11. Clinical Pharmacology, Pharmacokinetics, Pharmacogenomics and Toxicology

11.001 *In vitro in vivo* **correlation in the development of oral drug formulations**: **Case studies from a Pharmaceutical Industry in Brazil**. Davanço MG[1], Meulman J[2], Carvalho PO[1], Duarte FG[2], Campos DR[2] USF, Sanofi Medley Farmacêutica

Introduction: In vitro - in vivo correlation (IVIVC) allows prediction of the in vivo performance of an oral drug formulation based on its in vitro drug release profiles and can be used in the development of medicines to be more assertive, faster andreduce the number of human studies during the formulation development, once that IVIVC serves as a surrogate for in vivo bioavailability/bioequivalence testing [1,2]. The objective this study was to demonstrate the applicability of the IVIVC in the development of generic medicines in a Pharmaceutical Industry in Brazil. **Methods:** Three different IVIVC case studies were selected and evaluated, being: Case 1 - IVIVC for Desvenlafaxine succinate monohydrate 100-mg extended-release (XR) tablet (Low complexity XR formulation and BCS class I drug), Case 2 - IVIVC for Bupropion hydrochloride 150-mg XR tablet (High Complexity XR formulation and BCS class I drug); and Case 3 -IVIVC for Albendazole 400-mg immediate-release (IR) tablet (High Complexity IR formulation and BCS class II drug). For in vitro assessment, the apparatus 1 (basket), 2 (paddle), and 3 (reciprocating cylinder) were tested as well as different biopredictive dissolution media (pH 1.2, 4.5 and 6.8). For albendazole formulation (Case 3), a dissolution medium from literature [3] was tested to verify it is reproductibility. Wagner-Nelson and Loo-Riegelman models were applied for deconvolution ofin vivo data. Time-scaling approach was applied when was not possible to establish a linear correlation between in vitro and in vivo data. The capacity of predicting the bioequivalent result was considered to assess if the IVIVC was successful established. **Results:** Level A IVIVC was obtained in the cases 1 (using the Wagner-Nelson model) and 2 (using the Loo-Riegelman model); and for case 3, it was demonstrated that the dissolution medium published in literature was applicable and a Level D IVIVC was obtained. In all cases, the IVIVC demonstrated good capacity to predict the in vivo behavior and to support in the best prototype selection for bioequivalence studies. **Conclusion:** IVIVC is an excellent and useful tool to apply in the Research and Development (R&D) department of the Pharmaceutical Industry, permitting to predict the in vivo behavior and improving the rate of bioequivalent **Results**. **Acknowledgements:** The authors thank the Sanofi ID Campinas team for supporting the analytical and formulation development. **Financial Support:** the in vitro and in vivo studies were supported by Sanofi. **Ethics:** All in vivo studies were registered in the CEP/CONEP system and approved by a Human Research Ethical Committee. **References:** [1]Cardot & Davit. AAPS J. 2012 Sep;14(3): 491-9. [2] Emami. J Pharm Pharm Sci. 2006;9(2): 169-89. [3] Galia *et al*. Pharm Res. 1999 Dec;16(12): 1871-5.

11.002 Microdialys probes calibration for an application in pharmacokinetic study of amphotericin B. Santos VV, Araújo JMS, Pereira LC, Azeredo FJ UFBA

Introduction: Amphotericin B (AmB) is an antibiotic used to treat systemic infections. Its therapeutic response is obtained when the free concentration of this drug present at the site of infection is sufficient for it to have activity against the microorganisms that cause the infection. To quantify and evaluate the tissue penetration of this drug it is ideal to use a technique that only determines the free concentration in the tissue. Microdialysis (MD) is an approach in which the drug is directly determined in the tissues after probe implantation and from there the evaluation of the tissue concentration of the desired drug is performed. For this, the in vitro and in vivo calibration of the MD probes is necessary to determine the best workflow and relative recovery of the drug. Therefore, this study aimed to validate an analytical methodology for quantification of AmB in the MD of tissues of Wistar rats and to calibrate probes by in vitro and in vivo assays. **Methods**: An analytical method was validated according to RDC 166/2017 on HPLC/DAD using a C18 reverse phase column and a precolumn of the same material. The mobile phase consisted of a solution containing acetonitrile and acetate buffer (pH 4.0). Elution of the gradient is performed with a flow of 1.0 mL.min-1 and the detection was done at the wavelength of 407 nm. Solutions at serial concentrations of AmB (250-10000 µg/mL) and quality controls (400, 1500 and 6000 µg/mL) were made using methanol: dimethyl sulfoxide (95: 5, v/v) as the reagent. The MD system consisted of a syringe infusion pump connected to a controller, a syringe and MD probes. The infusion flow was evaluated by the method of retrodialysis and dialysis with the flows of 1, 1,5, 2 and 2,5 µL/min, and the influence of the concentration with concentrations of 2.5, 3 and 4 µg/ml of AmB. For in vivo recovery, the concentration of 3 µg/ml AmB was used by the retrodialysis method. **Results**: The method showed selectivity and linearity under the studied range, with r <0.99. Intra- and inter-day precision did not exceed 5% for concentrations, and intra- and inter-day precision did not exceed the 95-105% range for all concentrations, according to ROC 166/2017. The perfusion flow chosen was 1.5 µL/min with a relative recovery of 0.22 ± 0.08 for retrodialysis and 0.20 ± 0.06 for dialysis. Using this perfusion flow, the recovery in different concentrations was evaluated and it did not present significant difference among the concentrations, and between both retrodialysis and dialysis analysis. The in vivo recovery was not statistically different from the in vitro showing that AmB can have its pharmacokinetics performed by this technique. **Conclusions**: It was validated an analytical method capable of quantifying AmB in MD according to RDC nº166, dated July 24, 2017, proving to be selective, precise and accurate. Regarding the in vitro and in vivo calibration of the MD probes, it was possible to establish the ideal perfusion flow rate of the probes, to evaluate the influence of the concentration, and to determine the relative recovery. Financial Support: FABESB and CNPq. Ethical Aspects: This research was approved by the Ethics Committee on Animal Use of theSchool of Veterinary Medicine, Federal University of Bahia, under the protocol n° 26/2018.

