TITLE: *IN VITRO* SUSCEPTILITY OF CHROMOBLASTOMYCOSIS AGENTS TO SIMVASTATIN ISOLATED AND IN COMBINATION WITH TRIAZOLE ANTIFUNGALS

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ABSTRACT:

Chromoblastomycosis is an chronic disease caused by traumatic implantation of dematiaceous fungi. When not diagnosed in early stages, this infection reports low cure rate and high recurrence, especially in the most severe forms. Due to its difficult treatment, this mycosis is considered a challenge for the clinicians, not having a proper therapy or drug. Statins are hypolipidemic drugs that reduces serum cholesterol levels. One of the representatives of this class most commonly used is simvastatin. Considering that fungi have ergosterol as a constituent of their membrane, these drugs could have antifungal action. Thus, this work aimed to evaluate the *in vitro* susceptibility of chromoblastomycosis isolates to simvastatin alone and in combination with two azoles antifungals (itraconazole and posaconazole). The susceptibility assesment was carried out according to CLSI-protocol M38-A2. The interaction between simvastatin and the antifungal agents was evaluated through the chessboard techinique. For the analysis of morphological changes against *Fonseacaea pedrosoi* ATCC 46428, high resolution images were obtained by atomic force microscopy. Simvastatin could not inhibit anyone of the strains, even when the higher concentration was tested (MIC > 128 µg/mL). The combinations itraconazole-simvastatin and posaconazole-simvastatin demonstrate synergism against all of the investigated isolates (IFCI = 0,24 – 0,5). Microscopic images revealed morphological modifications in the fungal membrane, causing the fungus rupture and the extravasation of its intracelullar fluid when the strain was treated with itraconazole/simvastatin. In accordance with the results, it can be observed that simvastin in combination with itraconazole or posaconazole may be promising in the treatment of chromoblastomycosis.

Keywords: Antifungal activity, azoles, *Fonsecaea* spp., HMG-CoA reductase inhibitors.

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