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Rational Modification of a Lead Molecule: Improving the Antifungal Activity of Indole – Triazole – Amino Acid Conjugates

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Abstract. The modification of a molecule that was identified as highly efficacious in the previous studies could considerably improve the biological activity of the resulting compounds. While targeting lanosterol 14-α demethylase, the molecular modelling studies convinced that the extension of the phenyl ring of compound **1** deep into the hydrophobic pocket of the enzyme may increase the enzyme – ligand interactions and hence improve the anti-fungal profile of the molecules. As a result, the newly designed compounds **2** were synthesized and screened for their anti-microbial properties and these compounds were found to exhibit considerably better activity than the previous molecule **1**. Some of the compounds in this series exhibited MIC_{90} 16 μg mL^{-1} and 32 μg mL^{-1} against *Candida albicans* and *Aspergillus niger*, respectively as against 312 μg mL^{-1} for compound **1**.