

EFFECT OF MICRONIZED LACTOSE SOLID-STATE ON SALBUTAMOL SULFATE AEROSOLIZATION PERFORMANCE

^{a,*}Della Bella A., ^bMüller M., ^bSoldati L., ^aBettini R.

^aUniversity of Parma, Dept. Pharmacy, Parco Area delle Scienze, 27/A – 43124 Parma (Italy)

^bMicro-Sphere SA, Via Cantonale – 6996 Ponte Cremenaga (Switzerland)

*andrea.dellabella@nemo.unipr.it

Purpose

To investigate the effect of the micronization process on the physico-chemical properties of micronized lactose and the influence on the respirability performance of lactose/salbutamol sulfate formulations.

Methods

Micronization was performed using a fluid jet micronizer by varying three different parameters: the Venturi pressure P_V , the ring pressure P_R and the feed rate R_F .

The produced samples were characterized by laser diffraction, X-Ray Powder Diffraction (XRPD) and Differential Scanning Calorimetry (DSC).

Lactose-2 ($DV_{50} = 2.14 \mu\text{m}$) was chosen to be used in the preparation of formulations for inhalation. Coarse lactose/fine lactose/salbutamol sulfate mixtures containing the 1% (w/w) of active and different percentages of Lactose-2 were prepared using a Turbula® mixer.

The in vitro deposition studies were performed using a Next Generation Impactor (NGI) equipped with a pre-separator. A Turbospin® #2 was selected as device. Quantitative analysis of salbutamol sulfate was performed by UV-Visible spectroscopy.

Results

The X-Ray Diffraction showed that Lactose-2 had a degree of crystallinity lower than that of the other samples, suggesting the formation of a certain amount of amorphous lactose as a consequence of the micronization process.

This outcome was confirmed by the Differential Scanning Calorimetry which in addition revealed the presence of another form of lactose, the hygroscopic anhydrous α -lactose, in the samples with smaller particle size.

The in vitro deposition studies showed an improvement of salbutamol sulfate respirability with the increase of the amount of Lactose-2 up to 30% (FPF = 57%).

Conclusions

Micronized lactose has solid-state characteristics different from those of the starting material. Drastic conditions of micronization lead to the formation of amorphous and hygroscopic anhydrous α -lactose.

The presence of a fixed amount of micronized lactose in lactose/salbutamol sulfate mixtures has a significantly positive effect on the aerosolization performance of the formulations.