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Design, synthesis and evaluation of 3-hydroxy quinazolinone derivatives as urease inhibitors against *Helicobacter pylori*

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Gastritis is a common virulent disease found in the present world. The main pathogen which can cause gastritis is *Helicobacter pylori* and the infection from this bacterium in the upper gastrointestinal tract can lead to ulcers and gastric carcinoma. The activity and the growth of this bacteria in gastric juice of the stomach are favored by the bacterial urease enzyme. Therefore, urease enzyme inhibition plays a significant role in reducing the survival of the pathogen in the stomach. Apart from that, due to bacterial resistance and toxicity problems associated with the current drugs available against *H. pylori*, discovery of novel urease inhibitors is highly demanded. In this study, two 3-hydroxyquinazolinone derivatives were synthesized using anthranilic acid. Synthesized compounds were characterized using NMR spectroscopy. Urease inhibitory action of the synthesized compounds was measured by a colorimetric method called the Berthelot method. The amount of ammonia produced from urea due to urease enzyme activity was determined by this method. Inhibition of urease resulted low levels of ammonia produced and therefore low levels of absorbance. Among the two compounds, 3-hydroxy-2-phenyl-4(3H)-quinazolinone exhibited high levels of inhibition at low concentrations with an IC50 value of 19.95 ± 1.03 µg/mL. This experiment was supported by a computational approach with the use of Gold score software for docking analysis and Chimera 1.9 for visualization of the docked molecules. The computational scores resulted in which 3-hydroxy-2-phenyl-4(3H)-quinazolinone was shown to be a better urease inhibitor compared to 3-hydroxy-2-methyl-4(3H)-quinazolinone by providing higher binding affinity and better Gold score values. Both experimental and computational results favored 3-hydroxy-2-phenyl-4(3H)-quinazolinone as a preferable urease inhibitor.

Keywords: 3-Hydroxy quinazolinone derivatives, *Helicobacter pylori*, Urease enzyme

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