesp – Anatomia

Introduction: EPPIN (Epididymal protease inhibitor) is a cysteine-rich protein containing Kunitz-type and WAP-type four disulfide core protease inhibitor consensus sequences. Human EPPIN is expressed in testis and epididymis and it is present on the sperm surface. EPPIN is involved in the modulation of sperm motility acquisition after ejaculation, which makes it a promising target for male contraception. The development of a mouse model to further investigate EPPIN's functions will provide an important tool for its development as a contraceptive drug target and the understanding of its roles in reproduction. Herein, we characterized the expression and cellular distribution of EPPIN in male and female mouse tissues during different periods of post-natal life. **Methods:** Sexually maturing (10, 20 and 40 days-old) and adult (60 and 90 days-old) male and female C57BL/6 mice (n=3-5/group) were euthanized, their reproductive organs (epididymis, vas deferens, seminal vesicle, prostate, ovary, oviduct, and uterus) and several non-reproductive organs from cardiovascular, digestive, endocrine, respiratory, urinary and central nervous systems were collected and processed for RT-PCR and qPCR analysis to detect mouse *Eppin* and *Ppia* (cyclophilin A, endogenous control), or for Western blot and immunohistochemical studies using affinity purified anti-EPPIN antibody (negative controls were primary antibody pre-absorbed with recombinant EPPIN). qPCR data were analyzed by ANOVA followed by Tukey test; p<0.05 was considered significant. **Results:** In adult male mice, the presence of *Eppin* mRNA was abundantly detected in testis and epididymis, but also observed in vas deferens, seminal vesicle and adrenal gland. In females, the expression of *Eppin* mRNA was found in ovary, oviduct and uterus. Western blot analysis demonstrated the expression of EPPIN at apparent molecular masses of ~20 kDa in the testis, ~10 kDa in the epididymis (initial segment, caput, corpus and cauda) and seminal vesicle, and ~10, ~38 and ~60kDa in the vas deferens and adrenal gland, indicating that EPPIN is differentially processed in these tissues. EPPIN-positive immunostaining was observed in Sertoli cells, spermatocytes, round and elongated spermatids in the testis, and in epithelial cells and luminal sperm in the epididymis. For the first time, EPPIN-positive immunostaining was found in the ovarian germinal epithelium and in oocytes at different stages of developing follicles. qPCR and immunohistochemistry studies demonstrated an increase in the abundance of *Eppin* mRNA and protein levels, respectively, in the testis and epididymis of 60- and 90-day-old mice in comparison to sexually immature animals. **Conclusion:** The expression of EPPIN in mice suggests it has roles in both male and female fertility, as well as in adrenal gland function. The positive correlation between sexual maturation and increased EPPIN expression in testis and epididymis is consistent with androgen regulation and suggests a role in spermatogenesis and sperm maturation. **Support:** Fapesp (2017/11363-8 and 2015/08227-0). **Ethics Committee approval:** 1049-CEUA. **License number of ethics committee:** Ethics Committee approval: 1049-CEUA. **Financial support:** Support: Fapesp (2017/11363-8 and 2015/08227-0)

07.013 Effects of Cilostazol, A Phosphodiesterase 3 inhibitor, on male rat reproductive tract. Moreira TJ, Maia IC, Gontijo LS, Motta NAV, Lima GF, Lopes RO, Ribas JAS, Brito FCF, Maróstica E UFF – Fisiologia e Farmacologia

Introduction: Cilostazol is a phosphodiesterase 3 inhibitor, being classified as a vasodilator and antithrombotic agent. Although many PDE3 inhibitors have been found to arrest oocyte maturation and suppress meiosis in different species, including humans, this drug most commonly prescribed has not yet been evaluated in male reproductive tract. Thus, the aim of this study is to evaluate the effects of cilostazol on the male rat reproductive tract. **Methods:** Adult male Wistar rats (150-200g) were randomly divided in 4 groups (n=6/group): CO-fed with commercial chow; CLZ- fed with commercial chow, treated with cilostazol (30mg/kg, gavage) for 15 days; HC-fed with hypercholesterolemic diet (HCD) for 45 days; HC+CLZ-fed with HCD, treated with cilostazol in the last 15 days. Animals were anesthetized and testes, epididymis, prostate, seminal vesicle from different experimental groups were removed, weighed and the testes were processed for morphologic analyze. Spermatic evaluation (motility, vigor, sperm number, membrane integrity and hypo-osmotic swelling test) was performed using sperm from epididymis cauda. Values are mean±SEM (one-way ANOVA, Newman-Keuls; $P<0.05$).

Results: Cilostazol alone did not alter body weight or testis, epididymis, prostate and seminal vesicle relative weight when compared to control, but differences were found in these parameters when it was administrated with HCD: body weight (CO: 383±12; HC+CLZ: 260±13g), relative weight of testes (CO: 1.68±0.04; HC+CLZ: 0.96±0.06g), epididymis (CO: 0.15±0.01; HC+CLZ: 0.11±0.009g), prostate (CO: 0.07±0.005; HC+CLZ: 0.02±0.004g) and seminal vesicle (CO: 0.07±0.01; HC+CLZ: 0.02±0.001g). Testicular morphological analysis showed an increase in the diameter and area of the seminiferous tubules in the HC+CLZ group. Furthermore, a decrease in the number of spermatogonia and spermatocytes but not in the rounded spermatids and Sertoli cells was observed when compared to the CO group. Regarding spermatic evaluation, sperm count, membrane integrity and functionality were preserved and sperm progressive motility was increased in 17.5% by cilostazol. **Conclusion:** Our preliminary results showed that the cilostazol did not recover the deleterious effects of dyslipidemia mainly on the prostate and seminal vesicle, but it did not cause harmful effect on the male gamete and testicular parenchyma, as well as it did not affect the functional efficiency of Sertoli cells in male Wistar rats. However, its effects on the germ cell in the early stages of spermatogenesis should be investigated. **License number of ethics committee:** CEUA 858/16 **Financial support:** FAPERJ, CNPq, CAPES, PROPPI/UFF

