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Investigating the Dual-Action Potential of (Z)-6-methoxy2-(naphthalen-1-ylmethyle) Benzofuran-3(2H)-one (AU-23): A Novel Synthetic Aurone Derivative with Antibacterial and Anti-Inflammatory Activity

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Abstract Aim/Background: Aurone is a well-known, naturally occurring, minor flavonoid with significant biological properties. However, their low abundance in nature limits their application in the medical field. In this study, we investigated the antimicrobial and anti-inflammatory properties of a novel synthetic aurone, (Z)-6-methoxy-2-(naphthalen-1-ylmethylene) benzofuran-3(2H)-one (AU-23). Materials and Methods: AU-23 was synthesized via multistep synthesis reactions involving the oxidative cyclization of 2'-hydroxychalcones. AU-23 was tested for antibacterial, minimum inhibitory concentration and antibiofilm activity against several ATCC strains using agar well diffusion, broth-micro dilution and XTT assay methods respectively. Results: At various concentrations, it selectively inhibited the growth of four strains (*P. aeruginosa* ATCC 9027, methicillin-resistant *S. aureus* (MRSA) ATCC 33591, methicillin-sensitive *Staphylococcus aureus* (MSSA) ATCC 25923 and methicillin-resistant *S. aureus* (MRSA) ATCC 43300). Moreover, it was observed that AU-23 had a bactericidal effect on sensitive strains of MSSA ATCC 25923 and *P. aeruginosa* ATCC 9027, as well as a bacteriostatic effect on MRSA ATCC 33591 and MRSA ATCC 43300. AU-23 also displayed effective antibiofilm activity against monomicrobial biofilms but not against polymicrobial biofilms. The findings of PCR study revealed that AU-23 downregulates the expression of pro-inflammatory cytokines and mediators (i.e., IL-6, IL-1 beta, iNOS and TNF-alpha), as well as crucial pattern recognition receptors (TLR4 and CD14) in LPS-stimulated RAW 264.7 cells. Molecular docking studies demonstrated that the ability of AU-23 to bind to the mouse TLR4/MD-2 complex was comparable to that of dexamethasone. Conclusion: the results of several studies conducted, suggests that AU-23 has the potential to function as an effective dual-action agent with antimicrobial and anti-inflammatory properties.

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