BIO_16 - Evaluation effect of nanocarriers of AmB on pathogenics fungal

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Introduction: Globally, more than one billion people are affected by fungal infection, resulting in approximately 13.5 million life-threatening infections and more than 1.7 million deaths annually. Therapeutic strategies against systemic mycoses can involve antifungal resistance and significant toxicity. One of the main approaches to overcome biopharmaceutical challenges is the use of polymeric nanoparticles, which can carry drugs, such as amphotericin B. Its main advantages over other nanostructured systems are the increased potential for drug solubilization in small doses, great encapsulation capacity and possibility of functionalization of the surface of the nanocarriers.

Objective: To assess the *in vitro* effect of NanoAmB on pathogenics fungal.

Methodology: Polycaprolactone (PCL) and poly (lactic acid) (PDLLA) polymeric nanoparticles were produced by the nanoprecipitation method. Pathogenic fungal species, *Criptococcus neoformans* (serotype A clinical isolate H99), *Candida albicans* (ATCC 90028), THP-1 (ATCC TIB-202) and BHK (ATCC CCL-10) were grown *in vitro* in the presence of serial dilutions of NanoAmB alone or in combination with monoclonal antibodies (mAb). Cytotoxicity assay was performed by MTT and evaluation of viable yeast fungal and mammal cells was realized spectrophotometrically (540 nm).

Results: The PDLLA nanoparticles presented an average size of 137.3 ± 18.4 nm and an AmB concentration of 132.9 ± 17.6 mg/mL, while the PCL nanoparticles displayed an average size of 145.1 ± 11.5 nm. The cytotoxicity assay demonstrated that NanoAmB and nanocarriers without AmB does not show cytotoxicity against mammalian cells at concentrations ranging from 10 µg/mL to 0.1 µg/mL. However NanoAmB demonstrated that cytotoxic effect against *C. albicans* and *C. neoformans* after 24 hours in all concentration analyzed (10 µg/mL to 0.1 µg/mL) ($p<0.05$). However, nanocarriers without AmB showed a cytotoxic effect from 10 to 2.5 µg/Ml. NanoAmB showed an effect from 1.25 to 0.05 µg/mL in both fungal species and a partial effect at concentration up to 0.025 µg/mL only in *C. albicans* ($p<0.05$). Concentrations lower than 0.025 showed no cytotoxic effect.

Conclusion: Nanocarriers acted as an enhancing agent, potentializing the inhibitory growth effects of AmB on pathogenic fungi. Other novel antifungal therapeutic strategies using NanoAmB, isolated or in combination with mAbs, should be considered in the future.

Keywords: Nanocarriers of AmB; Pathogen fungi; Antifungal therapy