07.014 Excessive bladder relaxation and urethral contraction contributes to underactive bladder in old female mice. de Oliveira MG, Mónica FZ, Alexandre EC, Bonilla-Becerra SM, Justo AFO, Bertolotto GM, Antunes EFCM-Unicamp – Farmacologia

Introduction: Bladder underactivity is a highly prevalent condition in both men and women, particularly in the elderly, which undoubtedly impairs patient's quality of life [1]. Underactive bladder (UAB) is defined as prolonged urination time with or without a sensation of incomplete bladder emptying, usually with hesitancy, reduced sensation on filling, and slow stream [1]. Current understanding of the pathophysiology of UAB is limited and efficient pharmacological treatments are lacking. We investigated here the functional and molecular alterations of the contractile and relaxant machinery in the lower urinary tract smooth muscle of 18-month female mice, focusing on muscarinic and adrenergic receptors in bladder as well as the nitric oxide (NO)-soluble guanylyl cyclase (sGC) pathway in urethra. **Methods:** Female young (3-month old) and old (18-month old) C57BL/6 mice were used. Cystometry was performed in urethane-anesthetized mice for 45 min [3]. Neurogenic contractions were evaluated by electrical-field stimulation (EFS) in isolated bladders (1-32 Hz). Concentration-response curves to contractile (carbachol) and relaxing agents (mirabegron) in isolated bladders, as well as the contractile responses in urethral smooth muscle (phenylephrine) were also employed. mRNA expressions of muscarinic receptors (M2 and M3 subtypes), adrenergic (α -1A-, β 2- and β 3-adrenoceptors), sGC β 1, and nNOS were determined by RT-PCR, and results normalized to actin mRNA expression levels. Comparisons among the groups were evaluated using Student's *t* test. **Results:** In the cystometric study, young mice showed regular micturition cycles whereas old mice showed an atypical voiding pattern characterized by an incapacity to produce regular bladder contractions and emptying. In isolated bladders, EFS produced frequency-dependent bladder contractions in young and old groups, but the responses were significantly lower in old compared with the young group ($P < 0.05$). Bladder contractions to carbachol were also reduced in old compared with the young. Bladder responses to the selective β 3-adrenergic agonist mirabegron were enhanced in old compared with young mice. In isolated urethra, phenylephrine produced higher contractions in old compared with young group ($P < 0.05$). We next evaluated the muscarinic and adrenergic mRNA expressions in bladder and urethra (RT-PCR). In bladders, the mRNA assays revealed no differences for the muscarinic M2 and M3 receptors between young and old groups. The β 2 adrenergic receptor mRNA also remained unchanged, but a significantly higher expression of β 3 adrenergic receptors in old mice was found ($P < 0.05$). Urethra of old mice also displayed a significant increase in α -1A adrenergic receptor mRNA expression ($P < 0.05$). Because activation of nNOS-sGC-cGMP signaling pathway is crucial to promote urethral relaxations during the micturition cycle, we evaluated both nNOS and sGC mRNA expressions. We found a marked decrease in sGC β 1 and nNOS in urethra of old compared with young mice ($P < 0.05$). **Conclusion:** Taken together, our results demonstrate the presence of an age-associated UAB caused by an atonic and over relaxed detrusor smooth muscle and an overactive urethra, resulting in impairment of emptying efficacy. **License number of ethics committee:** CEUA UNICAMP 4121-1 **Financial support:** São Paulo Research Foundation (FAPESP, 2017/15175-1) Coordination of Improvement of Higher Education Personnel (CAPES, 1680776).

07.015 Relaxant effect of *Lippia origanoides* essential oil on rat isolated uterus. Paiva GO¹, Brito MC¹, Ribeiro LAA¹, Lucchese AM², Silva FS¹ ¹UNIVASF – Ciências Farmacêuticas, ²UESF – Ciências Exatas

Introduction: *Lippia origanoides* Kunth, popularly known as "salva de marajó " or "alecrim de tabuleiro", is quite common in Brazilian semiarid, and is used for the treatment of indigestion, diarrhea, nausea, menstrual cramps, uterine inflammation, vaginal discharge and fever. *L. origanoides* is rich in essential oil, and its' major component is carvacrol. The present study investigated the action of *Lippia origanoides* essential oil (LOO) through an experimental model of isolated rat uterus contracted with different agents. **Methods:** Virgin rats were treated before the start of the experiments with diethylstilbestrol (1 mg/kg) for estrus induction. After 24h, rat isolated uterus was incubated in 10mL chambers of tissue organ bath system filled with a Locke-Ringer solution at 32°C and constant oxygenation by 45min and tension of 1g. Uterus smooth muscle was contracted with carbachol (1µM), oxytocin (10⁻²UI/mL) or KCl 60mM and when contractions had reached a plateau, cumulative concentrations of LOO (1-729µg/mL) was added. A preparation was maintained without addition of the contracting agent to evaluate the LOO effect on the basal tonus. To elucidate the relaxant mechanism of LOO, set of experiments were performed in the presence or absence of 4-aminopyridine 1mM, tetraethylammonium 5mM, glibenclamide 1µM, CsCl 5mM, propranolol 10µM, phentolamine 1µM, L-NAME 100µM, methylene blue 1µM, or aminophylline 10µM. The effect of LOO on carbacol-induced contractions in Ca²⁺-free medium was also evaluated. **Results:** LOO reduced spontaneous uterine contractions in a concentration-dependent manner [CE₅₀=2.54 (2.02-3.23) µg/mL]. In the presence of agonists, LOO relaxed the pre-contracted rat uterus with oxytocin [CE₅₀=94.83 (67.71-132.80) µg/mL], carbachol [CE₅₀=34.12 (29.74-39.15) µg/ml] and KCl [CE₅₀=33.98 (26.62- 43.47) µg/ml]. There are no significant differences between the CE₅₀ values in the absence or presence of K⁺ channel blockers, as well as in the presence or absence of adrenergic receptor antagonists, suggesting that the related mechanisms are not involved in the LOO relaxing effect. The increased potency of LOO by L-NAME suggests that endogenously released nitric oxide stimulates prostaglandin synthesis by activation of the cyclooxygenase enzyme. In the presence of methylene blue, the CE₅₀ of LOO was reduced and is explained by the fact that this blocker is involved in redox reactions. When the organ was pre-incubated with aminophylline, there was a potentiation of the LOO effect, leading to the suggestion that the essential oil effect is favored by increased cAMP concentrations or by a direct action of aminophylline on intracellular Ca²⁺. The addition of LOO in Ca²⁺-free medium prevents extracellular contraction, suggesting that LOO action may be related to the decrease of Ca²⁺ release from intracellular stores. **Conclusion:** Relaxant effect of LOO on rat isolated uterus involves the cAMP signaling pathway and inhibition of the intracellular release of Ca²⁺. **License number of ethics committee:** CEUA/UNIVASF 0001/010617 **Financial support:** FINEP, FAPESB

