Overcoming the challenge of filling highly cohesive spray-dried powders

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Introduction

- Capsule filling processes via a dosator are widely applied in the pharmaceutical industry. Capsule filling of **spray dried powders** using a dosator-based capsule filler can be challenging due to the **cohesive properties** inherent to those powders.

MG2® Flexalab is a dosator-based capsule filler suitable for precision capsule filling, integrated with a 100% weight control system, MultiNETT, controlling in process the net weight contained in each single capsule.

- For carrier-based powders, two main attributes were identified as major players in a low-dosage dosator-based capsule filing process: **the ratio between the dosing chamber length and powder layer height** and a **homogenous powder layer**[1, 2].

The **mains goal** of this work were to assess precision capsule filling of a model spray dried powder using a dosator-based **MG2® Flexalab unit**, optimize the filling process and evaluate its impact on powder in-vitro aerodynamic performance.

Materials and Methods

Capsule filling set-up

Figure 1 – MG2® Flexalab set-up: machine, rotary container and dosator.

Dosator-based filling mechanism

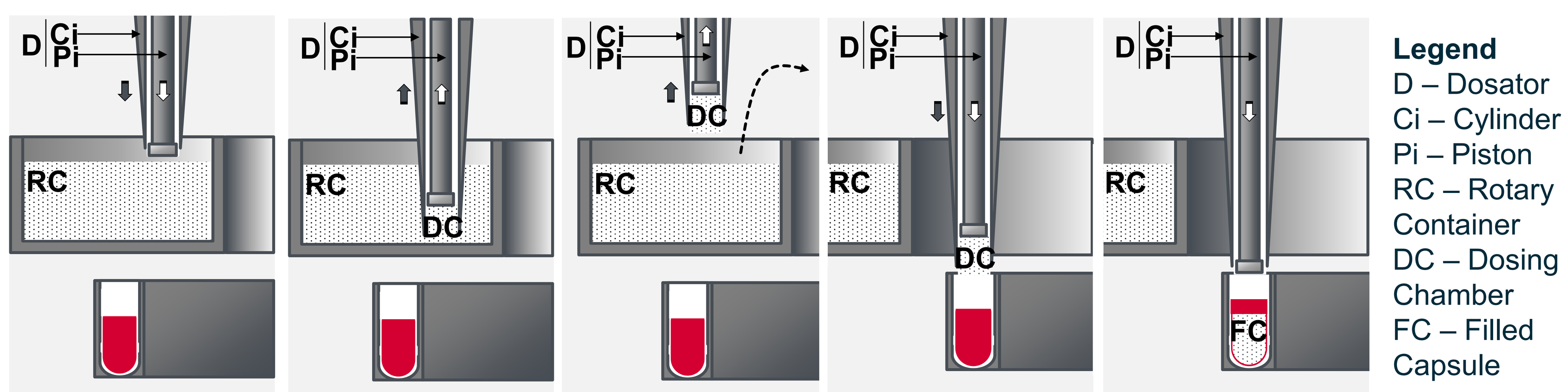


Figure 2 – Schematic representation of a dosator-based filling mechanism.

Spray drying process parameters

Table 1 – Spray drying process parameters.

Composition (% w/w)	Solids concentration (%)	Solvent system (% w/w)	Feed rate (g/min)	Atomizing rate (mm in rotameter)	Dry gas flow rate (kg/h)	Outlet temperature (°C)
Trehalose: L-leucine 80:20	2	Water: Ethanol 50:50	7	50	35	70

Experimental Design

Capsule

Clear HPMC Size #3

Fill weigh

20 mg ±1	10 mg ±1	5 mg ±0.5

Experimental Set-up

Speed (caps/h)

1500 **2000**

Dosator Diameters (mm)

1.9 **2.2** **2.8** **3.4** **3.7**

Chamber / Layer ratio

From **0.5** To **0.9**

Aerodynamic Performance

Andersen Cascade Impactor

Plastiape
60 L/min (4 kPa pressure drop)

N=3

Results and Discussion

Capsule filling optimization

- **Powder adhesion**: internal walls and behind the scrapper
- **Agglomerates** in powder layer
- Powder **accumulation around the dosator**
- High powder **compaction** in layer
- High **rejection rates** during capsule filling

