10. Cancer Pharmacology

10.001 Evaluation of the toxicities presented by patients with lung cancer treated with carboplatin and paclitaxel. Seguin CS[1], Vasconcelos P[1], Cursino M[1], Bastos L[1], Vaz C[1], Quintanilha J[1], Barbeiro A[1], Zambom L[1], Perroud Jr M[1], Moriel P[1], Pincinato E[2]
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Introduction: Cancer is one of the leading causes of death worldwide, currently more than 32 million people live with this disease, with lung cancer being the second most common in men and women in Brazil. It is estimated that by 2020 there will be more than 2.2 and 1.9 million new cases and deaths, respectively. Lung carcinoma is the leading cause of cancer-related morbidity and mortality in the world, smoking and passive exposure to tobacco being important risk factors for the development of lung cancer. In about 85% of the diagnosed cases, lung cancer is associated with the consumption of tobacco derivatives. Although the risk factors for the development of lung neoplasm are well known,about 75% of patients present the disease locally advanced or metastatic at the time of diagnosis, the reason being the lack of effective **Methods** for an early diagnosis. The main therapeutic agents used for treatment of this carcinoma are platinum-derived chemotherapeutics associated with other chemotherapeutic agents. The aim of this study isto evaluate the prevalence of major toxicities resulting from treatment with carboplatin and paclitaxel in patients with lung cancer treated at hospital of clinics of UNICAMP **Methods:** This is a clinical and observational study that is being carried out at the Clinics Hospital of Unicamp, which started in March 2018. This work has been approved by the Ethics Committee CEP n° 83196318.8.0000.5404. Blood is collected from patients prior to initiation of treatment before and after 15 and 20 days of chemotherapy sessions for toxicity analysis. The toxicities evaluated in this study are: nephrotoxicity (increased serum creatinine, decrease creatinine clearance, hypocalcemia, hypomagnesemia, hyponatremia, hypokalemia, hypophosphatemia and hyperuricemia), gastrointestinal toxicities (nausea, vomiting and diarrhea), hepatotoxicity (increased total bilirubin, increased alkaline phosphatase (FALC), increased aspartate aminotransferase (AST), increased alanine aminotransferase (ALT), and increased total protein) and hematological toxicity (anemia, leukopenia, neutropenia, lymphocytopenia and thrombocytopenia). All toxicities are classified according to the Common Toxicity criterial (CTCAE-version4). **Results:** In this study, up until the present, nineteen patients were included. Regarding the socio-demographic data, the average of age, education and income are: 63,8 years old, 5,6 years, 2.1 minimum wage, respectively. The patients are mostly women (64%), Caucasian (94%), married (53%), retired (42%), heavy smokers (47%), alcohol abstemious (47%), with performance status 100 (68%) with the histological type epidermoid carcinoma (52,6%).Toxicity occurrences were observed in all evaluated parameters, but at high grades (2-3), they appeared in particular in hematological parameters evidenced by neutropenia (7,7%), leukopenia (7,7%) and lymphocytopenia (15,4%).**Conclusion:** A high prevalence of toxicities was observed after chemotherapy with carboplatin and paclitexel, hematological toxicity being the most pronounced in patients with lung cancer treated at Hospital of Clinics of Unicamp.Financial Support: CAPES and MackenzieUniversity.

10.002 Evidence of interaction in the association of *Matricaria recutita* and 5-Fluorouracil on toxicological and histomorphological analysis in mice with cancer. Santos SA[1], Amaral RG[1], Menezes Filho RO[1], Graca AS[1], Mendes Neto JM[1], Andrade LN[1], Albuquerque Júnior RLC[2], Pereira Filho RN[2], Gomes SVF[2], Santos SL[1], Carvalho AA[1] [1]UFS, [2]Unit

Introduction: Popular knowledge provides a basis for the use of plants with antitumor potential and many patients associate their use with standard cancer treatments, but the existence of possible drug interactions may occur. Infusions of the medicinal plant *Matricaria recutita* (Chamomile) have been used in association with chemotherapy in the treatment of cancer, as observed by Caetano et al. (J. Health Biol. Sci., v. 5, p.163, 2018) in a study performed at private oncology clinics in the state of Sergipe. Therefore the aim of this study was to evaluate theeffect of Aqueous Extract of *Matricaria recutita* (AEMR) associated with 5-fluorouracil (5-FU)in animals transplanted with tumor Sarcoma 180 (S180).**Methods:** Animals transplanted with S180 ($2x10^6$ cells/0.5 mL, subcutaneous) were used. Mice were separated in six groups (n=7/group): vehicle (distilled water, gavage), 5-FU (25mg/kg/day, intraperitoneal), AEMR (100mg/kg/day, gavage), AEMR (200mg/kg/day, gavage),AEMR (100mg/kg/day, gavage) + 5-FU (25mg/kg/day, intraperitoneal)and AEMR (200mg/kg/day, gavage) + 5-FU (25mg/kg/day, intraperitoneal), treated and weighed daily (1x/day) for 7 consecutive days. After 24 hours of the last day of treatment the animals were anesthetized, the blood collected via the retro-orbital plexus and performed the following toxicological tests: biochemical analyzes (Aspartate transaminase - AST, Alanine transaminase - ALT, urea and creatinine);hematological analyses(hemoglobin - HB, hematocrit - HEM, hematocrit - HT, platelet counts - PLT and total leukocyte counts), analysis of body mass variation andafter euthanized animals were removed liver, spleen and kidney to analyze the mass of the organs. Histomorphological analysis was performed on the organs removed and tumor by hematoxylin / eosin staining method. **Results**:In the biochemical analysis it was observed that the groups treated in association showed ($p < 0.05$) of a decrease in AST levels without significant alterations in ALT, urea and creatinine. In hematological parameters, it was observed that the associated groups showed reduction of platelets and leukocytes similarly to the 5-FU group alone, and there was no potentiation of myelosuppression in these groups. The other hematological parameters showed no alterations ($p > 0.05$). There was reduction of body mass from the 3rd day of treatment in groups associated with apparent diarrhea. Spleen atrophy was observed in the 5-FU and associated groups. Histopathological analyzes showed reduction of mitoses and presence of apoptotic areas in excised tumors of the associated groups. There was also a reduction in spleen extension in the associated groups. **Conclusion:** The results suggest that the association between AEMR and 5-FU did not intensify myelosuppression, but intensified some adverse effects, such as weight loss and diarrhea, in addition to histopathological changes in the spleen and tumor of the associated groups. **License number of ethics committee**: 60/2016. **Financial support**: FAPITEC and CAPES.

10.003 Benefits of the FFA1 and FFA4 receptors modulation in a pre-clinical model of cancer associated cachexia. Freitas RDS, Muradás TC, Dagnino AP, Greggio S, Venturin G, Costa J, Campos MM PUC-RS

Introduction: Cancer cachexia (CC) is a metabolic wasting syndrome that leads to impaired quality of life (Argiles et al., Nat Rev Endocrinol;5:9, 2019). Free fatty acid (FFA) receptors have been investigated as pharmacological targets for metabolic diseases. So far, their role in CC remains to be investigated (Ulven & Christiansen. Annu Rev Nutri; 35;239, 2015). We previously demonstrated that treatment with the dual FFA1/FFA4 agonist GW9508 improved behavioral impairments and adiposity levels in cachectic mice (Freitas et al., 2018. 50th Brazilian Congress of Pharmacology and Experimental Therapeutics). This study investigated further mechanisms underlying GW9508 effects in a mouse model of lung CC. **Methods:** The Animal Ethics Committee (PUCRS/CEUA 7164) approved the experimental protocols. Lewis lung carcinoma (LLC) cells were cultured under standard conditions. On day 0, the cells were resuspended at 5 x 106/100 µL of phosphate-buffered saline (PBS) and injected subcutaneously (s.c.) in the right flank of C57BL/6jUnib male mice (20-15g; 8-10 weeks old). Mice were divided into three groups: tumor-free control + PBS; LLC + PBS; LLC + GW9508 (8 mg/kg; every other day, s.c.). After 21 days, mice were euthanized. Serum, epididymal (epWAT), retroperitoneal (rWAT) and intrascapular (isWAT) adipose tissues were isolated for further analysis. Brain glucose metabolism was assessed by microPET scanning analysis, with intravenous administration of 18F-[FDG]. **Results:** LLC-mice treated with GW9508 showed elevated serum leptin levels, when compared to tumor-free and LLC-controls ($P<0.05$). The isWAT and epWAT adipocyte area did not display any alterations among the experimental groups. However, epWAT adipocyte area frequency distribution showed a higher frequency of smaller adipocytes in GW9508-treated group, compared with LLC-controls ($P<0.05$). In rWAT, LLC-bearing mice showed a reduced adipocyte area, regardless of GW9508 treatment ($P<0.05$). In the adipocyte area frequency distribution, rWAT from LLC-bearing mice treated with GW9508 showed a higher frequency of smaller adipocytes, compared to control groups ($P<0.05$). LLC-injected mice displayed an upregulation of FFA1, but not FFA4, in isWAT ($P<0.05$). The uncoupling protein (UCP)-1 protein expression was downregulated in epWAT from LLC-cachectic mice, regardless of GW9508 treatment ($P<0.05$). In microPET scanning, the striatum, cortex, left hypothalamus, thalamus, superior colliculus and right inferior colliculus presented a significant hypometabolism in LLC-hosts ($P<0.05$), an effect that was recovered by GW9508. **Conclusion:** FFA1/FFA4 receptors likely participate in peripheral and central cachexia alterations. FFA1 upregulation in isWAT might indicate an important role for this receptor in the regulation of lipolysis. It is tempting to suggest that the dual modulation of FFA1/FFA4 receptors is a promising pharmacological tool for CC management. **Financial Support:** CAPES (Financial code 001), CNPq.

