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Evaluation of *Helicobacter pylori* urease inhibitory activity of (*E*)-1-(4-methoxybenzylidene)-2-phenylhydrazine

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Helicobacter pylori attacks and subsequently damages the stomach and duodenum of humans. It secretes the urease enzyme, which catalyzes urea hydrolysis, producing ammonia in the stomach and creating a suitable pH environment for the bacterium to survive and colonize. Though, several therapies and medications are available to treat H. *pylori*, they have several inherent problems, including allergies, severe complications, associated adverse effects, the emergence of antimicrobial resistance, and a high cost. Therefore, the discovery of new urease inhibitors with no toxicity, fewer undesirable side effects, and better stability is highly demanded. In this study, a hydrazone derivative, (*E*)-1-(4-methoxybenzylidene)-2-phenylhydrazine was evaluated for its potential to act against *Helicobacter pylori*. Hydrazones are a significant class of biologically active drug molecules, drawing attention from medicinal chemists due to their diverse pharmacological properties. Researchers are actively synthesizing these compounds as potential drugs to combat diseases with minimal toxicity and maximal efficacy. (*E*)-1-(4-methoxybenzylidene)-2-phenylhydrazine was successfully synthesized using a condensation reaction with 4-methoxybenzaldehyde and phenylhydrazine and characterized by FT-IR, ^{1}H NMR, and ^{13}C NMR spectroscopy. The anti-urease action of the compound was analyzed using a modified Berthelot reaction assay, which is a well-established colorimetric method for the determination of ammonia. (*E*)-1-(4-methoxybenzylidene)-2-phenylhydrazine showed inhibitory activity of 12.089±0.0008 μg/mL against urease enzyme rather than standard thiourea (4.885±0.0007 μg/mL). In addition, an in-silico study was carried out to analyze the binding interactions of (*E*)-1-(4-methoxybenzylidene)-2-phenylhydrazine with the active site (two nickel atoms) of the urease enzyme of *Helicobacter pylori*. In-silico studies showed that (*E*)-1-(4-methoxybenzylidene)-2-phenylhydrazine interacts with H. *pylori* urease with a high binding affinity (-5.3 kcal/mol), compared to thiourea (-3.3 kcal/mol). Therefore, it can be concluded that further structural optimization of (*E*)-1-(4-methoxybenzylidene)-2-phenylhydrazine will result in potent drug candidates to work against *Helicobacter pylori*.

Keywords: Berthelot reaction, Hammett correlation, Hydrazone, *Helicobacter pylori*, Thiourea