11.003 ALDH2 Activity recovery by nicotinamide adenine dinucleotide (**NAD+**) **treatment in neuroblastoma SH-SY5Y cells exposed to lead and ethanol**. Deza-Ponzio R, Cejas RB, Albrecht PA, Fernández-Hubeid LE, Cancela LM, Irazoqui FJ, Virgolini MB Universidad de Córdoba

Introduction: Several evidences demonstrate that the neurotoxicant lead (Pb) induces neurobehavioral alterations, including an altered response to drugs. We have previously reported that perinatally-Pb-exposed rats showed elevated ethanol (EtOH) intake. It is known that EtOH metabolism determines its motivational properties. In fact, centrally formed acetaldehyde (ACD) promotes EtOH consumption, while peripheral ACD accumulation induces aversive effects. In both cases, aldehyde dehydrogenase (ALDH) is responsible for ACD oxidation to acetic acid, a step determined by nicotinamide adenine dinucleotide (NAD^+) availability. In the Pb-exposed rats, the elevated EtOH intake seems to be mediated by brain ACD accumulation, probably due to a reduced mitochondrial ALDH (ALDH2) activity and expression evidenced in these animals. **Methods**: In search of a mechanistic approach, *in vitro* experiments were performed in SH-SY5Y cells, aimed to evaluate ALDH2 activity in a brain like-environment. Neuroblastoma cells were exposed to Pb (5-200µM), EtOH (100-200 mM) or Pb plus EtOH (10µM/200mM) for 24 h. **Results** AND CONCLUSION: The results resembled the *in vivo* data showing that Pb alone (5µM and 10µM) or in combination with EtOH inhibited ALDH2 activity in SH-SY5Y cells. Concomitant supplementation with 1mM NAD^+ seems to recover the enzyme activity. Provided the importance of NAD^+ in EtOH metabolism, the Results suggest either a reduction in NAD^+ biodisponiblity or an altered affinity of the enzyme for its cofactor as a putative combined mechanism of the neurotoxic effects of Pb and EtOH in neuroblastoma-derived cells. Current studies are focalized in the assessment of ALDH2 expression and mitochondrial functionality in this model to explore the mechanisms that modulate ALDH2 function and ACD toxicity in the presence of Pb and EtOH. **Key Words:** Lead-exposure, Ethanol, ALDH2, NAD^+

11.004 Analysis of Gene Polymorphisms Related to NSAIDs Metabolism and Pain Modulation. Calvo AM[1], Weckwerth GM[1], Oliveira GM[1], Dionisio TJ[1], Faria FAC, Moore T[2], Santos CF[1] [1]USP, [2]Kailos Genetics

Introduction: Polymorphisms in genes that regulate the production of enzymes responsible for drug metabolism, such as anti-inflammatory drugs, are also known to modulate the plasma concentration and excretion of these drugs. The efficiency of NSAID metabolism, for example, can determine the occurrence of adverse effects on users.Pharmacogenetics concept has become the object of study in order to customized prescription in the near future. The objective of the present study was to genotype 36 volunteers for several genes associated with drug metabolism, aimingin the next research step relates the occurrences of these polymorphisms with the pharmacokinetic and pharmacodynamic data of each individual. **Methods:** The research was approved by the Ethics Committee (# 2,768,156 and # 2,768,177), all volunteers participating in the surveys were informed in detail about their content and procedures to be performed and agreed to sign the Informed Consent Form. Multiple genotypes were performed for several genes of interest through panel PGx2018.1.4.1 developed by Kailos Genetics, Inc. (Huntsville, Alabama, USA). Thirty-six lyophilized DNA samples from saliva were analyzed after rehydration. All samples were quantified in Spectrophotometer SpectraMax® M2 (serial number: SMP500-18752-RCHQ), from Kailos Genetics® laboratory, to check the new concentration. Then, they were distributed in 96-well plate and were storage in a –80°C freezer, until the start of the Library preparation, with the TargetRich™ PGx Panel Protocol (Kailos Genetics®) and standardized sequencing in MiSeq® Illumina. The results of genotyping determine whether the subject is a normal (NM), slow (SM) or intermediate metabolizer (IM). These ratings are based on the literature and on Kailos Genetics®' software. Since the experiments are in the process of standardization, some genotypes could not be determined (NA). **Results:** The results reveal the following genotypes: CYP1A2 (17 NM, 13 SM, 6 NA); CYP2C8 (15 NM, 14 SM, 4 IM, 3 NA); CYP2C9 (16 NM, 10 SM, 7 IM, 3 NA); CYP3A4 (32 NM, 2 MI, 2 NA); CYP3A5 (1 NM, 25 SM, 8 IM); COMT (4 NM, 11 SM, 8 IM); and, OPRM 1 (24 NM, 7 SM, 1 IM, 4 NA). **Conclusion:** From the present results, pharmacokinetic and pharmacodynamic (PK / PD) tests will be performed for several NSAIDs using saliva samples LC-MS / MS and joint analysis of genes will provide a very broad panel to our pharmacogenetic study.

11.005 New insights from the study of vulnerable populations exposed to mercury: **genetic susceptibility**, **peripheral markers of neurotoxicity and the impact of large-scale projects in Amazon**. Crespo-Lopez ME[1], Arrifano G[1], Macchi BM[1], Oliveira MA[1], Araújo AL[1], Sacramento L[1], Takeda P[1], Martin-Doimeadios RCR[2], Moreno MJ[2], Trujillo SF[2], Oria R[3], Leite JA[4] [1]UFPA, [2]Universidad Complutense of Madrid, [3]UFC, [4]UFMG

