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Quercetin Assists Fluconazole to Inhibit Biofilm Formations of Fluconazole-Resistant Candida Albicans in In Vitro and In Vivo Antifungal Managements of Vulvovaginal Candidiasis

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Abstract

Background: Vulvovaginal candidiasis (VVC) is a common gynecological disease. Candida albicans is believed to be mainly implicated in VVC occurrence, the biofilm of which is one of the virulence factors responsible for resistance to traditional antifungal agents especially to fluconazole (FCZ). Quercetin (QCT) is a dietary flavonoid and has been demonstrated to be antifungal against C. albicans biofilm.

Methods: 17 C. albicans isolates including 15 clinical ones isolated from VVC patients were employed to investigate the effects of QCT and/or FCZ on the inhibition of C. albicans biofilm.

Results: We observed that 64 μg/mL QCT and/or 128 μg/mL FCZ could (i) be synergistic against 10 FCZ-resistant planktonic and 17 biofilm cells of C. albicans, (ii) inhibit fungal adherence, cell surface hydrophobicity (CSH), flocculation, yeast-to-hypha transition, metabolism, thickness and dispersion of biofilms; (iii) down-regulate the expressions of ALS1, ALS3, HWP1, SUN41, UME6 and ECE1 and up-regulate the expressions of PDE2, NRG1 and HSP90, and we also found that (iv) the fungal burden was reduced in vaginal mucosa and the symptoms were alleviated in a murine VVC model after the treatments of 5 mg/kg QCT and/or 20 mg/kg FCZ.

Conclusion: Together with these results, it could be demonstrated that QCT could be a favorable antifungal agent and a promising synergist with FCZ in the clinical management of VVC caused by C. albicans biofilm.

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