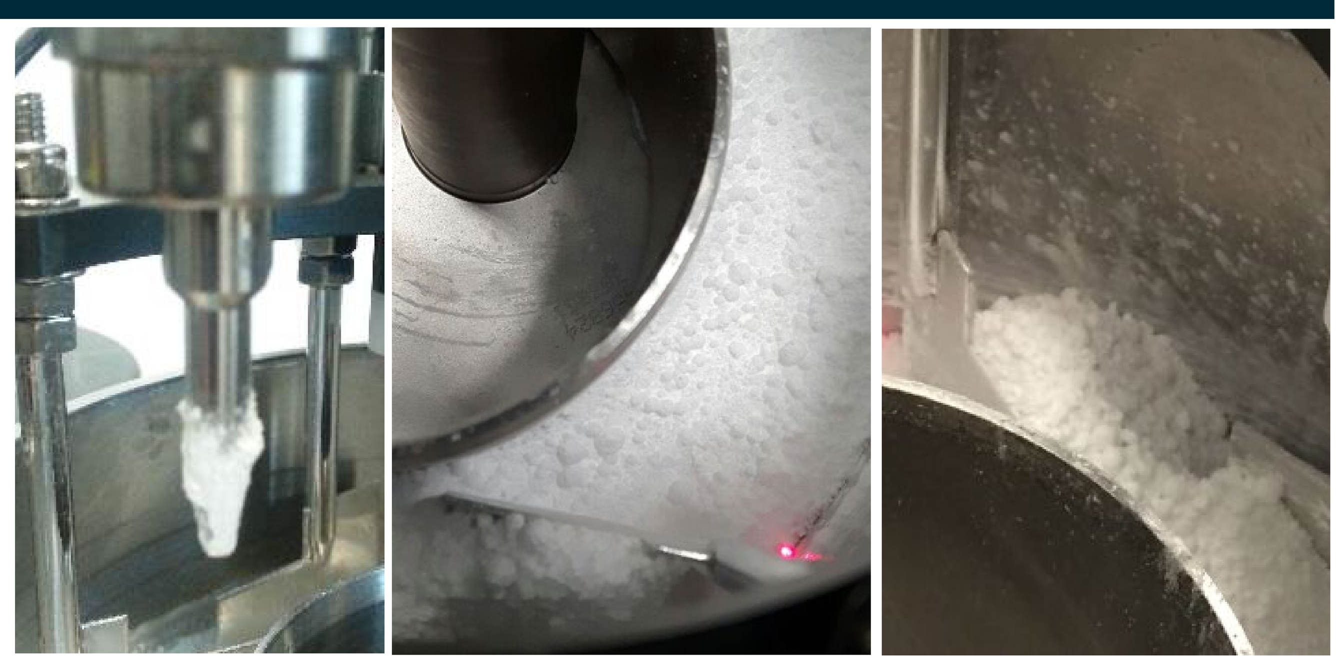


Figure 3 – Set-up and powder appearance before optimization.

- **Cleaning system** for the removal of the excess powder from the dosator;
- **Engineered mixing powder rod** to homogenize the powder bed and decrease the powder adhesion to the walls of the rotary container;

Table 2 – SD powders capsule filling optimization: process parameters and results for five experimental runs.

Run	Fill weight (mg)	Rejection rate (%)	Dosator diameter (mm)	Chamber / Layer ratio	Speed (caps./h)	Capsule visual observation
1	20	0	2.8	0.9	1500	High
2	20	0	3.4	0.7	1500	Medium
3	20	3	3.7	0.5	2000	Low
4	10	0	2.8	0.6	2000	Low
5	5	0	1.9	0.8	2000	Low