07.016 The lower urinary tract smooth muscle dysfunction in ovariectomized rats is ameliorated by testosterone replacement via activation of non-classic genomic pathway. Bonilla-Becerra SM¹, Rojas-MoscOSO JA¹, Antunes E¹ ¹Unicamp – Farmacologia

Introduction and Aim: Urological complications are observed in the postmenopausal women and the hormone replacement therapy with testosterone has been used to alleviate certain symptoms of androgen deficiency (1). Studies in animals and human have shown the presence of androgen receptors in the lower urinary tract organs, suggest that androgen may play an important role in the urinary continence (2, 3). However, little is known about the role of androgen in LUT smooth muscle (bladder and urethra) in menopausal condition. Therefore, this study was undertaken to evaluate the effects of testosterone on bladder and urethra isolated from 4-month ovariectomized rats to mimic menopause. **Materials and Methods:** Two-month old female Sprague Dawley rats were anesthetized (ketamine/xylazine; 60: 6 mg/kg, IP) and submitted to bilateral ovariectomy, whereas Sham-operated rats were manipulated but the ovaries were left intact. After 4 months of ovariectomy, the bladder and urethra were removed. Concentration-response curves to carbachol (bladder) and phenylephrine (urethra) were performed in the presence of testosterone (100 nM, 30 min). The neurogenic contractions by electrical-field stimulation (EFS; 1-32 Hz) were also carried out. **Results:** Bilateral ovariectomy significantly reduced the bladder contractions to either carbachol or electrical-field stimulation compared with control rats ($P < 0.05$). Instead phenylephrine-induced urethral contractions were increased compared with Sham rats ($P < 0.05$). In bladder of ovariectomized rats, testosterone significantly prevented the alterations of bladder and urethra contractions. Pre-incubation of flutamide did not significantly change the testosterone effects in bladder and urethra of ovariectomized rats. **Conclusion:** These results suggest that protective effect of testosterone on *in vitro* response of smooth muscle of bladder and urethra of ovariectomized rats does not involve the activation of the classical genomic pathway through androgen receptors. **References** 1. Sassarini et al. Age Ageing, (4), 551-558; 2015. 2. Wilson et al. Moll Cell Endocrinol, (120), 51–57; 1996. 3. Pelletier. Histol Histopathol, (4), 1261-1270; 2000. **License number of ethics committee:** (CEUA/UNICAMP; No. 4421-1) **Financial support:** CNPq (146942/2016-7), FAPESP (2017/26564-9).

07.017 Preclinical evaluation of the diuretic and saluretic effects of (-)-Epicatechin and the result of its combination with standard diuretics. Boeing T, Mariano LNB, da Silva RCMVAF, Cechinel-Filho V, Niero R, da Silva LM, Andrade SF, de Souza P Univali – Ciências Farmacêuticas

Introduction: Several studies have suggested that (-)-epicatechin-containing foods and plant extracts benefit conditions that affect the cardiovascular and renal systems, such as hypertension and endothelial dysfunction. However, no study was conducted so far to evaluate the potential of this flavonoid in diuretic activity assay. **Methods:** For that, female Wistar normotensive (NTR) and spontaneously hypertensive rats (SHR) received a single oral treatment with (-)-epicatechin (EPI), hydrochlorothiazide (HCTZ) or just vehicle (VEH). The effects of EPI in combination with diuretics for clinical use (i.e. HCTZ, furosemide and amiloride), as well as with L-NAME (a non-selective nitric oxide synthase inhibitor), atropine (a non-selective muscarinic receptor blocker) and indomethacin (an inhibitor of the enzyme cyclooxygenase) were also explored. Cumulative urine volume and urinary parameters were evaluated at the end of 8 h experiment. **Results:** When given to NTR and SHR, at doses of 0.3, 1 and 3 mg/kg, EPI was able to stimulate both diuresis and saluresis (Na^+ , K^+ and Cl^-), without interfering with urinary pH and uric acid values, when compared with VEH-treated only rats. Interestingly, only the highest dose of EPI was able to reduce urinary Ca^{2+} excretion in the SHR group, similarly to the HCTZ-treated group. The combination with HCTZ (a thiazide-type diuretic, inhibits the $\text{Na}^+\text{-Cl}^-$ transporter in the distal tubule), but not with furosemide (a loop diuretic, acts by blocking ion transport directly through its bind to the $\text{Na}^+\text{-K}^+\text{-2Cl}^-$ cotransporters) or amiloride, successfully strengthened EPI-induced diuresis. However, this effect was not accompanied by a potentiation of the saluretic effects. On the other hand, when given EPI in combination with amiloride (an antikaliuretic-diuretic agent, works by directly blocking the epithelial sodium channel in the nephron), a significant increase in Cl^- excretion and maintenance of the potassium-sparing effects characteristic of this class of diuretics were detected. In addition, the diuretic effect of EPI was enhanced after pretreatment with L-NAME and its action was significantly precluded in the presence of indomethacin, suggesting that endogenous prostanoids generation seem to be important for the effects described in this study. On the other hand, EPI-induced natriuretic effect was fully prevented either in the presence of atropine or in the presence of indomethacin, which reinforces the hypothesis of the participation of endogenous vasodilator mediators in the diuretic effects evoked by EPI. **Conclusion:** Taking together, the present findings indicate that EPI seems to be one of the bioactive compounds responsible for the diuretic and saluretic properties previously described for several extracts preparations and might contribute to explain and support their use in traditional medicine. **License number of ethics committee:** Authorization from CEUA/UNIVALI: 028/17p **Financial support:** Research support: CNPq, CAPES, FAPESC and UNIVALI.

