Microcomposite particles for drug delivery to the lungs: Can they be administered as dry powders or blending with a carrier is still needed?

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Introduction: The classical formulation approach for dry powder inhalers (DPIs) is drug micronisation and then mixing with coarse carrier particles (e.g. lactose). But often, it is inefficient, as only 12–30% of the emitted dose is delivered to the lungs [1]. Also, micronisation may generate amorphous domains on the drug particle surface that can adversely influence the performance of the formulation [1]. Nanocomposite and microcomposite particles prepared by wet milling and spray drying have been proposed as a universal particle engineering approach to combine the advantages of nanoparticles with the aerodynamics of microparticles [2].

Aims and Objectives: To assess the flowability and in-vitro aerosolisation of theophylline (THEO) microcomposite particles either as drug-alone or drug-carrier aerosols and to compare them with the performance of the adhesive mixtures of micronised THEO with lactose carrier.

Methods: THEO microcomposite particles containing various amounts of mannitol were prepared as reported by Malamatari et al. [2]. Adhesive mixtures were prepared by mixing weighed amounts of formulations with lactose carrier (63-90 μm) using a Turbula mixer. The initial and compact bulk density, the Carr's index and Hausner ratio of the microcomposites were determined by uniaxial compression test using a texture analyser. The aerosolisation performance from an Aerolizer® inhaler was assessed using the next generation impactor.

Results and Discussion: The microcomposite particles of theophylline with different amounts of mannitol exhibited poor flowability (Carr's index > 31%) which can be attributed to their small size, high porosity and surface roughness. Due to their poor flowability, handling difficulties may arise at different stages of the powder processing (e.g. capsule filling). Preparing adhesive mixtures of the microcomposite formulations with lactose carrier increased the emitted fraction of the drug while no significant differences in the fine particle fraction were observed. In all cases, the engineered microcomposite particles either as drug-alone formulations or adhesive mixtures exhibited enhanced aerosolisation performance compared to the adhesive mixture of micronised THEO. All in all, engineered microcomposite particles with enhanced aerosolisation properties still benefit from mixing with coarser carriers as their flowability and handling are improved while their aerosolisation performance is not deteriorated.

Keywords: microcomposite, dry powder inhalers, adhesive mixtures, flowability, aerosolisation

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