



Introduction

- Formulation excipients play a critical role in the performance, safety, and stability of nasal spray products.
- Excipients influence spray performance through changes in viscosity and surface tension¹.
- Spray performance affects regional deposition within the nasal cavity¹.
- Understanding formulation-performance relationships enables targeted delivery design.
- Objective: Leverage formulation-performance relationships to design a formulation intended to improve olfactory deposition for potential N2B applications.

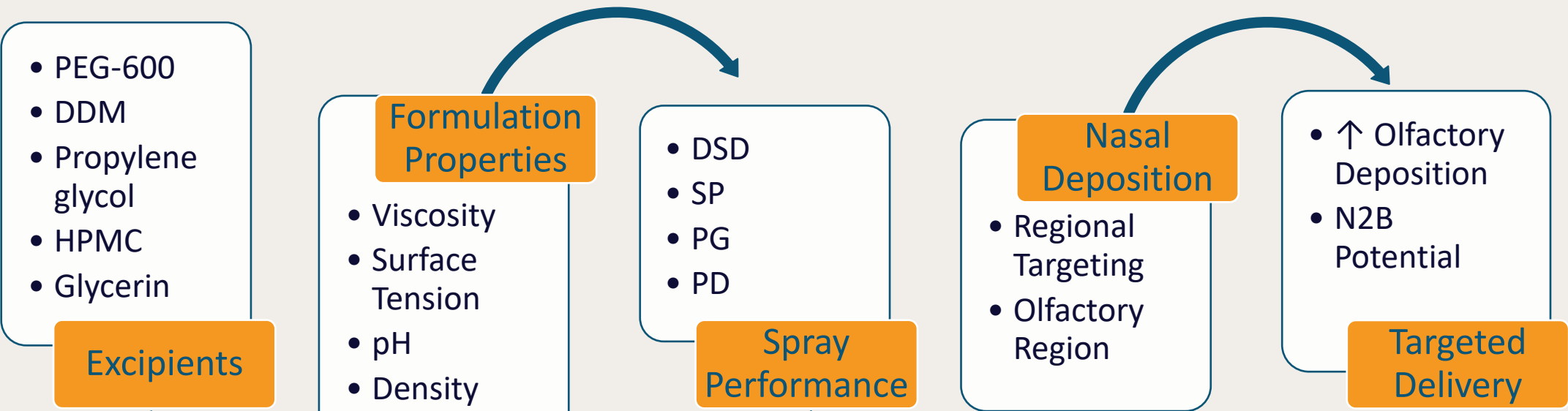


Figure 1. Excipient Performance Design Space for Rational Design of Targeted Nasal Delivery Systems. Formulation excipients alter formulation physical properties, which drive spray performance and ultimately influence regional nasal deposition.

Formulation Design Space

Twelve excipient formulations were prepared using the surfactants n-dodecyl β-D-maltoside (DDM), polyethylene glycol 600 (PEG-600), and propylene glycol with the viscosity enhancers hydroxypropyl methylcellulose (HPMC) and glycerin, at concentrations aligned with FDA Inactive Ingredient Database limits².

Formulation ID	Excipient
0	9 mg/mL NaCl
1	20 mg/mL glycerin
2	1 mg/mL HPMC
A	2.5 mg/mL DDM
B	50 mg/mL PEG-600
C	25 mg/mL propylene glycol

Device Selection

The Aptar UDS device was selected due to its established use in unit-dose nasal delivery and reproducible spray characteristics, allowing formulation effects to be isolated from device-driven variability.

Materials and Methods

Materials: Unidose (UDS) Liquid Nasal Spray System (Aptar Pharma), glass vials (Nipro PharmaPackaging), rubber stoppers (West Pharmaceutical Services)
Instrumentation: DV-II+ Pro Viscometer (Brookfield), Orion Versa Star Pro pH meter (ThermoFisher Scientific), pycnometer, Traube stalagmometer (Wilmad-Labglass), Vereo® Actuator NSx (Proveris Scientific), SprayVIEW Measurement System (Proveris Scientific), SprayTec (Malvern Pananalytical), Cary 3500 Compact UV-Vis Spectrophotometer (Agilent)
Nasal Cast: VCU M Adult Nasal Cast
Statistical Software: Minitab® version 22.4.0 (Pearson correlation, one-way ANOVA, Dunnett's multiple comparison)

Formulation Screening

Unit-dose nasal spray devices were assembled for each formulation and spray characteristics (DSD, spray pattern, and plume geometry, and pump delivery) were evaluated. HPMC-containing formulations (2, A2, B2, C2) produced significantly larger Dv10/50/90 values compared to control (0) (Figure 2). The HPMC + PEG-600 combination (B2) generated the largest droplet sizes, consistent with reports of HPMC and PEG mixtures forming a viscous gel matrix, providing a potential explanation for the observed effect³.