07.018 The Role of 1,25(OH)₂ Vitamin D₃ on glucose homeostasis on target tissues of insulin. Mendes AKB¹, Sulis PM¹, Frederico MJ¹, Gaspar JM¹, Silva FRMB¹, Rey DM², Novoa DMA² ¹UFSC – Bioquímica, ²Universidad Nacional de Colômbia - Bioquímica

Introduction: Several drugs are used to maintain glycemia in subjects with diabetes. Type 2 diabetes (T2D) is characterized by the final stage of insulin resistance, it is completely associated with risk factors such as advanced age and obesity. 1,25(OH) Vitamin D₃ (1,25-D₃) is a seco-steroid hormone and its therapeutic effect on glucose homeostasis has been described. **Aim:** To access the role of 1,25-D₃ on insulin resistance and glycemia. **Methods:** Male *Wistar* rats (50-day-old), were fasted for 2 h and divided into four groups: Group I, Control rats (2U/kg insulin, via intraperitoneal (*i.p.*)), Group II, VitD₃ rats (2.640 UI, via oral (*v.o.*), during the 5 days before insulin overload), Group III, Dexamethasone rats (0,1 mg/mL, *i.p.*, during 5 days before insulin overload), Group IV, VitD₃ + Dexamethasone rats. Blood samples were collected prior to insulin overload (time 0); and 10, 20 and 40 min after (ITT), to quantify glycemia. After, the animals were euthanized and blood samples were collected to quantify total cholesterol and triacylglycerol. The adipose tissue was taken to analyze the relative epididymal fat. The static insulin was measured *in vitro* in rat pancreatic islets incubated with 1,25-D₃. Results were expressed as Mean ± Standard Error Mean and level of significance of 95% (p <0.05), (CEUA protocol approved: 2119280317/UFSC). **Results:** 1,25-D₃ induced insulin secretion with 10 min of incubation, showing an acute effect. Dexamethasone induced insulin resistance measured at 20 and 40 min compared to control and VitD₃ group. No change in epididymal fat was observed in Dexamethasone, VitD₃ or Dexamethasone+VitD₃ groups in relation to the control group. The triacylglycerol and cholesterol concentrations were higher on Dexamethasone + VitD₃ group. **Conclusions:** The *in vitro* study revealed the acute effect of 1,25-D₃ on insulin secretion. *In vivo*, VitD₃ did not induce insulin resistance nor alter the insulin resistance induced by dexamethasone in 20 and 40 min. VitD₃ also did not alter the epididymal fat weight and induced an increase in triacylglycerol and total cholesterol concentrations. **Financial Support:** CNPq; CAPES; PPG-Bioquímica PROAP-UFSC. **Key-words:** insulin resistance, vitamin D₃, diabetes, lipid metabolism. **Acknowledgments:** Laboratório Multiusuário de Estudos em Biologia – LAMEB and professor Ariane Zamoner Pacheco de Souza for support in the use of analytical equipment. **References:** DeFuria J. PNAS. B-cells promote inflammation in obesity and type 2 diabetes through regulation of T-cell function and an inflammatory cytokine profile. v. 11, 2013. NORMAN, A.W. From vitamin D to hormone D: fundamentals of the vitamin D endocrine system essential for good health. Am J Clin Nutr, v. 88, p. 491S-499S, 2008. **License number of ethics committee:** 2119280317/UFSC **Financial support:** CNPq; CAPES; PPG-Bioquímica PROAP-UFSC.

07.019 Study of the acute effect of chalcones on glycemic, lipid and insulinemic response. Sulis PM¹, Fernandes TA¹, Mendes AKB¹, Frederico MJ¹, Rey D², Aragon M², Ruparelia K³, Silva FMB¹ - ¹UFSC – Bioquímica, ²Universidad Nacional de Colombia – Farmácia, ³University of Leicester - Pharmaceutical Sciences

Introduction: During the last decades, there has been an increase in the prevalence of type 2 diabetes mellitus (DM2) in the world population. The insertion of technological innovations in the pharmaceutical market has contributed to a series of changes in therapy that positively affect the quality of life of these patients. The Chalcones are currently of great interest for research because of their diverse pharmacological properties. Previous studies have demonstrated the influence of synthetic chalcones on carbohydrate metabolism, and thus indicating a potential therapeutic target in the treatment of metabolic diseases such as DM2. This study aimed to evaluate the antihyperglycemic effect of chalcones in the oral glucose tolerance (oGTT). Next, we evaluated the effect of chalcone on insulin secretion, glucose uptake and glycogen, as well as its repercussion in lipid metabolism was studied. **Methods:** First, the antidiabetic effect of 11 different derivatives chalcones was tested in the oral glucose tolerance test. For this, male Wistar rats (60 days-old) were divided into the following groups: hyperglycemic rats (received 4 g/kg glucose, via oral (v.o.)); and plus chalcones hyperglycemic (animals received 10 mg/kg treatment, v.o., 30 min prior to glucose overload). Blood samples were collected before glucose overload (time zero) and, at 15, 30, 60 and 180 min after glucose, from the glycemia, triacylglycerol and cholesterol measurements. Then, we studied the effect of chalcona 1 in the other assays: The muscle and hepatic glycogen content was analyzed at 180 min, fragments of soleus muscle and adipose tissue were used for the glucose uptake, and pancreatic islets were isolated to measure insulin *in vitro*. Results were expressed as Mean ± Standard Error Mean and the level of significance 95% ($p < 0.05$), (PP00862/CEUA protocol/UFSC). **Results:** The chalcones 1 and 11 demonstrate a significant decrease in glycemia at 180 min, and the chalcones 4 and 9 demonstrated this same significant effect at 15 min on oGTT. The Chalcone 1 demonstrated an antihyperglycemic effect justified by a glycemia reduction over 180 min as well as an improvement in plasma concentration of triacylglycerol and total cholesterol. In addition, to the aforementioned actions, chalcone 1 promoted an increase in muscle glycogen content, in the glucose uptake in the soleus muscle, and demonstrated a significant *in vitro* insulin secretion. **Conclusions:** Our data suggest that the chalcone 1 has a regulatory effect on glucose homeostasis. The demonstrated effects involve increased glucose utilization by peripheral tissues, stimulation of insulin secretion, and improvement in lipid profile. These effects suggest that the compound may be a potential target for DM2 therapy. **Financial Support:** CNPq; CAPES; PPG-Bioquímica-PROAP-UFSC. **Keywords:** Chalcone, antihyperglycemic effect, lipid metabolism, insulin resistance. **Acknowledgments:** The authors thank to LAMEB/CCB/UFSC, Prof. Bóris Stambuk and Profa. Ariane Zamoner for the technical support. **License number of ethics committee:** PP00862 **Financial support:** CAPES; CNPq; PROAP-UFSC

