

## Abstract

# Small Molecule Inhibitors of Bacterial Quorum Sensing <sup>†</sup>

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**Abstract:** Quorum sensing is a bacterial mechanism that is essential in the pathogenesis of many infections, such as *P. aeruginosa*. These infections are strongly influenced by specific quorum sensing molecules, such as Autoinducer-2 (AI-2). AI-2 binds to quorum sensing receptors within bacteria, leading to the up-regulation of virulence genes that cause biofilm formation and toxin production. Naturally-occurring brominated furanones isolated from the marine algae *Delisea pulchra* were previously found to possess properties which inhibited bacterial quorum sensing in AI-2 sensitive species. The aim of this work was to create a series of novel halogenated furanones which can function as quorum sensing inhibitors of AI-2. Based on the lead from *Delisea pulchra*, a library of compounds was synthesised via the functionalisation of *gem*-dibromoolefin and *gem*-dichloroolefin intermediates using palladium-catalysed couplings, namely Suzuki and Sonogashira reactions. These compounds were subsequently evaluated for their effects on biofilm formation in selected microbes. Several molecules were confirmed to be highly effective biofilm inhibitors in multiple pathogens, including *P. aeruginosa* and *C. albicans*.

**Keywords:** quorum sensing; resistance; biofilms; furanones



**Citation:** O'Sullivan, T.P. Small Molecule Inhibitors of Bacterial Quorum Sensing. *Med. Sci. Forum* **2022**, *14*, 16. <https://doi.org/10.3390/ECMC2022-13264>

Academic Editor: Alfredo Berzal-Herranz

Published: 1 November 2022

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**Supplementary Materials:** This is a invited talk. The video and presentation files are available at <https://www.mdpi.com/article/10.3390/ECMC2022-13264/s1>.

**Funding:** This research received no external funding.

**Conflicts of Interest:** The author declares no conflict of interest.