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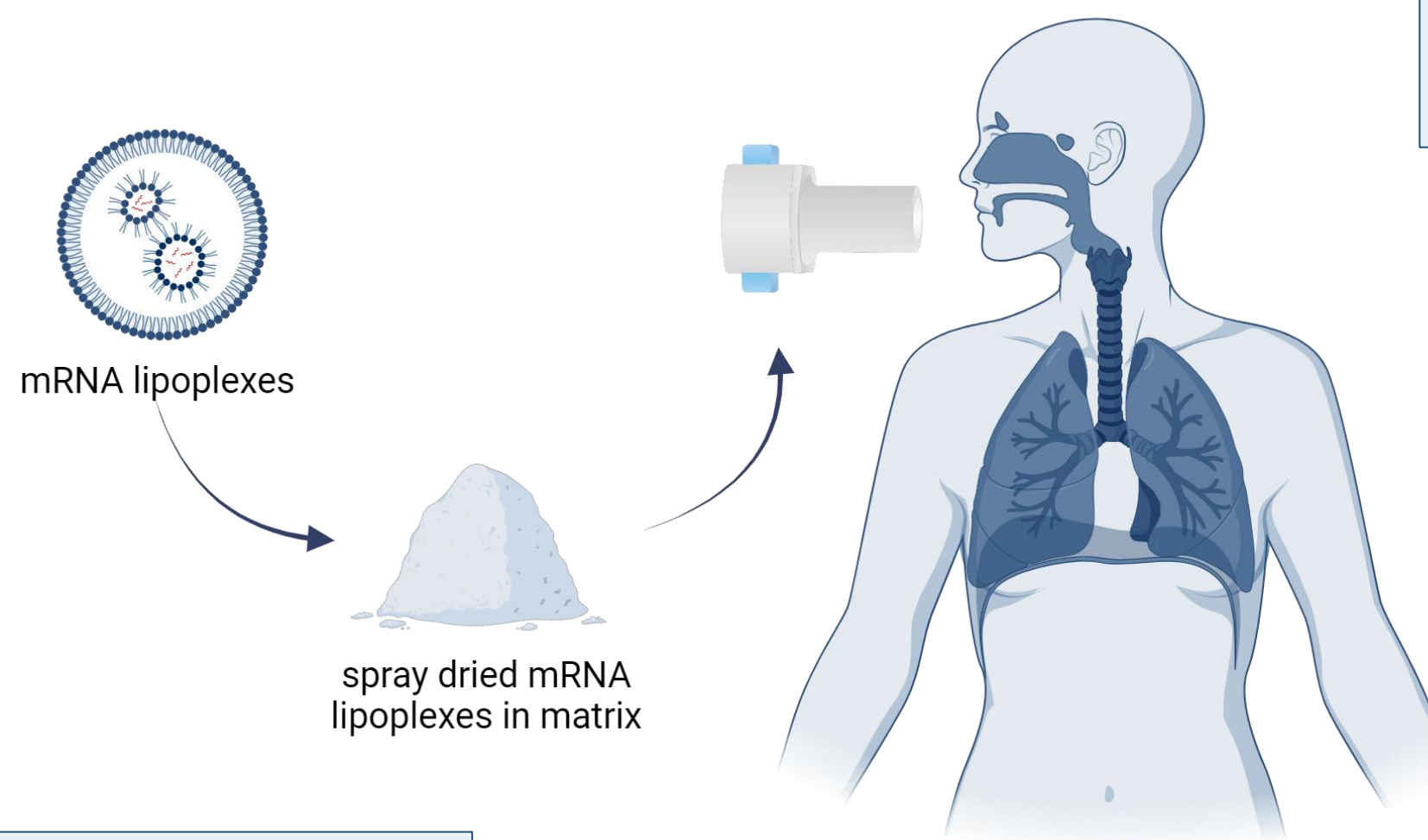
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Introduction

- Many respiratory pathogens enter the body through the respiratory tract, the lungs and the mucosal immune system are promising targets for therapeutic interventions.
- Liquid vaccines face the risk of chemical degradation and physical instability
→ Solid formulations can secure stability without challenging storage conditions. Since spray drying offers continuous manufacturing with high yields, we chose spray drying as production technic.