07.020 Activation of the cold-sensing TRPM8 channel triggers relaxation of corpus cavernosum due RhoA/ROCK pathway inhibition and reduction of adrenergic nerve activity. Silva DF¹, Cruz de Jesus RL¹, Wenceslau CF², McCarthy CG², Szasz T², Ogbi S², Webb RC² ¹UFBA – Bioregulação, ²Augusta University - Physiology

Erectile dysfunction (ED) is frequently encountered in patients with arterial hypertension. Due a low pharmacological response to phosphodiesterase type 5 (PDE-5) inhibitors in patients with vascular endothelial damage, the search for new drugs and therapeutic targets is of paramount importance to ED treatment. The aim of this study was to investigate the expression and function of cold-sensing TRPM8 channel in the corpus cavernosum (CC) as well as to clarify the mechanism of action involved on the observed responses in both normotensive and hypertensive rats. For this, we performed experiments integrating physiological, pharmacological, biochemical and cellular techniques, to better understand the effects of TRPM8 activation on the penile function in spontaneously hypertensive rats (SHR). All procedures were performed in accordance with the Guide for the Care and Use of Laboratory Animals of the National Institutes of Health (NIH) and were reviewed and approved by the Institutional Animal Care and Use Committee of Augusta University. Our results demonstrated the expression of TRPM8 channels in the CC by western blotting and immunofluorescence technique. Furthermore, TRPM8 activation, by a cooling compound icilin (10^{-8} – 10^{-4} M), induced relaxation of CC strips pre-contracted by phenylephrine (10^{-6} M). To understand the mechanism of action in the TRPM8 activation-induced relaxation, the effect of icilin was observed in electrical field stimulation (EFS)-induced contractions. TRPM8 activator decreased of EFS-induced contraction in the presence of atropine (1 μ M), indomethacin (10 μ M) and L-NAME (100 μ M), suggesting that icilin seems to inhibit the adrenergic nerve. In other set of experiments, the concentration-response curve to icilin was shifted to the right in the presence of Y27632 (ROCK inhibitor, 10^{-6} M), suggesting that, ROCK, at least in part, is important to relaxation induced by TRPM8 activation. Supporting these cavernosal function data, western blotting was performed for RhoA, ROCK II and RhoA/ROCK substrate myosin phosphatase target subunit 1 (MYPT1), with the phosphorylated form of this protein being an indicator of active RhoA/ROCK signaling. We observed that CC treated by either vehicle, Phe or Phe+icilin were not changed the expression of RhoA or ROCK. However, the levels of phospho-MYPT1 normalized by total MYPT1 were increased by Phe compared to control and Phe+icilin reverted this effect, suggesting that TRPM8 activation inhibits RhoA/ROCK pathway. Interestingly, icilin-induced relaxation was significantly smaller in CC from SHR compared to normotensive Wistar rats. However, we could not observe significant difference of the TRPM8 expression in CC from SHR and Wistar, suggesting that probably the sensitivity of TRPM8 channels is smaller in CC from SHR compared to normotensive rats. In conclusion, the data demonstrates, for the first time, the expression and function of TRPM8 channels in the CC, emphasizing the importance of these channels in the penile function, the mechanism of action underlying their activation and decreased sensitivity of these channels in CC from SHR, and all together, demonstrating the potential of this channel as a marker of hypertension associated-ED. **License number of ethics committee:** All procedures were performed in Augusta University, in accordance with the Guide for the Care and Use of Laboratory Animals of the National Institutes of Health (NIH) and were reviewed and approved by the Institutional Animal Care and Use Committee of Augusta University. **Financial support:** CNPq and CAPES

07.021 *Spirulina platensis* reverses the damage to cavernous contractile reactivity in wistar rats fed with a hypercaloric diet. Diniz AFA¹, Souza ILL¹, Ferreira ES¹, Carvalho MTL², Cavalcante FA³, Silva BA⁴ - ¹UFPB, ²UFPB, ³DFP-UFPB, ⁴DCF-UFPB