10.004 The antitumor potential of polysaccharide extracted of *Anacardium occidentale* **L. stem**. Barros AB[1], Araújo AJ[1], Oliveira TM[1], Iles B[1], Medeiros JVR[1], Silva DA[1], Moura AF[1], Moraes Filho MO[2], Marinho Filho JDB[1] [1]UFPI, [2]UFC

Cancer is characterized by a group of diseases related to the disordered growth of the cells, which invade tissues and organs. Several new drugs, derived from plants, algae, microorganisms and other sources, have been investigated due to their potential to treat different types of cancer. Polysaccharides extracted from plants have innumerable applications described in the literature, such as antibacterial, antifungal, antioxidant and antitumor activities, *in vitro* and *in vivo*. However, the antitumor effects of these polysaccharides are not fully elucidated yet. This study aimed to evaluate the antitumor potential of the cashew gum, through *in vitro* and *in vivo* models. The cashew gum did not demonstrate cytotoxic and antimigratory activity *in vitro* in murine and human tumor cells at the concentration of 100 µg / ml. *In vivo* assays showed that cashew gum was able to inhibit in 35% and 40% the tumor growth in murine metastatic melanoma (B16F-10), at doses of 50 and 100 mg / kg, respectively. In addition, the polysaccharide does not decrease the weight of the animals, since it is composed basically of sugar chains. Regarding hematological components, cashew gum did not cause leucopenia, and not significant hematological alterations, demonstrating that this polymer does not cause depletion of the immune system of the animal. Histological sections of the organs have shown that cashew gum did not caused toxic lesions in the liver, kidney, lung and spleen. Tumor slices indicated a cell death process indicative of apoptosis in treatment with cashew gum. The analysis of the tumor tissue by FTIR indicated a similar death process in treatments with cyclophosphamide and cashew gum, by the stretching of lipids representative bands, and groups present in the DNA. With regard to the analysis of enzymatic and non-enzymatic antioxidant components (GSH, MDA and MPO), Cashew gum did not indicate the production of these antioxidant agents, possibly demonstrating that this polymer does not cause tissue oxidative stress. Therefore, it is concluded that this polysaccharide could help in the treatment of neoplasias, by possibly reducing the side effects generated by the chemotherapeutic, besides helping in the tumor reduction.
Supported by: CNPq, CAPES, FAPEPI and INCT BioNat. **Keywords:** Polysaccharides. Cashew gum. Antitumor. Cancer.

1010.005 *In vivo* **and** *in vitro* **antineoplastic effect against mammary cancer of polysaccharides extracted from sweet green pepper** (*Capsicum annuum* (**CAP**). Adami ER, Acco A, Corso CR, Turin-Oliveira NM, Galindo C, Stipp MC, Dittrich RL, Telles JEQ, Klassen G, Cavaliere E, Cordeiro LMC, Silva LM, Milani L UFPR

Introduction: Breast cancer represents a public health problem, as it is the most incident in women. The treatment involves chemotherapy with cytotoxic drugs that cause several side effects. Therefore, new antineoplastic agents are required. **Methods**: This study was approved by the local Ethics Committee for Animal Use (CEUA/BIO – UFPR, # 1063) in order to investigated the antineoplastic effects of polysaccharides from sweet green pepper (*Capsicum annuum (*CAP) in mice with Ehrlich tumor in 3 protocols *in vivo*: (a) Conventional (21 days), (b) Long treatment (LT, 31 days) and (c) Associated with methotrexate (CAP+MTX, 21 days).CAP was also tested in vitro in human mammary tumor cells (MCF-7, MDA-MB-231 and MDA-MB-436). The action mechanisms regarding oxidative stress, inflammation, angiogenesis, apoptosis and cell cycle were investigated. **Results:** The results of the (a) Conventional protocol showed that CAP, at the three doses tested (50, 100 and 150 mg kg^{-1}) was able to reduce the tumor volume by 28%, 40% and 54%, respectively, while the positive control Methotrexate (MTX 2.5 mg kg^{-1}, via i.p.) reduced tumor volume by 85%. Thereafter, a dose of 100 mg kg^{-1} CAP was chosen for the next protocols and techniques. CAP treatment increased IL-6 tumor levels, but did not alter MPO, NAG, Nitrite, TNF-α, IL-10 and IL-4 levels in tumor. CAP did not alter the expression of apoptosis-related genes (Bcl-2, Bax and Caspase-8) and cell proliferation (Cyclin D1) in the tumor tissue, but reduced the expression of Vegf by 40% when compared to the Vehicle.This result was confirmed by the reduction of vessel area in the histological sections of the tumor. CAP did not alter oxidative stress parameters in the tumor, nor did it show antioxidant effects in vitro in the DPPH test, demonstrating that its mechanism of action does not involve the redox pathway. The protocol (b) LT, which started 10 days prior to inoculation of Ehrlich tumor cells and persisted for up to 21 days thereafter, also reduced the tumor development by 91%, increased tumor levels of IL-6 (85%) and MPO (37%), reduced IL-10 (95%) and IL-4 (94%), and reduced the gene expression of Vegf (55%) and the vascular area (47%) in the tumor. In protocol (c) CAP + MTX treatment reduced the tumor development in 95%, elevated tumor levels of IL-6 (702%) and TNF-α (390%), and decreased the levels of Nitrite (62%), IL-10 (57%), IL-4 (85%), the Vegf expression (43%) and the vascular area (48%) in tumors. CAP slightly induced variation at hematological parameters, but not at plasma biochemistry. In parallel, CAP acted in vitro reducing cell colonies of human tumor lineages MCF-7, MDA-MB-231 and MDA-MB-436, but had less effect upon non-tumor mammary HB4a cells. CAP also reduced VEGF gene expression in MCF-7 and MDA-MB-436 cells, but not in MDA-MB-231 cells, a triple-negative and aggressive cell lineage. CAP+MTX association decreased the viability of MDA-MB-231 and MDA-MB-436 cells more significantly when compared to both compounds isolated. Conclusions: CAP has an antineoplastic effect against mammary tumor cells, since it was able to reduce the tumor volume in three protocols tested in vivo. Additionally, CAP reduced the viability of human mammary gland tumor cells in vitro. Its antineoplastic mechanism seems to depend on the regulation of inflammation and angiogenesis, triggering necrosis in tumor cells. CAP is promising as adjuvant therapy in the treatment of breast tumors, both isolated or combined with chemotherapy. Financial support: CAPES, CNPQ.

10.006 Gedunin Effect on Glioblastoma Progression. Costa TEMM[1], Seito LN[1], Krahe TE[2], Henriques MG[1], Penido C[1] [1]Fiocruz, [2]UERJ
Introduction: Glioblastoma is the most common highly aggressive primary tumor in the central nervous system. Glioblastoma treatment is challenging because of its invasive behavior and resistance to existing therapies. The standard protocol used is tumor resection followed by radiotherapy and chemotherapy temozolomide (Stupp protocol), that results in a survival time of approximately 14 months. Heat Shock Protein 90 (Hsp90) is a molecular chaperone that regulates the folding and maturation of its client's proteins in normal cells. During stress conditions as well as in tumor cells, HSP90 is overexpressed. In fact, several oncoproteins are among its client proteins. Gedunin is a naturally occurring limonoid that exhibits in vitro and in vivo cytotoxic activity against different tumor types. Indeed, gedun in antitumor effect relies on its ability to inhibit Hsp90 activity, by binding to its p23, destabilizing the multichaperone complex. In the present study, we evaluated the antitumor activity of gedunin on murine glioblastoma GL261 cell line. **Methods**: GL261 cell line ($2x10^5$/well) were seeded on 24 well plate and treated with gedunin (100 –6.25µM), or with the selective HSP90 inhibitor 17-N-allylamino-17-demethoxygeldanamycin (17-AAG, 1µM)for 24, 48 and 72h. Vascular endothelial growth factor (VEGF) levels were evaluated in the supernatant, by ELISA. Phosphoinositide 3-kinase (PI3K), protein kinase B (Akt/PKB), Signal Transduction Activator of Transcription 3 (STAT3) and caspase-3 expressions were evaluated in cell lysates by western blot. MMP-2 activity was evaluated on a serum free GL261 supernatant zymography. GL261 invasiveness was evaluated by Scratch Assay. Cytotoxic effect of gedunin incubation on GL261 was measured by MTT reduction method. Cell proliferation, apoptosis and cell cycle were evaluated by flow cytometry. **Results:** Gedunin has in vitro anti-GL261 activity, reducing cell proliferation and related proteins expressionsuch as PI3K.It also induces apoptosis in a concentration-dependent manner as well as acted on the release of factors involved in tumor progression VEGF and MMP-2. **Conclusion:** Gedunin has antitumoral activity against glioblastoma GL261 cells by inducing cell death am decreasing growth and invasiveness in vitro.
Financial support: CAPES, CNPq, Farmanguinhos, Fiocruz.

10.007 NQO1 enzyme and cancer: **Scientific and technological mapping**. Costa PMS, Paier CRK, Oliveira FCE, Rebouças LV, Silva MFS, Pessoa C UFC

Cancer is one of the most complexes diseases affecting thousands of people every year and has high mortality rates. Pharmacological treatment of this disease causes several side effects and is very unspecific (FERLAY, J. et al. Int. J. of Cancer, vol 136(5), p359, 2014). In this sense, therapeutic alternatives needs to be developed to ensure a safer and more effective treatment with fewer side effects. NAD(P)H dehydrogenase quinone 1 (NQO1) is a cytosolic enzyme that arouses considerable interest as cancer target because it is over expressed in some types of tumors such as lung, pancreas and prostate (MARIN, A. et al. Br. J. Cancer, vol 76, p923, 1997; DONG, Y. et al. Clin. Cancer Res., vol 15, p131, 2009). This work aimed to map the state of scientific and technological development of the enzyme NQO1 in the context of cancer. **Methods**: A survey of patents and scientific articles published during the period from June/2009 to June/2019 using the descriptors: “NQO1”, “NQO1 e cancer” or “NQO1 and cancer”, “NQO1 e neoplasia” or “NQO1 and neoplasm”. Patents were consulted at the National Patent Institute (INPI), European Patent Office (Espacenet), United States Patent and Trademark Office (USPTO) and United States Patent and Trademark Office (WIPO). The articles were mapped to the Pubmed, Web of Science and Science Direct databases, and those containing the descriptors in the title or abstract, and the first page for the WIPO database were considered valid. Survey was realized in June 2019. **Results:** The WIPO patent bank presented the largest number of records of deposits related to the term “NQO1” (107), as well as for the term “NQO1 and cancer” (32). According to the International Patent Classification (ICP), the category with the highest deposit records was "preparations for medical, dental or hygienic purposes" (18) followed by measurement or assay procedures involving enzymes, nucleic acids or microorganisms (8). The number of patents per country, considering the term “NQO1 and Cancer”, the United States had the highest number of patents registered (15), followed by China (8). Regarding the scientific publications, Pubmed had the largest number of documents related to the descriptor “NQO1” (2152, on average 197 articles/year) while Web of Science had largest number for the descriptor “NQO1 and cancer” (841, on average 82 articles/year). **Conclusion:** Enzyme NQO1 has a high potential for application in the scientific and technological development related to cancer, especially in generation of products for medical purposes. Acknowledgements/Financial support: CAPES; FUNCAP

