

Poster abstract submission

Approval Status

Not Started

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Poster title

First-in-class metalloid-based antibiotics to overcome antimicrobial resistance

Poster abstract

Compounds incorporating non-essential elements, e.g. metals, have recently gained prominence as potential antibiotics [1], displaying high hit-rates against resistant bacteria and exhibiting low toxicity and potent antibacterial activity [2]. To address the urgent need for new antibiotics, we introduce a first-in-class metalloid-based antibiotic class. Small molecules containing metalloid atoms, elements with properties intermediate between metals and non-metals, have not yet been explored as antibacterial agents.

The developed compounds are highly active against Gram-positive bacteria, including resistant strains and clinical isolates, indicating a reduced susceptibility to established resistance mechanisms. Additionally, they exhibit improved activity against Gram-negative bacteria in combination with polymyxin nonapeptide, highlighting a clear opportunity for chemical optimisation toward standalone Gram-negative efficacy. Finally, this antibiotic class exhibits a unique mechanism of action distinct from those of clinically used antibiotics, suggesting a reduced potential for cross-resistance. The lead compound is well tolerated in mice and increases survival in infected *Galleria mellonella*. Collectively, the results support further clinical development for a truly novel antibiotic candidate with the

potential to overcome infections caused by resistant bacteria that could arise as an alternative treatment option where current therapies might fail.

- [1] A. Frei, A. D. Verderosa, A. G. Elliot, J. Zuegg, M. A. T. Blaskovich. "Metals to combat antimicrobial resistance" *Nat. Chem. Rev.* 2023, 7, 202-224
- [2] M. A. T. Blaskovich, et. al. "Metal-complexes as a Promising Source for New Antibiotics" *Chem. Sci.* 2020, 11, 2627-2639

Research topic

Small molecule therapeutics