Selection and Investigation of Inhibitors Targeting the LuxN Protein of Vibrio harveyi Through Molecular Docking

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Antimicrobial resistance (AMR), often referred to as a “silent pandemic” in scientific discussions, has become one of the most pressing threats to global health. AMR plays a key role in microbial recombination, impacting ecosystems due to microorganisms' constant interaction with other life forms. The WHO advocates for the One Health approach, which integrates human, animal, plant, and environmental health to ensure ecosystem sustainability in the fight against AMR. Current AMR mitigation strategies focus on quorum sensing (QS) inhibition, targeting the regulatory mechanisms of virulence factor production and bacterial cell-to-cell communication. Unlike traditional antibiotics, QS inhibitors do not exert bactericidal effects but instead reduce pathogen virulence, minimizing resistance development. In this study the LuxN gene, encoding the QS sensor kinase in Vibrio harveyi, was amplified by PCR, sequenced, and modeled in 3D. The effects of potential QS inhibitors chosen based on literature review—imidazole, methylimidazole, quercetin, and bergamottin—were initially assessed through molecular docking and simulation studies. Among them, bergamottin showed the highest binding affinity to LuxN, and its effect was evaluated in vitro by testing the MIC and biofilm inhibition in V. harveyi cultures. Bergamottin was found to inhibit biofilm formation by 76%. Our findings provide the first insights into the QS-inhibitory effects of bergamottin on V. harveyi. Our study paves the way for developing novel eco-friendly antimicrobials by combining bioinformatics and wet-lab methods. This approach has the potential to be expanded to other pathogens, contributing to a future where biodiversity is preserved, ecosystems remain sustainable, and public health is safeguarded.

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