Powder characterization

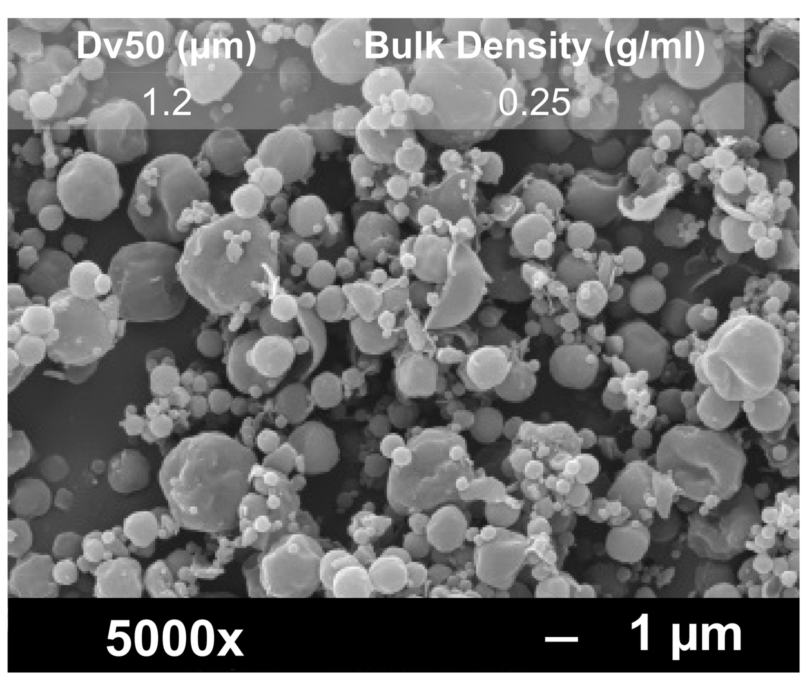


Figure 4 – SEM images of the spray dried powder.

Aerodynamic performance

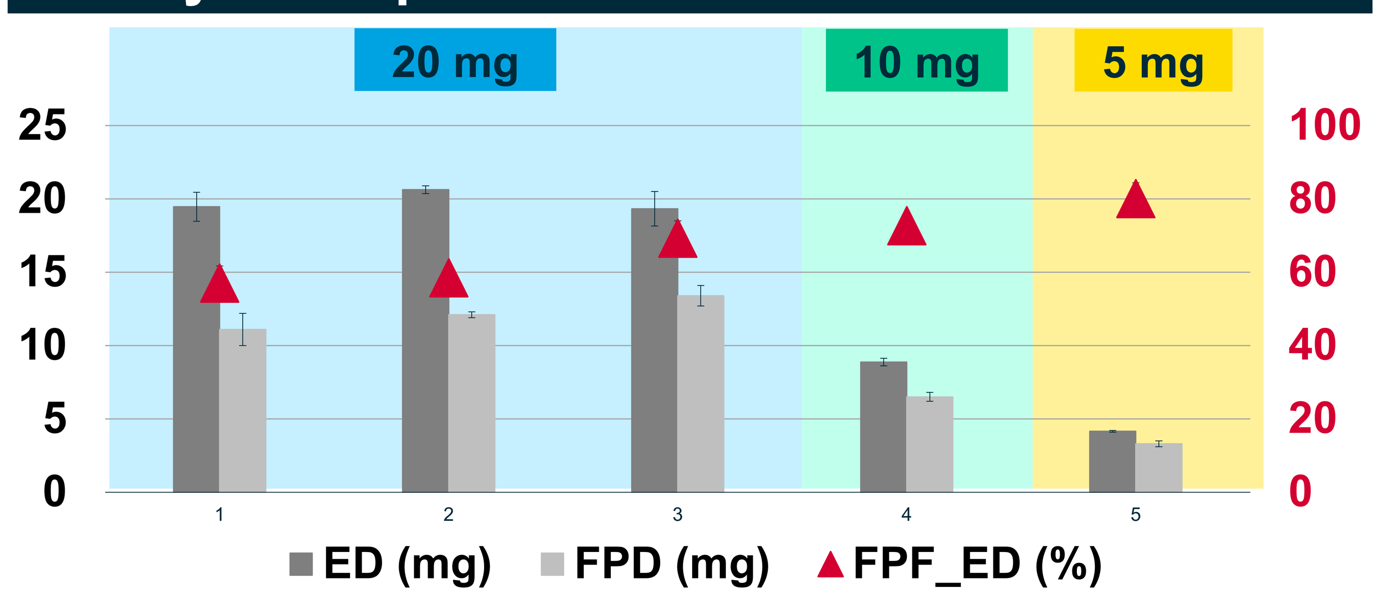
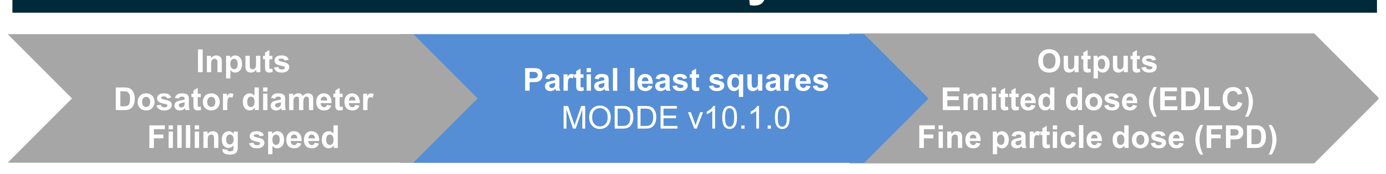


