Assessment of the In Vitro Performance of A GLP-1 Analogue Spray Dried Powder Combined with Sunriser® Capsule-Based Device

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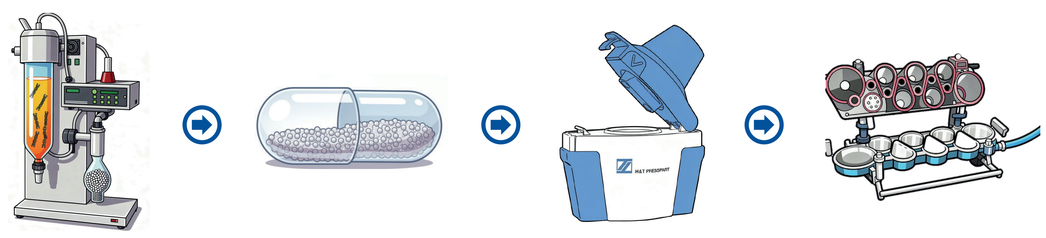
INTRODUCTION

Glucagon-like peptide-1 (GLP-1) regulates insulin secretion, slows gastric emptying, and promotes satiety via central pathways. Engineered GLP-1 agonists with reduced enzymatic susceptibility now achieve extended half-lives—up to ~180 h for semaglutide (SMG)—and are approved for type 2 diabetes and, at higher exposures, for obesity management via subcutaneous and oral routes.[1] Yet these routes face cold-chain constraints and limited oral bioavailability, motivating a more patient-friendly alternative: high-dose delivery as a dry powder for inhalation (DPI) to enable rapid, systemic exposure without injections and avoid cold chain storing.[2] In a previous study Glieca et. al. already presented the best conditions to formulate SMG as a spray-dried powder for inhalation maintaining the peptide stable and reaching a satisfactory respirability.[3] Here this powder was tested with the Sunriser® capsule-based Inhaler to assess the in-vitro performance at different flowrates.

MATERIALS AND METHODS



- Semaglutide
- Trehalose dihydrate (DFE)
- L-Leucine

- Quali_V capsule #3 (Qualicaps)
- 20 mg powder for cps
- 3 cps for RUN

- Sunriser device with medium resistance
- Oscillating capsule
- IP protected

- Flow rate: 50.0 L/min (4kPa)
- Flow rate: 32.8 L/min (2kPa)
- Film: Tween 80 (0.1% v/v in ethanol)

RESULTS

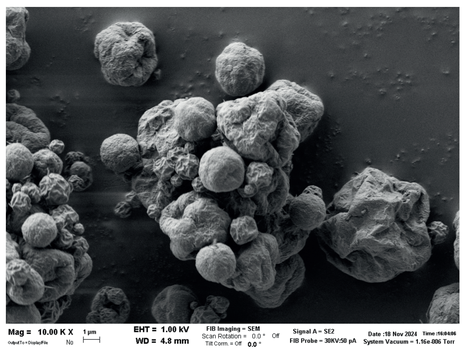
SMG formulation

The optimal formulation found during pre-formulation studies used a higher buffer concentration, producing a respirable and stable powder. Spray-drying yielded 86% with no detectable impact on peptide stability. The drug content was 1.76 ± 0.07 (n=3) at release and remained stable over 2 months under laboratory conditions, showing only a slight decrease to 1.54 ± 0.02 (n=3).

Table 1. Composition of the spray-dried powder, API content (%w/w) determined by HPLC-UV and water content (%w/w) determined by TGA (n=3, mean ± std. dev.).

Powder	Composition (%)				% Drug content	% Drug content after 2 month
	Semaglutide	L-Leucine	Trehalose	Buffer Salt		
SMG 1.5_SD	1.5	15	74.5	9	1.76 ± 0.07	1.54 ± 0.02

A



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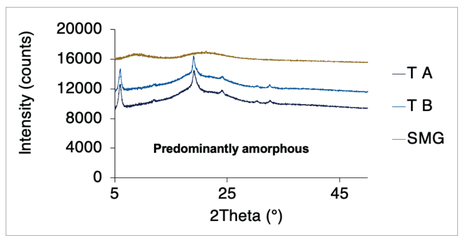


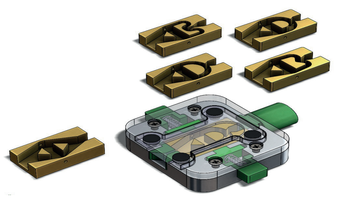
Spray-drying parameters

- T INLET 135°C
- T OUTLET 78-80°C
- AIR FLOW 55
- ASPIRATION 90%
- FEED RATE 3,5mL/min
- NOZZLE 0.7mm

Figure 1: A) scanning electron microscopy (SEM) image of SMG with a magnification of 10k. B XRD of starting material SMG and formulations with Sucrose and Trehalose as excipients showing limited crystallinity, due to crystalline Leucine.