Objective

- This study aimed to produce a dry powder formulation with intact mRNA and a satisfactory aerodynamic performance.
- To achieve that goal, we aimed to find the optimal spray drying parameters. Then, we assessed and optimised the aerodynamic performance.

Determining the Optimal Outlet Temperature

Why?

During spray drying, mRNA lipoplexes have to withstand several stress factors, especially thermal stress. The maximum temperature a product is subjected to during this process is the outlet temperature.

→ What is outlet temperature at which the mRNA remains intact?

How?

- Spray drying firefly luciferase mRNA lipoplexes in mannitol matrix at:
 - inlet temperature 120 °C
 - outlet temperature 50, 60, 70 °C
- Transfecting spray dried powder into CALU-3 und A549 cells
- DLS measurements to analyse z-average and zetapotential

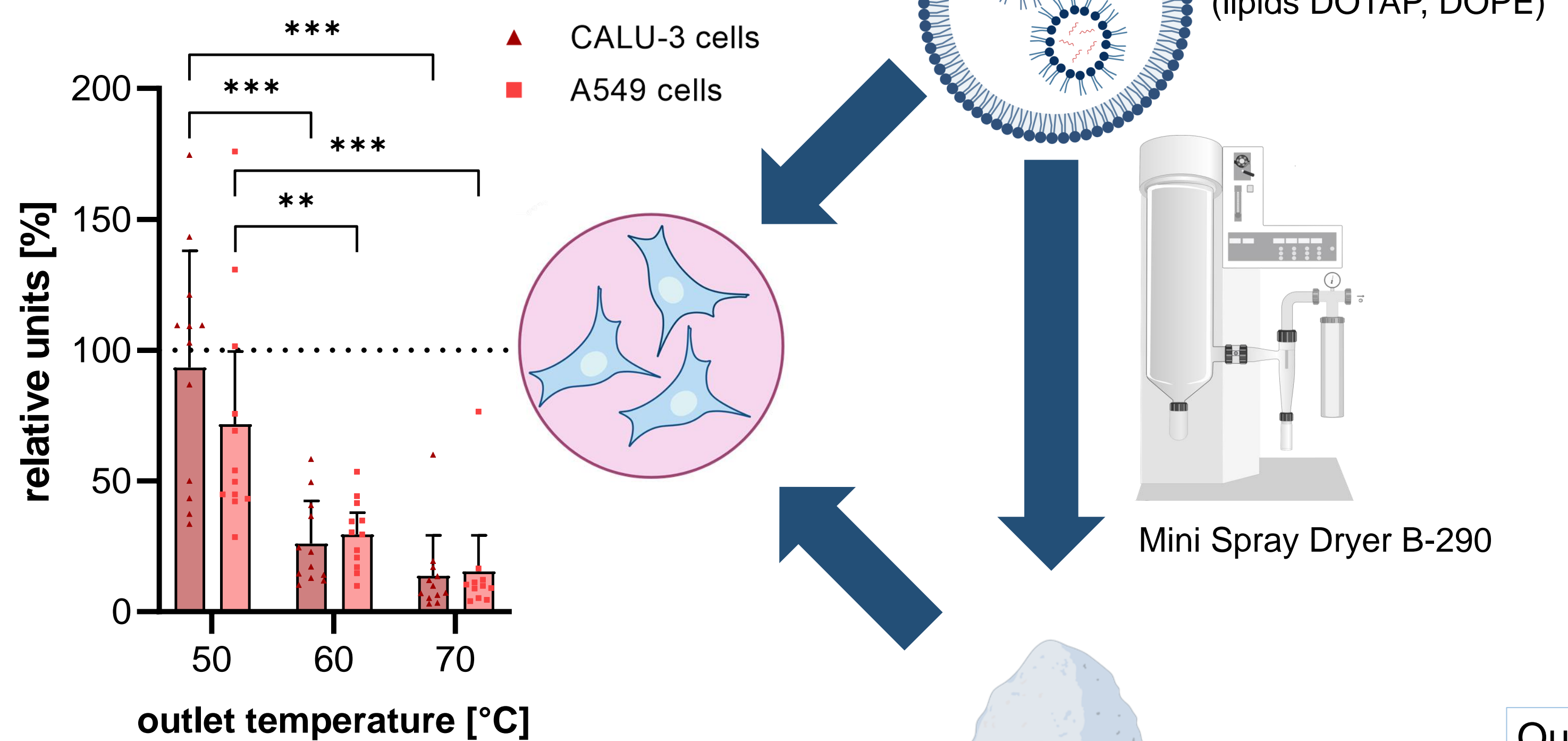


Figure 1: Transfection efficiency of lipoplexes. Relative units: normalised to non-spray dried lipoplexes. n = 3, bar = mean, error bars = SD, *p < 0.05; **p < 0.01; ***p < 0.001; ****p < 0.0001

