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Development and evaluation of a quinazolinone derivative as a urease inhibitor for reducing nitrogen loss in agricultural soil

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Plants often can't fully utilize nitrogen from urea due to losses from volatilization, nitrification, and denitrification. This research aimed to reduce these losses by inhibiting soil bacteria urease, which slows urea breakdown into ammonia, thereby improving nitrogen availability for plant uptake. Literature indicates that quinazolinone derivatives have diverse bioactivities. In this study, a quinazolinone derivative was synthesized as a urease inhibitor, with the optimal urea-inhibitor ratio determined to maximize efficiency against soil bacterial ureases. The binding affinity of the inhibitor to *Bacillus pasteurii* (*PDB code 4UBP*) urease was assessed through molecular docking using AutoDock GOLD 5.0.3 and Discovery Studio v16.1.0.15 software. The PLP fitness (Piecewise Liner Potential) of the synthesis compound was 50.3 compared to the thiourea PLP fitness of 25.0, which was used as a standard compound. The synthesis process involved two steps. First, a benzoxazinone intermediate (IM-01) was synthesized using anthranilic acid, a benzoyl chloride, and pyridine, achieving an 80% yield. Next, (IM-01) was refluxed with hydrazine monohydrate to produce the quinazolinone derivative (Q-01). The structures of the synthesized compounds were confirmed through FTIR, ^{1}H and ^{13}C NMR, and High-Resolution Mass Spectroscopy, while the *in vitro* urease inhibitory activity of the compound (Q-01) was assessed using a modified Berthelot's spectrophotometric method. The urease required for the assay was extracted from the germinated seeds of *Macrotyloma uniflorum* (Horse gram). The IC_{50} value of (Q-01) was 17.5 ± 1.9 ppm compared to thiourea IC_{50} 14.5 ± 1.8 ppm, which was used as a standard compound ($P < 0.05$). Different ratios of (Q-01) were then mixed with a constant amount of urea to identify the optimal ratio. The pellets with the optimal 250:1 (urea: Q-01) ratio were formulated using a binder to compress the urea and inhibitor mixture. Further studies will assess the efficacy of the urea: Q-01 (250:1) pellet in soil by evaluating its impact on plant growth and microbial activity.

Keywords: Quinazoline, Urease enzyme, Urease inhibitor, Urea.

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