Segregation and distribution of different particle sizes in the components of a capsule filling machine based on the vacuum drum filler for DPI applications

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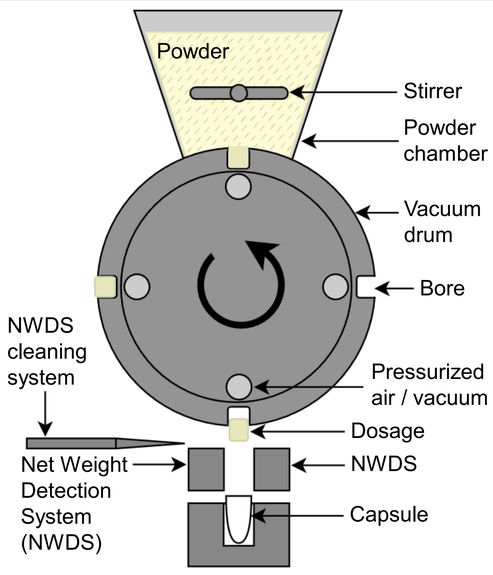
Introduction

- Dry powder inhalation (DPI) formulations are used to treat diseases by delivering the active pharmaceutical ingredient (API) to the lungs[1]. Capsules for DPI formulations can be filled with a vacuum drum, allowing doses as low as 1 mg to be filled.
- The GKF 720 capsule filling machine is mainly composed of a feeding station, a powder chamber with a stirrer and a vacuum drum with 4 lines, each with 5 bores. The powder is filled into the bores of the drum using vacuum, and then the drum rotates and ejects the powder with pressure to fill the capsules (Fig 1).
- Due to the low amount of powder dosage, accurate fill weight and uniform content of API in the capsules are critical[2].



▶Fig 1. Representation of the filling process with the vacuum drum

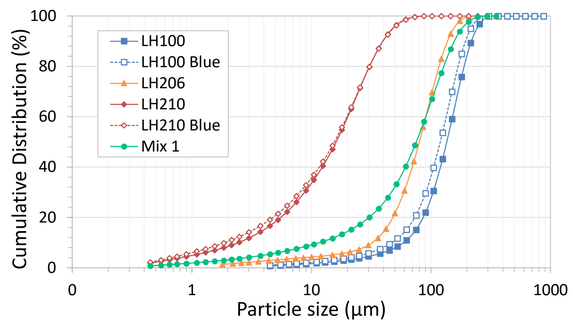
Objective

- Evaluate the segregation of powder during the capsule filling process and the influence of using different types of stirrers, by measuring the content uniformity in the capsules using a blue tracer.

Methods

Materials: Lactose for inhalation (DFE-Pharma)

- Mix 1 (10% LH100, 80% LH206 and 10% LH210)
- Small (LH210) or big (LH100) particles were replaced with their respective tracer (lactose dyed with methylene blue)

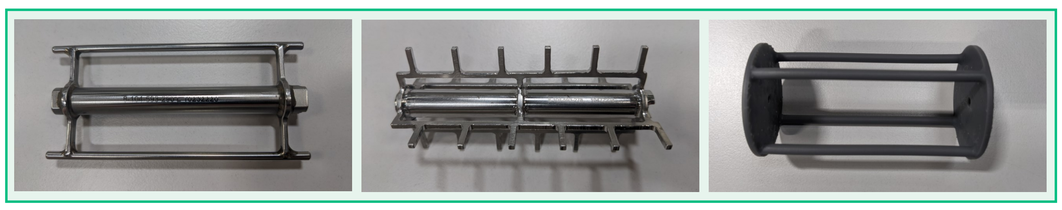


► Fig 2. Cumulative density distribution of the materials, their respective blue tracer and Mix 1

- The powder chamber and vacuum drum of the GKF 720 (Syntegon Technology GmbH, Waiblingen, Germany) with a filling weight of 5 mg were used for the study.
- The powder chamber was filled with 120 g of Mix 1 and 25 dosages from each of the bores were collected every 5 minutes for 25 minutes. The powder was analysed using UV-Vis spectroscopy.
- Different stirrers (Fig 3) were used to evaluate their influence on the segregation.