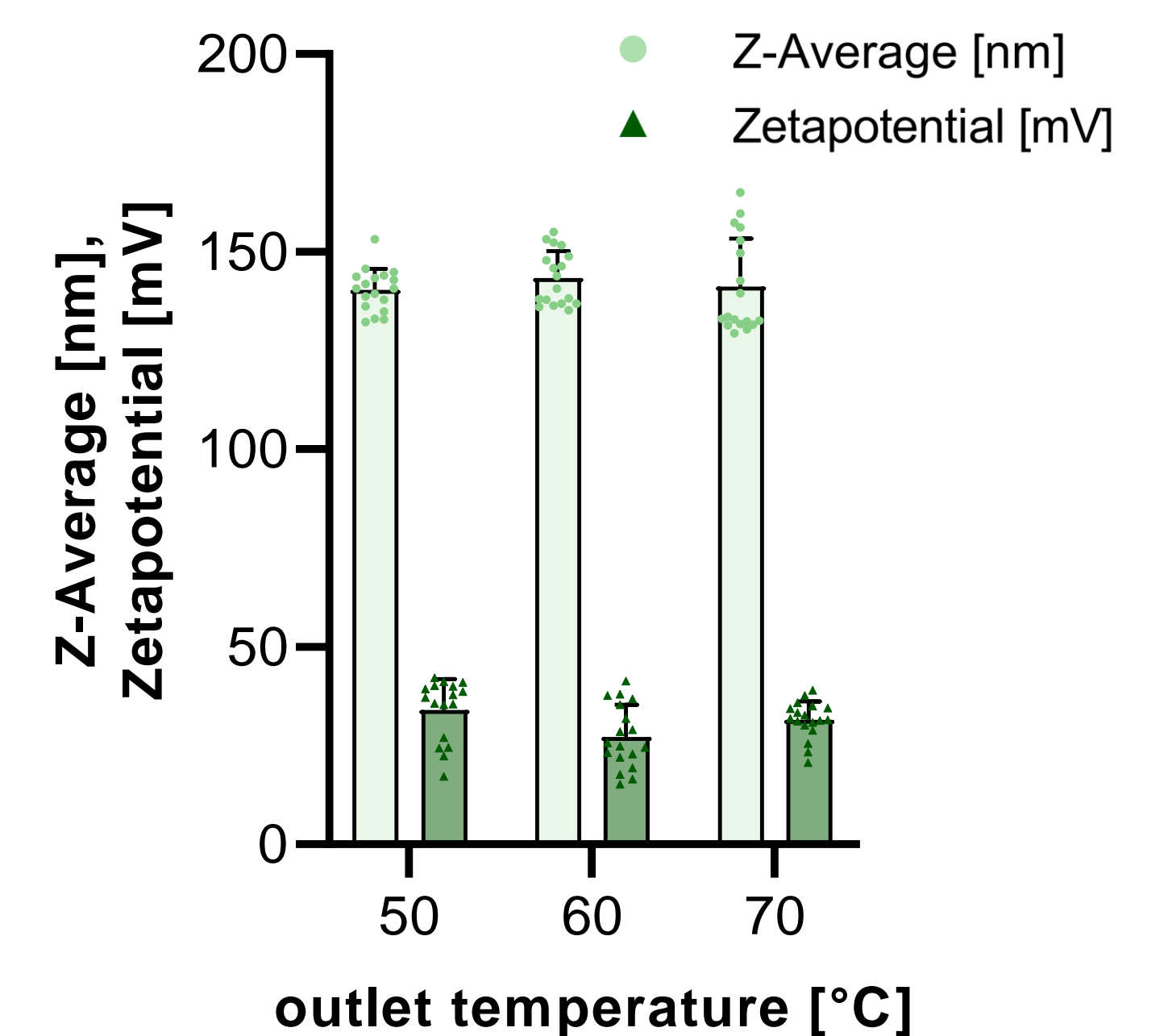


Figure 2: Z-average and zetapotential of lipoplexes after redispersion of the spray-dried powder. n = 3, bar = mean, error bars = SD.

