G.15 - Hyaluronic Acid Incorporation Modulates Rheological and Drug Release Properties in Poloxamer-Based Hydrogels

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INTRODUCTION: Synthetic polymer Poloxamer (PL) 407 (15% and 30% w/w) and binary formulation PL 407 15% + PL 338 15% (BF), with natural polymer hyaluronic acid 0.5% w/w, were designed as bupivacaine or ropivacaine thermosensitive release systems. OBJECTIVES: The aim of this work is to characterize structure and stability of drug delivery systems. MATERIALS AND METHODS: These systems were characterized by calorimetry, rheology, SANS, and release profile. DISCUSSION AND RESULTS: Calorimetry results demonstrated all formulations are stable at storage and physiological temperatures. PL 407 30% and BF systems are structurally more organized and with higher consistency (G'/G'' ~ 50) at 37 °C and with lower gelation temperature (Tg ~ 14 °C) than PL 407 15% ones (G'/G'' ~ 0.30 and Tg ~ 45 °C, respectively), however BFs have increased viscosity and slightly higher stiffness (G'/G'' ~ 60) when compared to PL 407 30% formulations, due to more hydrophilicity of PL 338 chains than PL 407. Adding HA, it is observed enhanced viscosity but diminished consistency (G'/G'' ~ 0.40). When a drug is incorporated, it is seen that it promotes increased interaction between chains. Although material alteration when incorporating HA or drug is observed, SANS results showed that the type of supramolecular structure is dependent on the concentration of Poloxamer. Systems with low concentration of Poloxamer have lamellar type, while formulations with 30% of Poloxamer have both cubic and hexagonal structures. In addition, PL 407 30% formulations undergo greater compression when bupivacaine is added (~ 29.7 nm at 25 °C and 37 °C). As drug release profiles showed, BFs release drugs in a more controlled way than other formulations. Moreover, HA hinders the release of both drugs. CONCLUSION: Thus, it is clear that the incorporation of more hydrophilic polymers is able to modulate the drug release rate according to the hydrogels rheological parameters.

Keywords: Supramolecular structures, Physico-chemical analysis, Drug delivery / **Supported by:** CNPq

G.16 - Lunatin-1: A Scorpion Venom Peptide That Induces Cellular Death In LNCap And MDA-MB-231 Cancer Cell Lines

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INTRODUCTION: Previous studies demonstrated that Lunatin-1, a peptide isolated from *Hadruroides lunatus* scorpion venom, regulates apoptosis in human promyelocytic leukemia HL-60 cell line as well as induces death in MCF-7 and MDA-231 human metastatic cancer cells lines by unknown mechanisms. OBJECTIVES: Evaluate the possible Lunatin-1 anti-tumor activity in metastatic human cancer cells, focusing on its mode of action MATERIALS AND METHODS: Synthetic Lunatin-1 was purified by high-performance liquid chromatography (HPLC). Purified Lunatin-1 was analyzed by mass spectrometry (MALDI-TOF/TOF) for synthesis and purification quality control. Lunatin-1 similarity search against human proteins was performed by Blast online tool. Gene ontology was done by GhostKOALA and David online tools. LNCap and MDA-231 cells were treated with different concentrations of Lunatin-1, and cell viability was evaluated by Resazurin assay. IC50 was determined by GraphPad Prism. DISCUSSION AND RESULTS: Lunatin-1 was successfully purified, as confirmed by mass spectrometry. Lunatin-1 induced cytotoxicity in LNCap cells even in the lowest concentration used (1.5 μM, $p < 0.001$). In the MDA-MB-231 cell line, Lunatin-1 presented cytotoxic activity with IC 50 of 20.1 μM. On the other hand, Lunatin-1 was cytotoxic for non-tumoral cells HEK-293 with concentrations higher than 25 μM. Therefore, Lunatin-1 presents different cytotoxic activity when comparing tumoral and non-tumoral cell lines (LNCAP x HEK293, $p < 0.001$). The bioinformatic analysis demonstrated that Lunatin-1 has similarities with proteins related to alternative splicing, phosphoproteins, transporter proteins, breast cancer proteins and prostate neoplasm proteins. Due to Lunatin-1 similarity to breast cancer proteins and prostate neoplasm proteins, its mechanism of action may be related to these proteins. CONCLUSION: Lunatin-1 may represent a potential prototype for developing anti-tumor drugs.

Keywords: Lunatin-1, scorpion peptides, anticancer peptides / **Supported by:** FAPEMIG, CAPES, CNPq