Introduction: Accompanying riverine Amazonian populations since 2006, we demonstrated that Hg is present in human populations (adults and children) under the influence of artisanal small-scale gold mining areas (ASGM), but also in those areas with no ASGM. Accurate measurement of genetic susceptibility and early neurotoxicity is especially challenging due to confounding factors in neurobehavioral evaluations and the scarce literature about reliable peripheral markers in humans. Both apolipoprotein E (APOE) and S100B protein were recently associated with Hg neurotoxicity as well-established biomarkers of genetic susceptibility and brain damage, respectively, that can be detected in blood. **Methods:** the largest epidemiological study of mercury-related genetic factors ever conducted in Amazonian riverine populations was performed with 823 individuals (CAAE nº 43927115.4.0000.0018). Anthropometric data, self-reported symptoms, routine clinical data, APOE genotyping, S100B expression and ancestry markers were recorded or analyzed in blood by qPCR. Total Hg and its species were quantified by ICP-MSand by a GC-pyro-AFS system. **Results and Conclusions:** Additionally, to areas with ASGM, riverine populations living at the areas of large-scale projects such as dams are also exposed to medium-to-high levels of Hg. Exposed individuals present long-term deleterious problems such as classical symptoms of neurotoxicity and high prevalence of non-communicable diseases (diabetes and hypertension).Due to the difficulty of adequate protein conservation in remote populations, we used S100B mRNA levels in blood as a way to assay mercury neurotoxicity, and its expression in exposed individuals was more than twice that of non-exposed individuals, supporting this peripheral marker as an useful tool for the early diagnosis of Hg-induced neurotoxicity. For the first time, we described the prevalence of APOE4-carriers (susceptible individuals) being 30% of the total riverine population of Amazon. Interestingly, the Amerindian genetic background was associated with a higher genetic susceptibility to Hg neurotoxicity. Moreover, our data support a kinetic influence of APOE isoforms on metal bioaccumulation, pointing to APOE genotyping as a valuable marker in preventive strategies. The combination of both prevention and early diagnosis biomarkers, in addition to exposure parameters, supports the screening and early identification of high-risk individuals in isolated populations. **Financial Support**: CNPq, CAPES, PROPESP-UFPA

11.006 Toxicity of the herbicide metribuzin on the development and antioxidant enzymes in drosophila melanogaster. Silva CM, Oliveira J, Silva E, Neiva G, Araújo LA UFAL

Introduction: Brazil is one of the leading countries in agrochemicals use in agriculture. These pesticides can leach and accumulate in soil, water and animals, which makes it mandatory to investigate the toxic effects of these substances on non-target organisms. The herbicide metribuzin is part of the class of triazinones and is used to control weeds in different crops[1]. It is suggested that the exposure of non-target organisms to triazinones induces cancer, oxidative stress and metabolic imbalance[2,3,4]. The aim of this work was to evaluate the potential effects of the herbicide metribuzin on the development and antioxidant activity of Drosophila. **Methods**: Adult flies were placed in oviposition medium to carry out a controlled collection of embryos. After 24 hours, the larvae were transferred to vials (n=35 larvae/replicate, four replicates per concentration) containing different concentrations of the herbicide (0.01 mg/mL - 0.2 mg/mL and control media) and its development followed during subsequent developmental stages. In order to evaluate the effects of the herbicide on the antioxidant enzymes, adult flies (males and females) were separated (3-5 days old) and exposed to different concentrations for 24h (acute) or 7 days (chronic). The animals (n=25/replicate, eight replicates per concentration) were placed in 3mL of standard culture medium containing the herbicide (0.01 mg/mL and 0.05 mg/mL). Following the exposure, the animals were anesthetized and quickly frozen. Analyzis of nitric oxide (NO), superoxide dismutase (SOD), catalase (CAT), and lipid peroxidation levels (through malondialdehyde - MDA) were performed. **Results**: Larvae that developed in metribuzin containing medium showed a delay of 2 to 5 days in total development when compared to control animals, besides larval lethality ranging from 25% to 40%, indicating that metribuzin caused deleterious effects capable of delaying or even inhibiting the larval development. Analysis of antioxidant capacity demonstrated that both acute and chronic exposure caused redox imbalance and led to oxidative stress in animals of both sexes, when compared to control group. Due to the fact that the metribuzin herbicide acts in plants as a photosystem II inhibitor, specifically in the transfer of electrons, the exposure of the animals probably led to the production of oxygen reactive species in its cells, triggering oxidative stress, which was not observed in the control group. **Conclusion:** Altogether, our data shows that the exposure of Drosophila to the herbicide metribuzin is capable of inducing delay and death during larval and pupal development, in addition to cause significant redox imbalance. These **Results** indicate that metribuzin might cause important deleterious effects to human health and other non-target organisms. **References**: [1] Maksymiv, Ivan V. et al. Pestic Biochem Phys. 122: 67, 2015. [2] Figueira, Fernanda Hernandes. et al. Comp Biochem Physiol. 191: 78, 2016. [3] Chiali, F.Z. et al; Pestic Biochem Phys. 106, 38, 2013. [4] Delancey, John Oliver L. et al. Ann Epidemiol.19, 388, 2009. **Financial support**: We are not funded

11.007 Toxicological evaluation of the insecticide imidacloprid and the herbicide hexazinone in *Drosophila melanogaster*. Floresta LRS, Silva KTR, Oliveira JM, Silva EA, Neiva G, Araújo LAD UFAL

Introduction: Brazil is one of the countries that most use pesticides in agriculture. These substances affect human health and the environment as they contaminate soil and water bodies, affecting non-target organisms. The imidacloprid insecticide, of the class of neonicotinoids, acts on the central nervous system of herbivorous invertebrates and is considered genotoxic for non-target organisms such as bees[1,2]. Hexazinone is an organic compound of the class of herbicides known as triazinones, classified as moderately toxic; it is known that this herbicide causes delay in fish development, behavioral changes and genotoxicity[3]. The main aim of the present study was to evaluate the toxicity of imidacloprid and hexazinone using the well-established toxicology model Drosophila melanogaster. **Methods**: Acute toxicity bioassays were performed for both substances, in which female flies (n=25/replicate, 8 replicates) were exposed in vials with standard Drosophila medium (4 mL) containing imidacloprid concentrations (0,001–0,004 mg/mL) or Hexazinone (0,05-0,4 mg/mL). The rate of mortality was determined after 24 hours of exposure. The toxicological effect of the pesticides on development was assessed by putting 35 first stage larvae (6-8 replicates) to develop in standard medium containing each pesticide concentration (0,0001 mg/ml for imidacloprid / 0,5-2,0mg/mL for hexazinone). The number of individuals that reached each developmental stage was analyzed and the rate of lethality could be determined. The antioxidant capacity of the exposed larvae and adults was assessed through nitric oxide assay, by measuring the activity of superoxide dismutase and catalase, and lipid peroxidation through malondialdehyde. **Results**: The acute toxicity bioassay showed lethality in a concentration-dependent fashion for both pesticides. In the developmental assay the animals that developed in imidacloprid medium showed a delay of 2-5 days in larval development while those in hexazinone medium delayed 4-7 days. Additionally, both pesticides caused a concentration-dependent larval lethality rate. This result reflected the lower number of animals that reached adulthood in higher concentrations. Some of the emerged adults showed aberrant phenotypes as deformed wings and black spots in the abdomen. All animals showed an increase in the parameters of antioxidant capacity, indicating that both pesticides caused oxidative stress. **Conclusion:** Taking together, our toxicological results demonstrate that both pesticides can be considered toxic to non-target organisms, as indicated by developmental delay, larval lethality and oxidative stress in Drosophila. **References:** [1] Raymann K. Appl Environ Microbiol. 84. 18. 2018. [2] Toniêto, Thiago. J. Agric. Food Chem. 64. 3960. 2016. [3] Buckingham S. J Exp Biol. 200. 2685. 1997.

