TITLE: EXPRESSION OF THE *SAP9* AND *SAP10* GENES, OF BIOCHEMICAL AND ULTRASTRUCTURAL ASPECTS IN *Candida albicans* STRAINS IN PLANKTONIC STATE AND BIOFILM, BEFORE AND AFTER THE ASSOCIATION OF FLUCONAZOL AND GUTTIFERONA A

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ABSTRACT

Among the species of fungi that cause bloodstream infections, *Candida albicans* is the most prevalent. The understanding of the factors associated with the virulence of this fungus, among them, the expression of the Secreted Aspartic Proteases isoenzymes (Sapp) and the formation of biofilms, are of great relevance in the attempt to find possible therapeutic targets. Evaluate the interaction between Fluconazole and Guttiferone-A, in planktonic cells and biofilms, through morphotopographic analysis and gene expression of *SAP9* and *SAP10*, in order to verify possible mechanisms of action of Guttiferone-A in *C. albicans*. We evaluated the gene expression of *SAP9* and *SAP10*, quantified the ergosterol produced in the cells under treatment and evaluated by means of atomic force microscopy (AFM) ultrastructural characteristics in planktonic cells and biofilms of *C. albicans* before and after isolated and associated treatment between Fluconazole (FLC) and Guttiferone A (GUT). The planktonic cells SC5314 strain was sensitive to FLC (0.125 µg / mL) and GUT (7.5 µg / mL). The associations showed a synergistic effect with inhibition of 75% growth of *C. albicans* (FICI = 0.156). Cells under association showed morphological changes, such as increase size ($p<0.001$), reduction ergosterol production ($p<0.001$), and reduction in *SAP9* and *SAP10* expression in planktonic cells when compared to control. In the biofilms, the fungus presented resistance of more than 2000 times when treated with the substances alone and there was no activity in the associations. GUT 1024 µg/mL promoted an increase in biofilm biomass ($p<0.001$) and, under treatments with 16 µg/mL, the cells had an increase in size compared to the control ($p<0.001$). The association of GUT to FLC has pharmacological potential against *C. albicans*, promoting a synergistic activity with significant changes in the structure of this fungus.

Key words: Biofilms. *Candida albicans*. Fluconazole. Gene Expression.

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