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Poster abstract submission

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Poster title

ZnPor (II): a novel cationic Zinc Porphyrin based anti-infective platform

Poster abstract

AMR is one of the top global public health threats in the 21st century according to the WHO. Many pathogenic bacteria form biofilms which exhibit up to a thousand-fold increase in antibiotic resistance and the formation of MDR strains. The NIH has estimated that 65% of all human bacterial infections involve biofilms; 80% of chronic infections. There is a great need for antimicrobials that can destroy the protective biofilm matrix. We present data of a novel Zinc porphyrin molecule, ZnPor (II), with potent antimicrobial activity that can disrupt biofilms on medically relevant substrata. Photoactivation is not required but provides further effectiveness. We tested ZnPor (II) against planktonic cells and biofilms of Pseudomonas aeruginosa (PsA) and Staphylococcus aureus MRSA (Sa MRSA) strain as well as the bacteriophage PEV2 and an ATCC Coronavirus isolate. The MIC and MBC of ZnPor (II) was 4 µg/ml and 8 µg/ml, respectively, against planktonic cells of PsA strains PAO1 and PA14. At 8 ug/ml ZnPor (II) there was more than a 6 log reduction in planktonic populations. PsA biofilms were disassembled in less than 2h at a concentration of 16 µg/ml (Fig. 1). At 4 µg/ml ZnPor (II) there was more than a 6 log reduction of Sa MRSA planktonic cells in 7h. Biofilms of Sa MRSA were similarly disrupted. The bacteriophage PEV2 and an ATCC Coronavirus strain isolated from an URI were inactivated without photoactivation. ZnPor (II) enhanced the effect of Tobramycin as shown in Fig 1. Tobramycin alone had little effect on PsA cells in biofilms or on the structure itself. When combined with 4 µg/ml of ZnPor (II) there was substantial killing of PsA cells and a less structured biofilm. ZnPor (II) alone at a concentration of 4 µg/ml did not affect biofilms (A). This indicates potential synergy between ZnPor (II) and Tobramycin. An in vivo model of PsA pulmonary infection ZnPor (II) caused a significant decrease in PsA populations in mouse lungs. There were no overt toxic effects on the mice or lung cells. Further RBCs and platelets were unaffected. Extensive in vitro toxicity testing using a variety of human lung cells (e.g. H441) failed to show toxicity at concentrations exceeding effective doses. ZnPor (II) is the first porphyrin, to our knowledge, that kills both Gram-negative and Gram-positive planktonic and biofilm associated bacteria directly without photoactivation. Resistance to ZnPor (II) has not arisen in PsA cells in 5 years of testing.

Research topic

Small molecule therapeutics

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AMR.pdf