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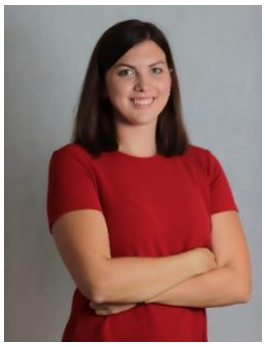

High-dose ibuprofen containing carrier-free dry powder inhalers for the therapy of cystic fibrosis

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Cystic fibrosis (CF) is characterized by inflammation, which contributes to lung damage. The nonsteroidal anti-inflammatory ibuprofen (IBU) significantly slows the progression of the illness. IBU should be taken in large doses, therefore inhalable particles could be beneficial to administer IBU directly to the lung.

We aimed to develop a carrier-free dry powder inhaler (DPI) system containing IBU. Inhalable powders were formed by wet milling and spray drying. We hypothesized a spherical shape, enhanced drug release, and optimal aerodynamic properties to provide a local treatment for CF.

The IBU was milled in a high-performance planetary mill. Solid particles were formulated from the microsuspension by spray-drying (Büchi Mini and Nano Spray-dryer). The following investigations were implemented: laser diffraction, scanning electron microscopy, density, solubility, X-ray powder diffraction, differential scanning calorimetry, dissolution test (Watchglass/PTFE disk assembly), and aerodynamic investigation (Andersen Cascade Impactor).

Wet milling led IBU to become micronized. The particle sizes of the spray-dried formulations were in the required pulmonary size range. The shape of the particles appeared spherical with hollows. The rheology measurement presented low density values. The structural analysis revealed that IBU becomes amorphous. The formulations demonstrated enhanced solubility and drug dissolution. The in vitro aerodynamic investigation showed proper lung deposition.

We successfully formulated high-dose ibuprofen containing DPIs. We aimed to improve the water solubility by reducing particle size. The particle size, shape, and density properties resulted in an efficient in vitro aerodynamic behavior. The compositions could offer a novel therapy for CF.

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