

TITLE: THERAPEUTIC EFFECT OF HYDROETHANOLIC EXTRACT OF *Fridericia chica* (BONPL.) L. G. LOHMANN LEAVES AGAINST VULVOVAGINAL CANDIDIASIS

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ABSTRACT:

Vulvovaginal candidiasis (VVC) is one of the most frequent causes of gynecological consultations. For instance, it is estimated that 75% of women will have at least one episode of candidiasis in their lifetime, and 40%–45% will have two or more episodes. Moreover, approximately 10%–20% of women will have complicated cases of VVC, which includes severe VVC, persistent non-*Candida albicans* infection, and recurrent VVC. However, public health authorities have neglected this disease, which reflects the limited therapeutic arsenal currently available. Therefore, the development of new antifungal therapies is crucial. In this context, medicinal plants represent a promising source for the development of new antimicrobials. The leaves of *Fridericia chica* (Bonpl.) L. G. Lohmann are considered a therapeutic alternative since they are traditionally used in VVC therapy. However, no scientific evidence has supported this use against fungal vaginal infections. Then, we aimed to characterize the antifungal effect of a hydroethanolic extract of *F. chica* leaves (HEFc) and evaluate the therapeutic potential of this extract in a VVC model. HEFc inhibited the growth of *Candida albicans* (512 µg/mL), *C. krusei* (512 µg/mL), and *C. dubliniensis* (256-1,204 µg/mL) *in vitro* without detectable resistance during 21 days. The antifungal effect of the extract was associated with its ability to form pores in the fungal membrane, which is independent of ergosterol binding. HEFc inhibits important virulence factors of *C. albicans* (i.e., biofilm and yeast-to-hypha transition), interacts synergistically with ketoconazole, and its antifungal activity is stable under several biological conditions. Intravaginal use of the HEFc at 50 mg/mL induces mycological cure in animals with VVC after 6 days of treatment, similar to the effect observed for the commercial antifungal nystatin. Treatment with the lowest dose of HEFc (5 mg/mL) did not reverse the deleterious effects of the infection of the vaginal tissue. However, a significant therapeutic effect of HEFc was observed at the higher doses evaluated (5 and 50 mg/mL) with reduction in inflammatory infiltrate and in the number of epithelial vacuoles. In addition, at 50 mg/mL, a greater integrity of the epithelium was observed, in which its thickness was comparable to the untreated control. In conclusion, these results support the traditional use of *F. chica* leaves as a topical therapeutic option to treat VVC.

Keywords: *Candida*; Vulvovaginal candidiasis; Natural products; Antifungal development; Vaginitis; Medicinal plants

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