Introduction: Body adiposity increased causes endothelial damage that favors the development of erectile dysfunction (ED). ED is defined as an inability to achieve and or maintain a penile erection sufficient for sexual satisfaction (Costa, *Drugs*, v.72, p.2243, 2012). Recently, it was demonstrated that food supplementation with *Spirulina platensis*, a blue-green algae, in rats fed with a hypercaloric diet prevents damage to erectile function (Souza, *Front Physiol*, v.8, p.1, 2017). Thus, we aimed to evaluate whether *S. platensis* supplementation also reverses the damage to cavernous reactivity, triggered by a hypercaloric diet consumption. **Methods:** Wistar rats (8 weeks of age) were divided into rats that received standard diet (DP), hypercaloric diet (DHC) or hypercaloric diet + orally supplementation with *S. platensis* powder at 25, 50 or 100 mg/kg (DHC25, DHC50 and DHC100, respectively). Animals received different diets for 16 weeks and started the supplementation with the algae on week 8, except DP that received saline solution. Cavernous reactivity was monitored. Results were expressed as mean and standard deviation of the mean and analyzed by one-way ANOVA followed by the Tukey post-test (n=5). **Results:** On cumulative concentration-response curves to phenylephrine (PE) 10^{-8} - 10^{-3} M, was observed an increase on PE efficacy in DHC ($E_{max}=161.5\pm9.3\%$) compared to DP ($E_{max}=100\%$). Supplementation with the algae at 25 mg/kg ($E_{max}=147.3\pm13.4\%$) did not alter the corpus cavernous contractile reactivity. However, 50 mg/kg of *S. platensis* ($E_{max}=224.2\pm22.2\%$) increased the PE contractile reactivity compared to both DHC and DP groups. Interestingly, *S. platensis* at 100 mg/kg ($E_{max}=98.0\pm6.8\%$), reversed the increased of contractile reactivity to PE caused by a hypercaloric diet consumption seen in DHC. Concerning the action mechanism involved on the alteration promoted by the hypercaloric diet consumption, it was observed that PE curve in the presence of L-NAME, an inhibitor of nitric oxide synthase, had its E_{max} increased ($E_{max}=153.8\pm17.9\%$) in DP group compared to the absence of this inhibitor. As expected, the removal of nitric oxide (NO) favors cavernous contraction. However, the PE curve in the presence of indomethacin, a cyclo-oxygenase inhibitor, in DP ($E_{max}=90.5\pm2.6\%$) was similar to the absence of this inhibitor, suggesting no involvement of prostanoids on cavernous contractility. In DHC, PE efficacy was reduced in the presence of both L-NAME and indomethacin ($E_{max}=80.0\pm9.5$ and $70.8\pm10.1\%$, respectively) when compared to the absence of these inhibitors. The supplementation promoted on DHC + SP50 did not alter the PE curves in the presence of both L-NAME ($E_{max}=179.8\pm10.4\%$, $pCE_{50}=5.6\pm0.08$) and indomethacin ($E_{max}=183.3\pm12.0\%$, $pCE_{50}=5.5\pm0.08$) when compared to the absence of these inhibitors. DHC + SP100 increased the PE efficacy in the presence of both inhibitors ($E_{max}=186.7\pm18.6$ and $216.7\pm10.3\%$, respectively) when comparing to the curve in the absence of these inhibitors. **Conclusion:** Supplementation with *Spirulina platensis* reverses the damage to cavernous contractile reactivity in Wistar rats fed with a hypercaloric diet, by positively modulation NO and prostanoids pathways. **License number of ethics committee:** 0201/14 **Financial support:** CNPq, CAPES, PPgPNSB/UFPB

07.022 Regulation of renal lipid metabolism in diet-induced obesity - The adiponectin role. Pereira BMV, Rodrigues AC USP – Farmacologia

Introduction: Obesity is an important and independent risk factor for the development and progression of chronic kidney disease, a condition that is increasing worldwide and may lead to complete loss of renal function (Redon, *Curr Hypertens Rep*, v. 17, p.555, 2015). Associated with this obesity related-renal dysfunction is the abnormal metabolism of fatty acids in the kidney represented by a tissue accumulation of lipids and lipotoxicity (Kume, *J Am Soc Nephrol*, v.18, p.2715, 2007). Adiponectin, an adipokine secreted by adipose tissue, exerts effects on insulin sensitization, lipid metabolism and inflammatory processes when interacting with its receptors and it is often decreased in obese individuals. In kidney this adipokine is especially important for the function of podocytes and proteinuria (Sharma, *J Clin Invest*, v.118, p.1645, 2008). Here, we investigated the role of adiponectin in fatty acid metabolism and renal injury induced by a high-fat diet.

Methods: Male C57BL/6 mice adiponectin knockout (AdipoKO) and wild-type (WT) were fed a control or high fat diet for 16 weeks to induce obesity and the levels of mRNA expression of genes involved in the synthesis and oxidation of fatty acids were assessed and associated with histological and functional findings. **Results:** High fat-diet fed mice, independent of genotype, increased, on average, 56% ($p < 0.001$) their initial body weight (BW) while mice fed a control diet had just an 14% BW increase. This BW increase was accompanied by increase in both visceral and subcutaneous fat pads, higher serum cholesterol and triglycerides levels (57% higher on average; $p < 0.05$) and glucose and insulin intolerance ($p < 0.05$). In the kidney of WT mice fed high fat-diet, the mRNA level of the transcription factor *Srebp-1* and its targets enzymes *Acc* and *Fasn* was higher indicating that the fatty acid synthesis is increased. On the other hand, it was not true in animals lacking adiponectin. Similarly, the *Ppara* mRNA expression level is higher in WT but not in AdipoKO mice that received high-fat diet. Meanwhile, the levels of ureia and creatinine did not increase and glomerular enlargement and glomerulosclerosis was not observed, despite albuminuria in obese animals. Of interest, AdipoKO mice receiving control diet showed high levels of albumin in urine. **Conclusion:** The accumulation of lipids in renal tissue may be a result of the imbalance between fatty acids synthesis (mediated by SREBP-1c and its target enzymes including ACC and FASN) and oxidation (mediated by PPAR α and its target enzymes) and here we show that after 16 weeks of high-fat diet, WT animals showed an increase of enzymes involved in the synthesis and oxidation of fatty acids and adiponectin may be involved in fatty acid homeostasis at least at kidney level since the lack of its expression prevents the observed increased mRNA expression levels of WT animals. **License number of ethics committee:** 137/2015 **Financial support:** Fapesp (2015/24789-8) and CAPES

07.023 Regulation and functional aspects of innate immunity components during epididymal morphogenesis. Ferreira LGA¹, Ribeiro CM¹, Hinton BT², Avellar MCW¹ - ¹Unifesp-EPM – Farmacologia, ²University of Virginia – Cell Biology