11.008 Biocompatibility of the Eu doped TiO2 nanocrystals and CdSe/CdS magic sized quantum dots in *Drosophila melanogaster*. Silva KTR, Oliveira JM, Silva EA, Carvalho JPS, Silva U, Silva CJ, Dantas NO, Silva ACA, Araújo LA UFAL

Introduction: The development of different materials at the nanoscale has increased for several applications. The titanium dioxide (TiO_2) nanoparticles has been used in several types of products such as cosmetics and food. Europium ions that emit in the red was incorporated to TiO_2 nanocrystals (NCs) structure, enabling the tracking of luminescence[1,2]. The CdSe/CdS magic sized quantum dot (MSQD) can be used in the biomedical field for applications such as disease diagnostics, cellular and molecular tracking and therapeutic drug delivery[3]. However, the nanoparticles may present toxic effects such as inducing oxidative stress, cytotoxity and genotoxicity[3,4]. Here, we evaluate the in vivo toxicity of Eu doped TiO_2 NCs and CdSe/CdS MSQDs during the development and lifespan in Drosophila melanogaster. **Methods**: Thirty-five first instar larvae were placed in 4ml of standard *Drosophila* culture medium (4 replicates) containing the nanoparticle in increasing concentrations of Eu doped TiO_2 NCs (0.249 - 8.0 mg/mL) and CdSe/CdS MSQDs (100 ng/mL - 100 µg/mL). We determined the rates of larval lethality, pupae formation, and lifespan of emerged adult flies. Moreover, we track the location of these nanoparticles in larvae and adult flies by epifluorescence. **Results**: Larvae that developed in culture medium containing Eu doped TiO_2 NCs presented higher larval lethality and consequently lower number of adults when compared to control. A very small percentage of the adult animals showed aberrant phenotypes, such as crooked wings and dark spots on the abdomen and thorax. In addition, large vesicles containing nanoparticles were observed in the fat body of adult animals from all tested concentrations. Although the animals presented these alterations the lifespan was the same as in the control group. The larvae that developed in medium containing CdSe/CdS MSQDs showed increased larval lethality and reduced number of adult animals only at the highest concentrations (10, 50 and 100 µg/mL). At these same concentrations, a three-day delay in larval development was observed. However, the lifespan of these animals did not differ from the control and in none of the concentrations tested we could observe adults showing aberrant phenotypes or nanoparticle vesicles.

Conclusion: Our results demonstrated that the Eu doped TiO_2 NCs is not biocompatible and can be considered toxic even at low concentrations while the CdSe/CdS MSQDs was biocompatible at concentrations below 10µg/mL. **References:** [1] Sario et al., Mutat Res Gen Tox Em, 831, 19, 2018. [2] Jovanovic et al., Scientific Reports, 8, 17922, 2018. [3] Nagy et al., ACS Nano, 6, 4748, 2012. [4] Alaraby et al., Science of the Total Environment, 530–531, 66, 2015.

11.009 Adverse Drug Reactions of Magnesium Sulfatein High-Risk Pregnancy and puerperium in Intensive Care. Borges MAH[1], Costa T[2], Cunha MD[2], Bezerra PKV[2], Azeredo F[1], Martins R[2], Oliveira A[2] [1]UFBA, [2]UFRN

Introduction: There is a limited selection of medications that may be prescribed to pregnant women because safety information related to use during this period is not available for most drugs, magne.However, some clinical conditions require extensive use of medications, for example, high-risk pregnancies where there is a greater probability of negatives outcomes for the mother and/or fetus. This study aimed to characterize the prevalence of adverse drug reactions (ADR), medications implicated and risk factors in high-risk pregnancy and puerperium under intensive care. **Methods:** This study was approved by the Institutional Review Board and written informed consent was obtained from all patients. From June 2016 to December 2017, all patients admitted to a maternal intensive care unit (ICU) because of high-risk pregnancy and puerperium were included in this observational, longitudinal, prospective study. Women admitted due to non-obstetric conditions, with an ICU stay less than 24 hours or readmitted to the ICU were excluded. Patients were investigated daily for the occurrence of ADR through pharmaceutical anamnesis, active search in medical records and questioning of the health team. Logistic regression was used to identify risk factors for ADR. **Results:** The study population consisted of 607 women aged 27.0±7.5 years-old, with mean gestational age of 33.8±6.3 weeks. The main admission diagnoses were preeclampsia/eclampsia (315, 51.9%) and gestational hypertension (108, 17.8%). ADR were observed in 165 women (27.2%). No severe ADR was observed and 29.7% were of moderate severity. The drug most often implicated was magnesium sulfate (25.2%) with 44.5% of patients administered that drug experiencing ADR that consisted of drowsiness (68.6%), absent patellar reflex (21.6%) and hypotension (9.8%). Risk factors of ADR were blood pressure (adjusted odds-ratio (AOR) 1.02), hemoglobin level (AOR 1.21) and body temperature (AOR 0.71). **Conclusion:** ADR affect about one third of high-risk pregnancies and puerperium, mainly due to magnesium sulfate administrations. High blood pressure, lower body temperature, and high hemoglobin concentration on admission were associated with an increased risk of ADR. The monitoring of the use of this medication, given its importance of its indication, allows it to be safely used by pregnant women and high-risk puerperae.

