

8.2 CONCLUSION

Delivering large dose of medication to the lung has been a challenging task for scientists and manufacturers. Patients with cystic fibrosis and chronic pulmonary infection of *Pseudomonas aeruginosa* require much larger doses of antibiotics. In this investigation, particle engineering was attempted to deliver large dose antibiotics to the lower airways i.e. site of diseases. Aerodynamically light and large particles of tobramycin sulfate and amikacin sulfate were prepared and optimized by response surface methodology using hydrogenated soya phosphatidyl choline, L-leucine and poloxamer 188 by both spray drying and freeze drying techniques. Particles produced by enlarging particle size and decreasing aerosol particle mass density were aerodynamically light and large particles ideally suited for inhaled therapies i.e. diseases involving infection of the airway (cystic fibrosis, non cystic fibrosis-bronchiectasis). It were characterized for particle size, polydispersity, tap density, moisture content, crystallinity, shape, topographical features and aerosolization properties. L-leucine was found to be most influencing formulation component in aerosolization of the developed light and large particles. Engineered particles produced by spray drying provided particles having low area of contact and reduced cohesive forces. This lower area of contact facilitated powder flowability, high fine particle fraction (lung deposition) and minimized deposition of particles in the extrathoracic and tracheobronchial airways. Particle engineering also resulted into prolonged lung residence of drug, reduced clearance by alveolar macrophage action and slow systemic dilution, and hence, expected to reduce systemic toxicities.

The data of aerodynamically light and large particles developed in this investigation conclusively supported the efficient delivery of high therapeutic dose antibiotics (tobramycin sulfate and amikacin sulfate) to the target site of the disease. It also demonstrated prolonged residence of drug within the lungs compared to conventional dry powder inhalers of drugs prepared for comparison. Hence, it is expected to maximize the therapeutic index, reduce dose and/or frequency of dosing and thereby; reducing systemic side effects of the drugs, and probably, cost of the therapy. However, the role of aerodynamically light and large particles for pulmonary delivery of high therapeutic mass, tobramycin sulfate and amikacin sulfate, can only be settled after extensive studies on at least two more animal species followed by clinical trials. However, this investigation has provided preliminary evidence that delivery of high

dose antibiotics through aerodynamically light and large particles can confine the drug primarily to lower airways providing effective treatment of the disease and prevent creation of drug resistance normally associated with antibiotic therapy.

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