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Molecular docking of biaryloxy-substituted triazoles as lanosterol 14-demethylase inhibitor

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Background and Aims: During the past three decades, the incidence of invasive fungal infections has been increasing dramatically. Clinical available antifungal agents have several drawbacks such as limited potency and spectrum, drug related toxicity, non-optimal pharmacokinetics and severe resistance. 14α-demethylase (CYP51) inhibitors have been widely used in the treatment of fungal infections. In this research a group of newly synthesized triazole derivatives with CYP51 inhibitory activity, that possessing a variety of substituent at the different positions of the phenyl ring, were subjected to docking analyses.
Methods: Desired azoles were built using HYPERCHEM program, and conformational studies were performed through semi-empirical method followed by PM3 method. The conformers with global minimum energy was used in docking studies. Docking study was performed using Auto-Dock 4.2 program on the all compounds.
Results: The obtained results show all of compounds, interact with the 14-alpha-demethylase and azole-heme coordination, pi-pi and pi-cation interactions are involved in drug-receptor interaction.
Conclusions: Computational modeling was used to rational design of novel antifungal azoles which the structure activity relationship (SAR) of compounds were efficiently explained by flexible molecular docking. Results were shown the coordination between nitrogen of triazole and iron of heme is the most important interaction to inhibitory activity.

Keywords: Docking; Antifungal; Triazole; 14α-demethylase