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10.008 Synthesis and antiproliferative activity of novel derivates of alpha-lapachone on tumor cell lines. Lima DJB[1], Pessoa C[1], Silva Júnior EN[2], Valença W[2], Rebouças LV[1], Costa PMS[1] [1]UFC, [2]UFMG

Introduction: Cancer is a set of proliferative diseases, which has become a growing public health problem worldwide (Hartmann, L. et al., N Engl J Med, vol 353, p229, 2005). Brazilian biodiversity, coupled with the search for more selective therapies, has inspired the advancement of pharmacological strategies to seek substances derived from natural molecules and modify them, thus expanding the therapeutic arsenal and improving its activity (Newman, DJ Braz. Chem. Soc. Vol 28, p402, 2017). Quinones are metabolites of wide distribution in nature that have several pharmacological activities of clinical importance (Monks, JT et al., Curr Drug Metab, vol 3, p425, 2002). In this context, α-lapachone naphthoquinone, a prototype for the development of substances with anticancer properties (Garkavtseva, I. et al., PNAS, vol 108, p11596, 2011), was used to origin analogous molecules, aiming to compare and establish their antiproliferative activity. **Methods**: 8 novel molecules derived from reactions between α-lapachone naphthoquinone and calcogen-coupled alkynes (Se and S) were synthesized via copper (I) catalyzed click reactions. The antiproliferative activity of the samples was established by the MTT method, for an incubation period of 72h, against 5 tumor lines: PC-3 (prostate carcinoma), HCT-116 (colon carcinoma), NCI-460 lung), SNB-19 (glioblastoma), and RAJI (Burkitt's lymphoma) and a non-tumoral cell line: L929 (murine fibroblast) for selectivity index to be accessed. The molecules were tested at the maximum concentration of 20 μM. **Results:** IC50 values (inhibitory concentration of 50% of cell growth) were obtained ranging from 2.10 to <20μm among the tested analogues. Best activity was observed in HCT-116 and lower in NCI-460 cells. Sample 037 presented relevant activity in practically all tested strains and also a higher selectivity index (6.5x). That analog showed antiproliferative activity superior to the molecule of origin, α-lapachone. **Conclusion:** From 8 novel analogues of α-lapachone, the molecule 037 presented a relevant antiproliferative activity in relation to the positive control, and a remarkable index of selectivity comparing to the lineage of colorectal cancer. Future perspectives include trials to establish the mechanisms of action. Acknowledgments/ Financial support: CNPq, CAPES, FUNCAP

10.009 Prospection of new synthetic molecules and determination of anticancer effect of a new synthetic chalcone-sulfonamide (**CSS185**). Moura AF[1], Araújo AJ[1], Marinho Filho JDB[1], Santos MCL[2], Silva MFS[2], Oliveira FCE[2], Castro MRC[3], Peres CN[3], Pessoa C[2], Moraes Filho MO[2] [1]UFPI, [2]UFC, [3]UFG

Introduction: Cancer is a complex diseases characterized by the uncontrolled growth of abnormal cells with high invasive potential and is considered a global public health problem(WEINBERG, 2013). The incidence of cancer has increased every year, showing the relevance in conducting research on cancer treatment in its various modalities. New chalcones have been developed from the insertion of organic groups, among them sulfonamides. The anticancer effect of some chalcone-sulfonamides have been described, however, few studies have described the cytotoxic mechanism of action of these molecules (LEE et al, 2010; SILVA et al., 2015; EJAZ et al., 2017). With this, the aim of this study was to determine the cytotoxicpotential of new synthetic chalcone-sulfonamides and the mechanisms involved in the antiproliferative activity of synthetic chalcone-sulfonamide 185 (CSS185). **Methods:** Four synthetic chalcone-sulfonamides with similar molecular structure were tested against tumor cell lines to evaluate the cytotoxic potential of these molecules using MTT assay.Among them, chalcone-sulfonamide 185 (CSS185)was selected for further investigations, like viability assay by Trypan blue; real-time monitoring of cell growth at XCelligence system; analysis of mechanism of cell death by optical microscopy and fluorescence, flow cytometry and Western blot. **Results:** Two of four compounds showed potential antiproliferative effect against tumor cells. Chalcone-sulfonamide 185 (CSS185)curiously showed a selective cytotoxic effect against colorectal cancer cell lines, with an IC_{50} (half maximal inhibitory concentration) value four times lower when compared to the other cell lines tested. Therefore, the cytotoxic effect of CSS185 against the metastatic lymph node-derived colorectal cancer cell line (SW-620) was carried out. The molecule induced a cytostatic and cytotoxic effect against this cell line in a time and concentration dependent manner, interfering with cell cycle progression with increasing G2/M cell number, inducing DNA damage and consequent cell death with the appearance of cell morphology alterations associated with apoptosis and necrosis characteristics, loss of membrane integrity and mitochondrial depolarization. Cell death was associated with activation of PARP and expression of proteins related with necroptosis cell death, like RIP and MLKL. These proteins are phosphorylated during the necroptosis process. **Conclusion:** With this, it is suggested that the mechanism involved in the *in vitro* cytotoxic effect of CSS185 may be related to induction of cell cycle arrest in the G2/M phase and consequent DNA damage and cell death by necroptosis, being a promising molecule against cancer. **Supported by:** CNPq, PRONEX, CAPES, FAPEG and FUNCAP. **References:** WEINBERG, R.A. TheBiology of Cancer. 2 ed., 2013; LEE, M. et al.Int J RadiatOncolBiol Phys., v. 76,p. 1528, 2010; SILVA, C.R. et al. PLoS One, v.10, 2015.

Key Words: antitumor; cell cycle; cell death.

10.010 Evaluation of the chemopreventive effect of *Cordia lutea* L flower ethanolic extract on prostate carcinogenesis induced by N-methyl-N-nitrosourea and testosterone in rats. Armas JPR, Ortiz-Sanchez JM, Aguilar-Carranza C, Palomino-Pacheco M Universidad Nacional Mayor de San Marcos

Introduction: *Cordia lutea* Lam (Boraginaceae) is an indigenous plant of Peru known by the common name of overo; in Traditional Peruvian medicine, overo flowers are used to treat prostate inflammation (Bussmann, 2010). In this plant has been reported the presence of flavonoids and leucoanthocyanidins, of which the majority compounds were utin and quercetin (Mayevych, 2015), substances with anticancer properties. That is why we carried out the present study to evaluate the in vivo activity of the ethanolic extract of *Cordia lutea* flowers on prostate cancer induced in rats. **Methods**: The induction of prostate cancer was carried out with cyproterone acetate 50 mg/kg/day for 18 days, followed by 3 days of testosterone propionate 100 mg/kg; and finally, an intraperitoneal injection of N-methyl-N-nitrosourea (NMU) 50 mg/kg. Were used 40 male Holtzman rats assigned to 5 groups (n = 8). Group I: received saline (control); Group II: rats induced for prostate cancer; Groups III, IV and V: induced for cancer and received the extract of the flower of *C. lutea* daily in doses of 50, 200 and 500 mg/kg of bodyweight, respectively, for 5 months. After the treatment period, a blood sample was collected for the determination of Prostate-Specific Antigen (PSA) and the rats were sacrificed by pentobarbital overdose. The prostate was dissected and weighed, the ventral lobe of the prostate was processed for histopathological examination. **Results**: The somatic prostate index decreased with the treatment of *Cordia lutea* in a dose-dependent manner, the best effect occurred with the dose of 500 mg/kg, from 0.34 ± 0.04 to 0.23 ± 0.05 ($p < 0.05$). PSA levels also decreased with the dose of 250 and 500 mg/kg, from 0.34 ± 0.05 ng/ml (induced) to 0.15 ± 0.06 and 0.12 ± 0.05 ng/ml ($p < 0.05$), respectively. Histopathological analysis showed a decrease in the number of layers, as well as high grade and low grade prostatic intraepithelial neoplasia, from> 5 layersin the induced group, to 1 to 2 layers, and absence of high-grade and low grade prostatic intraepithelial neoplasia with the dose of 500 mg/kg. **Conclusion**: The ethanolic extract of *Cordia lutea* has chemopreventive effect on prostate cancer induced by NMU and testosterone in rats. **References**: Bussmann R, J Ethnobiol Ethnomed. 6:30, 2010; Mayevych I, Nat Prod Chem Res. 3: 194, 2015. **Financial Support**: Vicerectorate of Investigation of the Universidad Nacional mayor de San Marcos. Ethical Approval: 0261-17.

10.011 Extract of the leaves of *Passiflora alata* induces apoptosis and necrosis in leukemic cell line. Nascimento DS[1], Amaral RG[1], Santos SA[1], Mendes Neto JM[1], Andrade LN[1], Gomes SVF[2], Severino P[2], Menezes Filho RO[1], Santos SL[1], Carvalho AA[1]
[1]UFS, [2]Unit

