Softpellets Production by Self-Agglomeration Process

E. Gresse[1], T. Gemine[2], L. Renauld[1,2], G. Lumay[2], B. Evrard[1], A. Lechanteur[1]

[1] Laboratory of Pharmaceutical Technology and Biopharmacy, Center for Interdisciplinary Research on Medicines (CIRM), University of Liège, Avenue Hippocrate 15, 4000 Liège, Belgium

[2] Group of Research and Applications in Statistical Physics, CESAM Research Unit, University of Liège, Allée du 6 Août 19, 4000 Liège, Belgium

✉ anna.lechanteur@uliege.be

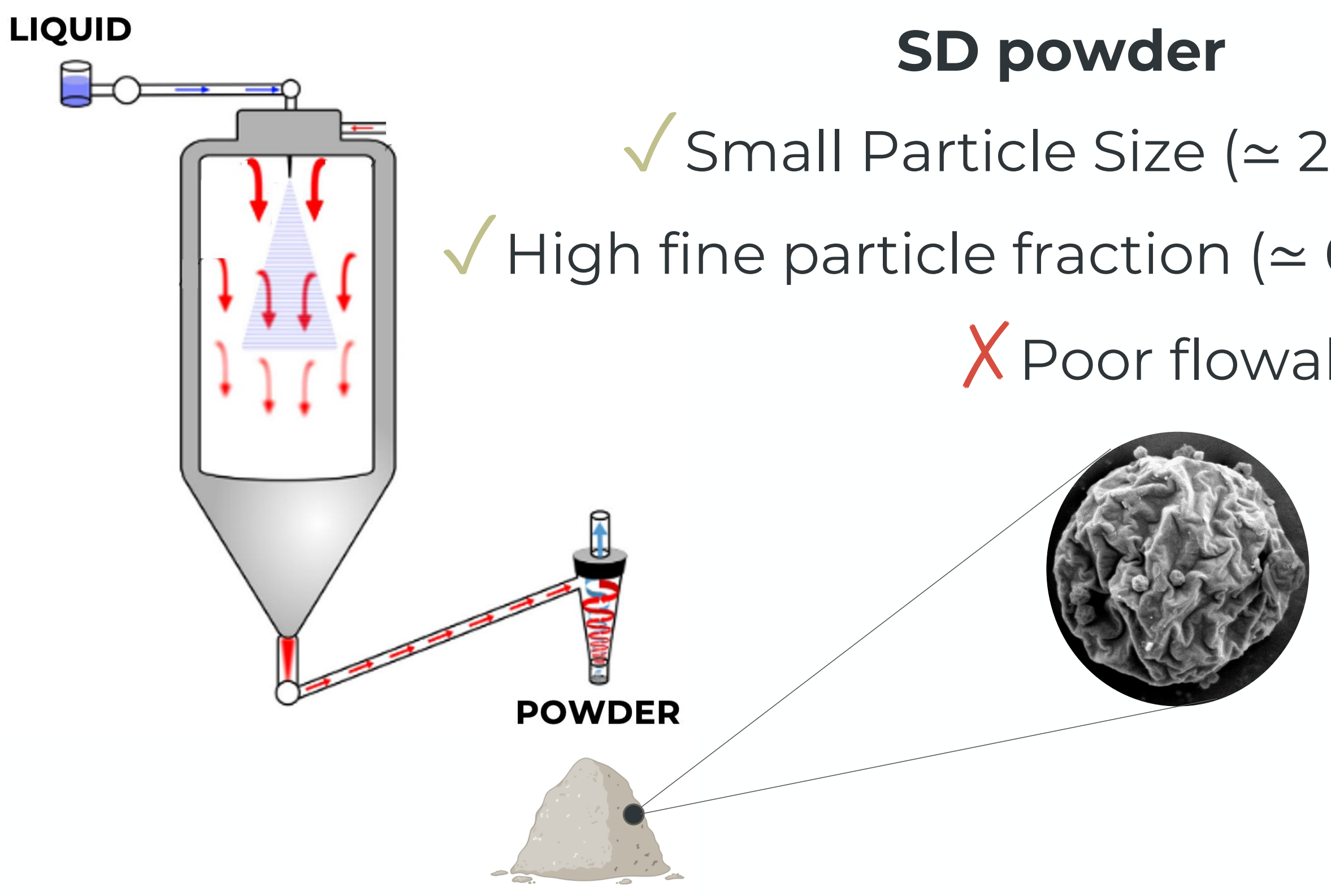
LIÈGE université
LTPB
Center for Interdisciplinary Research on Medicines

