Polymeric Nanogel based on Polyetheramine-bisepoxide Containing Amphotericin B for reduced Biofilm Growth

ANA FLÁVIA ALVES PINTO CUNHA[1], REGINA HELENA PIRES[1], DENISE CRISPIM TAVARES[1], ARTHUR BARCELOS RIBEIRO[1], PEDRO HENRIQUE OLIVEIRA DOS SANTOS[1], EDUARDO FERREIRA MOLINA[1]

[1.] UNIVERSIDADE DE FRANCA, FRANCA/SP, BRASIL

The persistence and recurrence of fungal infections associated with species of the genus *Candida* are directly related to biofilm formation and increased antifungal resistance, factors that compromise the effectiveness of conventional therapeutic approaches. In this context, nanostructured systems have been explored as promising strategies to optimize drug delivery and enhance their activity in organized microbial communities. Thus, this study aimed to synthesize and characterize a polymeric nanogel as a carrier system for amphotericin B (AmB), evaluating its antifungal efficacy against *Candida* species under planktonic conditions and in biofilms, as well as its cytotoxicity. The nanogel was obtained through a reaction between a bisepoxide and a polyetheramine at a 1:1 molar ratio, followed by heating, dilution, and purification by dialysis. Subsequently, the nanogel was characterized by dynamic light scattering (DLS), zeta potential, and transmission electron microscopy (TEM). Antifungal activity was determined by minimum inhibitory concentration (MIC) and by evaluation in biofilms of *Candida tropicalis* and *Nakaseomyces glabrata*, while cytotoxicity was assessed in HaCaT keratinocytes. The system exhibited an average diameter of approximately 270 nm, low polydispersity, and a positive surface charge, maintaining stability after AmB incorporation. From a microbiological perspective, the nanogel without drug did not exhibit relevant antifungal activity. In contrast, the formulation containing AmB demonstrated greater efficacy compared to the free drug, as evidenced by reduced MIC values. In mature biofilms, free AmB showed activity only at concentrations higher than those used clinically, whereas its incorporation into the nanogel resulted in a significant reduction in MIC, highlighting the superiority of the nanostructured formulation. Regarding biocompatibility, encapsulation of AmB significantly reduced cytotoxicity, as indicated by increased IC_{50} values. Overall, these findings indicate that the developed system improves the therapeutic profile of AmB by combining enhanced antifungal efficacy with reduced cellular toxicity. Therefore, the nanogel represents a promising platform for controlled drug delivery, supporting further investigations toward clinical application.

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