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Abstract

Design, Synthesis Molecular Docking Study and Antifungal Activity Evaluation of New Benzimidazole-Triazole Derivatives †

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Lanosterol 14α-demethylase (CYP51) is an essential enzyme in the fungal life cycle and also an important target for antifungal drug development. Selective inhibition of the enzyme would cause depletion of ergosterol and accumulation of lanosterol and result in the growth inhibition of the fungal cell [1].

In this study, a series of benzimidazole derivatives containing a triazole ring that are structurally related to the famous antifungal azole pharmacophore were synthesized and their structures were characterized by spectral (IR, ^{1}H-NMR, ^{13}C-NMR, and MS spectra) analyses. Compounds **5i** and **5s** showed the most promising antifungal activity with a MIC_{50} value of 0.39 ug/mL against *Candida* species. Molecular docking studies were performed to investigate the mode of action towards the fungal lanosterol 14α-demethylase. ADME studies were carried out and a connection between activities and physicochemical properties of the target compounds was determined. The effect of the active compounds against ergosterol biosynthesis was observed by the LC-MS-MS method.

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