Context & Methods

1

PARTICLE ENGINEERING

Spray drying enables the production of inhalation powders with **high aerosolization performance** through particle engineering. However, the small aerodynamic diameter of these particles leads to strong **interparticle forces**, resulting in **poor flowability**.



SD powder

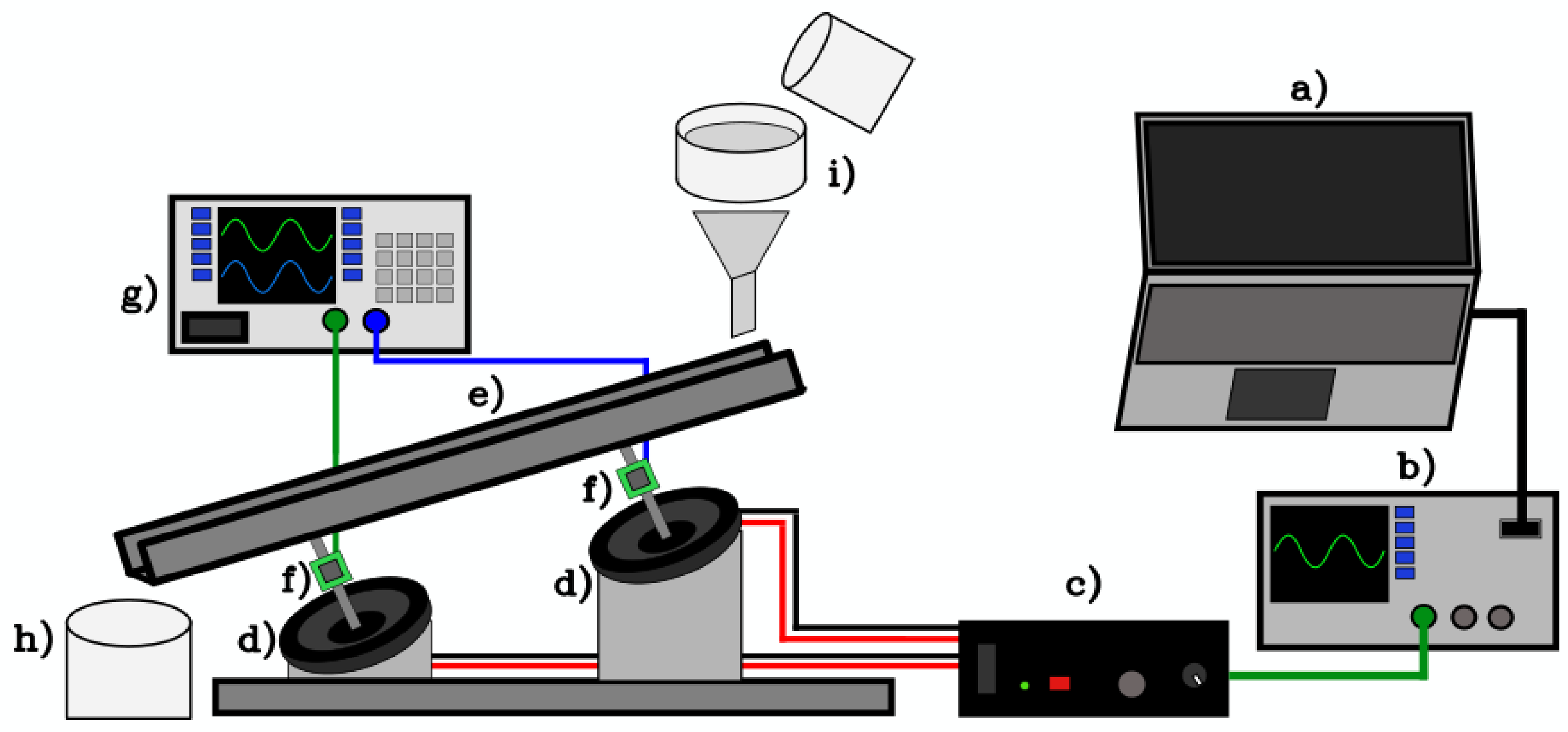
✓ Small Particle Size (≃ 2 µm)
✓ High fine particle fraction (≃ 60%)
✗ Poor flowability

