(ERS) covered with poloxamer 188 (P188) and loaded with loperamide (NP-Lop), for crossing the BBB and reduce protein oxidative stress. **Methods:** Central biodistribution was assessed by evaluating NP-Lop supraspinal analgesic effects in rats naive submitted to the Hot Plate Test, after its oral and intraperitoneal administration. Protein oxidative stress was measure in prefrontal cortex (PFC) of rats submitted to traumatic brain injury (TBI), by advance oxidative protein products (AOPP) colorimetric assay, after NP-Lop intravenous administration. Confidence interval was set at 95%; statistical analysis was performed by t-student comparison or ANOVA and Tukey test. **Results:** NP-Lop increased maximum possible effect in the Hot Plate test at 30 min, 2 and 24 h after both, ip and vo NP-Lop administration, in about 20 and 60-fold regarding loperamide in solution (Lop/Sol). In addition, NP-Lop reduce AOPP in about 6.7-fold regarding TBI. **Conclusion:** NP-Lop enhance loperamide CNS biodistribution, and reduces AOPP in a TBI rat model. Finally, the nanocarriers synthesized are potentially a nanopharmaceutical form that may enhance gastrointestinal absorption of drugs like loperamide.

70. (425) **Risk of QT Prolongation related to Drug used in COVID-19: Use of a database mining strategy to detect risk and predict adverse reactions.**

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Introduction: The search for effective drugs in COVID led to an insufficient assessment of adverse reactions. Hydroxychloroquine was has a known risk of arrhytmia and was used without proven efficacy. This situation may have been partially repeated for other drugs. We analyzed the FAERS database in search of signals of new associations. Methods: FAERS reports (2004 to 2020) were analyzed. The Medical Dictionary for Regulatory Activities (MedDRA) was used to identify TdP/QTP cases. We calculated the Reporting Odds Ratios (RORs), Proportional Reporting Ratio (PPR), Yule's Q, and Chi Square with Yate's correction for the association between each Drug used in CoViD treatment, moxifloxacine (positive control) and ceftriaxone (negative control) using MedDRA Standarized Medical Querry for QT Prolongation. Signals were defined as lower limit of the 95%CI greater than 1.0 (for ROR or PPR), greater than 0 (Yule's Q) or a P value less than 0,05 (Chi Square). Results: 17.734.379 reports (including 48.364 arrhytmias) were analyzed. No significant signals were found for Dexamethasone, Remdesivir, ritonavir / lopinavir, and Ceftriaxone. A significant signal was found for prolonged qt prolongation and arrhythmias for: hydroxychlorocine 1.23 (1.10 to 1.56); ivermectin 1.63 (1.09 to 4.51); tocilizumab 1.07 (1.02 to 0.28); ticarcilina clavulanico 3.57 (2.60 to 4.91); piperacillin + tazobactam 2.32 (2.17 to 2.48); ampicillin + sulbactam 1.91 (1.68 to 2.17); clarithromycin 1.46 (1.37 to 1.55); azithromycin 1.54 (1.44 to 1.64); and moxifloxacin 1.84 (1.76 to 1.93). Discussion: There is not only a risk of arrhythmias with drugs such as hydroxychloroquine, but also with antibiotics used in the management of COVID (ampicillin + sulbactam, clarithromycin), and other drugs under study for potential efficacy in COVID (azithromycin, toxilizumab, ivermectin). This information must be taken into account to monitor the ECG and prevent pharmacodynamic interactions that enhance the effect.

71. (492) **PHARMACOLOGICAL INHIBITORS OF THE MOLECULAR CHAPERONE HSP90**

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Hsp90 is a molecular chaperone that stabilizes in an ATP-dependent manner the active conformation of many proteins with stable tertiary structure. Several substrate proteins of this chaperone are related to tumor development and progression, hence making Hsp90 an attractive target for antitumor therapy. The inhibition of Hsp90 activity shows strong anticancer effects, and Hsp90 inhibitors seem to be the only chemotherapeutic agents capable to affect all cancer hallmarks. Unfortunately, one of the most efficient inhibitors, Geldanamycin (GA), cannot be used in clinical trials because of its harmful side-effects.

In the present work we evaluated the capability of synthetized compounds designed by molecular modelling to inhibit the ATPase activity of Hsp90, and their effects on the biological actions mediated by this chaperone, such as PC3 cell viability and migration, as well as GR transport to the nucleus after hormonal stimulation in HEK293T-transfected cells. In all the cases, GA was used as an inhibitory control. Nine compounds named S3, S8, S31, S42, A15, C3, C6, N15 and P1 were tested. All of them confirmed the *in silico* predictions regarding their ability to inhibit the intrinsic ATPase activity of Hsp90. The S-series of dihydroxybenzaldheyde-derived Schiff bases and C-series of pyrazoline-derived drugs (especially C3 and C6) showed a decreased action on cell viability comparable to that shown by GA, but only S3, S8, S31 and S42 decreased cell migration comparable to the positive control. None of the synthetics drugs affected the GR nuclear import.

In summary, in this study we described various synthetic candidates with high pharmacological potential. Importantly, it is also shown that Hsp90 ATPase activity is not an essential requirement for cell viability and GR nuclear import, which opposites the prevailing dogma.

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72. (154) **EFFECTS OF OXIDIZED LOW-DENSITY LIPOPROTEIN (OXLDL) ON PROSTATIC STROMAL CELLS DERIVED FROM PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA**

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Benign Prostatic Hyperplasia (BPH) affects elderly men, being the result of an excessive and uncontrolled cellular proliferative process of both epithelial and stromal prostatic compartments. Novel evidence suggests that dyslipidemias and other factors of the Metabolic Syndrome are associated to BPH progression and aggressiveness. However, little information is available about the pathogenic mechanisms promoting prostatic growth in atherogenic contexts. We therefore aimed to analyze *in* vitro the effects of OxLDL on primary cell cultures. Prostatic stromal cells, surgically harvested from patients with BPH (n=3), were isolated, cultured, and stimulated with OxLDL (20 μM or 100 μM, simulating an atherogenic state) or vehicle for 24h and 48h.

OxLDL induced cell proliferation, as assessed by BrdU incorporation and Ki67 immunocytochemistry, mainly at lower concentrations and in a time-dependent manner ($p<0.001$ vs. vehicle). OxLDL-treated cells also displayed a myofibroblastic phenotype with high metabolic activity, characterized by an increase of cytoplasmic granules, dilated endoplasmic reticulum, and the presence of prominent nucleoli, as evaluated by transmission electron microscopy (TEM). Furthermore, the release and characterization of Extracellular Vesicles (EVs) were determined in supernatants, which were isolated by ultracentrifugation steps and observed by TEM using negative staining. BPH-derived stromal cells showed a very low frequency of secreted EVs, with OxLDL inducing a 10-fold increase, especially in a fraction of 15-20nm ($p<0.001$). At ultrastructural level, these vesicles exhibited an artificial concave shape appearance, compatible with exosomes. Taken together, these findings indicate that OxLDL promotes cell proliferation, stimulation, and EVs release in BPH stromal cells, pointing OxLDL as a strong pathogenic factor in atherogenic contexts supporting uncontrolled prostatic growth.

73. (285) **CHARACTERIZATION OF OUTER MEMBRANE VESICLES FROM MULTIDRUG RESISTANT BACTERIA**