Enhancing the performance of dry powder inhalers by tailoring interparticle forces via surface modification of carrier and active

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The aim of this work is to improve the performance of carrier based dry powder inhalers (DPI) via the modification of interparticle interactions between the drug and the carrier. In order to reach the deep lung active pharmaceutical ingredient (API) particles must have an aerodynamic diameter of 1 µm to 5 µm. Particles of this size range are very cohesive and exhibit rather poor flow properties [1] what makes volumetrically dosing very difficult. To overcome this problem and to improve flowability the API is attached to larger carrier particles (50 µm – 200 µm). Drug detachment from the carrier during inhalation is essential to ensure that the drug particles reach their targeted site, the deep lung. Otherwise they will impact together with the coarse carrier on the upper airways. Thus interparticle interactions play a crucial role in carrier based formulations. It is important, that they are on the one hand high enough that uniform dosing is possible and on the other hand low enough that drug detachment during inhalation is guaranteed.
In the present study interparticle interactions were altered by the surface modification of glass beads, used as model carrier because of their ideal geometry and the various options to modify their surface chemically as well as physically, without affecting other factors that also influence interparticle forces like particle shape and size. Furthermore interparticle forces were modified by spray drying of the API. Salbutamol sulphate and salbutamol base, used as model drug, were spray dried using different solvents, different concentrations and spray drying conditions. The sphericity and cristallinity of the generated particles was analyzed dependent on these parameters. The challenge is to generate particles of appropriate size (1 µm – 5 µm) which are spherical and crystalline. Experiments of Chawla [2] showed that spray drying of salbutamol sulphate produces spherically shaped particles with a mass median diameter of 4.5 µm. But compared to micronized salbutamol sulphate the spray dried powder tends to be less crystalline [2]. In contrast our first experiments have shown that spray drying of ethanolic salbutamol base solutions seems to be most promising to create crystalline particles with the requested size. Figure 1 shows a scanning electron micrograph of a salbutamol base particle spray dried at 100 °C from ethanol.

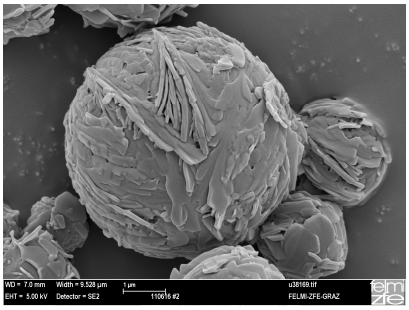

Fig. 1: SEM of salbutamol base, spray dried at 100 °C from ethanol

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2. Chawla A, Taylor K M G. (1994) International Journal of Pharmaceutics. 108: 233-240.