Research in Pharmaceutical Sciences, 2012;7(5)
School of Pharmacy and Pharmaceutical Sciences
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Design, synthesis, antifungal and antibacterial activity of some new fluconazole derivatives

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Background and Aims: Fluconazole is a wide spectrum triazole antifungal agent with inhibitory effect on the 14-αdemethlase enzyme. In this study a novel series of fluconazole derivatives with 3-nitro-1,2,4-triazole or piperazine moieties were designed and synthesized as antifungal and antibacterial agents.
Methods: In order to synthesis of these compounds at first, several structures were designed and then the structures were docked into the active site of 14-α-demethylase (MT-CYP51), using Autodock program. Twelve compounds with the best binding energy were selected and synthesized. The chemical structures of the new compounds were confirmed by elemental and spectral (1H-NMR and Mass) analyses. All compounds were investigated for antifungal activity against Candida albicans, Candida tropicalis, Candida glabrata, Candida parapeilosis, Candida kruzei, Candida dubliniensis, Aspergillus fomigatus, Aspergillus flavus, Microsporum canis, Microsporum gypseum, Trichophyton mentagrophyte, Epidermophyton floccosum. Six compounds were investigated for antibacterial activity against some gram positives and gram negatives microorganisms.
Results: These compounds showed excellent in-vitro antifungal and antibacterial activity against most of the tested microorganisms. Also many the synthesized compounds had antifungal activity against several resistant fungi against fluconazole and itraconazole. There is a correlation between docking energy and antifungal activity.
Conclusions: Therefore, the synthesized compounds could be candidates as antifungal agents with inhibition of 14-α-demethylase enzyme. In addition, these compounds showed antibacterial activity against several the tested gram positives and gram negatives microorganisms.

Keywords: Antifunga; Antibacterial; Fluconazole Derivatives; Docking; Nitro-triazole