Manufacturing of Taylor Made Carrier Particles for Inhalation Therapy by Spray Drying

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Abstract

Dry powder inhalers usually contain ordered mixtures of active species preferably in the low micron size $d_p < 5\mu m$ and carrier particles typically in the mean size range of 50 to 100 µm. The separation of the active fines from the carrier during inhalation in an inhaler is fundamental for the drug deposition in the lung. During inhalation, the particles impact onto the walls of the inhaler at given air speed and lead to detachment of the active fines from the carrier and their entrainment into the aerosol. Carrier particles are deposited in the upper airways by impaction whereas drug particles are transported into the deeper areas of the lung. There are several tasks to be fulfilled by the carrier particles. On one hand they must provide a good flowability of the particle mixture favored by large carrier particle sizes. Carrier particles however should also provide a large enough surface area for the adhesion of the active fines, on the other hand they should not break during impact, handling and processing. Only particles below a certain diameter are expected not to break into fragments during impact, i.e. too large carrier particles should also be avoided. Besides a given target particle size, equal or close to equal surface characteristics can only be expected from narrowly sized particles. Only those particles would undergo uniform transport, drying and solidification processes in the drying tower. Lactose is the carrier material preferably applied in commercially available ordered powder mixtures. However, the surface of the particles as obtained from spray drying of lactose solutions appears to be always smooth within a large range of drying temperatures. In contrary mannitol allows for tailoring the surface morphology of the particles by variation of the drying air temperature as already confirmed in a small lab dryer producing carrier particles $d_{v.50} < 20$ µm with high speed commercial rotary atomizers [1]. It was found that high drying air temperatures leads to rough surfaces, structured by larger crystals, and fairly smooth particles are formed at low drying air temperatures. It is demonstrated for the active species to adhere stronger to rough surfaces compared to smooth surfaces. New experiments were performed spraying 15% by weight mannitol with a new rotary atomizer in combination with a larger tower. This atomizer with D = 100mm diameter is equipped with 50 inclined bores operating within the laminar open channel flow range. The atomizer is able to generate sprays with low span values SP = (dv.90-dv.10)/dv.50 < 1, [2] and to adjust the mean drop size in a very distinct manner. The target particle size was 62 µm achieved at 7200 rpm out of drops with $d_{v50} = 99$ µm diameter. The morphologies of these larger particles could be modified again by changing the air inlet temperature into the dryer leading to air outlet temperatures within the range of 80°C to 130°C. The particles as obtained from the mannitol solution are characterized by different analytical methods relevant for their pharmaceutical application. Details on the PSD are reported.

1. Maas, S.G., Schaldach, G., Walzel, P., and Urbanetz, N.A., Tayloring Surface Topography of Mannitol by Spray Drying, *Powder Technol.*, submitted for publication in 2008

2. Walzel, P., Schaldach, G., Wiggers, H., paper ID ILASS08-1-1. *Proc. Inst. Liquid Atomis. and Spray Sys. (ILASS Europe)*, Como, Italy, 08-10 Sep. 2008

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