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Poster abstract submission

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Poster title

Novel thiourea antibiotic against MDR Acinetobacter baumannii with in vivo activity

Poster abstract

The increasing prevalence of drug-resistant pathogens is a looming crisis that risks to set back decades of advances in global health. Among these superbugs, carbapenem-resistant Acinetobacter baumannii stands out as one of the most serious threats, according to the World Health Organization.
In 2018, CDRI identified the thiourea derivative SRI-12742 as an antibiotic against AB (Chopra et al, Int. J. Antimicrob. Agents (2018) 22–27). The compound's MIC is 4 µg/mL against the MDR AB isolate BAA-1605 and activity for clinical strains was assessed (MICs 4 µg/mL to >64 µg/mL). SRI-12742 exhibited concentration-dependent bactericidal activity. In a murine neutropenic thigh infection model of AB infection, SRI-12742 reduced CFU counts by ca. 0.9 log10 CFU, comparable to polymyxin B.
In our collaborative work, the hit was synthetically expanded with over 250 synthetic derivatives and an SAR was established. A highly active derivative was identified with MICs down to 0.125-0.5 µg/mL against 220 clinical isolates of diverse Acinetobacter species including multidrug resistant strains and CRAB. A novel mode-of-action has been suggested based on absence of cross resistance and affinity proteomics. First safety pharmacology assessment revealed good selectivity. The frontrunner showed efficacy in A. baumannii infection experiments in zebrafish and mice.

Research topic

Small molecule therapeutics