Sunriser from Idea to final prototypes

Concept Development

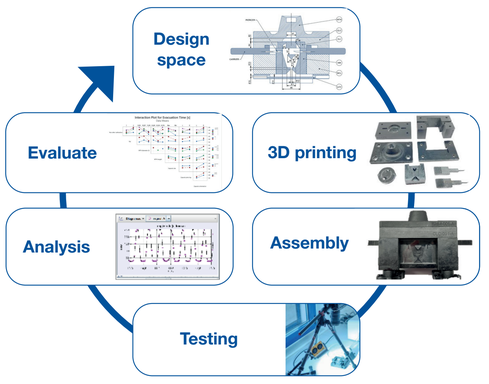


Brainstorming:
Innovative concepts based on patient needs, customer requirements and unmet needs from the market.

Early- stage feasibility

Testing of first prototypes:
Spray-dried powder: FPF > 70%
Carrier-based: FPF > 35%

Device Development



Modular approach:
Critical dimensions varied and subsequently tested until optimized capsule movement, aerodynamic performance and minimized powder retention was obtained. In addition usability enhancing features were integrated.

Final Prototype

Sunriser Device:
Patented engine with oscillating capsule and classifier for superior de-agglomeration across flow rates. Improved usability: easy capsule loading, automatic opening for cleaning, large ergonomic buttons.

Aerodynamic performance Sunriser at different Flowrates

At both pressure drops the combination powder/device reported a very high emitted fraction (~ 84%), indicating a low drug retention in the capsule and device. Moreover, Sunriser® was very effective in aerosolizing the powder, especially at lower flow rate. Fine Particle Fraction (< 5 µm) and extra-Fine Particle Fraction (< 2 µm) were both positively impacted by the lower pressure drop, due to a higher drug deposition in Stage 2-8 when the device was tested at 32.8 L/min.

Table 2. Aerodynamic parameters obtained by aerosolizing 20 mg of powder, containing approximately 290 µg of SMG, using Sunriser® into the NGI (n=3, mean ± std. deviation).

Flow Rate	kPa	Drug Content (%)	Emitted Dose (µg)	Emitted Fraction (%)	MMAD (µm	GSD	FPD (µg)	FPF (%)	EFPD (µg)	EFPF (%)
32.8 L/min	2kPa	1.76 ± 0.07	295.0 ± 3.7	84.3 ± 2.8	3.0 ± 0.3	4.0 ± 0.1	188.6 ± 4.1	64.0 ± 2.0	112.7 ± 4.9	38.2 ± 1.8
50 L/min	4kPa	1.76 ± 0.07	289.1 ± 10.8	82.6 ± 0.1	3.0 ± 0.1	4.4 ± 0.4	156.4 ± 1.5	54.2 ± 1.7	95.2 ± 2.7	33.0 ± 0.5

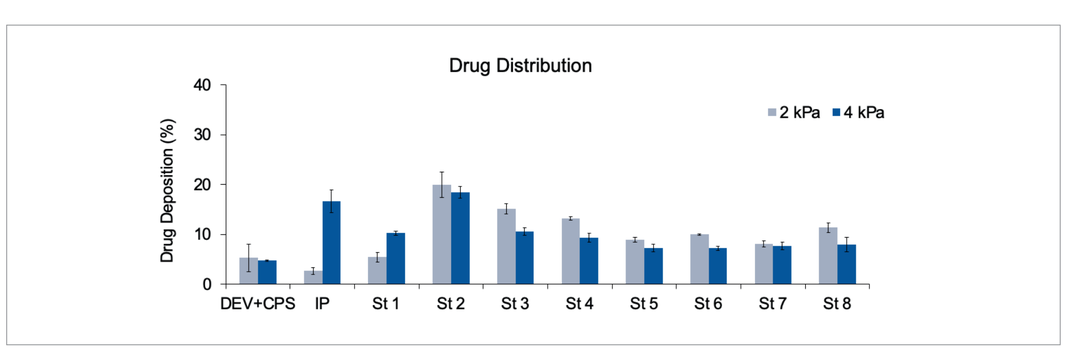


Figure 2. SMG deposition (%) in the various stages of the NGI: induction port (IP), stages 1 to 7 (St1-St7) and micro orifice collector (MOC) (n=3, mean ± std. deviation).

CONCLUSION

These preliminary findings indicate that the SD SMG- formulation/Sunriser® combination is a promising approach for repurposing a GLP-1 analogue as a dry powder inhaler (DPI). The system delivered high and consistent emitted doses across clinically relevant flow rates (30–60 L/min), with elevated fine particle fractions reflecting efficient de-aggregation. Notably, strong performance at lower flow rates. On the device side, further work will target reducing device retention and increasing fine-particle fraction with the Sunriser®. To that end, new 3D-printed prototype designs are being produced to fine-tune the device and formulation performance and maximize pulmonary delivery efficiency. Also further studies will be carried out to assess the DPI long term stability.

References

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[2] Yang et. Al. Enhanced semaglutide bioavailability via spray freeze dried powder for inhalation: Unveiling safety and broad potential applications. Drug Deliv. Sci. Technol, Volume 111,2025.
[3] Glieca S. et al Semaglutide Powder for Inhalation, Pre-formulation and in vitro Characterization. DDL poster 2024.