

Antibacterial Activities of Meldrum's Acid Derivatives: In Vitro and Molecular Docking Studies

Puteri Najihah Mat Latip & Muhd Hanis Md Idris*

Structured Abstract

Background: Antimicrobial resistance (AMR) is an escalating global health threat driven by the widespread emergence of antibiotic-resistant bacterial strains. This crisis is undermining the effectiveness of many conventional antibiotics and complicating the treatment of infectious diseases. According to Murray et al. (2022), AMR accounted for approximately 1.27 million deaths worldwide in 2019, a figure expected to rise if no effective interventions are taken. The growing resistance not only impacts clinical outcomes but also increases healthcare costs and the risk of outbreaks. In Malaysia, the government has launched the Malaysian Action Plan on Antimicrobial Resistance (MyAP-AMR) to address this concern by promoting awareness, rational antibiotic use, and the discovery of novel antibacterial agents (Morris et al., 2021). Among the potential candidates for drug development are Meldrum's acid derivatives, a class of compounds known for their synthetic flexibility and promising biological activities.

Methods: This study evaluates the antibacterial potential of five synthesized Meldrum's acid derivatives through both in vitro and in silico approaches. Antibacterial activity was tested against *Bacillus cereus*, *Bacillus spizizenii*, *Shigella sonnei*, and *Proteus vulgaris* using the disk diffusion, minimum inhibitory concentration (MIC), and minimum bactericidal concentration (MBC) methods. Molecular docking was performed using SwissDock against *Bacillus subtilis* DNA gyrase subunit B (PDB ID: 4URM).

Results: Among the tested compounds, M3A demonstrated moderate antibacterial activity with observable inhibition zones and measurable MIC and MBC values. In molecular docking, M3A recorded a docking score of -7.1 kcal/mol and formed hydrophobic interactions with isoleucine residues. The positive control, Cefotaxime, showed a slightly stronger binding affinity of -7.4 kcal/mol with two hydrogen bonds involving ARG144.

Conclusion: To conclude, M3A shows potential as a lead antibacterial compound, supported by both experimental and computational results. Further structural optimization and biological evaluation could enhance its efficacy and broaden its antibacterial spectrum, contributing to the ongoing search for effective alternatives to combat AMR.

Keywords: Meldrum's acid derivatives, antibacterial activity, molecular docking, MIC, MBC

*Correspondence: muhdhanis@uitm.edu.my

School of Biology, Faculty of Applied Sciences, Universiti Teknologi MARA, Shah Alam, Malaysia