Characterization of Dry Powder Aerosols of Albuterol Sulfate/Lactose Monohydrate and Cromolyn Sodium/Lactose Monohydrate Delivered by Standardized Entrainment Tubes

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MOTIVATION

Standardized entrainment tubes (SETs) with defined flow parameters provide a great opportunity to examine the dispersion of various batches of Respitose products. Together with other powder techniques, they are aimed to shed light on the fundamental characteristics of pharmaceutical dry powder formulation, and to achieve performance prediction.

OBJECTIVE

To evaluate the effects of morphology, lactose grade, and surface energetics on in vitro aerosolization and particle deposition of drug/lactose blends using SETs with varying shear stress and power.

MATERIAL

Pulmonary Drugs
Micronised Albuterol Sulfate \((C_12H_22O_{11})\)
Micronised Cromolyn Disodium \((C_{23}H_{14}Na_2O_{11})\)

Respitose Carriers
Lactose monohydrate \((C_12H_22O_{11})\)

- MW 342.30 g/mol;
- Analysis led to selection of four batches;
- Sieved batches: SV-A, SV-B;
- Milled batches: ML-A, ML-B.

METHODS

Particle sizing was performed using Malvern laser diffraction for volume particle size distribution and inertial sampling aerosol particle sizing techniques for aerodynamic particle size.

Drug/lactose interactive physical mixtures were prepared at drug concentrations of 0.5%(w/w) and 2%(w/w). Solid-state characterization of phase behavior and molecular interactions was performed using differential scanning calorimetry (DSC) and X-ray powder diffraction (XRPD).

Particle morphology was examined using scanning electron microscopy (SEM). Atomic force microscopy (AFM) was utilized for topographical imaging and surface energetics characterization of these drug powder particulate systems.

RESULTS & DISCUSSION

Jet-milled drug particles were in the respirable sized range (< 5 mm) with a narrow normal size distribution (Span < 0.5).

Aerosol dispersion, distribution, and performance were assessed and characterized by twin-stage liquid impinger (TSLI) to measure the proportion of the aerosol particles delivered in a sized range less than 6.4 mm and Anderson 8-stage non-viable cascade impactor (ACI) as an in vitro lung model of aerosol particle deposition. Aerosolization was performed using a series of SETs with well-defined shear stress \((\tau)\), Reynolds number \((Re)\), pressure drop \((AP)\) and power. \((Q=60\ L/min)\) Dispersion data were evaluated with Design-Expert ver. 5.0.9, 2-level full factorial analysis.

For all aerosol systems studied, the lowest shear stress SET \((\tau = 0.624\ N/mm^2)\) gave a higher emitted dose \((ED = 83-94\%)\) but lower fine particle fraction \((FPF_{6.4} = 8-29\%)\).

Comparison of drug/lactose interactive physical mixtures revealed significant differences in macroscopic aerodynamic properties, lactose grade, molecular interactions, interfacial chemistry, and nanotopography.

The favorable interfacial and self-assembling properties of cromolyn sodium are reflected in its superior aerosol performance through decreased interparticulate interactions leading to aggregation.

CONCLUSIONS

- Significant differences in macroscopic aerodynamic dispersion and performance were correlated with differences in drug physicochemical properties, lactose grade, molecular interactions, interfacial chemistry, and nanotopography.
- The favorable interfacial and self-assembling properties of cromolyn sodium are reflected in its superior aerosol performance through decreased interparticulate interactions leading to aggregation.

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REFERENCE