11.010 Exposition to Water Containing Traces of Heavy Metals And Pesticides From Alagoas' Water Basins Induces Behavioral Alterations In Adult Zebrafish (**Danio rerio**). Santos ORS, Santana DB, Sousa MAS, Oliveira AAR, Nascimento TG, Reys JRM, Moura MABF UFAL

Introduction: Water quality is currently a major global concern and considered a vital parameter for ecosystems' maintenance, in addition to its impact on public health (PARRIS, Int. J. Water Resour. Dev., v. 27, p. 33, 2011). Previous studies conducted by our group have identified the presence of pesticides and heavy metals in surface water bodies used as source of drinkable water in theMaceió's water supply system. In bioassays performed to evaluate the influence of toxic chemicals on the neurological-behavioral activity of fish, the study of swimming behavior is key because it has a direct impact on social interaction, reproduction, and ability to avoid and escape predators. Acceleration, velocity, and distance traveled are important factors in the evaluation of fish's locomotive capacity (RIEHL, Neurotoxicol. Teratol., n. 33, p. 658. 2011). **Methods**: *In vivo* assays were approved by CEUA/UFAL, through the authorization number 72/2017. The collection of water in areas of environmental protection was authorizedthrough the letter of consent No. 05/2018(IMA/AL). The environmental samples were collected from three sampling near the water catchment stations, located on the banks of the Pratagy River and the Catolé dam. Toxic effects evaluated in the trials were of the acute type, in the neurological/behavioral modality. We adopted fish at approximately 3 months of age in these trials. The exposure test was based on the methodology of video monitoring conducted by Riehl et al (RIEHL, Neurotoxicol. Teratol., n. 33, p. 658. 2011), with some modifications. The video recordings were performed at moments of 0, 3, 6, 12 and 24 hours after exposure. Animals were not fed during the tests; its distribution was random, and tests were performed in triplicate. Video analysis was performed using ToxTrac open source software (RODRIGUES, **Methods** Ecol. Evol., v. 9, p. 460, 2018). Data obtained in the exposure tests were subjected to the normal test (Shapiro-Wilk test, for alpha = 0.05). Significance ($P < 0.05$) of the difference between the control and test groups was assessed using the Student's T-Test. **Results**: No fish death was observed during the exposure period nor after the trials (0% mortality), characterizing a low acute toxicity of the samples tested. The same lethality was found in the control group. Final values obtained after video analysis and statistic treatment point to a higher average acceleration ($P = 0.0024$), higher mean velocity ($P = 0.0003$), and greater average distance traveled ($P = 0.0458$) relative to individuals exposed to the complex mixture of substances present in the samples from the Catolé Dam, when compared to the individuals in the negative control group, which were immersed in deionized water; this indicates that the exposure had a direct effect on the animals' locomotor activity ($P <0.05$). **Conclusion:** Behavioral endpoints were more sensitive in the tested conditions than the mortality. In vivo exposure tests using the selected animal model indicated that the substances present in the environmental samples of water were able to cause neurological-behavioral changes in the fish ($P <0.05$), in comparison to the control group. Further physical-chemical tests for identification and quantification of other toxic components in these water sources, and in-depth studies on exposed animals are necessary for a better understanding of the toxicity mechanisms. Acknowledgments and funding: ORSS holds a grant from FAPEAL/CAPES (agreement, grant number 88887159647/2017-00). Access to paid publications was subsidized by CAPES.

11.011 Biochemical effects of a two-week exposure to Aflatoxin B1 and aspartame to Wistar rats. Silveira AR, Souto NS, Rosa EVF, Dassi M, Braga ACM, Vaz AA, Furian AF UFSM

Introduction: Food products rich in fiber can serve as substrates for fungi proliferation that produces mycotoxins, like aflatoxin B1 (AFB1). AFB1 is converted in the liver in AFB1-8,9-epoxide, promoting an imbalance in the oxidative system. AFB1 isliposoluble and its existence in the postmortem brain tissue suggest its ability to cross the blood brain barrier promoting damages. Food contaminated with AFB1 can be consumed in the same meal that contains aspartame (ASP), a food additive developed to replace the conventional sugar, widely diffused by having a high sweetness power with low caloric value. The mechanism of its toxicity is based mainly on the induction of oxidative stress and can act on different tissues. Among all the metabolites of ASP, methanol is the most toxic and was related to induce neurological disorders. Thus, the aim of this study was to evaluate the effect of exposure to AFB1 (250 µg/kg, i.g.) and/or ASP (75 mg/kg, i.g.) for 14 days on the cerebral cortexof male Wistar rats, on biochemical parameters. **Methods**: 24 male Wistar rats (40-50g) with 21 days of age that were randomly divided in 4 groups: group I received DMSO (2%; ig) + NaCl (0,9%, ig); group II received AFB1 (250µg / kg; ig)+ NaCl (0,9%, ig); group III received ASP (75mg / kg ig) + DMSO (2%; ig) and group IV received AFB1 (250µg / kg; ig) + ASP (75mg / kg ig). After 14 days of treatment, the animals were euthanized and the cerebral cortex was removed for the analysis of ascorbic acid content, non-protein thiols (NPSH), antioxidant power of iron reduction (FRAP) and thiobarbituric acid reactive substances (TBARS). Data were analyzed by a two-way ANOVA, followed by Newman-Keuls. The protocol was approved by Animal Ethics Committee license number 3403220317 (CEUA-UFSM). **Results**: Exposure to AFB1 and ASP, alone or in combination have shown to induced oxidative stress. It has been shown increased TBARS in AFB1+ ASP group, when compared to control or AFB1 in the cerebral cortex of rats. Ascorbic acid, NPSH and FRAP levels were reduced in AFB1 + ASP group, when compared to control or AFB1. **Conclusion:** Association ofAFB1 + ASP for 14 days was able to cause neurotoxic effects evidenced by the reduction in the levels of antioxidant compounds in the cerebral cortex of the rats and increased TBARS levels. Further studies are needed to elucidate the effects of exposure to these compounds involving other protocolsin order to clarify the mechanisms involved in the toxic action promoted by this exposure. **References:** Abhilash, M., et al., Int J Toxicol, v. 33, p. 332, 2014 Ashok, I. et al., J Nutr Intermed Metab, v. 2, p. 76, 2015 Qureshi, H. et al., Med Mycol, v. 53, p. 409, 2015 Rushing, B. R. et al., *Food* Chem Toxicol*.*, v. 124, p. 81, 2018 Souto N. S. et al., World Mycotoxin J, v. 00, p. 1, 2019 Acknowledgments and Financial Support: CNPq, FAPERGS, CAPES

11.012 A study of the hypothalamic-pituitary-adrenal axis in depression and its genetic vulnerability. Pereira SC[1], Figaro-Drumond FV[2], Menezes IC[1], Baes CW[1], Coeli-Lacchini FB[3], Juruena MFP[4], Lacchini R[2] [1]FMRP-USP, [2]EERP-USP, [3]FCFRP-USP, [4]King´s College

