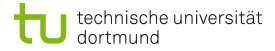


Tailor-made carrier particles for dry powder inhalers

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We present an overview of our current work on spray dried carrier particles of D-Mannitol for dry powder inhalers. The aim of this study is to control and optimize the performance of carrier-based inhaler formulations by carrier surface modification via spray drying.

Introduction

The purpose of this study is to generate tailor-made carrier particles of D-Mannitol for DPI by spray drying. Tailor-made refers to the interparticle interaction between drug and carrier particles which affects the aerosolisation performance of the drug. By varying surface roughness of spray dried mannitol particles interparticle interactions may be tailored. Experiments on a Niro laboratory spray dryer showed that by variation of the air outlet temperature different surface roughness was obtained [1]. However problems encountered by Maas [1] were on the one hand broad particle size distribution and on the other hand too low particle size. For this reason the aim of this study is to first achieve an appropriate atomizing spray with convenient droplet size and narrow droplet size distribution as a prerequisite for adequate particle size and narrow particle size distribution of the final spray-dried product.

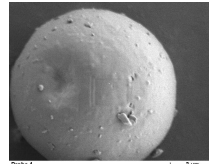


Photo 1
Air outlet temperature: 60 °C [1]

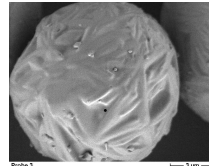


Photo 2
Air outlet temperature: 120 °C [1]

Schematic of potential drug-carrier adhesion interaction scenarios dependent on surface roughness [2]



Smooth carrier: high contact area
 Pros: good blend content uniformity
 Cons: increased adhesion- decreased drug liberation



Commercial grade carrier: variation in contact area
 Pros: commercially produced- low cost
 Cons: contact area variation- drug liberation variation



Microscopic roughness: high contact area
 Pros: good blend uniformity
 Cons: increased adhesion- decreased drug liberation



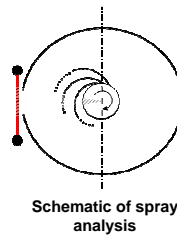
Ideal morphology: reduced contact area
 Pros: consistent adhesion profile- controllable adhesion (through void space) good content uniformity- good drug liberation



Nanososcopic roughness: low contact area
 Pros: increased liberation- decreased adhesion
 Cons: poor content uniformity- blend segregation

Experimental methods

Atomizing spray was measured by laser diffraction (Malvern 2600, Malvern Instruments) as function of feed concentration (7.5 % [w/w] and 15.0 % [w/w]), feed rate (10 l/h and 20 l/h) and rotation speed (5400 rpm, 6300 rpm, 7200 rpm and 8100 rpm). Variables used for spray characterization were volume mean droplet size and droplet span $[(d_{90}-d_{10})/d_{50}]$. Droplet span is conventionally calculated with volume droplet size values. The laser beam was positioned 30 cm vertically from the atomizer edge.



Schematic of spray analysis

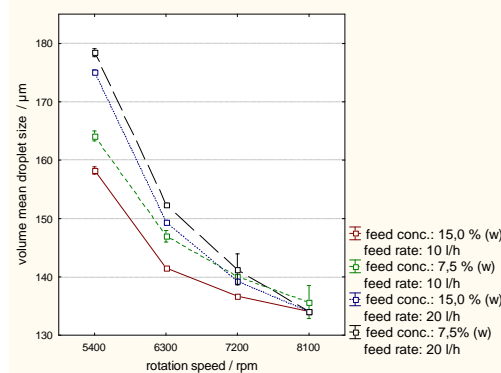


Used atomizer
 proprietary developed^b
 60 bores (laminar flow through)

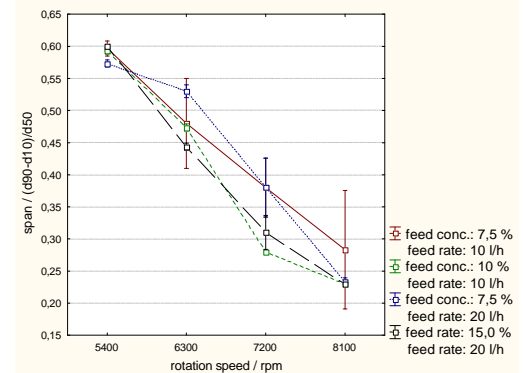
Laminar rotary atomization
 Atomization of liquids by laminar jet break-up leads to narrow droplet size distribution with low plugging-tendency even at high throughputs.

Results and discussion

Mean droplet size as well as droplet span is inversely proportional to rotation speed. The decrease of the span is most likely caused by the gradual change from dripping regime to laminar jet break-up which is characterized by a narrow droplet size distribution. A further increase of the rotation speed might have led to an even lower span however the maximum working speed of this kind of atomizer is limited at 8100 rpm. The decrease of droplet size is caused by increased forces on the jet which leads to the thinning of the jet resulting in smaller droplets after break-up. Especially because of the narrow droplet size distribution at higher rotation speed we decided to use 7200 rpm and 8100 rpm for a fractional design at two levels for spray drying experiments.



Dependence of volume mean droplet size on rotation speed (n = 3; mean ± SD; feed temperature: 23 °C)



Dependence of volume droplet span on rotation speed (n = 3; mean ± SD; feed temperature: 23 °C)

Outlook

Based on results achieved by analysis of atomizing spray an experimental design for spray drying will be planned and carried out. Five factors, feed temperature, rate and concentration, air inlet temperature and atomizer rotation speed will be studied in a fractional factorial design at two levels.

Acknowledgement

References

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