Abstract No: TC 43

In-silico investigation on derivatives of (*Z*)-*N*-phenyl acetamidoximes as potential inhibitors against *Helicobacter pylori*

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Helicobacter pylori is a major cause of gastrointestinal diseases, including gastritis, gastric and duodenal ulceration, gastric carcinoma, and gastric cancer. Urease enzyme secreted by *H. pylori*, hydrolyses urea, generating ammonia which neutralizes stomach acid and create a suitable pH environment to the bacterium to survive and colonize in the stomach. The structural unit (UreB) of urease contains two nickel ions (Ni^{2+}) at its active site and they are essential for the catalytic effect of urease. Therefore, inhibition of the urease enzyme is a good strategy for controlling *H. pylori*. In this study, (*Z*)-*N*-phenyl acetamide oxime and its phenyl substituted derivatives were designed and their binding affinities to the active site of the urease enzyme were studied using molecular docking. The binding results indicated that the oxygen of the (*Z*)-*N*-phenyl acetamidoxime derivatives interacts with the bi-nickel center of the enzyme with metal acceptor interaction. The ligand–enzyme complex is stabilized mainly by hydrogen bonding interactions and hydrophobic interactions. Hydrogen bonding interactions were observed with polar side chain residues of ASP 362, ALA 365, ALA 169, ASN 168, GLY 279, HIS 322 and the ring and other side chain carbons formed strong hydrophobic interactions with nonpolar residues ASP 362, ALA 169, ALA 168, ALA 365, and CYS 321. Further, ionic interactions were found with the side chain residues of ASP 223, HIS 322, ASP 362, KCX 219. Binding energies were found to increase with the electron withdrawing ability of the groups attached to the phenyl, hence, the electron withdrawing groups will have higher urease inhibitory activities than the electron-donating groups. Hammett correlation plot results showed that, there is a considerable correlation between the ligand binding energies and the electronic effects exerted by the substituent groups. Substitution of groups with inductively electron-withdrawing effects at the para position of the phenyl ring increased the binding energies of the ligand-enzyme complex. Therefore, derivatives of (*Z*)-*N*-phenyl acetamidoxime can act as potential inhibitors against *Helicobacter pylori*.

Keywords: *Helicobacter pylori*, Urease enzyme, Derivatives of (Z)-N-phenyl acetamidoxime, In silico, Urease inhibition