Introduction: Depression is a chronic and incapacitating disease that leads to great personal and social prejudice. In most severe cases of depression, patients may try to commit suicide. Depression may be due to several factors, including early stress and genetic polymorphisms. Several studies suggest an important role of stress on Hypothalamic-Pituitary-Adrenal (HPA) axis hyperactivity and represent one of the most consistent pathophysiological findings in depressive disorders. This deregulation of the HPA axis can reduce the cortisol ability to exert negative feedback, which can lead to hypercortisolemia. We have studied the following genes: *HSD11B1*, *HSD11B2, NR3C1, NR3C2* and *MDR1*, which are genes responsible for cortisone conversion to cortisol and vice-versa, glucocorticoid and mineralocorticoid receptors and an efflux pump that transports cortisol, respectively. Thus, genetic polymorphisms may affect the risk of developing depression and the risk of suicide. The aim was to evaluate whether genotypes of genes in cortisol axis are associated with the risk for depression, with the severity of symptoms and with suicidal behavior. **Methods:** In this study it were included 130 depressives. All subjects was submitted a psychometric evaluation with the MINI Scale, GRID-HAMD-21 Scale, Infant Trauma Survey Questionnaire CTQ, and Beck Suicidal Ideation Scale (BSI). **Results:** Our **Results** showed a significant association of the genotype of the polymorphism (rs2070951) in the *NR3C2* gene with the severity of depressive symptoms (HAMD) (P= 0.03*); risk of suicidal ideation (BSI) (P= 0.01*) and in relation to the number of suicide attempts (P= 0.03*). In addition, a significant association of the genotype of the polymorphisms (rs11119328) in the *HSD1B1* gene was observed with the increased risk of at least one suicide attempt (odds ratio (OR): 10.80, P= 0.03*) and with euthymic humor after optimized pharmacological treatment (OR: 36.01, P= 0.04*). Finally, we also observed an association of the genotype of the polymorphism (rs1128503) in the *MDR1* gene with the number of suicide attempts (P=0.02*). **Conclusion:** The polymorphisms of genes involved on the HPA axis may be relevant biomarkers for detecting genetically vulnerable individuals to develop depression, commit suicide and achieve symptoms remission under pharmacological treatment. **Financial support:** Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES). Approved by the committee of ethicsof the University of São Paulo at Ribeirão Preto College of Nursing at CAAE 33001414.1.0000.5393

11.013 Population pharmacokinetics of magnesium sulfate in pregnant women with preeclampsia. Azeredo F[1], Costa T[2], Cunha MD[2], Ururahi M[2], Martins R[2], Oliveira A[2] [1]UFBA, [2]UFRN

Introduction: Magnesium sulfate is the drug of choice to treat seizures in preeclampsia, despite your extensive use, dosage and great concentration has not been conclusively established.The aim of this study was to develop a population pharmacokinetic (PK) model of magnesium sulfate in preeclampsia and determine key covariates that impact the pharmacokinetics. **Methods:** Prospective cohort performed in patients with PE in use of magnesium sulfate from June to February 2016-2018. Serum magnesium concentrations were obtained from 114 patients who received 4 g by injection of magnesium sulphate and subsequent infusion of 10 g in 1 g/h for 24 hours. Maternal blood samples were obtained before administration and after 2, 6, 12 and 18 hours of the initial dose. Population pharmacokinetic parameters of magnesium sulfate (clearance, volume of distribution, half-life) were estimated using the Monolix software ® 2018 Suite (Lixoft ®, Antony, France). A pharmacokinetic model including demographic, clinical and laboratory covariates of patients was developed. **Results:** The PK profile of magnesium sulfate was well characterized by a one-compartment model. The population clearance 1.38 L/h, volume of distribution 13.3 L and the baseline magnesium concentration was 0.77 mmol/L (1.87 mg/dL). The covariates weight and serum creatinine statistically influence the clearance and volume of magnesium distribution values, respectively. The model was parameterized as clearance (CL) and volume of distribution (V). **Conclusions**: The pharmacokinetics of magnesium sulfate in pregnant women with PE are significantly affected by creatinine and maternal weight. Pregnant women with PE and higher body weight have a higher volume of distribution and, consequently, a lower elimination rate of magnesium sulfate. Pregnant women with PE and higher serum creatinine value show lower clearance and, therefore, lower magnesium sulfate elimination rate. **Financial support**: CNPq. **Ethical Approval:** The present study was submitted to and approved by the Ethics and Research Committee of UFRN, according to determinations of Resolution 466/13 of the National Health Council, presenting CAAE with the following n No.: 49959215.8.0000.5292.

11.014 Limited sampling modeling for estimation of phenotypic metrics for CYP enzymes and the ABCB1 drug transporter using a cocktail approach. Ximenez JPB[1], Coelho EB[1], Cusinato DAC[1], Lanchote VL[1], Suarez-Kurtz G[2] [1]USP, [2]INCa
Introduction: Phenotyping for drug metabolizing enzymes and transporters using simultaneous administration of "cocktails" of selective probes is frequently adopted in drug interaction studies and pharmacogenetic trials. We applied limited sampling strategy (LSS) modeling to plasma concentration data from a trial in which a cocktail of subtherapeutic doses of selective probes was used to investigate the effects of a Brazilian green propolis formulation on the activity of CYP enzymes and the ABCB1 transporter. The trial was approved by the Human Research Ethical Committee of School of Pharmaceutical Sciences of Ribeirão Preto (ReBEC: RBR-9zmfs9). **Methods:** Plasma concentration data (n = 2640) from 16 healthy adults exposed twice to a drug cocktail comprising caffeine (probe for CYP1A2), metoprolol (CYP2D6), midazolam (CYP3A), omeprazole (CYP2C19) and fexofenadine (ABCB1) were used for LSS modeling of the area under the plasma concentration versus time curve between 0 and 12 hours (AUC0-12h) of caffeine, fexofenadine and midazolam and the ratio of the AUC0-12h of metoprolol: alfa-OH metoprolol and omeprazole/5-OH omeprazole. Data from the first exposure to the cocktail were used for development of LSS models, while the data from the second dose were used for model validation. Computations were performed using function leaps to generate linear regression equations, which were ranked according to the correlation coefficient (R2) between the LSS-derived metrics and the parameters´ best estimates, obtained using all plasma concentration data points. **Results:** The LSS modeling disclosed single time-points which provided accurate (R2 > 0.95) estimates of the AUC0-12h ratios for metoprolol: alfa-OH metoprolol and omeprazole: 5-OH omeprazole. This supports the adoption of single point metabolic ratios for metoprolol and omeprazole as reliable parameters of CYP2D6 and CYP2C19 activity, respectively. For the other drug probes, namely caffeine, fexofenadine and midazolam, 2-timed samples were required to obtain predictions of the respective phenotypic metrics, with R2 > 0.95. Although the most informative time points differed among the drug probes, LSS models based on paired samples collected at 90 and 120 min or 90 and 240 min provided R2 values in the range of 0.88 to 1.0 for their respective phenotypic metrics in the development cohort. Increasing the number of sampling points to three led to relatively minor increases in R2 and/or reductions in the bias or precision of the estimates. Validation tests confirmed the robustness of the 2-point LSS models over wide ranges (>5 fold) of phenotypic metrics´ values.**Conclusion:** We suggest that the validated LSS models are appropriate for predicting phenotypic indices for CYP1A2, CYP2C19, CYP2D6 CYP3A and the ABCB1 transporter, using subtherapeutic doses of caffeine, omeprazole, metoprolol, midazolam and fexofenadine, respectively. **Financial support:** This project was funded by CNPQ, FAPESP and FAPERJ.