Introduction: Cancer is a group of diseases of cellular origin, responsible for one of the greatest causes of death in the world, with an estimate of new cases and increasing mortality. These data demonstrate the need for social-scientific engagement in the search for more effective anticancer agents. In this context, Amaral *et al*. (2013) evaluated the cytotoxic potential of leaf extract from 16 Passiflora species cultivated in Brazil, obtained by accelerated solvent extraction and detected that the extract of the leaves of *Passiflora alata* (ELPA) has promising activity cytotoxic activity against cancer cell lines. In view of this, the objective of this work was to determine the process of ELPA-induced cell death in the leukemic cell line. **Methods:** The identification of the cytotoxic activity of EFPA was performed by colorimetric analysis, based on the conversion of MTT to formazan (Mosmman, 1983) blue in 7 tumor cell lines: Promyelocytic Leukemia (HL-60), Prostate Carcinoma (PC-3), Ovarian adenocarcinoma (OVCAR-8), chronic myelocytic leukemia (K-562), and hepatocellular carcinoma (HepG2). For identification of the cell death process, Ethidium Bromide/Acridine Orange (EB/AO) staining and Hematoxylin/Eosin (H/E) staining were used. The cytotoxicity data were presented as values of the inhibitory concentration capable of causing 50% of the maximum effect (IC_{50}) in µg/mL, EB/AO staining analyzed by the percentage quantification of each cellular event (viable, necrotic and apoptotic) and H/E were analyzed by cellular morphological characteristics. Doxorubicin was used as a positive control. **Results:** The extract showed high potency (IC_{50} < 30 µg/mL) against HL-60 (IC_{50} = 19.37 µg/mL), followed by PC-3 (IC_{50} = 20.24 µg/mL), HCT (IC_{50} = 20.79 µg/mL), SF-295 (IC_{50} = 21.87 µg/mL) and OVCAR-8 (IC_{50} = 28.26 µg/mL), respectively. In the present study, the identification of the cell death process was studied in the presence of the extract (HL-60), at the concentrations of half of the IC_{50} (9.69 µg/mL), the IC_{50} itself (19.77 µg/mL) and 2 x IC_{50} (38.74 µg/mL). Morphological analysis by incorporation of ethidium bromide / acridine orange showed an increase ($p < 0.05$) in apoptosis and necrosis in the ELPA-treated groups at concentrations of 9.69 µg / mL (30.74 and 44.7%), 19.77 µg / mL (32.44 and 26.88%) and 38.74 µg / mL (35.88 and 29.45%), respectively. H/E staining shows a distinct reduction in cell numbers and morphological changes characteristic of cell death by apoptosis (cell volume retraction, nuclear fragmentation and formation of apoptotic bodies) and necrosis (loss of membrane integrity and swelling). **Conclusion:** The ELPA shows high cytotoxic activity for the 5 cell lines with IC_{50} ranging from 19.37 to 28.26 µg/mL with higher activity for HL-60. The incorporation of EB/AO and H/E in the treated cells, suggests the process of cell death via apoptosis and necrosis for the 3 concentrations front HL-60. **References**: Amaral RG, J. Med. Plants. Res., v.1, p.157-166, 2019; Mosmman, TJ, Immunol **Methods**. v. 65. p. 55, 1983. Financial support: CAPES and FAPITEC.

10.012 Investigation of the cytotoxic activity of quinones β -lapachone and lapachone in cell lines *in vitro*. Sousa AC[1], Queiroz RRM[1], Silva MFS[1], Oliveira FCE[1], Abreu BB[1], Rebouças LV[1], Silva Júnior EN[2], Pessoa C[1] [1]UFC, [2]UFMG
Introduction: The cancer is characterized by the uncontrolled growth of mutated cells of the body, and it is currently one of the largest causes of mortality in the world (Ferlay,Int. J. Cancer, v.5, p359, 2014). The search for the development of new drugs to treat cancer has been the target of several studies and naturally occurring secondary metabolites are promising for this purpose. The β-Lapachone (β-Lap) and Lapachone (Lap) quinones, belonging to the class of natural products derived from the oxidation of phenols, were studied to determine their cytotoxic properties against tumor lines (Ferreira, Rev. Virtual Quim., v2, p140, 2010). **Methods:** The colorimetric assay of MTT (3- (4,5-dimethyl-2-thiazolyl) -2,5-diphenyl-2H-tetrazolium bromide) was used to determine the antiproliferative activity of these lines treated with the two compounds under study (Mosmann, J. Immunol, v65, p55, 1983).The antiproliferative activity obtained by the MTT assay was expressed as IC50 values. These values measure the ability of a substance inhibit 50% of a biological process. Two experiments were performed with two independent replicates, in the SNB19 (glioblastoma), HCT-116 (colorectal cancer) and PC-3 (prostate cancer) cell lines. Results - β-Lap presented IC 50 values of 4.442 µg/mL, 3.911 µg/mL and 3.842 µg/mL for the SNB19, HCT-116 and PC-3 cell lines, respectively. These results show that β-Lap quinone has cytotoxic potential in inhibiting cell growth in tumor cell lines *in vitro*. The other substance, Lap, showed higher IC 50 values than β-Lap. Lap presented IC 50 values of 10 µg/mL, 7.22 µg/mL and 10.79 µg/mL, for the SNB19, HCT-116 and PC -3 cell lines, respectively. **Conclusion**: Natural products are rich sources of substances with diverse pharmacological properties of interest for scientific research. The β-Lap and Lap substances are presented promising results against the cell lines tested and could be indicated as future prototypes for antitumor drugs. **Acknowledgments** / **Financial support**: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). **References**: FERREIRA, S. B. et.al. β-Lapachona: Sua Importância em Química Medicinal e Modificações Estruturais. Revista. Virtual Quimica, 2 (2), 140-160, 2010. MOSMANN, T. Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays. J. Immunol. Methods, v.65, p 55-63, 1983.FERLAY, J. et al. Cancer incidence and mortality worldwide: Sources, Methods and major patterns in GLOBOCAN 2012. International Journal of Cancer, 136(5), p359-386, 2014.

10.013 Antitumor activity of *Eplingiella fruticosa* **Salmz Benth. in swiss mice transplanted with sarcoma 180**. Mota DCS[1], Lima ACBL[1], Almeida SM[1], Souza JB[1], Moraes SZC[1], Graça AS[1], Amaral RG[1], Shan AYKV[1], Barreto E[2], Albuquerque Júnior RLC[3], Araújo BS[1], Estevam CDS[1] [1]UFS, [2]UFAL, [3]Unit

Introduction: Cancer is a disease of high incidence, mortality and difficult to treat, therefore there is a constant interest in more efficient therapies and with fewer side effects. In this sense, natural products have been shown to be potential antitumor agents. Therefore, the objective of the present study was to evaluate the cytotoxicity of the hydroalcoholic extract, and its phases obtained from *Eplingiella fruticosa* leaves against human tumor cell lines, to select the sample with the highest cytotoxicity in vitro and to evaluate it for the antitumor potential *in vivo*. **Methods**: The hydroalcoholic extract was obtained by maceration of the dried leaves in 90% (v/v) ethanol, resuspended and re-extracted with solvents of increasing polarities. The cytotoxicity assay was performed using Ovarian adenocarcinoma tumor cells (OVCAR-8), colon carcinoma (HCT-116) and glioblastoma (SF-295) and test samples (25 µg/mL) were used for the first MTT test and the results were expressed by cell growth inhibition percentage (GI%) by the formula: [GI% = 100 − [(Test/Control) × 100%]. In the second test, the sample most active in vivo antitumor activity was evaluated in mice transplanted with Sarcoma 180 (n= 10) in two doses (100 and 200 mg/kg/day) and two administration routes (oral and ip). Biochemical and hematological parameters were also obtained as well as anatomopathological analysis of vital organs. For multiple comparisons of the data Kaplan-Meyer test or ANOVA was used, followed by Student's-Newman-Keuls test. This study was approved by the animal research ethics committee of UFS, with License Number 06/2012, executed in 2013 and released for publication after patent filing (BR10 20190020652) in 2018. **Results**: The chloroform phase (CP) presented the best GI result of 97.55, 98.79 and 98.09% and IC_{50}3.55; 3.74 and 3.67µg/mL, for HCT-116, OVCAR 8 and SF-295, respectively. The CP presented inhibition of 46 and 56% (oral) and was 53.9 and 70.4% (ip) for the doses of 100 and 200 mg/kg/day, respectively. In addition, the parameters (AST, ALT, urea and creatinine) did not change. There was a significant increase in the spleen mass of the CP treated animals relative to the negative control. In hematological analyzes, the two doses, both per oral and per ip presented leukocytosis. **Conclusion**: The chloroform phase of leaves of *E. fruticose* shows anticancer activity *in vitro* and *in vivo*, without large variations in toxicological parameters. **Financial support**: To CAPES.

10.014 Phytochemical analysis and biological activity of the leaves extracts of *Montrichardia linifera* (**Arruda**) **Schott** (**Araceae**). Araújo JI, Pereira FIA, Barros AB, Araújo AR, Araújo GS, Silva DA, Marinho Filho JDB, Araújo AJ UFPI

Introduction: *M. linifera*, is an aquatic macrophyte that occurs in tropical regions and develops in soaked soils. Several studies report the presence of different phytochemical compounds in *M. linifera* extracts, such as alkaloids, flavonoids and terpenes, with antibacterial, antiplasmodic, insecticidal and antimalarial activity. Therefore, this study aimed to evaluate the phytochemical composition of *M. linifera* extracts and their antioxidant and antibacterial activities. **Methods**: For the analysis of *M. linifera* phytochemical profile, the methanolic and hydroalcoholic leaves extracts were used. The samples were obtained in five collection points: Santa Quitéria (SQ), Galego (G), Porto dos Tatus (PT), Morros da Mariana (MM) and Lagoa do Bebedouro (LB). The process was carried out according to the reported by Barbosa et al. (2004). The antioxidant effect of the methanolic and hydroalcoholic extracts from the locality of PT was evaluated by the DPPH method (Khoshnamvand, Huo e Liu, 2018) The minimum inhibitory (MIC) were determined following CLSI recommendations (2015), against *Staphylococcus aureus* (ATCC 29213) and *Escherichia coli* (ATCC 25922). **Results:** In the phytochemical analysis of the hydroalcoholic extracts, it was observed the presence of alkaloids, organic acids, flavones and flavonoids in the samples from all localities. Saponin in SQ, while phenols and tannins were found in LB and SQ. For the methanolic extracts, the presence of organic acids was observed for the samples from all of the localities. Saponins were found only for the locality of SQ, alkaloids in LB, MM, G and SQ, phenols and tannins in PT, Mm and G, flavones and flavonoids in the locality of PT. Regarding the antioxidant potential of the methanolic and hydroalcoholic extracts, it was observed that the analysed samples indicated 50% sequestration of radicals at concentrations of 62 µg/mL and 121 µg/mL, respectively, and could be related to the presence of secondary metabolites with antioxidant activity, suggesting that the extracts may serve as promising anti-radical agents. The hexane extract of MM showed activity against the *S. aureus* with MIC value of 1.25 mg/mL, indicating that the metabolites present in this extract have potential against gram-positive bacteria. **Conclusion**: This study demonstrated that the phytochemical composition of the extracts, as well as their biological activity, might vary according to the region where the plant develops, demonstrating the importance of natural products phytochemical composition studies. **Supported by**: CNPq, CAPES, INCTBioNat. **References:** KHOSHNAMVAND, Mehdi; HUO, Can; LIU, Jingfu., Journal of Molecular Structure, v. 1175, p.90, jan. 2019.