Introduction: Several components of host defense are expressed in the epithelium of postnatal and adult epididymis. Among them are the β -defensins, a family of multifunctional proteins with antimicrobial and immunomodulatory properties, which also have a role in male fertility. We have detected a subset of β -defensin genes located within a gene cluster on chromosome 16 that is differentially expressed at mRNA level in the developing rat Wolffian duct (WD), the embryonic precursor of the epididymis. Next, we showed that one of these β -defensins, named sperm associated antigen 11 C (SPAG11C), was detected at both mRNA and protein levels between embryonic days (e) 12.5-20.5 and identified as an androgen-regulated mesenchymal factor with a role in WD morphogenesis. Transcripts for another β -defensin of this gene cluster, β -defensin 2 (*Defb2*), was only detected in WDs from e20.5 fetuses. Thus, the present study was designed to unveil the androgen regulation and potential role of DEFB2 in WD morphogenesis. Among other mechanisms, β -defensins can exert their functions by modulating Toll-like receptor (TLR) and chemokine receptor signaling pathways. For this reason, the expression levels of *Tlr4* and CC chemokine receptor 6 (*Ccr6*) mRNA were also evaluated in the developing WD. **Methods:** WDs were isolated from male Wistar rat fetuses at e17.5 and e20.5 and used for total RNA extraction. Expression levels of *Defb2*, *Tlr4* and *Ccr6* mRNA were assayed by RT-qPCR using ribosomal protein L19 (*Rpl19*) as reference gene. Androgen-dependency studies were performed using WD (e17.5) organotypic culture kept for up to 96 h in the absence or presence of testosterone (T; 10 nM) and OH-flutamide (10 μ M), an androgen receptor (AR) antagonist. Tissues were collected at 72 h and used for RT-qPCR. To determine a functional response of the DEFB2 on WD morphogenesis, the effect of recombinant human DEFB2 (hDEFB2, 3 nM) was also studied on WD organotypic culture. Washout experiments were conducted to remove hDEFB2 after 48 h of culture. Gross morphology of cultured WDs was evaluated. **Results:** Between e17.5 and e20.5, the period when fetal plasma T raises and WD morphological differentiation occurs in the rat, an increase in *Defb2* and *Tlr4* and a decrease in *Ccr6* mRNA levels were detected, indicating that these innate immunity components are expressed and differently regulated during WD development. The influence of androgens on *Defb2* mRNA expression was confirmed, since T/AR signaling sustained the expression levels of *Defb2* mRNA in 72 h cultured WDs, an effect prevented by T/OH-flutamide co-incubation. hDEFB2-treated WDs were shorter in length after 72 h and 96 h of culture when compared to the control ducts. These effects were rescued following washout of hDEFB2 and change to normal culture medium, showing the specificity of the recombinant protein-induced effects. **Conclusion:** The present data shed light in the role of innate immunity components during epididymal morphogenesis and imply a role for DEFB2 in the androgen-induced morphological differentiation of WD. Funding support: FAPESP, CNPq and CAPES. Ethics approval: CEUA-Unifesp-EPM#1776201213. **License number of ethics committee:** CEUA-Unifesp-EPM#1776201213 **Financial support:** FAPESP, CNPq e CAPES

07.024 Multiple protein disulfide isomerases in the epididymis: Novel roles in an androgen dependent tissue? Fernandes SG¹, Benham AM², Avellar MCW³ ¹Unifesp – Farmacologia Básica e Clínica, ²Durham University - Biosciences, ³Unifesp-EPM – Farmacologia

Introduction and Aim: Protein disulfide isomerase (PDI) is a member of the thioredoxin superfamily of redox proteins. Currently the *Pdi* gene family contains 21 members varying in amino acid sequence, domain composition, tissue expression and cellular processing. Their vital role in protein-folding have associated them with the pathogenesis of diseases, most commonly related to unfolded protein response during inflammatory conditions. PDIs are present in the male gonad and contribute to the ability of the spermatozoa to fertilize an egg. Some PDIs have also the ability to bind steroid hormones *in vitro*, suggesting their potential as hormone reservoir in the male reproductive tissues that are primarily regulated by androgen/androgen receptor (AR) signaling. Surprisingly, we have previously identified by RT-PCR that 20 *Pdi* genes are differentially expressed along the adult rat caput epididymis. Herein we evaluated the androgen modulation of a subset of *Pdi* genes to gain insights into their role in the epididymis, an organ of the male reproductive tract that is crucial for sperm maturation and male fertility. **Methods:** Adult male Wistar rat (90 or 120 days old) were divided into the following experimental groups: 1) Bilateral Surgical Castration (to confirm gene expression dependence on androgens plasma levels): control (sham operated), surgically castrated for 7 days (C7d) or 15 days (C15d), and C7d rats treated with testosterone propionate (C7+T; daily for 6 days, i.p. 1 mg/kg); and 2) Efferent Duct Ligation (EDL; to confirm gene expression dependence on testicular factors): control (sham-operated) and rats kept for 15 days after EDL. Epididymal proximal regions (initial segment and caput epididymis) were isolated and were used for total mRNA extraction. RT-pPCR was performed to evaluate *P4hb*, *Pdip*, *Pdia3*, *Pdia5*, *Pdia6*, *Pdilt*, *Erp29* and *Txndc5* mRNA relative expression, using *Rpl19* transcript as reference gene and *Ar* and *Defb1* mRNA as a positive control for surgical castration and EDL, respectively. Proper negative controls were used. **Results:** RT-qPCR revealed that surgical castration significantly reduced *P4hb*, *Pdia3*, *Erp29* and *Txndc5* mRNA levels in C7d and C15d caput epididymis, an effect restored to control levels in C7+T tissues for all gene tested, except *P4hb* that had its mRNA levels only partially restored by T treatment. Conversely, *Pdia5* and *Pdia6* mRNA levels increased in the C7d group and returned to control levels in C15d and C7+T tissues. *Pdilt* and *Pdip* mRNA levels, on the other hand, were not affected by surgical castration. *P4hb* was the only transcript to be affected by EDL, being reduced in the caput, but not initial segment region when compared to control. **Conclusion:** The differential androgen modulation of the different *Pdi* transcripts present in the epididymis indicate potential novel roles for these protein in an androgen-modulated tissue such as the epididymis, with potential impact to epididymal function and male fertility. Ongoing experiments are exploring their role in the epididymis during different inflammatory conditions. **License number of ethics committee:** CEUA UNIFESP-EPM 5908210916 **Financial support:** FAPESP, SPRINT/FAPESP, CNPq, CAPES.