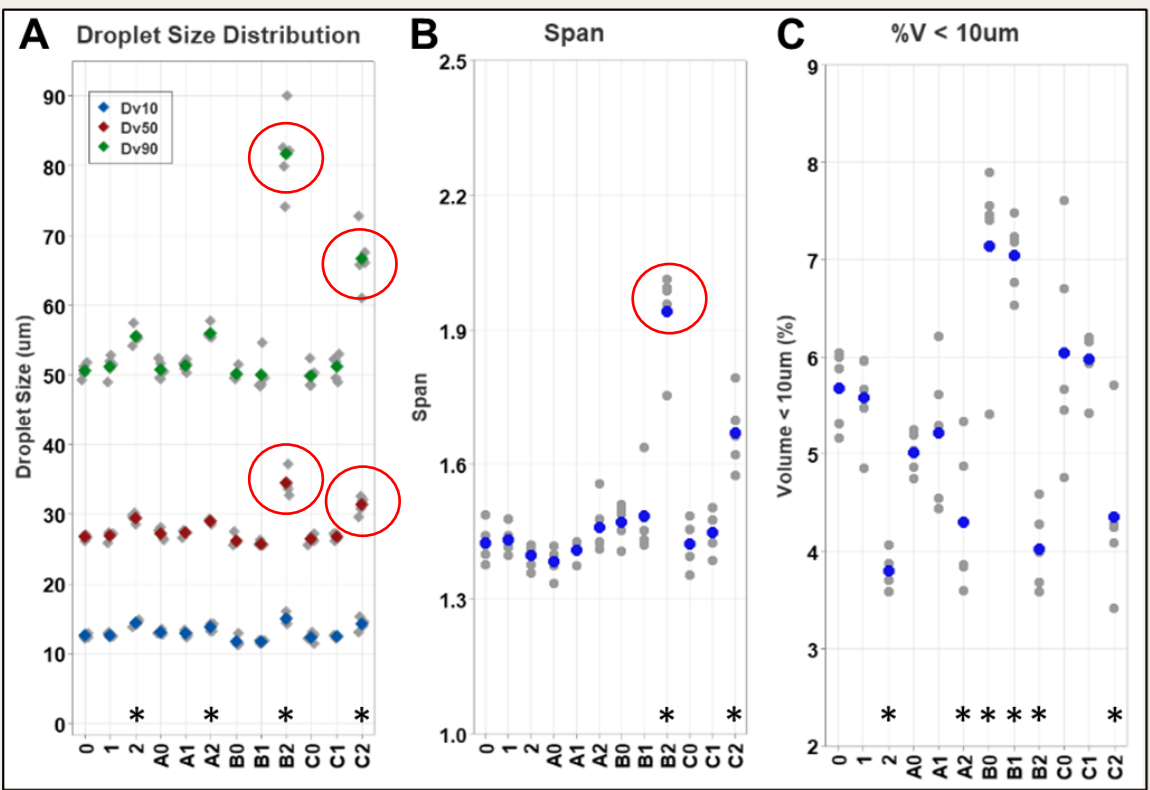


Figure 2. Impact of Surfactant and Viscosity Enhancers on Droplet Size Distribution. Individual values (gray circles) and mean values (colored symbols) for each formulation are shown. (ANOVA p < 0.001; *Dunnett's p < 0.05 vs. control).

Spray pattern analysis showed no differences in ovality (Figure 3). Dmax decreased for formulations containing PEG-600 (B0-B2) and propylene glycol (C0 and C2). Plume geometry was broadly similar among formulations, though B2 exhibited a trend toward narrower plume angle and width (Data not shown). Pump delivery was unaffected by formulation composition (Data not shown).