Outcome?

- Best transfection efficiency at an outlet temperature of 50 °C
- Z-Average and zetapotential show stable nanoparticles within the desired size range

Aerodynamic Performance

Why?

High Fine Particle Fraction (FPF) and low residue in the capsules are requirements for a satisfactory Aerodynamic Performance.

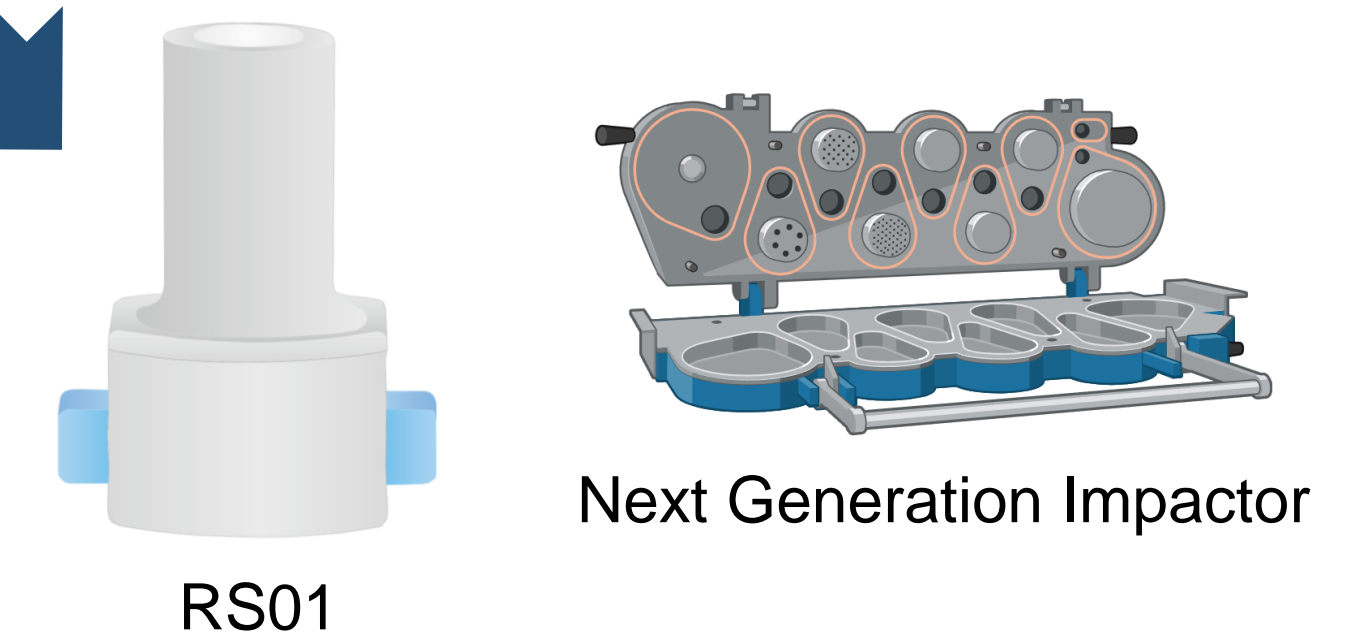
→ How is the aerodynamic performance of the spray dried formulation itself?

How?

- RS01 Inhaler, 5 capsules, 20 mg each, 80 l/min
- Next Generation Impactor

Outcome?

- FPF of 35%
- ca. 20% of powder remaining in the capsules
- Improvement necessary



Improving Aerodynamic Performance



Sweeper crystals

Why?

Sweeper crystals are intended to sweep the capsules' inner surface clean of remaining powder, allowing the powder to follow the air stream out of the capsule

→ Are sweeper crystals able to help the powder out of the capsule?

How?