07.025 Prenatal dexamethasone influences glucocorticoid receptor signaling during Wolffian duct morphogenesis. Sousa ME, Ribeiro CM, Calegare BFA, Avellar MCW Unifesp-EPM – Farmacologia

Introduction and Aim: Glucocorticoids are steroid hormones with crucial and unique roles during the pregnancy and fetal development. Their significant rise in fetal serum in late pregnancy is required to prepare the fetus for postnatal life and adulthood. They act through activation of the glucocorticoid receptor (GR) expressed in different tissues in the developing fetuses. Insufficient glucocorticoid/GR signaling can be fatal primarily due to impaired lung development, while its excess from chronic maternal stress or antenatal treatment with synthetic glucocorticoids may affect fetal growth and program the fetus for life-long diseases. Recently we reported the expression and potential role of glucocorticoid signaling components in the developing Wolff Duct (WD), the embryonic precursor of the epididymis (a tissue from the male reproductive tract with crucial role in sperm maturation). Herein we investigate whether synthetic glucocorticoid (dexamethasone, DEX) prenatal exposure alters GR expression and cellular localization during WD morphogenesis. Since the WD/epididymal development is primarily controlled by androgen/androgen receptor (AR) signaling, we have also studied the prenatal treatment effects on AR expression in this tissue. **Methods:** Pregnant Wistar rats (90 days of age) were treated daily with either saline (control, s.c., N=6) or dexamethasone during the embryonic age window e17.5-e19.5 (1.0 mg/kg, s.c., DEX-S, N=6) or e13.5-e19.5 (0.1 mg/kg, s.c., DEX-L, N=6). WD from the male fetuses were collected at e20.5 from all experimental groups. WD were dissected and processed for gross morphology and for immunofluorescence studies with antibodies against GR and AR. Serum corticosterone was measured by Elisa assays. **Results:** Compared to controls, body weight (g) and nasoanal length (cm) were lower in male fetuses from both DEX-S and DEX-L dams (N=7-8 per group, $p < 0.05$). Fetuses from DEX treated dams displayed reduced plasma corticosterone concentration (N=7, controls 115.8 ± 19.21 and 32.79 ± 9.24 versus 118.7 ± 13.87 and 13.88 ± 2.17 ng/mL, respectively to DEX-S and DEX-L, $p < 0.05$). WD gross morphology and its respective histological analysis of duct cryosections stained with hematoxylin and eosin indicated similar WD histomorphology among the different experimental groups. Immunofluorescence and confocal microscopy analysis revealed cytoplasmic/nuclear GR and AR immunolocalization pattern that varied from proximal (closer to the testis) to distal WD regions (named from A to F) in mesenchymal and epithelial cells from control ducts. Both GR and AR immunodistribution was influenced by the prenatal DEX treatments. Ongoing experiments are exploring expression changes of glucocorticoid- and androgen-dependent target morphogenes as readouts for the better understanding of the molecular consequences of the antenatal treatments. **Conclusion:** The results indicate that antenatal glucocorticoids may impact the normal GR-regulated trajectory of the WD morphogenesis with potential consequences to epididymal function and male fertility. **License number of ethics committee:** CEUA UNIFESP #1776201213 **Financial support:** CAPES, CNPq, FAPESP

07.026 The pro-ejaculatory effects of on-demand lorcaserin administration suggest 5-HT_{2C} receptors activation as a new approach to delayed ejaculation.

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Background: Lorcaserin [(1R)-8-chloro-2,3,4,5-tetrahydro-1-methyl-1H-3 benzazepine] is an antiobesity drug whose weight-loss effect results from 5-HT_{2C} receptors activation. Importantly, while the 5-HT_{2C} was shown to participate in the physiological control of ejaculation no data addressing the potential effects of lorcaserin on ejaculation are available. Therefore, in this study the effects of lorcaserin on different *in vitro* and *in vivo* experimental models of ejaculation were evaluated. **Methods:** All the experimental procedures were approved by the Institutional Ethics Committee for the Use of Experimental Animals of UNICAMP. Adult male Wistar rats (120-180 days old) were used in the different experiments. *In vitro contraction studies.* Rats were killed by isoflurane overdose and the seminal vesicles (SV), vas deferens (VD) and cauda epididymis (CE) were mounted in 10 ml organ baths to evaluation of isometric contractions. The effects of lorcaserin on VD, SV and CE resting tension and on neurogenic contractions induced by electrical field stimulation were evaluated. *Ejaculation in urethane-anesthetized rats.* Adult male Wistar rats were urethane-anesthetized (1.5g/kg, ip) and the right vas deferens (VD), left seminal vesicle (SV) and the bulbospogiosus muscle (BSP) were mounted to in situ evaluation of isometric tension, intraluminal pressure and electromyographic recording, respectively. Vehicle or lorcaserin (0.1, 0.3, 0.6 or 1.0mg/kg) were intravenously administered and the occurrence of ejaculation, i.e. the coordinated contraction of VD, SV and BSP were evaluated. The participation of 5-HT_{2C} on lorcaserin-induced ejaculations was investigated with the 5-HT_{2C}-selective antagonist SB 242084 (0.1 and 0.3 mg/kg, iv). Data are presented as mean ± sem and statistical analysis done with ANOVA + Newman-Keuls. p values <0.05 were taken as statistically significant. **Results:** *In vitro* lorcaserin (0.001-100 uM) administration had no effect on CE, SV and VD smooth muscle resting tension or on neurogenic CE, SV and VD contractions. *In vivo* lorcaserin 0.3, 0.6 and 1.0 mg/kg administration induced 3.8±0.58, 4.4±0.81 and 4.0±1.08 ejaculations (p>0.05 between all groups) in urethane-anesthetized rats. Lorcaserin-induced ejaculations were mediated via 5-HT_{2C} activation as they were dose-dependently prevented by the 5-HT_{2C}-selective antagonist SB 242084 (0.1 and 0.3 mg/kg, i.v.). **Conclusion:** Our results uncover a previously unrecognized pro-ejaculatory effect of antiobesity drug lorcaserin via 5-HT_{2C} activation. Due to its recognized safety profile it is tempting to suggest lorcaserin evaluation as a putative ejaculation facilitator in patients complaining of delayed ejaculation to which a few drug approaches are available. **License number of ethics committee:** CEUA: 4888-1/2018 **Financial support:** **Financial support:** FAPESP (2015/19677-6),CNPq (169694/2017-8).