

TITLE: SYNERGISTIC ANTIFUNGAL EFFECT OF FLUCONAZOLE COMBINED WITH PURE CULTURE EXTRACT OF *Candida parapsilosis* AGAINST *Trichophyton mentagrophytes*

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ABSTRACT:

Onychomycosis are nail infections caused primarily by dermatophyte fungi, followed by yeasts, characterized by being persistent infections with high recurrence rates. The interspecies interactions in infections of mixed etiology are mediated by small diffusible molecules and are fundamental for the survival of these microorganisms in competitive environments. The present study evaluated the synergistic interaction between a pure culture extract of *Candida parapsilosis* (ECP) and fluconazole against *Trichophyton mentagrophytes*. Clinical strains of *C. parapsilosis* from the Laboratory of Microbiology of the Medical School in São José do Rio Preto (FAMERP), Brazil were used. A 500-mL Inoculum prepared in Sabouraud Dextrose Broth was filtered through a 0.2 µm millipore membrane and separated using ethyl acetate as a counter-phase. The ethyl acetate phase was dried completely using a rotary evaporator and subsequently solubilized in sterile distilled water with 10% dimethyl sulfoxide (DMSO). Minimal Inhibitory Concentration (MIC) tests were performed for *T. mentagrophytes* strains. After obtaining the MIC of the extract, a checkerboard trial with fluconazole was performed to evaluate the synergistic interaction with ECP based on the calculation of the fractional inhibitory concentration index (ICIF) = (MIC fluconazole in the mix / MIC fluconazole alone) + MIC extract in the mix / MIC extract isolated). The synergistic interaction was classified using the method described by Kumar *et al.*, where values ≤ 0.5 indicate significant interaction. The results obtained for the MIC of ECP against the *T. mentagrophytes* strain and fluconazole in isolation were 1000 µg/mL and 16 µg/mL respectively. However, when the extract was used in combination with fluconazole, the MIC value of fluconazole it was 4 µg/mL with an ICIF value of 0,25. In conclusion, the ECP in isolation shows antifungal activity against *T. mentagrophytes* and the action is greater in association with fluconazole, thus proving synergy. In the future, the isolation and identification of extract compounds may allow new therapeutic approaches in the control of fungal infections.

Keywords: onychomycosis, dermatophytes, yeasts, synergism, fluconazole

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