A solution of budesonide, formoterol, hydroxypropyl-β-cyclodextrin, raffinose, and L-leucine is spray dried (15% w/w) using a Procept 4M8-Trix Formatrix spray-dryer[1].

2

FLOW IMPROVEMENT

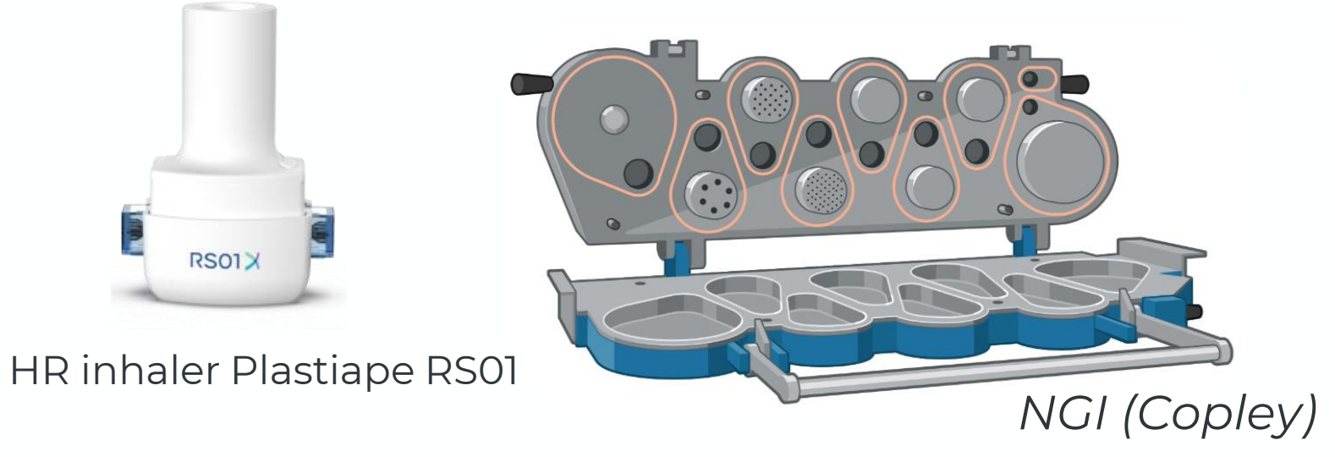
A previous study showed how to optimize powder flow by the mixing with coarse lactose and the impact on capsules filling[1]. In this study we evaluate **the use of a vibrating inclined plan to induce the self-agglomeration of micronized powder.**



Two powders were used: SD powder or lactose 500 They flow along a vibrating inclined plate, where particle collisions induce **tribocharging**, leading to the generation of soft pellets from either.

Figure 1: Schematic representation of the vibrating inclined plate. The experimental setup consists of a signal generator (b) controlled by a computer (a). The generated signals are amplified (c) and applied to the vibrators (d), which support a 50 cm U-shaped plate (e) with a variable incline set at 10°. The vibrators are attached to the plate 10 cm from the ends. The oscillation of the vibrating plate is monitored using an oscilloscope (g) with the aid of two accelerometers (f). The experimental protocol is as follows: the powder passes through a mesh sieve of 1.25 mm (i) before being introduced onto the plate via a funnel. The powder then flows along the vibrating plate before being deposited into the receiving container (h).

