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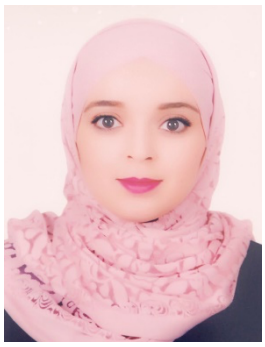

Optimizing aerodynamic performance of an anti-inflammatory-containing dry powder inhaler via nano-spray drying

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Inhaled products have proven effective in targeting lung diseases locally, minimizing systemic exposure and reducing adverse effects. The spray dryer is a particle engineering technique used to create inhalable powders with optimal characteristics, offering precise control over parameters like temperature, flow rate, liquid feedstock concentration, and mesh size (1). The Nano Spray Dryer (NSD) stands out for its vibration mesh spray technology, producing smaller droplets compared to conventional spray dryers (2).

Nanocrystals, a carrier-free nanotechnology, are gaining attention for pulmonary drug administration due to enhanced dissolution rates and solubility of poorly soluble drugs. However, delivering nanoparticles through the pulmonary route poses challenges, as particles <1 µm may be exhaled before deposition. An alternative approach involves nanocrystalline agglomerates (NCAs) characterized by large geometric but small aerodynamic diameters, thereby improved aerodynamic performance.

This study utilized the NSD to formulate ketoprofen (K), a poorly water-soluble drug, into NCAs. NSD parameters were optimised using a Box-Behnken design (3-levels, 3-factors). The optimized parameters were then employed to produce K-NCAs with and without a matrix (D-mannitol, L-leucine). Evaluation of the resulting powder included assessments of particle size, morphology, density, *in vitro* aerosol performance, and dissolution. Crystallinity index calculations from XRPD and DSC analyses were also conducted. The optimized formulation demonstrated improved aerodynamic performance, with ~90% Fine Particle Fraction (FPF) <5µm and ~80% FPF <3µm, confirming deep pulmonary deposition.

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