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Investigations on the Mechanism of Magnesium Stearate to Modify Aerosol Performance in Dry Powder Inhaled Formulations

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1. ABSTRACT

The potential of the force control agent (FCA) magnesium stearate (MgSt) to enhance the aerosol performance of lactose-based dry powder inhaled (DPI) formulations was investigated in this study. The excipient blends were investigated with analytical techniques including time-of-flight secondary ion mass spectrometry (ToF-SIMS) and Single Particle Aerosol Mass Spectrometry (SPAMS) and particle size, morphology and surface properties were evaluated. Excipient-blends were manufactured either by high-shear or low-shear blending lactose carrier with different amounts of MgSt in the range from 0-10% (w/w). Fluticasone propionate (FP) and salmeterol xinafoate (SX) used as model APIs were added by low-shear mixing. The *in vitro* aerosol performance in terms of aerodynamic particle size distribution (APSD) and fine particle fraction (FPF) of the FP and SX DPI formulations was evaluated with the Next Generation Impactor (NGI) and also with SPAMS using a Breezhaler® inhalation device.

The distribution of MgSt on the lactose carrier in the blends was visualized and found to depend strongly on the blending method. This affected drug particle detachment from the carrier and thus impacted aerosol performance for FP and SX. Compared to blends without FCA, low-shear blending of MgSt increases the FPF of the model drug SX, while high shear blending significantly increased FPF of both SX and FP. The interactions between drug and carrier particles were substantially affected by the choice of blending technique of MgSt with lactose. This allows detailed control of aerosol performance of a DPI by an adequate choice of the blending technique. SPAMS successfully demonstrated that it is capable to distinguish changes in DPI formulations blended with different amounts of MgSt and additional information in terms of dispersibility of fine particles could be generated.

KEYWORDS