Aerosolization measurements:



HR inhaler Plastiape RS01

NGI (Copley)

Flow measurements:

Soft pellets analysis:

Digital microscope

Setting of vibrating plane parameters

Influence of number of passages on Soft-pellets morphology

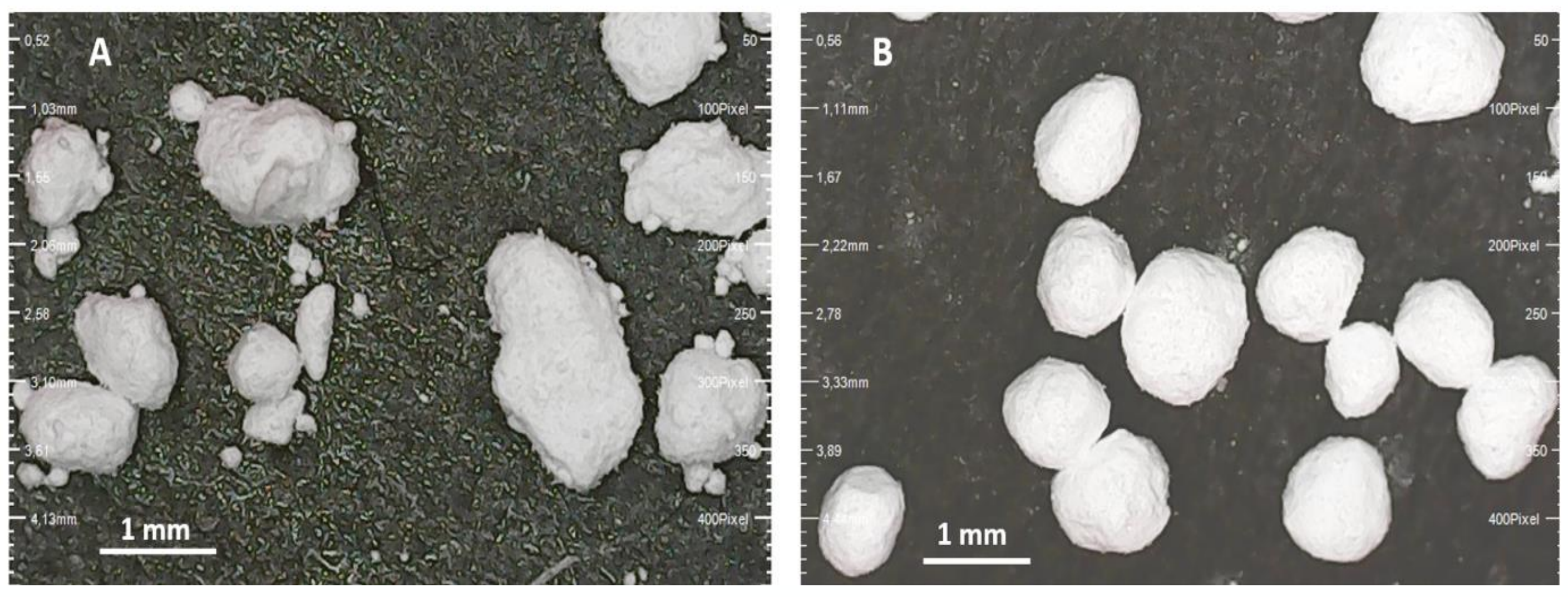


Figure 2: Digital microscopy images of Lac500 agglomerates after one passage (A) and three passages (B) on the vibrating inclined plate.

Parameters were selected for the self-agglomeration of micrometric powders, specifically a frequency of 40 Hz and amplitudes of 0.52 mm and 0.59 mm for the upper and lower speakers, respectively.

