Activity and Interactions of Liposomal Antibiotics in Presence of Polyanions and Sputum of Patients with Cystic Fibrosis

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Abstract

Background

To compare the effectiveness of liposomal tobramycin or polymyxin B against *Pseudomonas aeruginosa* in the Cystic Fibrosis (CF) sputum and its inhibition by common polyanionic components such as DNA, F-actin, lipopolysaccharides (LPS), and lipoteichoic acid (LTA).

Methodology

Liposomal formulations were prepared from a mixture of 1,2-Dimyristoyl-*sn*-Glycero-3-Phosphocholine (DMPC) or 1,2-Dipalmitoyl-*sn*-Glycero-3-Phosphocholine (DPPC) and Cholesterol (Chol), respectively. Stability of the formulations in different biological milieus and antibacterial activities compared to conventional forms in the presence of the aforementioned inhibitory factors or CF sputum were evaluated.

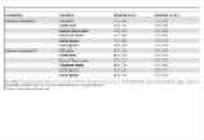
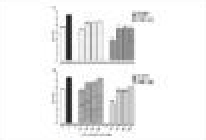
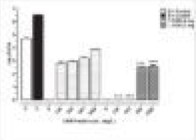
Results

The formulations were stable in all conditions tested with no significant differences compared to the controls. Inhibition of antibiotic formulations by DNA/F-actin and LPS/LTA was concentration dependent. DNA/F-actin (125 to 1000 mg/L) and LPS/LTA (1 to 1000 mg/L) inhibited conventional tobramycin bioactivity, whereas, liposome-entrapped tobramycin was inhibited at higher concentrations - DNA/F-actin (500 to 1000 mg/L) and LPS/LTA (100 to 1000 mg/L). Neither polymyxin B formulation was inactivated by DNA/F-actin, but LPS/LTA (1 to 1000 mg/L) inhibited the drug in conventional form completely and higher concentrations of the inhibitors (100 to 1000 mg/L) was required to inhibit the liposome-entrapped polymyxin B. Co-incubation with inhibitory factors (1000 mg/L) increased conventional (16-fold) and liposomal (4-fold) tobramycin minimum bactericidal concentrations (MBCs), while both polymyxin B formulations were inhibited 64-fold.

Conclusions

Liposome-entrapment reduced antibiotic inhibition up to 100-fold and the CFU of endogenous *P. aeruginosa* in sputum by 4-fold compared to the conventional antibiotic, suggesting their potential applications in CF lung infections.

Figures

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