10.015 Cytotoxic potential of pacharin and bauhiniastatin-1 isolated from Bauhinia sp. on tumor cells. Souza SMD[1], Militão GCG[1], Bezerra DP[2], Santiago GMP[3], Gois RWS[3], Andrade PGF[1], Souza JLC[1], Silva VR[2], Santos LDS[2] [1]UFPE, [2]UFBA, [3]UFC
Introduction: Cancer can be described as a set of complex processes involving impaired cells death, unlimited cell proliferation and temporal–spatial changes in cell physiology that often leads to tumor invasion and metastasis (SEYFRIED, 2010). In addition, it is a multifactorial heterogeneous disease, being one of the main causes of mortality worldwide (JEMAL et al., 2011). The genus Bauhinia (family Caesalpinioideae, Leguminosae) comprises more than 500 species located in tropical areas of the planet and has been used in folk medicine to treat various diseases because theier anti-inflammatory, antidiabetic, antimicrobial, antimalarial, antinociceptive, antitumor and antimutagenic properties (SOARES e SCARMINIO, 2008; KITTAKOOP et al., 2000; MOHAMED, 2009; CAGLIARI, 2018; AGRAWAL, 2009). Two oxepins, pacharin and bauhiniastatin-1 were isolated from Bauhinia acuruana qnd tested in a mini panel of tumor cell line, where antitumor activity was shown (GOIS, 2013; PETTIT et al., 2006). **Objective:** To determine the in vitro cytotoxicity of the compounds of pacharin and bauhiniastatin-1 isolated from Bauhinia Acuruana on tumor cells and in normal cells (peripheral blood mononuclear cells-PBMC). **Methodology**: The compounds of pacharina and bauhiniastatin-1 were isolated, characterized and supplied by Dra. Gilvandete Maria Pinheiro Santiago of the Federal University of Ceará, according to methodology described by Góis et al, 2013. The tumor lines studied MCF-7 (breast cancer), HT- 29 and HCT 116 (colon cancer), HeLa (cervix cancer), NCI H292 (lung cancer), HL-60 (leukemia), HepG2 (liver cancer) and normal cell lines (L292, MRC-5) were obtained from the Rio de Janeiro Cell bank; Human peripheral blood mononuclear cells (PBMC) were obtained from healthy volunteers. The Research Ethics Committee of the UFPE (Recife, Pernambuco, Brazil) approved the experimental protocol (no. Of opinion 2.980.861) for PBMC isolation. To evaluate the cytotoxic activity of the compounds, the MTT colorimetric method was used. Cells were seeded in 96-well plates and the test compounds were added to each well and incubated for 72 h. Doxorubucin was used as a positive control. Cell viability was evaluated after 24h and 48h treatment by tripan blue exclusion test. The analysis of morphological changes were determined by May-Grunwald-Giemsa staining, where slides of these cells treated with the compounds under study were made, stained and analyzed by optical microscope and photographed using the NIS Elements F software with the help of the camera (Digital Sight DS-U3, NIKON). **Results:** In the quantitative analysis of cell viability and proliferation, the compounds of pacharin and bauhiniastatin-1 were tested in different cell lines for cytotoxic screening using the MTT assay. Among the tested cell lines, HeLa and NCI H292 were the most sensitive to the cytotoxic effect of the compounds with the IC50 of 9.18 and 11.11 µM for the compound pacharin respectively. For the compound bauhiniastatin-1, the IC_{50} ranged from 10.6 to 21.83 µM for HL-60 and MCF-7, respectively. No cytotoxic activity was observed at PBMC. The trypan blue exclusion assay confirmed the cytotoxicity of the compounds pacharin and bauhiniastatin-1 in HL-60 and MCF-7 cells. At concentrations of 10 and 20 µM, pacharin reduced the number of viable cells in HL-60 by 25% and 39% after 24 h, and 61% and 70% after 48 h, respectively. For bauhiniastatin-1 at concentrations of 10 and 20 µM, there was a reduction in the number of viable cells in 32% and 52% after 24h and 50% and 74% after 48h, respectively. In MCF-7 cells, pacharin at concentrations of 20 and 40 µM reduced the number of viable cells by 36% and 47% after 24h and 50% and 65% after 48h, respectively. Bauhiniastatin-1 in MCF-7, at concentrations of 20 and 40 µM, had a 48% and 47% reduction in the number of viable cells after 24h and 71% and 79% after 48h, respectively. As regards the effect of the treatment with the compounds pacharin and bauhiniastatin-1 on the HL-60 and MCF-7 cell lines, it was observed morphological alteration after incubation such as reduction in cell volume, chromatin condensation, nucleation fragmentation and enhanced cells blocked at mitotic phases. **Conclusion:** Pacharin and bauhiniastatin-1 showed cytotoxic activity with significant inhibition of

growth for different cancer cell lines and induce mitotic blockage at HL60 an MCF-7 cancer cells. **Keywords**: Cancer, Bauhinia acuruana, Pacharin, Bauhiniastatin-1, cytotoxicity. **Financial Support:** CAPES, UFPE, FIOCRUZ-SALVADOR. **References:**
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10.016 Melatonergic System, but NOT Melatonin Content, Determines Differences in the Viability of Human Urothelial Carcinoma Cell Lines. Quiles CL, Moreno MOC, Muxel SM, Kinker GS, Fernandes PACM, Markus RP USP

The accumulation of melatonin in solid tumors, independent of pineal synthesis, is now considered a positive predictive prognosis factor (Markus et al., Br J Pharmacol, 175: 3239, 2018). Accordingly, in glioma (Kinker et al., J Pineal Res, 60:84, 2016), and other solid tumors (LV et al., J Pineal Res, 66:e12557, 2019) the index relating the expression of genes that codify synthesis/degradation enzymes (ASMT:CYP1B1) was a survival predictive factor. This *in silica* prognostic factor was confirmed in gliomas by showing an inverse correlation between proliferation/aggressiveness grade and the ASMT:CY1B1 index (Kinker et al., J Pineal Res, 60:84, 2016). Considering the enormous variation among solid cancers, here we tested whether human urothelial carcinoma cell lines viability could be classified according to their ability to synthesize melatonin. Thus, the genomic index, production of melatonin, as well as the expression and localization of melatonin receptors in two different cell lines, one representing grade II urothelial carcinoma (5637) and the other grade III/IV (T24). We also evaluated the effect of tumor-synthesized melatonin by measuring cell viability in the presence of the non-selective antagonist luzindole (MT1 pKA 6.2-6.8; MT2 pKA 7.6-8.8). **Methods**: Cell lines were purchased from the Cell Bank of Rio de Janeiro. The expressions of ASMT and CYP1B1 genes determined by qPCR was used to construct the ASMT:CYP1B1 index. Melatonin accumulation in the medium for 6 hours was quantified by ELISA. The presence of melatonin receptors (MT1 and MT2) was evaluated by confocal microscopy. Functional output was evaluated by the MTT assay in cells incubated with the competitive antagonist luzindole (1pM to1nM) per 48 hours. The results were normalized by the vehicle followed a Gaussian distribution and the data were compared by independent t-test. **Results:** The ASMT:CYP1B1 index was 25 times lower in GIII/IV than GII urothelial carcinoma cells. Both cell lines synthesized melatonin, GII (12.01 ± 0.73 pg/ml, N = 4 independent cultures), GIII/IV (8.78 ± 2.26 pg/ml, N = 4), and expressed melatonin receptors. Interestingly, the receptors were expressed predominantly in the nuclei of GII cells, and in the cytoplasm of GIII/IV cells. Surprising, luzindole induced opposite effect of the viability of each cell line. Luzindole (1pM – 10 pM) decreased GII, while (1pM – 100 pM) increased GIII/GIV viability, when compared to the corresponded vehicles. Conclusions: Here we show that melatonin synthesized by urothelial carcinoma cell lines have different effects according to the lineage studied, and that it is highly recommended to further understand the role of the melatonergic system in cell survival before using this indolamine and derivatives in clinics.

10.017 Antimigratory effect of a synthetic sulfonamide chalcone in metastatic melanoma cells (**B16-F10**). Araújo GS[1], Moura AF[1], Barros AB[1], Castro MRC[2], Peres CN[2], Marinho Filho JDB[1], Araújo AJ[1] [1]UFPI, [2]UFG

Introduction: Migration plays a primordial role in the progression of metastasis in cancer. Metastatic melanoma has high lethality, mainly due to resistance to conventional therapies (PRASAD et al., 2019). Thus, alternative approaches are necessary, including the production of new synthetic compounds for the management of metastatic cancer. Considering chalcones and sulfonamides as important classes of compounds with different pharmacological activities (BAHEKAR et al, 2016), new sulfonamides chalcones (CSS185 and CSS99) were synthesized to evaluate their antimigratory potential. Previous studies showed the cytotoxic potential of these compounds against tumor cells. **Methods**: The cytotoxic effect of CSS185 and CSS99 against metastatic melanoma cells (B16-F10) was assessed by MTT assay, after 24 h of incubation, for determination of non-cytotoxic concentrations then used in the cell migration assay. Cell growth was quantified by the ability of living cells to reduce MTT to a blue formazan product.To determine antimigratory effect of these compounds in B16-F10, scratch assay was performed. Cell migration images were monitored and photographed, at time 0 and 24h after incubation with compounds, using inverted microscope. Migration area was calculated using Image J software. Trypan blue dye was used to assess if cells were actually migrating and not proliferating Data analysis was performed using GraphPad Prism version 6.0 program. **Results:** Non-cytotoxic concentrations of CSS185 and CSS99 were determined by MTT assay. For cell migration assay, B16-F10 cells, after scratching and nutrient starvation, were treated with 2.5 µM and 5 µM of CSS185 and CSS99. The results showed that these compounds were able to inhibit the scratch closure in both concentrations, after 24 h of incubation. The antimigratory effect of another sulfonamide chalcone has been described by Ejaz et al. (2017) and may be related to the inhibition of extracellular nucleotides involved in the migration, invasion, tumor proliferation and angiogenesis processes. In another study, the role of chalcones in the inhibition of cell migration was associated with downregulation of matrix metalloproteinase, playing a key role in the degradation of the extracellular matrix related to cancer cell invasion and metastasis (PENG et al, 2018).**Conclusion:** The present study demonstrated antimigratory activity of new sulfonamide chalcones in B16-F10 cells. However, further studies should be performed to verify the mechanisms involved in this process. Supported by: CNPq, CAPES, FAPEG, FAPEPI and INCT BioNat. References: BAHEKAR, S.P., et al. European journal of medicinal chemistry, v. 124, p. 262-269, 2016. EJAZ, S.A. et al. Bioorg Chem, v. 70, 2017. PENG, Xiaolin et al. Life sciences, v. 206, p. 35-44, 2018.PRASAD, P. et al. International journal of molecular sciences, v. 20, n. 3, p. 608, 2019.

