Synthesis, Antibacterial, Enzyme Inhibitory, and Molecular Docking Studies of Pyrimido-Pyrimidine Derivatives as Urease Inhibitors

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Abstract

Urease dependent bacterial pathogens pose serious threat to human health due to rapid development of drug resistance and their involvement in urinary tract infections, gastric and duodenal cancers. This intensified the search for novel bioactive molecules with antibacterial and anti-urease potential. In present study a series of 16 pyrimido-pyrimidine derivatives is synthesized by substitution reaction and studied against growth and urease activity of four bacterial uropathogens (*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Klebsiella pneumonia*) isolated from urinary tract infected patients. Among the tested compounds, 6-amino-2,9-diimino-4,11-dimorpholin-4-yl-2*H*,9*H*-dipyrimido[1,2-*a*:1′,2′-*c*]pyrimidine-3,10-dicarbonitrile possessed significant activity against growth (18 mm) and ureolytic potential (51.18%) of *Pseudomonas aeruginosa* and jack bean urease (68.12%). Molecular docking studies performed for studying nature of binding interaction of this compound with jack bean urease demonstrated role of hydrogen bonding and ionic interactions in urease inhibition. ADME analysis of 6-amino-2,9-diimino-4,11-dimorpholin-4-yl-2*H*,9*H*-dipyrimido[1,2-*a*:1′,2′-*c*]pyrimidine-3,10-dicarbonitrile also showed satisfactory results indicating it as promiscuous lead for development of antibacterial and anti-urease molecule.