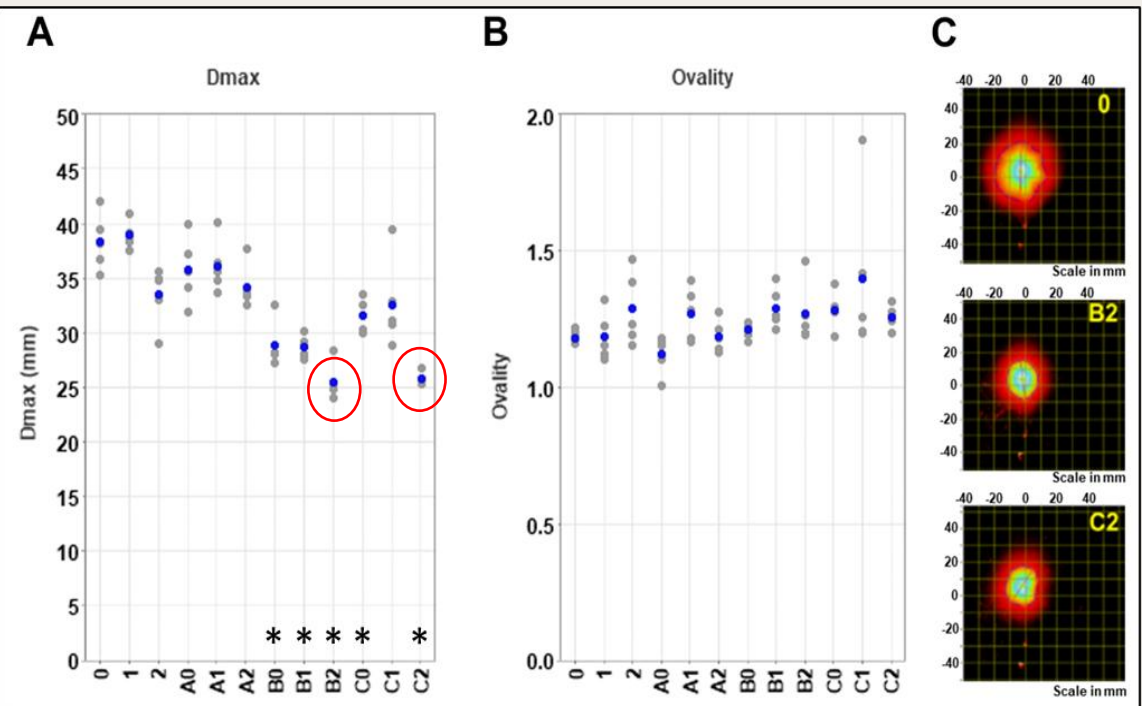


Figure 3. Impact of Surfactant and Viscosity Enhancers on Spray Pattern. (A) Dmax and (B) ovality results are shown with individual values (gray circles) and mean values (blue circles). (C) Representative images for formulations 0, B2, and C2. (Dmax ANOVA p < 0.001; *Dunnett's p < 0.05 vs. control).

Nose to Brain Formulation

Increased viscosity and narrower spray geometry were selected as design attributes to promote deposition in superior turbinate region of the nasal cavity and enhance access to olfactory-targeted delivery pathways associated with nose to brain (N2B) delivery.

The N2B formulation exhibited the smallest Dmax, indicating a narrower spray pattern. No differences in Ovality were observed across formulations.

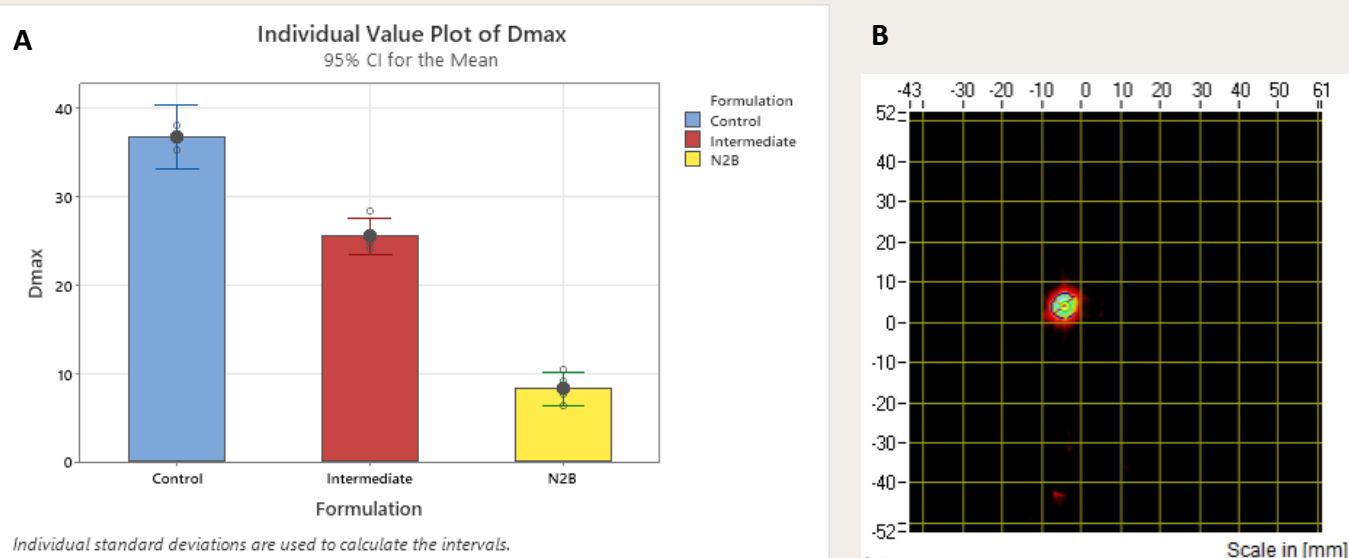


Figure 4. Spray Pattern analysis of N2B formulation. (A) Dmax results. (B) Representative spray pattern image for N2B formulation.