Influence of number of passages on electrostatic charge

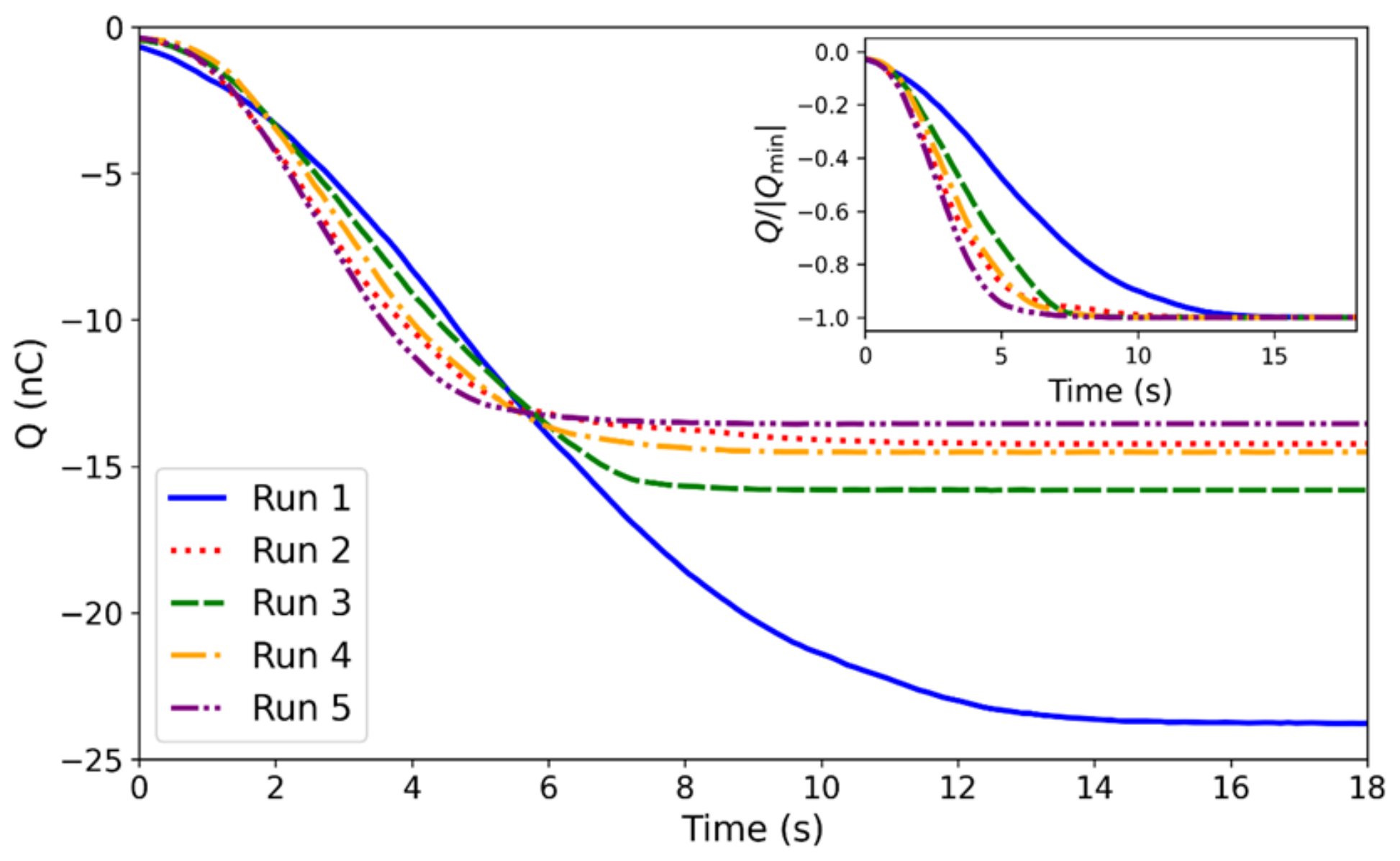


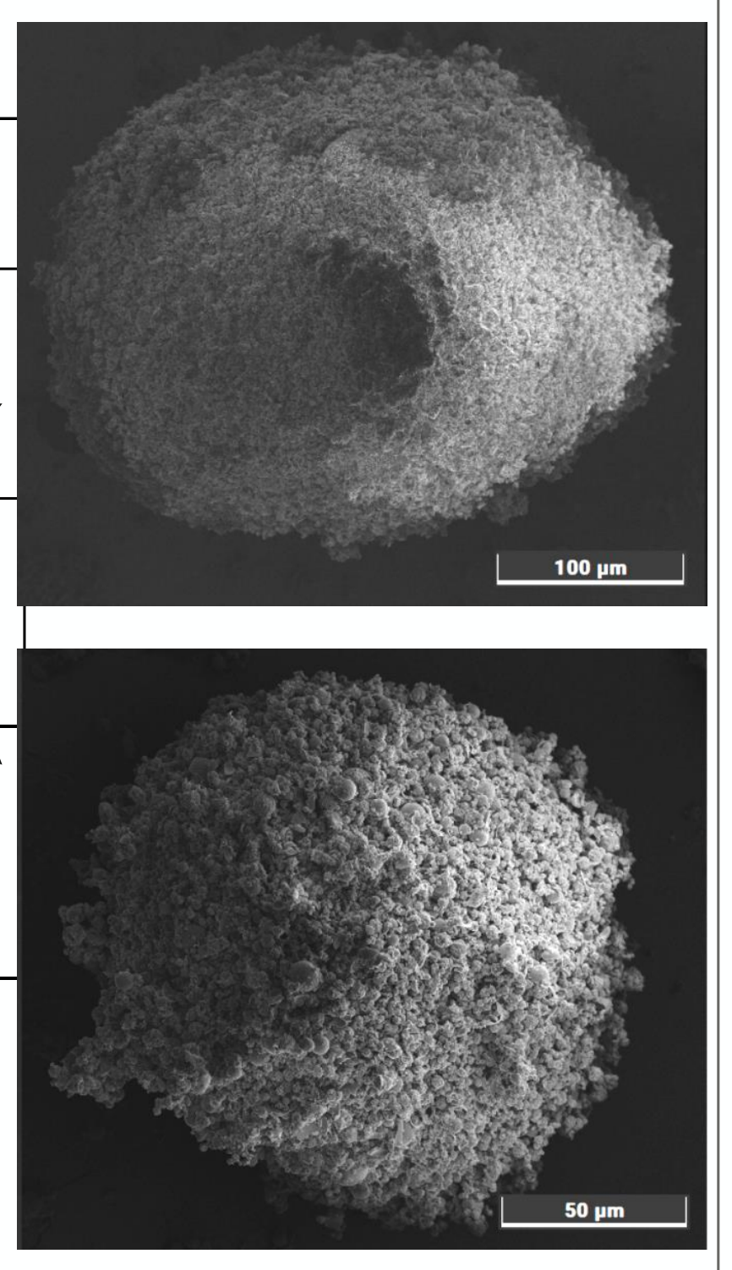
*Figure 3: Typical temporal evolution of the charge Q measured by the **Faraday cup** at the output of the inclined plane for the different runs of an experiment. The insert shows the normalized version of the curve to highlight the time needed to empty the inclined plane for each run.*

The time discharging time is longer for the first run and decreases in subsequent runs, indicating that the flowability increased due to the agglomeration process produced by the charge (Q)

Results of the soft pellets

LACTOSE 500 MESH and SD powder

	D_{10} (µm)	D_{50} (µm)	D_{90} (µm)	Sphericity
Lac500 Softpellet	315.81 ± 9.06	790.99 ± 7.52	1400.42 ± 8.86	0,83
SD Softpellet	464,93 ± 18,18	807,48 ± 58,57	1270,35 ±121,14	0,82
Pulmicort® Turbubaler [23]		519.6		0,91



The vibrating plate generates soft pellets from both powders, regardless of particle type.

