

Title: SYNERGISTIC EFFECT BETWEEN ACCA SELLOWIANA (OBERG) AND FLUCONAZOL AGAINST CANDIDA GLABRATA RESISTANT

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Abstract:

Fungal infections caused by opportunistic yeast non - *albicans Candida* (NAC) have dramatically increased in recent decades and could be related to the high number of immunocompromised patients. NAC have greater resistance to traditional antifungal agents such as fluconazole (FLZ), the drug of choice for the treatment of infections caused by *Candida* spp. The antifungal resistance leads to failures in clinical therapy and may cause an increase in morbidity and mortality rates. The species *Candida glabrata* have intrinsic resistance to FLZ. Thus, it becomes necessary to search for new treatment alternatives in cases of candidiasis and candidemias related to this *Candida* specie. Associations between drugs and natural substances can be a feasible alternative to overcome antifungal resistance in NAC. *Acca sellowiana* is a guava tree belonging to the Myrtaceae and has several proven biological activities. Thus, the aim of this study was evaluate the synergistic activity between the active fraction F2 from the freeze-dried aqueous extract of leaves of *A. sellowiana* with fluconazole (FLZ) in *Candida glabrata* isolates sensitive and resistant to FLZ. Ten isolates of *C. glabrata* were used: sensitive isolates (GC RL02S, CG RL03S, CG RL12S, CG RL34S and CG RL37S) and resistant isolates (CG RL12m, CG RL22, CG RL24, CG RL34m and CG RL37m) to FLZ. The methodology was carried out by the Checkerboard method and the result of interaction according to the value of the Fractional Inhibitory Concentration Index (IFIC): synergistic interaction (IFIC \leq 0.5), additive (0.5 < IFIC < 1), indifferent (1 \leq IFIC < 4) or antagonist (IFIC \geq 4). Strong synergistic effect was demonstrated in 80% of *C. glabrata* isolates. All isolates showed reduced its MIC for both FLZ as to active fraction F2 when evaluated in combination, compared to the MIC values evaluated separately. This combination can be used as an adjunct treatment for eradicate fungal infections caused by *C. glabrata* resistant.

Keywords: *Acca sellowiana*, *Candida glabrata*, antifungal agent, synergism, resistance

Fostering agency: CNPq