11.015 Pharmacokinetic assessment of two formulations of the anticancer drug Tamoxifen. Suarez-Kurtz G[1], Ximenez JPB[2], Bello MA[1], Obadia RM[1], Iocken FHS[1], Lanchote VL[2] [1]INCa, [2]USP

Introduction: Tamoxifen (TAM), a selective estrogen receptor modulator, used for treatment and prevention of breast cancer, is a pro-drug which undergoes extensive liver metabolism by cytochrome P450 enzymes, leading to the major active metabolite, endoxifen (END), and to N-desmethyltamoxifen (NDTAM) and 4-OH tamoxifen (4OHTAM). At the Instituto Nacional de Câncer (INCA), generic formulations, rather thereferenceTAM formulation (Nolvadex®) are routinely used. Bioequivalence between generic and reference oral formulations is conventionally assessed by pharmacokinetic metrics following single dose administration. This does not reproduce the usual dosing protocol of TAM in breast cancer patients, which consists of daily administrations for prolonged (up to 5 years) periods. The present study was designed to compare the plasma exposure of patients to TAM and its main metabolites during, repeated, stable administration of either the generic formulation in current use at INCa versus the reference formulation. **Methods:** The study protocol was approved by the Ethics Committee of INCa (CAAE 50456015.3.0000.5274). Breast cancer patients (n = 30) under daily treatment with TAM (20 mg p.o.) were recruited and consented to participate. A bracketed protocol, comprising 3 successive phases, each lasting 30 days was adopted: in phases 1 and 3, a generic TAM formulation was used, whereas the reference formulation was used in phase 2. Between days 27 and 30 of each phase, two blood samples were collected at 24-48 h intervals, for quantification of the plasma concentrations of tamoxifen and its metabolites by LC-MS/MS. The timing of the blood sampling assured that the concentrations of TAM and metabolites in plasma reached a steady-state. ANOVA was used for statistical analysis of the plasma concentration data. Statistical significance was set at p-value <0.05. **Results:** All patients completed the study protocol. The plasma concentrations of TAM in phase 2 (reference formulation) ranged between 43.5 – 240.9 ng/ml (mean 135.0; IC95% 114.2 - 155.8 ng/ml). The corresponding values for the TAM metabolites were: END, 10.3 - 71.3, 35.3, 30.0 - 40.8 ng/ml; 4OHTAM, 2.0 - 8.3, 4.8, 4. 2 - 5.4; NDTAM, 365 – 1709, 914, 791 – 1137 ng/ml. ANOVA showed no statistically significant difference between the plasma concentration of TAM and its metabolites in phase 2 versus phases 1 and 3**. Conclusion.** Despite the considerable range (4 – 6 fold) of variation in steady-state plasma concentrations of TAM and its metabolites, no statistically significant differences were observed between the reference and the generic formulations assessed. This conclusion is reinforced by the bracketed protocol adopted. **Financial support:** This project was funded by CNPQ and FAPERJ.

11.016 Validation of bioanalytical methodology and pharmacokinetic evaluation of Amphotericin B in Wistar rats. Araújo JMS, Azeredo F, Santos VV, Pereira LC, Gomes CA UFBA

Introduction: Due to the low drug options for candidemia's treatment, Amphotericin B(AmB) has been the drug of first choice for the treatment of the referred disease, even with its high toxic effects. Some studies show that AmB exerts interesting modulatory effects, interfering in many of the properties of leukocytes, such as in inhibiting chemotaxis, in producing antibodies, in the functional properties of leukocytes, in significantly decreasing phagocytosis and, specially, by killing *Candida* spp. In this context, this study aims to quantify plasma AmB concentrations in Wistar rats by validating a bioanalytical method and AmB pharmacokinetic evaluation. **Methods:** This validation was performed analyzing plasma concentrations of AmB after administration of 1mg/kg i.v. in Wistar rats (n = 4) (CEUA/UFBA 026/2018) using the High Efficiency Liquid Chromatography coupled to the ultraviolet-visible detector (HPLC/UV-Vis) and performing noncompartmental analysis. **Results:** After performing the plasma concentration analysis of AmB in rats it is possible to perceive that the samples had similar pharmacokinetic characteristics in comparison with the literature for the administration of 1mg/kg so that the elimination constant (ke) values were 0.04 h-1 ± 0.01, generating a half-life (t1/2) of 27h ± 23.3, distribution volume (Vd) of 0.23L/kg ± 0.12, clearance (Cl) of 0.02L/h/kg ± 0.008, area under curve (AUC) of 56360 ng.h/mL ± 27936, and mean residence time (MRT) of 11,7h ± 5.3. The bioanalytical method was linear in the working range of 250-8000 ng/mL, R^2 = 0.9967, achieving precision and accuracy lower than 20% for the lower limit of quantification and less than 15% for the other concentrations in the bioanalytical method. **Conclusions:** No other substance was detected, guaranteeing the specificity of the method, which was validated, being selective, accurate and accurate for AmB quantification. In addition, the method has been proven to be capable ofevaluating Pharmacokinetics of AmB. **Keywords:** Amphotericin B. *Candida albicans*. Pharmacokinetics. **Financial Support**: PROPCI-UFBA and Fapesb.