10.018 Modulation of short-chain free fatty acid receptors FFA2 and FFA3 in breast cancer cells. Muradás TC, Campos MM PUC-RS

Introduction: Breast cancer is a heterogeneous disease that presents a poor prognosis and low survival rates, affecting a high number of individuals globally (Tobin et al. Annals of Oncology. v. 26, n. 1, p. 81–88, 2015). Short-chain free fatty acid receptors, namely FFA2 and FFA3, has been recently described as modulators of breast cancer cell invasiveness (Thirunavukkarasan et al., Plos One, 12(10): e0186334, 2017). This study investigated the in vitro effects of the dual FFA2/FFA3 agonist sodium propionate and the selective FFA2 antagonist CATPB, in breast cancer cells. **Methods:** All the protocols were approved by the Institutional Ethics Committee (9011/18). Three different molecular subtypes of human breast cancer cell lines, MCF-7 (estrogen receptor-positive), SK-BR-3 (HER-2 positive), and MDA-MB-231 (triple-negative) were used. The cells were cultured under standard conditions in RPMI supplemented with 10 % fetal bovine serum (FBS). The cell viability was determined through MTT assay. The cells were exposed to different concentrations of sodium propionate (0.1, 0.3, 1, 3, 10 and 30 mM) or CATPB (0.1, 0.3, 1, 3, 10 and 30 μM), for 24, 48 and 96 h. The effects of sodium propionate (3, 10 and 30 mM) on cell proliferation were further examined by using the Cell Counting Kit 8 (CCK8/WST-8). CATPB (0.3, 1, 3, 10 and 30 μM) and sodium propionate (1 mM) were also tested under starving conditions, with a reduction of FBS to 0.5%. **Results:** Sodium propionate (3 mM to 30 mM) induced a concentration- and time-dependent reduction of the viability of the three tested cell lineages. The maximal inhibitions were obtained at the concentration of 30 mM, at 96 h, corresponding to 58 ± 6 %, 38 ± 8 %, and 49 ± 9 %, for MCF-7, SK-BR-3, and MDA-MB-231, respectively. However, the 1 mM concentration of sodium propionate significantly increased the cell viability of MDA-MB-231 cells ($P<0.05$). The reduction of viability induced by sodium propionate (3, 10 and 30 mM) was confirmed by using the WST-8; CCK8 kit, at 48 h, in the three tested cell lines. Under normal culture conditions, CATPB (0.1 and 0.3 μM) increased the cell viability of MDA-MB-231 cells, at 96 h ($P<0.05$). Alternatively, CATPB (1 μM) increased the cell viability of MCF-7 cells, whereas this FFA2 antagonist (0.3 μM to 30 μM) significantly diminished the viability of MDA-MB-231 cells ($P<0.05$), according to the assessment at 24 h under starving conditions. **Conclusion:** Our data suggest that pharmacological activation or inhibition of FFA2/FFA3 receptors might induce different effects depending on the tested concentration, the breast cancer cell lineage, or the culture conditions. Additional experiments are in progress to further investigating the involvement of both receptors in breast cancer. **Financial support:** CNPq, CAPES (Financial Code 001), PUCRS.

10.019 Gene expression profile as predictive response markers to neoadjuvant anastrazole in elderly women diagnosed with breast cancer. Lopes MHS[1], Barbosa LA[2], Torrezan GT[3], Olivieri EHR[3], Paula CAA[3], Gifoni MAC[2], Lima MVA[2], Carraro DM[3], Wong DVT[1], Andrade VP[3] [1]UFC, [2]ICC, [3]AC Camargo Cancer Center

Introduction: Estrogen receptor positivity remains the most important criteria for the indication of neoadjuvant hormone therapy. Conversely, up to 50% of patients have no clinical benefit. Currently, microarrays have been used to identify the molecular basis of hormone therapy response through the screening of genes expressed in tumors. This study aimed to identify a predictive gene expression signature to the neoadjuvantanastrozole response by a microarray gene expression platform. **Methods:**For that purpose, the correlation between immunohistochemical markers (HER-2, the estrogen (ER) and progesterone (PR) receptors and the proliferation marker Ki-67) and the clinical response was also assessed. Elderly women (42 patients, 61-91 years old) diagnosed with breast cancer and treated with neoadjuvantanastrozole (1 mg/day for 4 months before surgery) were enrolled for the study. (CEP protocol number/ICC: 734.463). **Results**: The HER-2, ER and Ki-67 immunoexpressions were not able to predict the clinical responses. However, the univariate analysis indicated that the low immunohistochemical expression of PR (<20%) was statistically associated with the objective response (P<0.05). In addition, the multivariate logistic regression also evidenced that the PR was associated with the objective response (Adjusted OR=7,19, CI 95% 1,07-48,40). The transcriptome comparison between six patients with objective response and six individuals with disease progression showed that 75 genes were differentially expressed among these groups of patients (Fold Change ≥ 2 and P-value ≤0.01). The gene expression profile-based unsupervised hierarchical clustering discriminated the type of response with 92% accuracy. In progressing tumors, the *TMEM26* and *GFRA1* genes were suppressed, while the *PBX3* and *ST6GALNAC* genes were the most hyper-expressed. **Conclusion:** These findings might help clinicians in their choice for the best therapy to be indicated to elderly women diagnosed with breast cancer. **Financial support**: CNPQ -Grants number: 428354/2016-5. Keywords: Breast neoplasms - Gene expression - Hormonal antineoplastic drugs - Aromatase inhibitors - Neoadjuvant treatment

10.020 Essential oil of *Schinus terebinthifolius Raddi* **leaves inhibits the growth of tumor in mice transplanted with sarcoma 180**. Graça AS, Almeida SM, Mota DCS, Amaral RG, Santos SA, Menezes Filho RO, Souza JB, Moraes SZC, Nogueira PCL, Carvalho AA, Shan AYKV, Araújo BS, Estevam CDS UFS

Introduction: Cancer is a set of more than 100 diseases responsible for the second leading cause of death in the world. It is estimated that in Brazil 600,000 new cases will occur each year for the 2018-2019 biennium, so the search for new antineoplastic drugs is essential, since the current ones still cause many undesirable effects. In this sense, natural products can be an alternative, especially for Brazil, which is a country rich in plant diversity. *Schinus terebinthifolius* Raddi, plant of the Anacardiaceae family found in the Brazilian coast, has cytotoxic activity *in vitro* against tumoral lines. However, *in vivo* assays have not yet been reported. Therefore, the aim of this work was to evaluate the chemical composition, antitumor activity of the essential oil of leaves of *S. terebinthifolius* Raddi, as well as toxicological parameters. **Methods**: The leaves were collected in the municipality of São Cristóvão (SE) and frozen until the extraction. The essential oil of *S. terebinthifolius* Raddi (EOST) was extracted by hydrodistillation and analyzed by GC/MS. *In vivo* antitumor activity was performed using animals transplanted with Sarcoma 180 ($2x10^6$ cells/0.5 mL, subcutaneous) were used and separated in 5 groups (n=10/group): healthy animals [saline, intraperitoneal (i.p.), without tumor]; control group [saline, intraperitoneal (i.p.)], 5- Fluorouracil (25 mg/kg/day, i.p.), EOST (25 mg/kg/day, i.p.), EOST (50 mg/kg/day, i.p.), treated and weighed daily for 7 days. After 24 hours of the last day of treatment the animals were anesthetized, the blood collected via the retro-orbital plexusand performed the following tests toxicologicals: hematological analyses (hemoglobin - HB, hematocrit - HEM, hematocrit - HT, platelet counts - PLT and total leukocyte counts); biochemical analyzes [Aspartate transaminase (AST), Alanine transaminase (ALT), urea and creatinine]; analysis of body mass variation and after euthanized animals were removed liver, spleen and kidney to analyze the mass of the organs. Data were expressed as mean ± SEM and analyzed by one-way analysis of variance (ANOVA) followed by Tukey post-test ($p<0.05$). **Results**: EOST showed predominance of monoterpene compounds (92.1%). Its main constituents were α-pinene (37.1%), β-carene (35.8%), (ε)-cariophilene (8.4%), limonene (7.4%) and myrene (3.2%). In the *in vivo* antitumor activity assay, EOST showed inhibition percentages of 48.7% and 76.0% at 25 and 50 µg/kg/day, respectively. In addition, the dose of 50 µg/kg/day had the same effect as 5-Fluorouracil, but did not cause any toxic effect to the treated animals when compared to the control group. **Conclusion**: Thus, it is concluded that the EOST is predominantly monoterpenic and has antitumor activity *in vivo*, without toxicity and at low dosage. **License number of ethics committee**: 35/2017. **Financial support**: To CAPES and FAPITEC for the scholarships.

10.021 The expression of cytoplasmic CCR7 (CCR7c) and mTOR associates with tumor relapse to chemotherapy and lower overall survival in Triple Negative Breast Cancer (TNBC). Cajado AG[1], Gurgel DC[2], Gomes-Filho JV[1], Pereira AC[1], Bandeira AM[1], Torres CS[1], Borges LFC[1], Pereira JFB[1], Uchôa PLO[1], Ferreira LMM[1], Silva PGB[1], Távora FR[1]F, Wong DVT[1], Almeida PRC[1], Lima-Júnior RCP[1] [1]UFC, [1]ICC

Introduction: Triple-negative breast cancer (TNBC) is a subtype of breast cancer, which tests negative for estrogen receptors, progesterone receptors, and excess HER2 protein, accounting for 10-20% of breast cancers. TNBC is unresponsive to hormonal therapy or drugs targeting HER2 receptors, contributing to a poor prognosis and reduced patient survival. The identification of new targets in cancer is essential to improve clinical therapeutic outcomes. In that context, chemokines and their receptors, such as the CCR7, have been described in the pathogenesis of several types of cancer as a consequence of transcription factors deregulation. Besides orchestrating the leukocyte migration, chemokines signal through a number of cell pathways, including the mammalian target of rapamycin (mTOR), and directly drive the tumor cell growth, angiogenesis, and metastasis. OBJECTIVE: To evaluate the expression of the CCR7 chemokine receptor and the mTOR protein in the TNBC, and to compare the basal-like and non-basal-like subgroups, correlating them with the clinic-pathological parameters.

