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Synthesis, evaluation and structure activity relationship study of 2-phenyl-3H-quinazolinone derivatives as urease inhibitors against *Helicobacter pylori*

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Urease is a nickel containing metalloenzyme, which catalyzes the hydrolysis of urea into ammonia and carbon dioxide. It is an essential enzyme for *Helicobacter pylori*, which is a bacterium that has an ability to colonize upon the gastric wall, causing gastric ulcers and development of adenocarcinoma. By inhibition of urease, their growth and colonization can be ceased and therefore can be used as a pharmaceutical agent against *H. pylori*. This research was focused on the synthesis of the derivatives of 2-phenyl-3H-quinazolin-4-one and on the evaluation of their urease inhibitory action. Six derivatives of 2-phenyl-3H-quinazolin-4-one were synthesized in good yields (64%-88%) by the oxidative cyclo-condensation of 2-aminobenzamide with benzaldehydes (namely 4-hydroxybenzaldehyde, 4-methoxybenzaldehyde, 4-chlorobenzaldehyde, 4-cyanobenzaldehyde, 4-hydroxy-3-methoxybenzaldehyde and benzaldehyde) in a refluxing aqueous solution of $FeCl_3$. The structures of synthesized analogues were confirmed using spectroscopic techniques such as ^{1}H-NMR, ^{13}C-NMR and FT-IR and by the determination of the melting points of compounds which were previously reported in literature. The urease inhibitory activities of synthesized compounds were quantified using an assay developed from Berthelot's reaction. Urease required for the assay was extracted from the germinated seeds of *Macrotyloma uniflorum* (Horse-gram) and thiourea was used as the positive control. The synthesized derivatives of 2-phenyl-3H-quinazolin-4-one showed moderate to high potencies in the urease inhibition, as the IC_{50} values of all compounds except 2-(4-cyanophenyl)-3H-quinazolin-4-one and 2-(4-chlorophenyl)-3H-quinazolin-4-one, were less than that of the positive control (i.e., 0.80 mg/mL). When a Structure Activity Relationship (SAR) study was carried out by building up a linear free-energy correlation diagram, the exponential of the potencies of synthesized compounds were found to be directly proportional to the substituent constants, where the potency increased with the electron donating nature of the substituent groups. Thus, 2-phenyl-3H-quinazolin-4-one derivatives can be further optimized as "hits" in the drug discovery against *H. pylori*.

Keywords: 2-Phenyl-3H-quinazolin-4-one derivatives, *H. pylori*, Urease inhibitors, SAR

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