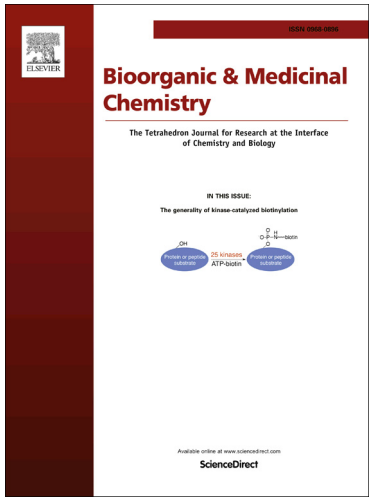

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Synthesis of antimicrobial glucosamides as bacterial quorum sensing mechanism inhibitors

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ABSTRACT

Bacteria communicate with one another and regulate their pathogenicity through a phenomenon known as quorum sensing (QS). When the bacterial colony reaches a threshold density, the QS system induces the production of virulence factors and the formation of biofilms, a powerful defence system against the host's immune responses. The glucosamine monomer has been shown to disrupt the bacterial QS system by inhibiting autoinducer (AI) signalling molecules such as the acyl-homoserine lactones (AHLs). In this study, the synthesis of acetoxy-glucosamides **8**, hydroxy-glucosamides **9** and 3-oxo-glucosamides **12** was performed *via* the 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC·HCl) and *N*,*N*'-dicyclohexylcarbodiimide (DCC) coupling methods. All of the synthesised compounds were tested against two bacterial strains, *P. aeruginosa* MH602 (LasI/R-type QS) and *E. coli* MT102 (LuxI/R-type QS), for QS inhibitory activity. The most active compound **9b** showed 79.1% QS inhibition against *P. aeruginosa* MH602 and 98.4% against *E. coli* MT102, while compound **12b** showed 64.5% inhibition against *P. aeruginosa* MH602 and 88.1% against *E. coli* MT102 strain at 2 mM concentration. The ability of the compounds to inhibit the production of the virulence factor pyocyanin and biofilm formation in the *P. aeruginosa* (PA14) strain was also examined. Finally, computational docking studies were performed with the LasR receptor protein.

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