Material and Methods: This was an observational, longitudinal and retrospective study. Surgical paraffin histopathology blocks and clinical-pathological data (tumor size, presence of lymph node metastasis, distant metastasis, progression-free interval, and overall survival) were prospected from 133 patients from January 2011 to December 2015. Healthy individuals that underwent reductive mammoplasty were included as the control group. Samples from both groups were analyzed by immunohistochemistry using the Tissue Microarray (TMA) technique for the evaluation of the immunoexpression of CCR7 and mTOR and scored according to the intensity of staining as absent (0), mild (1), moderate 2) and intense (3).The Ethics Committee approved the protocols (Approval Protocol CEP 407.395).Results were considered statistically significant when$P<0.05$.

Results: The clinicopathological data indicated that most of the patients were more than 50 years old, with advanced histological grade ductal carcinomas and lymphovascular invasion (46.4%), which responded in a variable manner to neoadjuvant chemotherapy and presented systemic tumor relapse (18.5%). The CCR7c immunohistochemical expression varied from discrete to intense in the cytoplasm of neoplastic cells. For them TOR, the absence or the discrete membrane expression was observed and intense cytoplasmic immunostaining. The overall survival was lower in patients with positive expression of CCR7c and mTOR (75%) when compared with the non-expressing group (89%, $P<0.05$). In addition, the relative risk of death was found to be 2.5-fold higher in patients who presented the over-expression of these markers. **Conclusion:** The high expression of CCR7c and mTOR was directly associated with tumor relapse, contributing to reduced overall survival. Therefore, CCR7 and mTOR are potential targets for the treatment of TNBC. **Financial Support**: Proc. PR2-0101-00054.01.00/15 – PRONEX /FUNCAP /CNPq

10.022 Systemic risk analysis of a rich antitumoral fraction in clerodanic diterpenes. Amorim VR[1], Santos DB[1], Bolzani VS[2], Cavalheiro AJ[2], Machado KC[1], Almeida AAC[1], Silva JN[1], Sousa Neto BP[1], Ferreira PMP[1] [1]UFPI, [2]USP

Introduction: Toxicological studies have the purpose of assuring or refuting the clinical applicability of a drug to investigate its safety, which occurs through tests to evaluate acute or chronic, systemic or site-specific effects(LANGMAN; KAPUR, 2006). As important as talking about toxicity studies for new drugs is correlating them with herbal medicine(LANINI et al., 2009).Among the available plant species stands out Casearia *sylvestris*, popularly known as "guaçatonga", "wild coffee" or "bush coffee", known for its popular use as antimicrobial, antifidic, antiulcerogenic and antitumor. The present work aimed to investigate the subchronic toxicity of Casearin Fraction (CF) in mice through hematological, biochemical and open-field and rotarod behavioral tests.**Methods**: the tests were adapted from the 90 day rodent oral toxicity study method - OECD 408 (OECD, 2018). To this end, female *Swiss* mice were randomly divided into 3 groups (n = 10 for each group) with weights ranging between 25 and 29 g. Each group received its specific treatment: a) negative control: vehicle (5% DMSO, oral); b) CF 2,5 mg / kg / day by gavage and; c) CF 5 mg / kg / day by gavage. The treatments were performed for 90 consecutive days. Every 30 days, the animals underwent behavioral tests. On the 91st day, blood was collected through the retroorbital plexus for hematological and biochemical tests. All procedures were approved by the Animal Research Committee of the Federal University of Piauí. (nº 373/2017). **Results**: Behavioral monitoring data (rotarod) showed no differences between groups. As for the open field test, a change in grooming effect at 5 mg / kg was evidenced. Hematological examinations detected significant changes in both doses. Such treatments (2.5 and 5 mg / kg / day) caused an increase in segmented leukocytes (26.0 ± 5.0; 42.7 ± 8.3, respectively), when compared to the control group (Segmented leukocytes: 19, 1 ± 3.0%) ($p < 0.05$). No significant changes in serum biochemical parameters were observed in TGO, TGP and creatinine parameters. **Conclusion**: The tests performed showed that CF at the doses used did not have a toxic profile for animals, changes in behavioral test could infer a sedative action, but as the change was not persistent, it cannot be inferred about this action in the CNS. Studies conducted by Ferreira et al (2016) showed that animals treated for 30 days with CF at doses 5 and 10 mg / kg / day i.p. induced lymphocytes and neutrophils and mice treated with Casearin X presented lymphocytopenia and neutrophilia after 7 days of exposure. These data corroborate in part with the subchronic test, where neutrophilia was verified at both doses (2.5 and 5.0 mg / kg / day) compared to the negative control. However, this data alone does not show a toxic potential for CF. **References**: FERREIRA, P. M. P, et al. Preclinical anticâncer effectiveness of a fraction from Casearia sylvestris and its componente CasearinX: in vivo and ex vivo Methods and microscopy examinations. Journal of Ethnopharmacology, v. 186, p. 270–279, 2016. LANGMAN, L. J., et al. Toxicology: Then and now. Clinical Biochemistry, v. 39, p. 498-510, 2006. LANINI, J., et al. "Natural and therefore free of risks" - adverse effects, poisonings and other problems related to medicinal herbs by "raizeiros" in Diadema/SP. Brazilian Journal of Pharmacognosy. v 19, p. 121-129, 2009. Organization for Economic co-operation and Development (OECD). 2018. Test No. 408: Subchronic Oral Toxicity. OECD, Paris. Financial Support: CAPES

10.023 Drugs safe association set to Neoplasis – Focus in pharmacokinetics investigation (**Pilot Group**). Godoy ALPC[1], Silva LP[1], Neves FMF[1], Silva ACSS[1], Yamamoto PA[2], Moraes NV[2], Machado MCA[1], Estrela-Lima A[1] [1]UFBA, [2]Unesp-Araraquara

Introduction: Multi-drug therapy has been shown to be a safe strategy for cancer treatment. The metronomic chemotherapy, which is based on oral drug administration of comparative low doses, can be used with the conventional cytotoxic chemotherapy in the treatment of different neoplasia. The aim of this study was to evaluate the effect of cyclophosphamide and ivermectin on the safety and in the kinetic disposition of carboplatin in a pilot study in rats. The histopathology of the kidneys, liver, intestine, and bone marrow was evaluated by the veterinary pathologist. **Methods:** The study was approved by the Ethics Committee for the Use of Animals of the Escola de Medicina Veterinária e Zootecnia – UFBA Campus (Protocol 01/2018). Female Wistar rats (n=24) were separated into 3 groups: G1 – Rats treated with a single intravenous (iv) dose of 300 mg/m^2 (50 mg/kg) carboplatin; G2 - Rats treated with a single iv dose of 300 mg/m^2 (50 mg/kg) carboplatin after pretreatment (48 h before) with 400 µL/kg ivermectin and G3 - Rats treated with a single iv dose of 300 mg/m^2 (50 mg/kg) carboplatin after pretreatment (21 days/once a day) with 12,5 mg/m^2 de cyclophosphamide – metronomic regimen. Serial blood samples were collected up to 120 min after carboplatin administration. After euthanasia, kidneys, intestines, liver, lung, and bone marrow samples were collected for anatomopathological analysis. Carboplatin was determined in plasma samples by LC-UV at 229 nm. Non-compartmental pharmacokinetic analysis was performed using the Excel add-in program Pk-Solver. **Results:** The area under the curve plasma concentration versus time extrapolated to the infinity ($AUC^{0-\infty}$) was 3309.57, 4661.82 and 7002.49 µg/mL.min for G1, G2 and G3, respectively. The histopathological did not demonstrated major changes. Discrete circulatory and degenerative alterations in renal and hepatic parenchyma were observed for G1, G2 and G3.This investigation suggests that carboplatin vs ivermectin or carboplatin vs cyclophosphamide associations are safe. **Conclusion:** Further investigation in female dogs with mammary neoplasia are being conducted based on the observed results. SIDDIK, Z.H.; Biochem Pharmacol, v. 36, n. 12, p.1925-1932, 1987. MUTSAERS, A.J; Top. Comp. Anim. Med., v.24, n.3, p.137-143, 2009. MASCI, G.; Ecancer medical science, v. 6, n. 1, p. 1–5, 2012. JUAREZ, M.; American journal of cancer research, v. 8, n. 2, p. 317, 2018 **Financial Support**: CNPq

10.024 Protective effect of *Senecio rhizomatus Rusby* (**Llancahuasi**) **ethanolic extract on 7**, **12-dimethylbenz [a] anthracene** (**DMBA**) **induced breast cancer in female rats**. **Arroyo** Acevedo JL, Justil Guerrero HJ, Calva Torres JC, Chaves Asmat RJ, Herrera Calderon O, Condorhuaman Figueroa MC, Martìnez Heredia J, Cieza Macedo E, Garcia Bustamante C, Arroyo Sandoval J Universidad Nacional Mayor de San Marcos

Objective: To determine the possible protective effect of the ethanolic extract of *Senecio rhizomatus* Rusby (Llancahuasi) ethanolic extract on 7, 12-dimethylbenz [a] anthracene (DMBA) induced breast cancer in female rats. **Design:** Experimental. **Location:** Medicine Faculty, National University of San Marcos, Lima, Peru. **Materials and methods:** Female holtzmann rats; aerial parts *Seneciorhizomatus*Rusby (Llancahuasi). Phytochemical study with identification of chemical components of the extract by Agilent Technologies 6890 N gas chromatograph, coupled to mass spectrometer 5973N (Santa Clara, CA, USA); acute toxicity in mice (LD50); Protective effect: 1) Normal; 2) DMBA inductor (I); 3) I + Llancahuasi 10 mg / Kg; 4) I + Llancahuasi 100; 5) I + Llancahuasi 200 mg / Kg; protective efficiency at experimental completion; animal sacrifice was performed with the VIP administration of pentobarbital 100 mg / kg and pathologic findings were evaluated as indicators of the breasts. Main measures of results: The chemical components of the extract was analyzed on a gas chromatograph and its antioxidant activity with DPPH test (1,1-diphenyl-2-picryl-hidrazil).Data were expressed percentage of effect, as mean and standard deviation compared by ANOVA and Tukey test with a confidence interval of 95% ($p < 0.05$). Care of animals: were taken in according to stipulated ethical standards for experimental animals. **Results:** 1,4-Benzenediol, mono-tetradecyl ether followed by Cyclopropylidenediethylidene) disemicarbazide, and Totarol<trans->, methyl ether, among others; a decrease in the number of breast tumors was observed, and there was also reduction of necrosis and mitosis in the treated rats; in mice with a single dose up to 5000 mg / kg, they showed no signs of toxicity, and no evidence of morphological changes by histopathological study of liver, kidney, heart and brain.There was an antioxidant effect in vitro against DPPH being 92.50 and 88.75% ($p < 0.005$) for llancahuasi followed by vitamin C correspondingly. **Conclusion:** Llancahuasi has shown a protective effect of breast cancer in rats, and the LD50 would be above 5000 mg / kg.Ethical approval 185-17. Financial support: Vicerectorate of Investigation of Universidad Nacional Mayor de San Marcos.