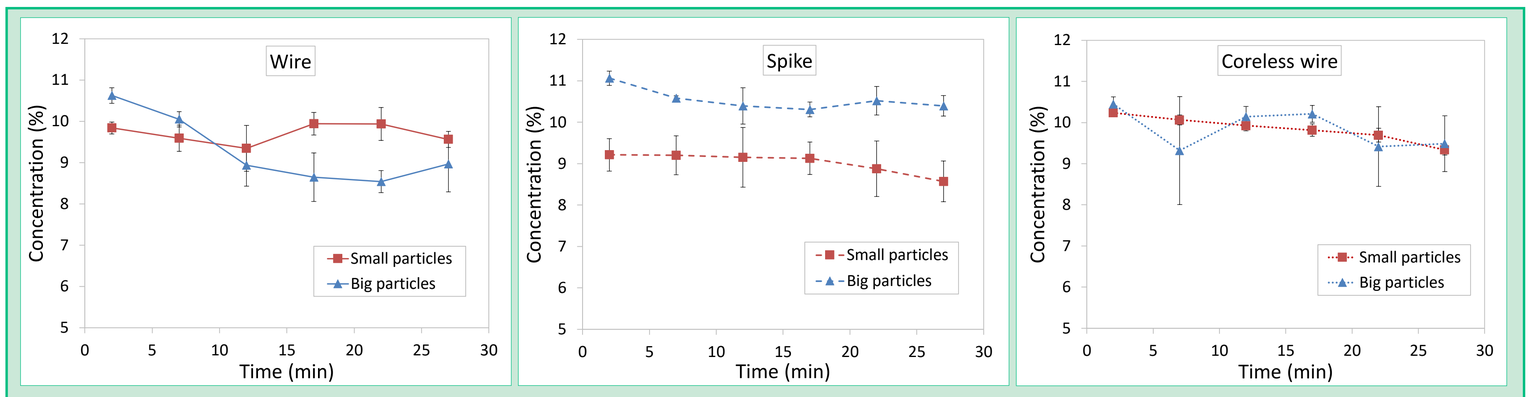
▼Table 1. Overview of the machine parameters used for experiments

Fixed parameters	
Machine speed	100 cycles/min
Stirrer speed	100 rpm
Stirrer rotation	to the right
Vacuum (drum)	-0.4 bar
Transfer pressure (drum)	0.4 bar

