Nebulization studies of chitosomes generated from spray-dried prochitosome using two anti-asthma drugs

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Background: Pulmonary administration presents advantages over alternative delivery methods for treating lung diseases. However, the duration of inhaled drug presence in the lungs is brief due to the thinness of the pulmonary epithelium and abundant blood supply, leading to systemic drug absorption and potential side effects. In this investigation, we employed spray-drying to produce bioadhesive chitosan-proliposome powder (Prochitosomes). These particles were then hydrated to generate chitosan-coated liposomes (Chitosomes), which were administered via nebulization into a two-stage impinger (TSI). Salbutamol sulphate (SS) and Beclometasone dipropionate (BDP) were included in the prochitosome formulations as representative hydrophilic and hydrophobic drugs, respectively.

Methods: Prochitosome powder was prepared through spray-drying an ethanolic mixture of lipids, mannitol, drugs (SS or BDP), and chitosan glutamate, utilizing various lipid to chitosan ratios (0:100, 10:100, 20:100, 30:100, and 50:100 w/w). These powders underwent hydration to form chitosomes, subsequent to which they were subjected to size analysis, electron microscopy examinations, and zeta potential measurements. The formulations were administered to a two-stage impinger (TSI), followed by the determination of parameters including "fine particle fraction" (FPF), drug output, and drug output rate.

Results: Liposomes exhibited sizes ranging from 3-6μm, contingent upon the formulation used. Zeta potential values were predominantly slightly negative across all formulations. Following nebulization, the drug output reached approximately 70% for SS formulations and 50% for BDP formulations. The "fine particle fraction" (FPF) neared 45% for SS formulations and hovered around 35% for BDP formulations. The median size of nebulized droplets remained below 6μm for all formulations, suggesting potential suitability for inhalation. Aerosol mass output consistently surpassed drug output, indicating some drug accumulation within the nebulizer during nebulization.

Conclusions: The findings of this study indicate that spray-dried prochitosomes have the capability to produce chitosomes suitable for delivery to a two-stage impinger (TSI) through nebulization. These formulations displayed outstanding aerosol performance, characterized by high drug output and "fine particle fraction" (FPF) values.