10.025 Cytotoxic and antimigratory potential of methanolic, **hydroalcoholic and hexanic extracts of leaves of** *Montrichardia linifera* (**Arruda**) **Schott** (**Araceae**). Pereira FIA, Pereira JIA, Silva DA, Barros AB, Marinho Filho JDB, Araújo GS, Araújo AJ
UFPI

Introduction: Natural products have been shown to be effective in the development of anticancer drugs over the past five decades, especially those derived from terrestrial microorganisms and higher plants, as well as providing many compounds that have led to the discovery of new biochemical mechanisms. Several biological activities of compounds extracted from *Montrichardia linifera* have already been reported, such as antioxidant, antibacterial, antimalarial and insecticidal activity. Studies have found that extracts of this plant showed toxicity against *Artemiasalina*, which used in the preliminary evaluation of toxicity, being useful in the detection of bioactive compounds in plant extracts and demonstrating a good correlation with the cytotoxic activity against human tumors. Thus, this study aimed to evaluate the cytotoxic and antimigrant activity of methanolic, hydroalcoholic and hexanic extracts of *M. linifera* leaves in tumor cell lines. **Methods**:The specimens of *M. linifera* used to make the extracts were collected in five collection points: Santa Quitéria (03°30'56''S; 42º32'48''O), Galego (2°46'49''S; 41°51'51''O), Porto dosTatus (2°50'17''S; 41°49'52''O), Morros da Mariana(2º51'15,9''S; 41º48'49,1''O) and Lagoa do Bebedouro (2°46'49''S; 41°51'51''O).An exsicata of number 3541 was deposited in the herbarium HDelta of the Federal University of Piauí. For the methanolic and hexane extracts, 100 ml of reagent was measured for 10 g of leaves and for the hydroalcoholic extract 20 ml of ethanol, 80 ml of water were measured for 10 g of leaves. To evaluate the cytotoxic potential of these compounds the MTT assay was used in the cancer cell lines B16-F10 (murine metastatic melanoma) and MDA-MB231 (human breast adenocarcinoma), after 72 hours of incubation at a concentration of 50 µg/mL. The cell migration assay was performed on 24-well plates with 0.25% BFS at concentrations of 50, 5 and 0.5 µg/mL of the hydroalcoholic extracts from Santa Quitéria and Bebedouro. A scar was performed on the cell monolayer and cell migration was monitored after 24 hours of incubation. The cells were visualized under an optical microscope, photographed at 50x magnification, and the scar area at the beginning and at the end of treatment were measured for comparative purposes. **Results**: For the B16-F10 line, the hexanic and methanolic extracts showed cytotoxic activity, mostly above 70% inhibition, but the best results were observed for hydroalcoholic extracts from Santa Quitéria and Bebedouro, which presented 92% inhibition. No cytotoxic activity was observed for the MDA-MB231 cell line. A cell migration assay was performed for the hydroalcoholic extracts from Bebedouro and Santa Quitéria, which showed the best cytotoxicity results against metastatic B16F-10 cells. Thus, the antimigratory activity of these extracts at a non-cytotoxic concentration, with inhibition of approximately 70% of the tumor cells, was observed. **Conclusion**: Thus, this work demonstrated that extracts of leaves of *M. linifera* indicated a strong cytotoxic and antimigratory potential, also observing that these activities were different depending on the location of the plant. **Support:** CNPq, CAPES, INCTBioNat.

10.026 Evaluation of the cytotoxic and antitumour effects of the hydroalcoholic extract of Propolis Green. Araújo SMS, Menezes Filho RO, Mendes Neto JM, Graça AS, Moraes SZC, Souza JB, Amaral RG, Santos SA, Andrade LN, Carvalho AA UFS
Introduction: It is known that cancer has disordered growth, invades tissues, organs and has systemic spread. For many years, natural products like green propolis are used for curative and chemopreventive purposes, representing a source rich in phenolic acids and flavonoids, which present a wide range of biological activities, including antineoplastic effects (Amaral et al., Clin. oncol., v.4, p.1562, 2019). Therefore, the aim of this study was to investigate the cytotoxic and antitumor effects of the hydroalcoholic extract of propolis green (HEPG). **Methods:** Hydroalcoholic extract preparation was with 4 g of green propolis crushed and homogenized in 400 mL of 70% alcoholic solution, filtered and maintained in an infusion. The extract was tested against five human cancer cell lines: human leukemia (HL-60), colon carcinoma (HCT-116), prostate adenocarcinama (PC-3), glioblastoma (SNB-19) and breast adenocarcinoma (MCF-7) using the MTT assay, in triplicate with a single concentration of 50 µg/mL (Mosmman, J. Immunol Methods. v. 65. p. 55, 1983). The treatment effects were expressed as the percentage of control absorbance of reduced dye at 595 nm. All absorbance values were converted into a cell growth inhibition percentage (GI%) by the following formula: GI% = 100 − [(T/C) × 100%. Where C is the absorbance for the negative control, and T is the absorbance in the presence of the tested compound. For the evaluation of the antitumor activity *in vivo* were implanted sarcoma 180 (S180) ascites tumour cells (2×10^6 cells/0.5 mL) subcutaneously into the right axillary region of mice swiss (25-35g). After inoculation, the animals were separated into 4 groups (n = 10/grups): negative control (saline, oral route), positive control (5-FU 25 mg/kg/day) and two test groups (HEPG 100 and 200 mg/kg/day, oral route). After 24 hours of inoculation, the treatments were administered for 7 consecutive days. On day 8 the animals were euthanized and then the tumors were removed for weighing. The percentage of tumor inhibition was calculated using the formula IT (%) = [(A-B) / A] × 100, where IT is tumor inhibition, A is the mean vehicle weights and B is the weight average of the treated groups. **Results:** The results of this study showed that the HEPG demonstrated intermediate cytotoxicity with GI 51% - 75% for the cells MCF-7 (GI = 68.16%) and SNB-19 (GI = 72.41%), and high cytotoxicity with GI > 75 % for HL-60 (GI = 95.61%), HCT-116 (GI = 89.56) and PC-3 (GI = 89.43 %). In view of these results the antitumor activity of HEPG *in vivo* was evaluated. It was observed that HEPG inhibited tumor growth in 47% and 48% at doses of 100 (0.73 ± 0.11g) and 200 mg/kg/day (0.71 ± 0.14g), respectively ($p < 0.05$). 5FU inhibited 69.2% ($p < 0.05$) at a dose of 25 mg/kg/day (0.47 ± 0.07g). **Conclusion:** The data suggest that HEPG has relevant *in vitro* cytotoxic activity against the tumor cell line (HL-60, HCT-116, PC-3) and presents reduction of the growth of tumors in front of the pre-clinical model of tumor S180 by oral route. However further investigations to identify extract toxicity are required. **License number of ethics committee**: 38/2017. **Financial support**: CAPES and FAPITEC.

10.027 Novel thiazacridine and imidazacrine derivatives and their binding behavior with bovine serum albumin. Tavares MAB, Souza GMM, Cavalcanti LAMN, Almeida SMV UPE

Cancer, one of the most devastating diseases in the world, shows great dynamicity and heterogeneity. These characteristics favor the emergence of resistance and hinder the therapeutic process. Thus, in the face of the therapeutic difficulty, the development of new alternatives for effective and safe interventions is essential. Among these alternatives are DNA intercalators, and between them, the acridine derivatives stand out as classic intercalators, presenting antitumor activity. In this perspective, considering the potential of acridine derivatives, new thiazacridine derivatives and imidazacridine derivatives were evaluated for their interaction properties with albumin, one of the main carriers of drugs in clinical use. Considering that studies on the binding characteristics of a new compound with protein are essential for the understanding of pharmacological efficacy and its clinical safety, this work presents as an attempt to evaluate the properties of the in vitro interactions of thiazacridine and imidazacridine derivatives with bovine serum albumin (BSA) by spectroscopic studies of UV-vis uptake and fluorescence emission. The thiazacridine derivatives (4) 5-acridin-9-ylmethylidene-3-amino-2-thioxo-thiazolidin-4-one (LPSF / AC-127), (5) 5-acridin-9-ylmethylidene-2-thioxo 4-one (LPSF / AC-157), (7) 3-acridin-9-ylmethyl-thiazolidine-2,4-dione (LPSF / AA-1A) and the imidazacridine derivative (6) 5-acridin- 9-ylmethylidene-2-thioxoimidazolidin-4-one (LPSF / AC-5) were successfully obtained. After interaction with the BSA, in the UV-vis absorption the derivatives tested exhibited changes in their spectroscopic properties, demonstrating hyperchromic effect with increasing absorption intensity for all compounds. In addition to this effect, derivatives 4 and 6 presented a hypsochromic shift, while derivatives 5 and 7 showed displacement to the red region, presenting a bathochromic shift. The derivatives showed intrinsic binding constants with BSA ranging from 0.78 to 10.5 x 105 M-1. Derivative 6, the only imidazacridine derivative, showed a greater increase in the peak of absorption intensity, greater displacement of the maximum wavelength and also a higher intrinsic binding constant (Kb), showing a better cytotoxic potential. Spectrofluorometric studies confirmed the interaction of the compounds with BSA, all of which showed marked decrease in fluorescence intensity of BSA in the presence of increasing concentrations of the compounds. According to the values of the Stern-Volmer extinction constant (Ksv) all derivatives had a constant of 104 (M-1), indicating the existence of interaction between the compounds and BSA. Such results demonstrate a mechanism for binding to BSA with thiazacridines and imidazacridines, showing that these derivatives are promising in the development of novel acridine analogues with potential albumin binding sites. Acknowledgments: authors are thankful to FACEPE (Fundo de Amparo à Ciência e Tecnologia de Pernambuco, Brasil) for financial support.