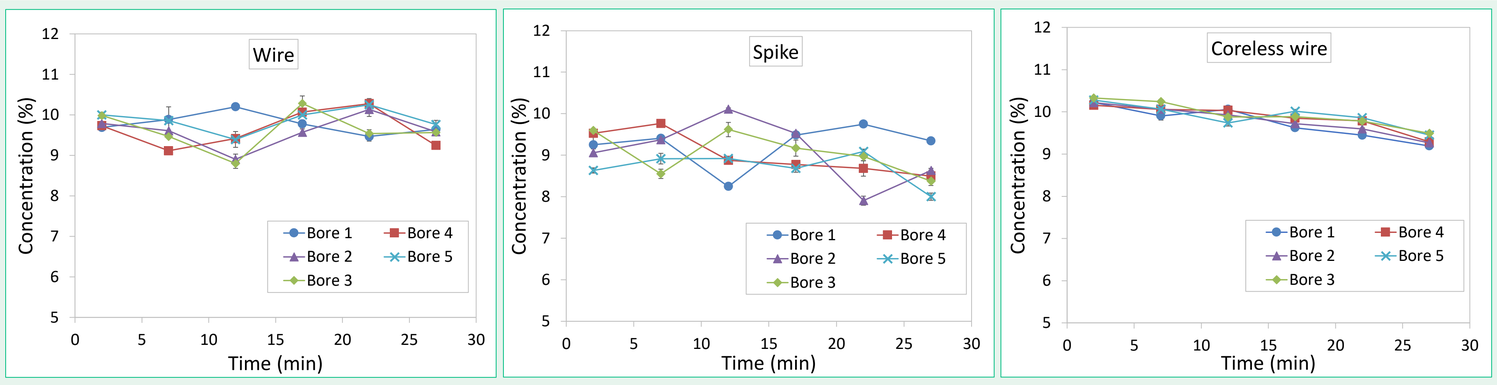


▲Fig 3. Wire (left), spike (middle) and coreless wire (right) stirrer

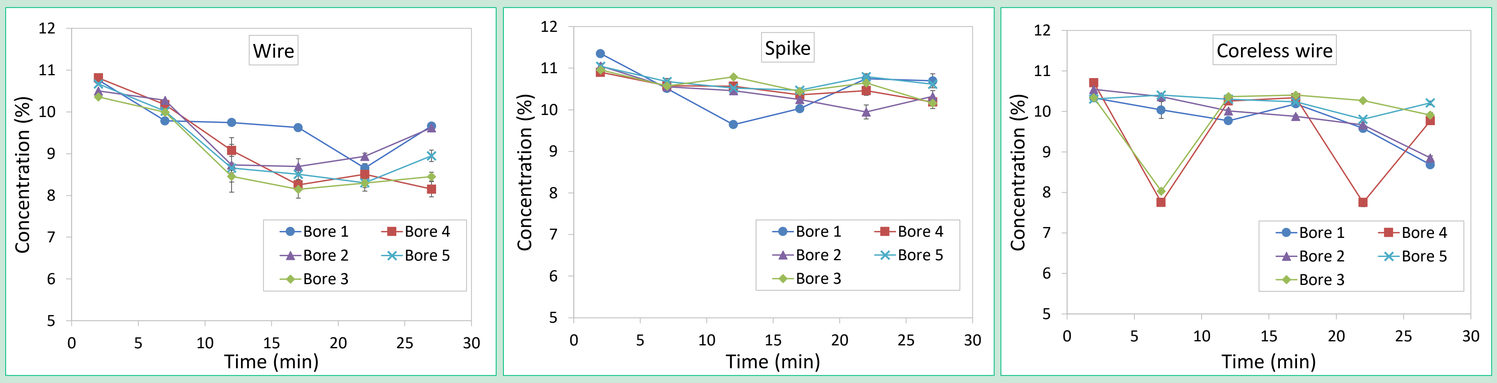
Results



▲Fig 4. Mean concentration in the line of bores of small (LH210) and big (LH100) particles over time with wire, spike and coreless stirrer (n=3 ± standard deviation)



▲Fig 5. Concentration of small particles (LH210) that come out of the bores of the vacuum drum over time with wire, spike and coreless stirrer (n=3 ± standard deviation)



▲Fig 6. Concentration of big particles (LH100) that come out of the bores of the vacuum drum over time with wire, spike and coreless stirrer (n=3 ± standard deviation)

- By replacing the small or big particles with the blue tracer, it was possible to experimentally measure the concentration of a specific particle size that came out of the bores of the drum over time (Fig 4).
- When using the spike stirrer, the bigger particles came out of the bores first, and the smaller particles stayed in the powder chamber (Fig 4).
- It was found that there are statistically significant differences ($p<0.05$) in the concentration of small and big particles coming out of the bores when using different stirrers.
- With this method, it was also possible to measure the concentration of small and big particles in each of the bores separately over time for the different stirrers (Fig 5 and Fig 6), allowing to determine the content uniformity in the capsules.

Conclusions

- With the help of a tracer, it was possible to measure the content uniformity of the powder coming out of the bores, to assess the segregation in the powder chamber.
- The type of stirrer used in the powder chamber influences the segregation of particles of different sizes, showing statistically significant differences.
- This method will help ensure uniform API content in DPI capsules.

Future work

- Other types of stirrers are going to be investigated, as well as other settings of the machine, such as machine speed, stirrer speed and powder bed height, among others.
- It is expected that in the future for each material, depending on its properties and particle size, the process will be optimized.

References

[1] L. Ding et al., Pharm. 2021; 13; p. 1213

[2] E. Faulhammer *et al.*, *Int. J. Pharm.* 2014; 473(1-2); pp. 617–626

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