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Effect of crystallinity on electrostatic charging in DPI formulations

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Introduction: Many physicochemical, mechanical and environmental factors can influence charging of dry powder inhaler (DPI) formulations - crystallinity is one of these factors. Due to differences in crystal packing and surface energies, there may be differences in charge transfer behaviours between amorphous and crystalline materials. Although the effect of crystallinity on electrostatic charging in DPI formulations has been investigated previously by other researchers, the reported data were inconclusive since the samples not only differed in crystallinity, but also in particle morphology and size distributions. Therefore, these variables are controlled in the present study to determine the role of crystallinity in electrostatic charging of DPI formulations. The objective of this study was to characterize inherent charges generated by amorphous and crystalline micron-sized salbutamol sulfate (SS) powders.

Materials and Methods: Amorphous SS was spray dried, whereas crystalline SS was produced by conditioning spray dried SS in the presence of supercritical CO₂ and menthol. Solid-state characterization was carried out using laser diffraction, scanning electron microscopy (SEM), X-ray diffraction (XRD), dynamic vapour sorption (DVS), atomic force microscopy (AFM) and nitrogen adsorption for multipoint BET measurement. In vitro aerosol performance and electrostatic charge were measured simultaneously by a modified Electrostatic Low Pressure Impactor (ELPI™). Triplicate samples (approximately 5 ± 0.2 mg) were dispersed by an Aerolizer®. Charge was defined as the area under the curve in the current-versus time plot. Net charge was defined as the sum of charges on a particular impactor stage. Specific charge was defined as the quotient of the net charge and deposited drug mass.

Results and Discussion: Amorphous and crystalline SS had comparable particle size distributions, where SEM images confirmed formulations showed comparable particle size and shape. The rougher surface of crystalline SS indicated that crystallisation had occurred.

Subsequent XRD and DVS data confirmed the crystalline nature of supercritically conditioned SS. On the other hand, amorphous SS showed the typical halo pattern and crystalline SS had peaks that generally overlapped with those of raw SS. AFM and BET measurements quantified the increased roughness and specific surface area, respectively, of crystalline SS. Both powders exhibited similar bipolar charging pattern, with a reversal in polarity was observed around the 1.60 µm cut off diameter. Crystalline SS charged to higher magnitudes with more consistent charge and mass deposition profiles, and an improved aerosol performance. There were significant differences in specific charges, in particular for particles with cut off diameters ≤ 0.615 µm.

Conclusion: A difference in charging behavior was observed between amorphous and crystalline SS. In vitro deposition studies found crystalline SS charged to higher magnitudes with more consistent charge and mass deposition. These results suggest that crystalline SS could lead to more predictable charging with improved aerosol performance.

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