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Acta Medica Iranica
2009;47(4) : 87-92

Interaction between ketoconazole, amphotericin B and terbinafin and three diazenumdiolates in concomitant uses against some fugal species

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Abstract:

A checkerboard broth microdilution method was performed to investigate the in vitro antifungal activities of three diazeniumdiolates derivatives (DETA/NO, DPTA/NO, DEA/NO) alone and in combination with ketoconazole, amphotricin B or terbinafine against five Candida species, Cryptococcus neoformance and four dermatophyte strains. MICs and MLCs were recorded, and synergy was calculated by using fractional inhibitory and fractional lethal concentration index. DETA/NO with a half-life of 57h at 25°C showed antifungal activity against all tested dermatophyte species (MIC 0.150 to 2.5mg/ml), DPTA/NO with a half life of 3h at 37°C showed antifungal activity against five species of Candida and Cryptococcus neoformans, and DEA/NO with a half life of 2 min at 37°C and 16 min at 25°C did not show antifungal activity against tested strains. Combinations of DPTA-NO with either ketoconazole or amphotericin B were either synergistic or indifferent for all tested strain of Candida and Cryptococcus neoformance. DETA/NO was unable to enhance the antifungal activity of terbinafine against dermatophyte strains. Even where no synergistic activity was achieved, there was still a decrease in the MIC of one or both drugs which were used in combination. Antagonism was observed between terbinafine and DETA-NO against Trichophyton rubrum. Our result suggests that DETA/NO and DPTA/NO may be useful for development of new therapeutic strategies for treatment of dermatophyte and Candida infections. Clinical studies are warranted to elucidate the potential utility of these combination therapies.

Keywords:

NO ، Diazeniumdiolates ، Antifungal activities ، Terbinafine ، Ketoconazole

TUMS ID: 2380

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