

Titre: *In vitro* synergy between fluconazole and citral against *Candida glabrata* strains

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Abstract:

Candida glabrata is a commensal fungus present in oral and vaginal mucosa and in gastrointestinal tract of humans. It may be the etiological agent of several opportunistic mycoses in immune compromised patients. *C. glabrata* is intrinsically resistant to the widely used triazole antifungals and its rapidly acquire azole resistance during therapy. Due to the increased bacterial resistance to multiple antibiotics, there are concerns about researching for new drugs and antibacterial therapy. In this way, the aim of this study was to determine the synergistic effect of citral in combination with fluconazole against *Candida glabrata* strains. Initially, it was determined the antifungal activity of fluconazole and three terpenes (citral, eucalyptol and limonene) against nine *C. glabrata* strains and *C. glabrata* ATCC 90030. The study of the interaction between citral and fluconazole was carried out by the checkerboard method on five *C. glabrata* strains. The criteria used to evaluate the synergistic activity was defined by the Fractional Inhibitory Concentration Index (FIC index). All *C. glabrata* strains showed a fluconazole resistance profile whose MICs were greater than 5120µg/mL. Amongst the terpenes, citral showed to be the most effective (MIC 320-80 µg/mL) and was chosen for the second step of this research. The synergistic effect was observed between the fluconazole and citral on all strains. The FICI values ranged from 0.18 to 0.25. The MIC reduction to fluconazole was greater than or equal to 87.5%. The citral associated with fluconazole acts synergistically and drastically decreases MIC values of this antifungal.

Key words: *Candida glabrata*, citral, fluconazole, synergistic effect.

Financial support – CAPES, UFPE