In vitro aerosolization of SD soft-pellets

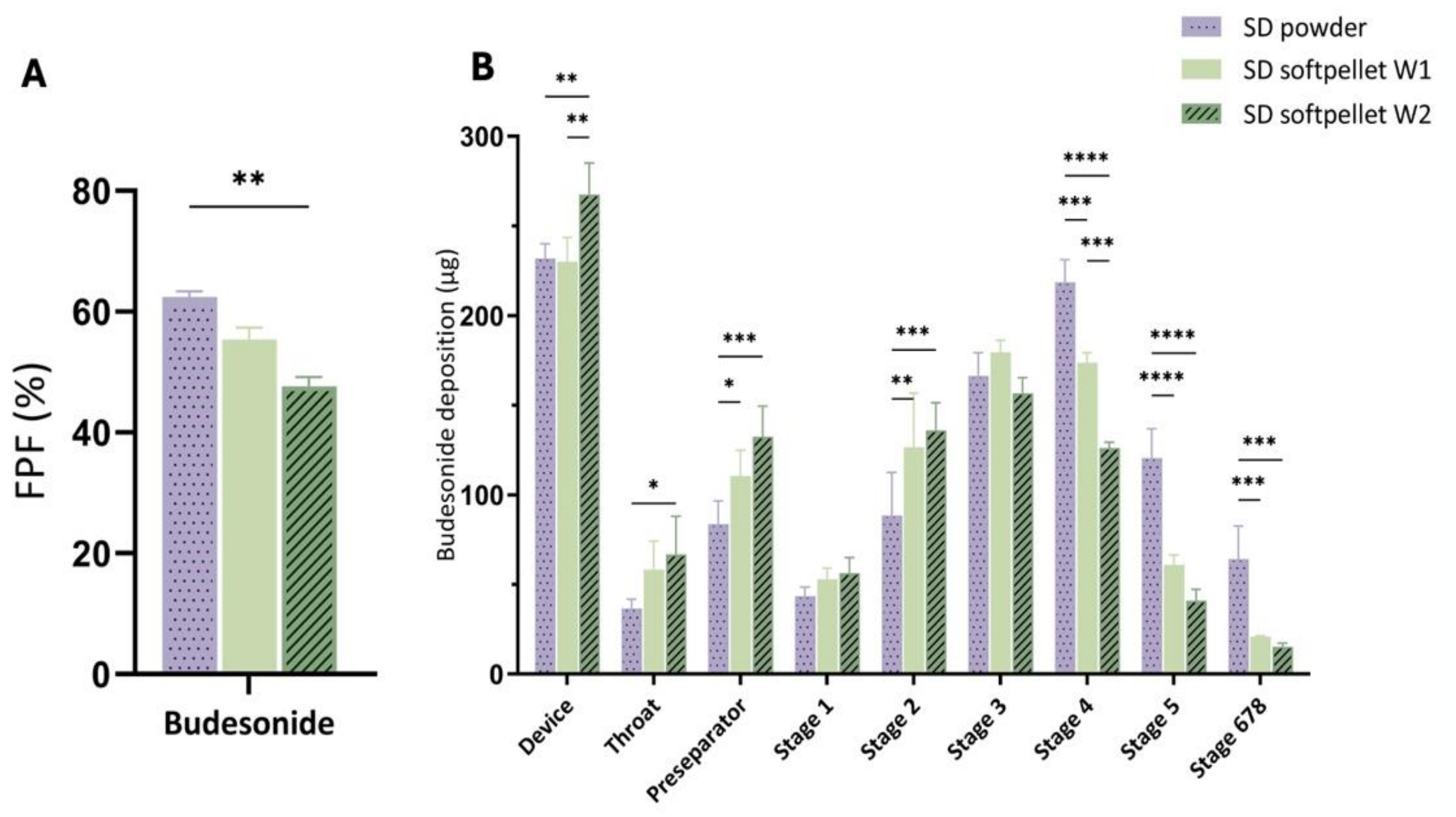


Figure 4: Fine particle fraction (FPF) (A) and budesonide deposition (B) for spray-dried (SD) powder and SD softpellets after one week (W1) and two weeks (W2) from production.

The forces maintaining the soft pellets do not hinder aerosolization performance, allowing for effective separation into individual particles. FPF is observed at a non optimal inspiration flow (low flow rate of 30 L/min). These results have been correlated to mechanical strength of agglomerates (texture analyser experiments).

Flowability

Self agglomeration improves the flowability of spray-dried powder (SD powder) and fine lactose (Lac 500) since the soft pellets have a lower cohesion index compared to native powders.

