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Poster abstract submission

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Potent bactericidal and therapeutic activities of lysocin E regarding refractory S. aureus infection

Poster abstract

The global spread of antimicrobial resistance has created an urgent need for novel antibiotics with mechanisms distinct from those of conventional agents, which primarily target actively growing bacteria and therefore show limited efficacy against non-growing or biofilm-associated Staphylococcus aureus implicated in refractory infections. In this study, we investigated the bactericidal activity of the novel antibiotic lysocin E against stationary-phase and biofilm-associated S. aureus and evaluated its therapeutic efficacy in severe infection models. The intracellular amount of the lysocin E target, menaquinone, was quantified during exponential and stationary growth phases, and bactericidal activity against growing and non-growing cells was assessed in vitro, while in vivo efficacy was evaluated using cyclophosphamide-induced neutropaenic mice and a delayed-treatment model. Menaquinone levels remained constant across growth phases, and lysocin E rapidly killed stationary-phase S. aureus, whereas daptomycin showed minimal activity; lysocin E also disrupted mature biofilms at low concentrations. In vivo, lysocin E demonstrated superior efficacy in severe infection models, exhibiting markedly lower ED_{50} values in neutropaenic mice (0.19 mg/kg; 0.072 mg/kg in untreated mice) than linezolid (31.6 and 1.47 mg/kg, respectively), and retaining substantial activity when treatment was initiated 6 hours post-infection (ED_{50}: 0.82 mg/kg), whereas vancomycin showed greatly reduced efficacy (46.3 mg/kg). These findings indicate that lysocin E exerts potent bactericidal activity against non-growing and biofilm-associated S. aureus and represents a promising therapeutic candidate for managing refractory infections in the context of antimicrobial resistance.

Research topic Small molecule therapeutics