- As sweeper crystals four lactose qualities were chosen: InhaLac 70, 120, 180, 251
- Blending spray dried powder + lactose sweeper crystals in a turbula mixer (weight ratio 2 + 1)

Outcome?

- In our blends, sweeper crystals...
 - did not reduce remaining powder in the capsules
 - did not significantly improve the FPF
 - facilitated (especially INH70) capsule filling with similar FPF

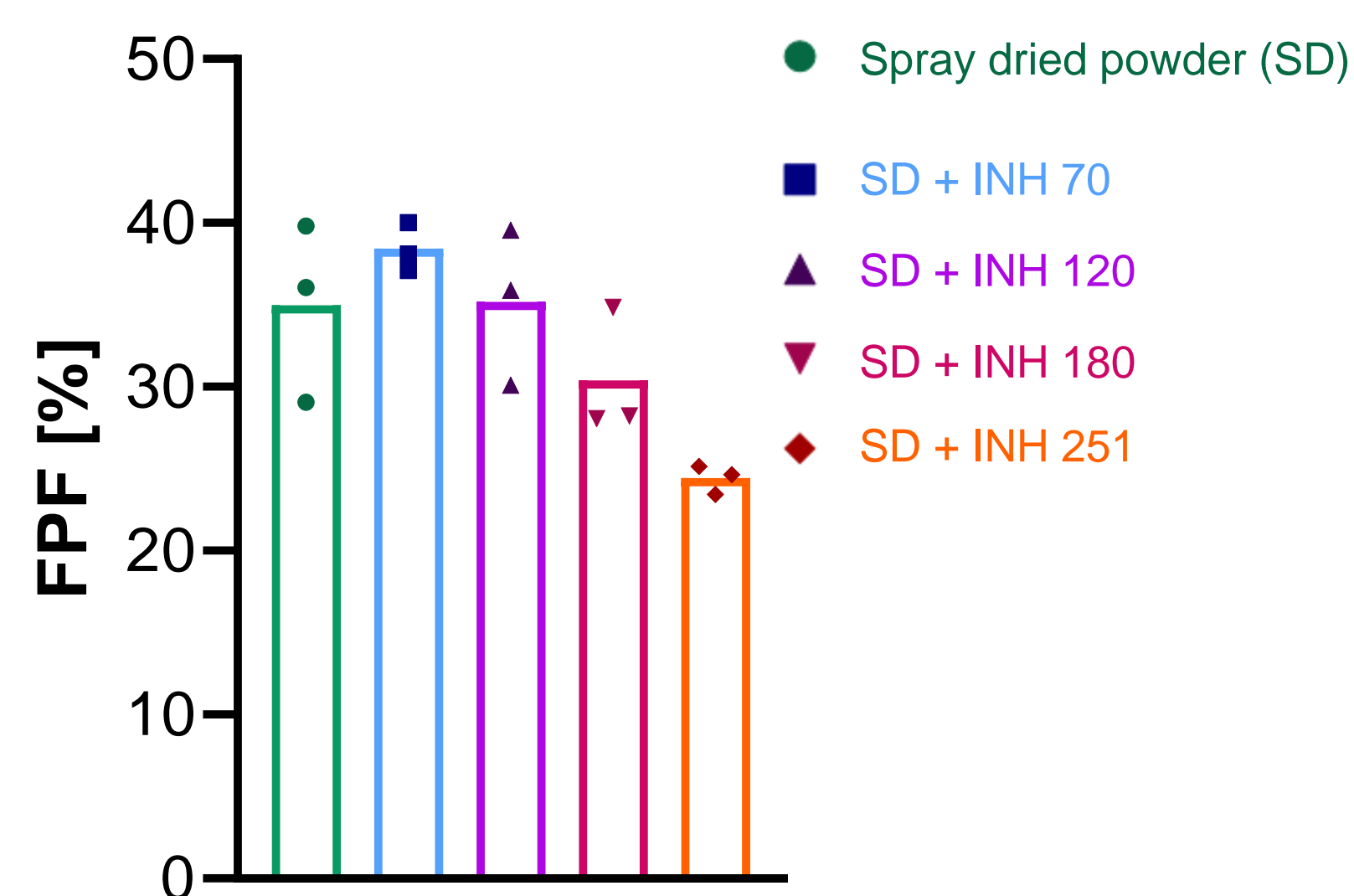