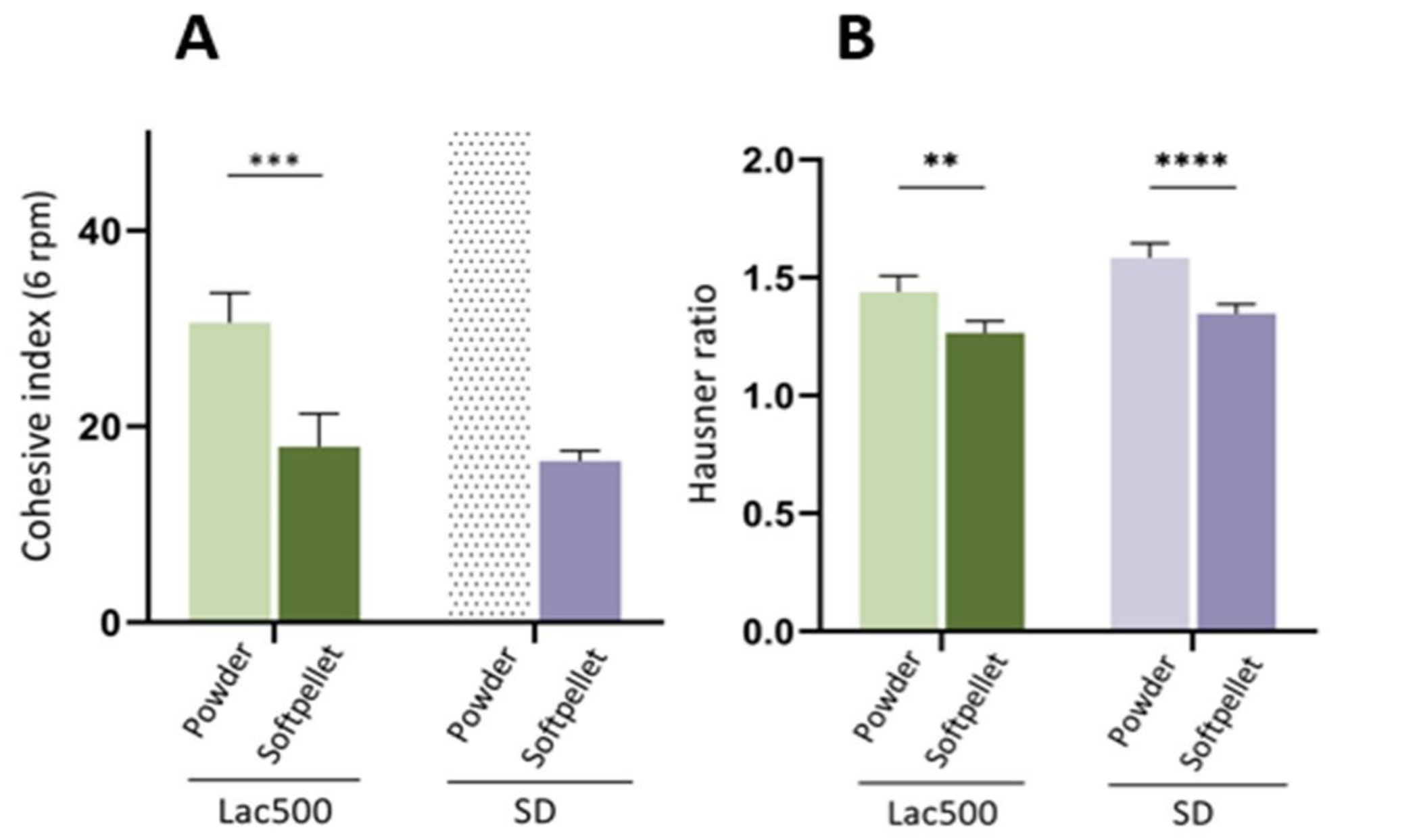


Figure 5: Cohesive index (A), Hausner ratio (B) of Lac500 and SD powders

References

1. E. Gresse *et al.*, Powder Technol., 2024
2. E. Gresse *et al.*, Powder Technol., 2025 (*In review*)

Acknowledgments

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