Title: EVALUATION OF ANTIFUNGAL ACTIVITY OF SIMVASTATIN AND ITS ASSOCIATION WITH FLUCANAZOLE AGAINST *Candida albicans*

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Abstract:

*Candida albicans*belongs to endogenous microbiota but is considered opportunistic yeast affecting both immunocompetent and immunocompromised patients. This species is the most common of its genus, causing superficial and invasive infections.Treatment of fungal infections is difficult because there are few available antifungal agents.The use of two or more antifungal agents concomitantly is a good alternative to increase the spectrum of action and reduce adverse effects. Fluconazole is anusual antifungal, and simvastatin is used to reduce blood cholesterol concentration in humans. However, it has the potential to inhibit the synthesis of ergosterol in the plasma membrane of fungi and so could be used as an antifungal.Our aim was to verify the antifungal activity of simvastatin and its synergism with fluconazole *in vitro*.In this study were used a clinical strain of *C. albicans* and a standard strain, *C. albicans* ATCC 90028. To evaluate the antifungal activity of those drugs, we performed an agar diffusion test (drug concentrations ranging from 1000-250 µg/mL), andestimated the minimum inhibitory concentrations(MICs) according to M27-A2 CLSI protocol. To evaluate the interaction of the drug,a checkerboard technique was conducted, using a starting concentration of 125 µg/mL for both drugs.For agar diffusion tests, our results demonstrated inhibitionzonesat a minimal concentration of 250 µg/mL for fluconazole and 750 µg/mL for simvastatin. In the MIC test, the standard strain growth was inhibited with 31.25 µg/mL of simvastatin and 0.24 µg/mL of fluconazole. For inhibiting the growth of the clinical isolate, it was necessary half of the concentration of both antifungals. Additionally, the drug interaction was synergistic against both strains tested (3.9 µg/mL of fluconazole and 0.03 µg/mL of simvastatin). Thus, our results showed that simvastatin has great potential as a topical antifungal.

Key-words: Simvastatin, fluconazole, *Candida albicans*, synergism.

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