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In vitro synergism between berberine and miconazole against planktonic and biofilm Candida cultures.

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Abstract

OBJECTIVES: To investigate the antimycotic activity of the plant alkaloid berberine (BBR), alone and in combination with antifungal azoles, against planktonic and biofilm Candida cultures.

DESIGN: The minimum inhibitory concentrations (MICs) of BBR, miconazole (MCZ), and fluconazole (FLC) towards Candida albicans, Candida glabrata, Candida kefyr, Candida krusei, Candida parapsilosis, and Candida tropicalis were determined by a microdilution method. For C. albicans, the synergistic effects of BBR combined with MCZ or FLC were examined in a paper disc agar diffusion assay and checkerboard microdilution assay. The effect of the BBR/MCZ combination was further investigated in a C. albicans biofilm formation model with a dual-chamber flow cell. The effect on metabolic activity of biofilm cells was established using 2,3-bis(2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxanilide (XTT)/menadione.

RESULTS: Berberine inhibited the growth of various Candida species (MICs 0.98-31.25mg/L) in the following order of susceptibility: C. krusei > C. kefyr > C. glabrata > C. tropicalis > C. parapsilosis and C. albicans. Synergism between BBR and MCZ or FLC was observed in the disc diffusion assay as well as in suspension showing an FIC index <0.5 (∑FIC=0.19). Whilst neither BBR (16 mg/L) nor MCZ (0.8 mg/L) alone significantly inhibited biofilm formation of C. albicans, their combination reduced biofilm formation by >91% after 24 h, as established from the reduction in surface area coverage (P<0.01). The BBR/MCZ combination also exhibited synergy against the metabolic activity of pre-formed C. albicans biofilms in polystyrene microtiter plates (∑FIC=0.25).

CONCLUSION: Berberine exhibits synergistic effects with commonly used antimycotic drugs against C. albicans, either in planktonic or in biofilm growth phases.

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