11.017 Non-clinical toxicity of the cashew gum (**a complex heteropolysaccharide extracted from the exudate of** *Anacardium occidentale* **L**.): **Absence of adverse effects in Swiss mice**. Oliveira ACP, Costa BNC, Araújo TSL, Pacheco G, Chaves LS, Pinho SS, Araújo AKS, Santos ES, Silva PC, Medeiros JVR UFPI

Introduction: With the biotechnological advances, natural products have become the largest source of inputs with applicability in the industry, mainly pharmaceutical.A product with great economic value and that has been gaining prominence due to its diverse applicability is the plant *Anacardium occidentale L*. (family: *Anacardiaceae*), better known as cashew tree. Among the various materials obtained from cashew tree, cashew gum (GC) has been outstanding for its numerous pharmacological applications.The present work aimed to evaluate the acute toxicity of cashew gum, a complex heteropolysaccharide extracted from the exudate of *Anacardium occidentale L*.**Methods:** The procedures were carried out according to accepted standards for the use of animals in research projects of BCOAE (Brazilian College of Animal Experimentation). The experiment followed the OECD 423 specifications governing in vivo toxicity tests. During the experimental procedure the animals received a dosage of 2000 mg / kg of the purified GC and were evaluated for 14 days following the parameters of the Hippocratic *screening*. On the fifteenth day the animals were anesthetized, and blood was withdrawn by cardiac puncture, for the biochemical and hematological analyzes. Then these animals were euthanized, and some organs removed for histological evaluation. **Results:** Among the results, it was possible to demonstrate that the CG did not show signs of intoxication, nor did it affect motor, physiological or behavioral changes in the administered dosage of 2000mg / kg.In this study, there were no significant alterations in the weight and macroscopic analyzes of the organs, nor in the evaluated masses. In our tests there were no significant changes in any of the parameters measured, thus highlighting the safety of the compound. **Conclusion:** The LD50 value for oral GC administration was estimated to be greater than 2000 mg / kg and could be classified as Class 5 toxicity according to GHS and considered to be of low toxicity. **Financial support:** CAPES/CNPq/FAPEPI-UFPI. **License number of ethics committee:** CEAU-UFPI 068/14.

11.018 Evaluation of the importance of therapeutic drug monitoring in a Teaching Hospital in Salvador- BA. Santos LO, Carneiro TLGO, Noblat LACB, Azeredo F UFBA **Introduction**: Therapeutic drug monitoring (TDM) is a technique that is based on the individualized and safe therapy of the patient, aiming to measure the pharmacological effects and plasma concentration of drugs according to their concentration in the action sites. This study aims to demonstrate the importance of TDM in patients who use digoxin and carbamazepine - drugs with a narrow therapeutic window to ensure that the plasma concentrations of these drugs are the main markers for assessing the safety and effectiveness of treatment through quantification and analysis of serum drug levels. **Methods**: Data from this study were extracted from electronic medical records of patients who had been admitted to the institution using digoxin or carbamazepine. For statistical analysis, it was used the software Excel and the ANOVA test was performed followed by the Student t test to compare the reasons that were extracted in the data collection. Values of $p < 0.05$ were considered statistically significant. **Results**: A total of 50 patients had serum digoxin, ages ranged from 4 years to 98 years, and the median age was 70 years among participants. The second group of the study were 50 patients on carbamazepine treatment, ages ranged from 7 to 87 years and median age was 18 years. In order to evaluate the plasma concentrations of digoxin and carbamazepine, the **Results** extracted were subdivided in three groups: underdose, overdose and normal dose, with reference to the therapeutic window of each drug under study. In the digoxin group, 23 patients (46%) had an ideal plasma concentration (> 0.8mg/dL and <2.0mg/dL), a total of 27 patients had plasma concentration outside the therapeutic window - 17 patients (34%; n = 50) had underdose and 10 patients (20%; n = 50) had serum levels of digoxin above the reference value and were considered a toxic dose. In the carbamazepine group, 20 patients (40%) had the ideal serum concentration (> 4ug/mL and <10ug/mL), with 30 patients with the therapeutic range outside the reference value - 17 patients (34%; n = 50) had underdose and 13 patients (26%; n = 50) presented a toxic dose. This fact makes evident the necessity of a care service that aims at the safety of the pharmacotherapy of patients receiving digoxin and carbamazepine in this institution, since the ideal serum concentration reached less than half of the patients who were treated with both drugs, more than 50% of the analyzed patients had the plasma concentration of the drugs outside the therapeutic window recommended in the literature. **Conclusion:** Therefore, a responsible service for understanding pharmacokinetics and dose accuracy is essential in clinical practice, given the diversity among individuals, which will contribute to better care for patients who currently lack this service in the hospital and in first aid post.

11.019 The importance of primary care and strategies used to improve adhesion to tuberculosis treatment. Brandão CM, Fernandes G, Azeredo F UFBA

Introduction: Tuberculosis (TB) is a serious public health problem in Brazil and avoiding treatment abandonment is one of the most important challenges, especially for Primary Health Care (PHC) professionals, as it is the health service where a patient with TB symptoms has her first contact and is followed throughout the treatment. This study is a descriptive observational one conducted at the Professor Bezerra Lopes Health Center, located in the city of Salvador, Bahia, in order to describe and analyze the main strategies used in the unit to improve patients' adherence to treatment and to know the main factors related to abandonment. **Methods**: Two instruments were used for data collection, an interview script employed by the pharmacist who works in the program and document analysis. For the documental analysis we used the patient record book and treatment follow-up of tuberculosis cases, in order to obtain the list of patients treated by the program in 2014, 2015 and 2016 and the pharmacotherapeutic follow-up form, only of patients who abandoned treatment to understand their profile and study the best treatment adherence strategies. Data were collected such as patient identification, occupation / income, drug usage, adverse drug reactions, treatment time and other associated comorbidities. **Results**: The study population consisted of 236 patients enrolled in the Tuberculosis Program from 2014 to 2016, of which 11 were discharged due to abandonment. Among the main factors associated with dropout found are the use of alcohol and illicit drugs, unemployment and feeling of cure after symptom improvement. As strategies used are frequent returns coupled with a good patient reception in the health unit as well as support to psychological, economic and nutritional issues such as distribution of basic baskets and the active search for missing patients. CONCLUSION: The study contributed with relevant information to better understand the profile of patients who abandon treatment and thus establish strategies for the proper control of tuberculosis in Salvador. Finally, it is expected that the results obtained with this study may contribute to the decision-making of health professionals aiming to improve the tuberculosis control program.