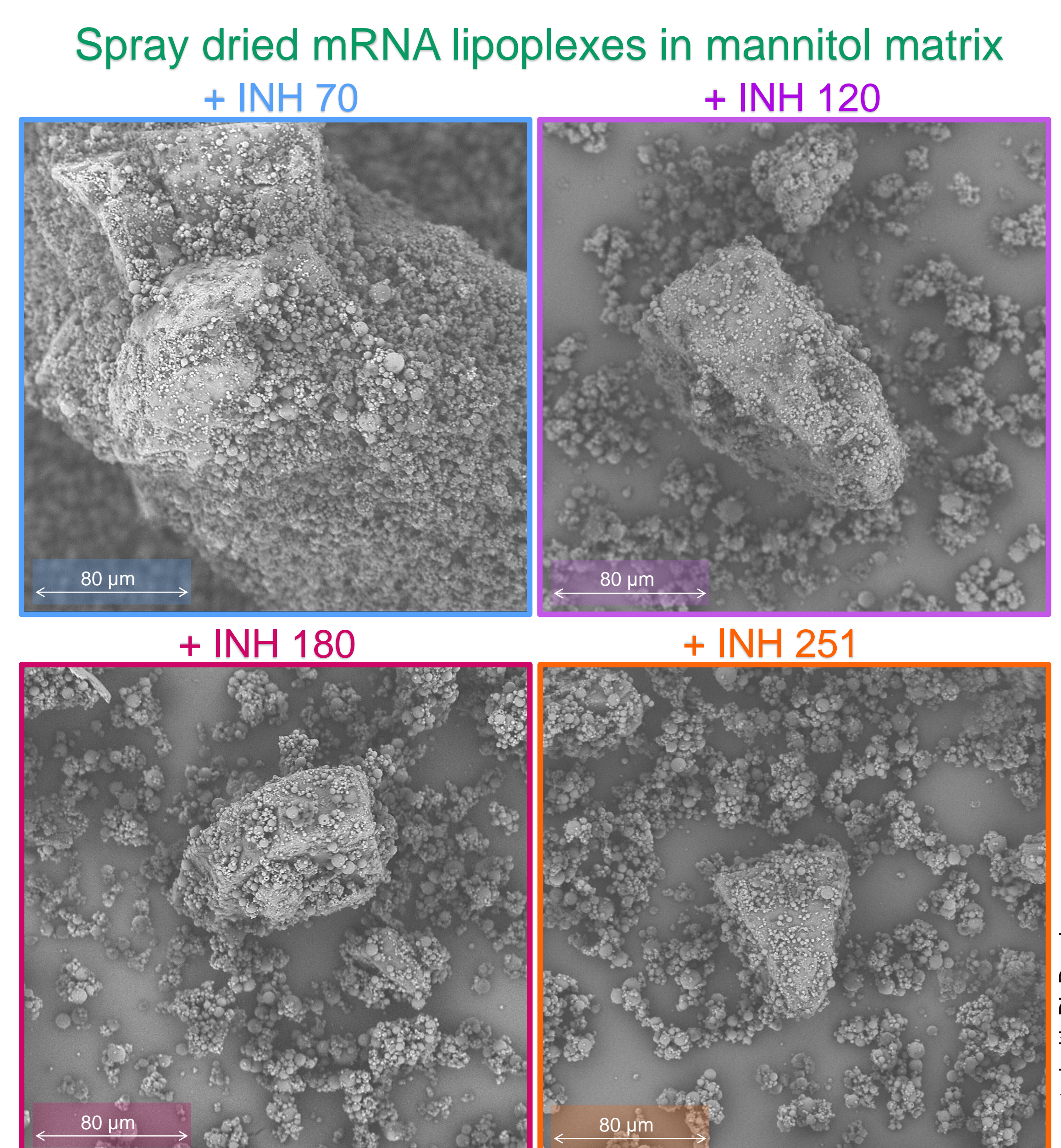


Figure 3: FPF of the spray dried material (SD) and its blends with sweeper crystals, bar = mean of 3 NGI measurements



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➔ In this study, sweeper crystals did not cause a significant improvement of FPF.

➔ Next step: increase dispersibility by adding leucine

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