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A Fresh Shine on Cystic Fibrosis Inhalation Therapy: Antimicrobial Synergy of Polymyxin B in Combination with Silver Nanoparticles

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This in vitro study aimed to investigate the synergistic antibacterial activity of polymyxin B in combination with 2 nm silver nanoparticles (NPs) against Gram-negative pathogens commonly isolated from the cystic fibrosis (CF) lung.

The in vitro synergistic activity of polymyxin B with silver NPs was assessed using the checkerboard assay against polymyxin-susceptible and polymyxin-resistant *Pseudomonas aeruginosa* isolates from the lungs of CF patients. The combination was also examined against the Gram-negative species *Haemophilus influenzae, Burkholderia cepacia, Burkholderia pseudomallei, Stenotrophomonas maltophilia, Klebsiella pneumoniae* and *Acinetobacter baumannii* that are less common in the CF lung. The killing kinetics of the polymyxin B-silver NPs combinations was assessed against *P. aeruginosa* by static time-kill assays over 24 h. Polymyxin B and silver NPs alone were not active against polymyxin-resistant (MIC ≥ 4 mg/L) *P. aeruginosa*. Whereas, the combination of a clinically-relevant concentration of polymyxin B (2 mg/L) with silver NPs (4 mg/L) successfully inhibited the growth of polymyxin-resistant *P. aeruginosa* isolates from CF patients as demonstrated by ≥2 log10 decrease in bacterial count (CFU/mL) after 24 h. Treatment of *P. aeruginosa* cells with the combination induced cytosolic GFP release and an increase of cellular reactive oxygen species. In the nitrocefin assay, the combination displayed a membrane permeabilizing activity superior to each of the drugs alone.

The combination of polymyxin B and silver NPs displays excellent synergistic activity against highly polymyxin-resistant *P. aeruginosa* and is potentially of considerable clinical utility for the treatment of problematic CF lung infections.

Biography:

Raad Jasim was born in Babylon, Iraq, in 1977. He received the bachelor degree in pharmaceutical sciences from Baghdad University, Iraq, in 2002. He worked as a pharmacist in the City of Medicine / Hospital of Special Surgeries, in Baghdad/ Iraq from December 2002 to October 2004. In November 2004 he joined the department of pharmacology and Therapeutics, Almustansria University/ College of Pharmacy as a demonstrator. In 2008 he received the Master degree in Pharmacology & Therapeutics from Kufa University/College of Medicine/Department of Pharmacology & Therapeutics, Iraq. In 2014 he has started his PhD in the department of Drug Delivery, Disposition and Dynamics (D4), Monash Institute of Pharmaceutical Sciences, Monash University, Australia.