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Development and formulation of a single dry powder inhaler combining ketoprofen nanoparticles-embedded mannitol microparticles for pulmonary inflammations: in vitro and in silico analysis, and cell line assessment

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Pulmonary inflammation is a common symptom of many lung diseases and can be threatening, especially when it involves abnormal mucus buildup. Despite the notable side effects, inhaled corticosteroids are frequently used for these conditions. To address this, a single dry powder inhaler (DPI) comprising two active ingredients has been created using advanced nano-in-micro approach. This system improves the delivery of medication directly to the lungs while avoiding clearance mechanisms.

Ketoprofen, an anti-inflammatory drug with low water solubility, was first dispersed and homogenised in a stabilizer solution. Next, a nanosuspension of ketoprofen was created through wet-media milling. Co-spray drying with L-leucine (a dispersity enhancer) and mannitol (a mucuactive agent) was then carried out. Spray-dried powders were characterised by size, shape, dissolution rate, permeation, viscosity, deposition in lung models (both in vitro and in silico), cytotoxicity, and anti-inflammatory properties.

The size of the ketoprofen nanosuspension particles was approximately 230 nm. Scanning electron microscopy (SEM) images revealed wrinkled and nearly spherical particles with a final size of about 2 µm (referred to as nano-in-micro). Mannitol-containing samples reduced the viscosity of a 10% mucin solution. Results of mass median aerodynamic diameter (2.4-4.5 µm), fine particle fraction (56-71%), permeation (enhanced by 5-fold), and dissolution (80% release within 5 minutes) confirmed the suitability of the system for local inhalation therapy. All samples exhibited significant anti-inflammatory effects and reduced IL-6 levels in LPS-treated U937 cells with minimal cytotoxicity. Thus, combining ketoprofen and mannitol in one inhaled system holds promise for effectively managing lung inflammations (1).

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