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Carrier free inhaled dry powder of budesonide tailored by supercritical fluid particle design

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Abstract: Budesonide (BUD) is a potent inhaled corticosteroid widely used for treatment of asthma and chronic obstructive pulmonary disease (COPD). The aim of the present study was to develop carrier free inhaled dry powder containing only BUD using supercritical fluid particle design (SCF PD) technique. The powder was perpetrated using the proprietary apparatus of SCF PD-Lab and characterized in terms of crystal behavior, surface property and suitability for pulmonary delivery. SCF PD-BUD powder shown itself large specific area and lower surface energy measured by iGC-SEA, and the aerodynamic performances relative to the milled powder and the marketed Pulmicort® powder was considerably improved, the pulmonary deposition rate increased substantially up to $FPF_{<5\mu m}$= 32.9% which was comparable to the Pulmicort® powder of $FPF_{<5\mu m}$= 28.4%. The proprietary SCF PD technique was capable of simultaneously tailoring particle size, morphology and physical properties toward an enhancing aerodynamic performance and pulmonary deposition rate of the carrier free inhaled dry powder.

Keywords: Carrier free inhaled dry powder, Budesonide, Supercritical fluid particle design, Surface energy, Aerodynamic performance, Pulmonary deposition rate.

1. Introduction

Last decades dry powder inhaler (DPI) of anti-inflammatory corticosteroids such as budesonide (BUD), formoterol fumarate dehydrate (FFD) and others have become more favorable for the treatment of asthma and chronic obstructive pulmonary disease (COPD) since it is usually easier and the problems associated with the propellants used in the pressurised metered-dose inhaler can be avoided. For effective deposition in the lower airways and deep lung, where drugs are most efficiently absorbed, the particle aerodynamic diameter [1] needs to be in the range of 1-5 μm.

Since such small micron size inhaled particles are extremely adhesive and cohesive, in order to achieve the best aerodynamic performance with effective lung deposition, different technologies and strategies [2] of DPI formulations have been developed and adopted.

There are three strategies of currently available DPI formulations in the market: (1) the carrier blended DPI where small drug particles are adhered on the large carrier surface; (2) the pure drug DPI consisting of small particles of drug alone; (3) the carrier free DPI containing only small particles of drug and excipients, shown as in Fig. 1. The carrier blended DPI has been the majority of marketed products. Symbicort® Turbuhaler® [3] is a typical brand in such DPIs, formulated by BUD/FFD particles with large coarse lactose of 50-100 μm as well as lactose fine of < 20 μm. Production of a stable and homogeneous powder blend requires an optimized interaction between carrier and drug particles. Interaction forces have to be strong enough for the drug to preferentially adhere to the carrier during mixing, but sufficiently weak to enable detachment of drug particles during inhalation. In fact, the mechanism of drug particle loading on formulation structure and drug particle liberation is quite complex, even not clear. Some inherent shortages like small dose, possible dose instability and non-uniformity are very difficult to be improved within the frame of current techniques. The smart

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