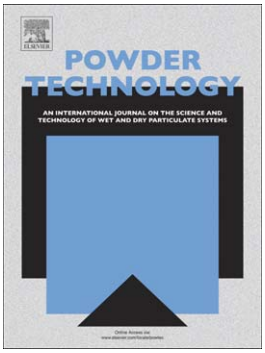

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PII: S0032-5910(14)00240-X
DOI: doi: 10.1016/j.powtec.2014.03.040
Reference: PTEC 10128

To appear in: *Powder Technology*

Received date: 5 June 2013
Revised date: 13 February 2014
Accepted date: 1 March 2014

Please cite this article as: Stefan Karner, Markus Maier, Eva Littringer, Nora Anne Urbanetz, Surface roughness effects on the tribo-charging and mixing homogeneity of adhesive mixtures used in dry powder inhalers, *Powder Technology* (2014), doi: 10.1016/j.powtec.2014.03.040

Surface roughness effects on the tribo-charging and mixing homogeneity of adhesive mixtures used in dry powder inhalers

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Abstract

For active pharmaceutical ingredients (API) delivered to the lung it is of main importance that they reach the deeper lung, in order to cause the intended therapeutic effect. To obtain inhalable powders that on the one hand are small enough to travel along the tiny airways finally reaching their target site and on the other hand show sufficient flowability, so-called adhesive mixtures are used. They consist of API particles in the size range of 0.5 µm - 5 µm and carrier particles in the size range of 50 µm - 200 µm, that, due to the size of the carrier, exhibit adequate flowability. However, when administered to the patient, the API has to separate from the carrier surface in order to be able to penetrate the deep lung. The performance of dry powder inhalers (DPIs) and adhesive mixtures are mainly governed by interparticle forces like Van der Waals and triboelectric forces. Carrier surface roughness modification is a new method to alter the contact area and thus the Van der Waals forces between API and carrier. Unfortunately the tribo-charging during handling, especially during the generation of the adhesive mixtures in a tumble blender, is strongly influenced by particle characteristics like particle surface roughness. Thus the mixing quality and stability and thereby the usability of the powder mixture might be additionally influenced by tribo-charging. Therefore the aim of the present work is to investigate whether tribo-charging during the mixing process is influenced by the carrier particle surface roughness. Further the influence of tribo-charging on mixing homogeneity is assessed. Netcharge measurements are performed using a faraday cup. As model API and carrier salbutamol sulphate and spray dried mannitol, respectively are used. It is shown that the carrier particle characteristics impact tribo-charging of the pure carriers in a tumble blender. This influence is not observed for the adhesive mixtures of carrier and API. Nevertheless the homogeneity of the adhesive mixtures is still influenced by the charging of the carriers.

1. Introduction