Figure 5 – Aerodynamic performance results measured by ACI for the different fill weights.

Aerodynamic performance in **accordance** with **visual observation** of capsules.

Multivariate statistical analysis



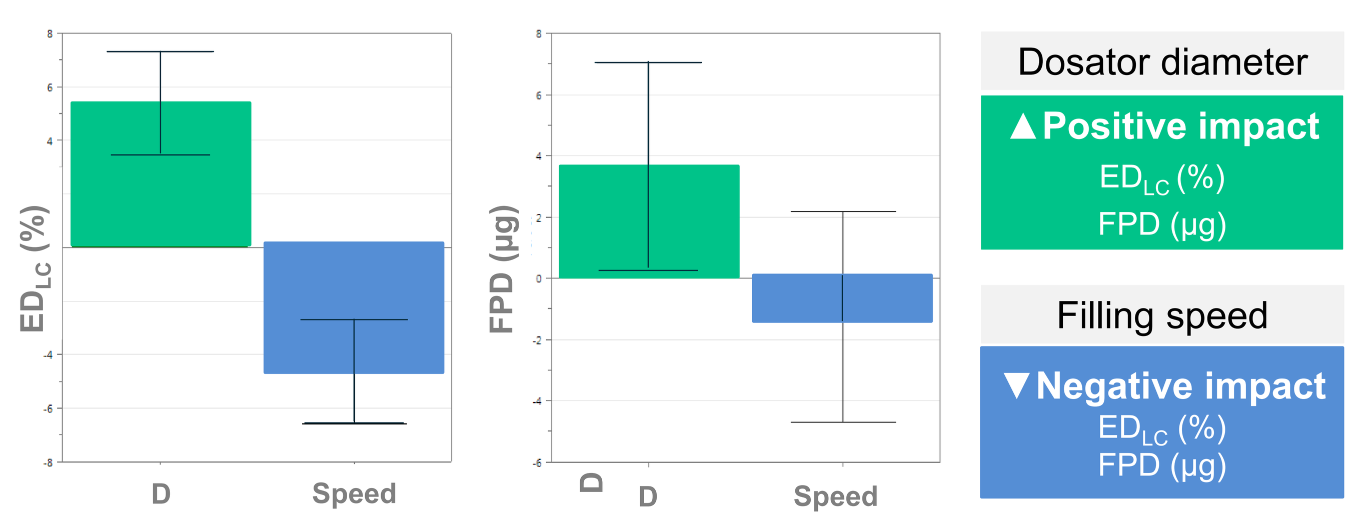


Figure 6 – Regression coefficient plots for ED_{LC} (%) and FPD (µg/capsule))

Conclusion

Capsule filling process of spray dried composite particles using a MG2 Flexalab machine was **successfully achieved**.

Low powder compaction in capsules and low rejection rates were possible to obtain by **optimizing process parameters** and by **implementing appropriate engineering solutions**.

Good aerodynamic performances were obtained using a **reliable and robust technology** in a manufacturing environment, which is **easily scaled-up**.

REFERENCES: [1] Eva Faulhammer, Marlies Fink, Marcos Llusa, Simon M. Lawrence, Stefano Biserni, Vittorio Calzolari, Johannes G. Khinast: *Low-dose capsule filling of inhalation products: Critical material attributes and process parameters*, International Journal of Pharmaceutics 2014; 473: pp617-626. [2] S. Stranzinger, E. Faulhammer, V. Calzolari, S. Biserni, R. Dreu, R. Šibanc, A. Paudel, J.G. Khinast: *The effect of material attributes and process parameters on the powder bed uniformity during a low-dose dosator capsule filling process*, International Journal of Pharmaceutics 2017; 516: pp9-20.