The N2B formulation was subsequently evaluated in the VCU M Adult Nasal Cast to determine whether formulation-driven changes in spray characteristics translated into altered regional deposition patterns.

Nasal Deposition Analysis



Figure 5. Image of VCU M Adult Nasal Cast assembled (left). Formulation deposition in Superior turbinate (right).

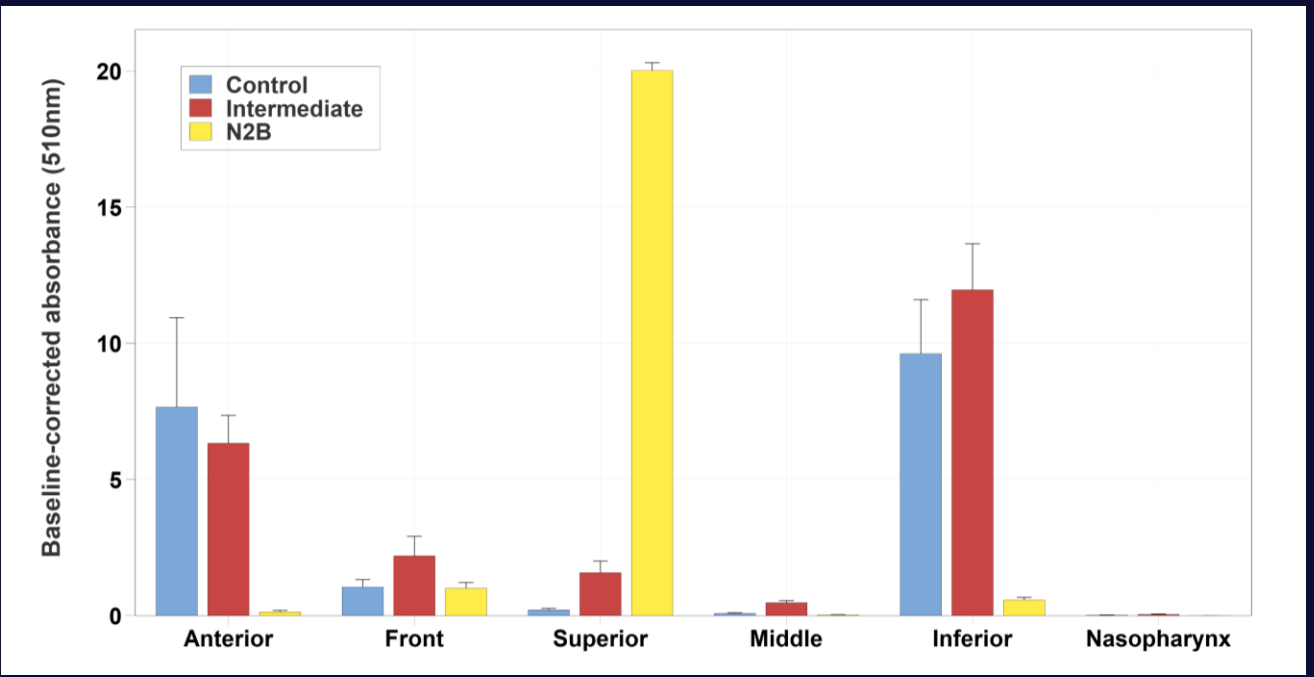


Figure 6. Impact of Surfactant and Viscosity Enhancers on Nasal Spray Deposition

Relative to the control and intermediate formulations, the N2B formulation exhibited concentrated deposition in the superior turbinate region. This shift in deposition demonstrates the impact of spray performance on delivery to anatomically relevant target sites.

Key Takeaway

- Excipient selection provides a practical formulation lever for tuning nasal spray performance and directing regional deposition, enabling rational design of targeted intranasal drug products.

Conclusions

- Formulation excipients influence spray performance through changes in viscosity and surface tension.
- Improved understanding of formulation rheological properties is critical for more precise control of nasal deposition and enhanced bioavailability.
- Rational formulation design – paired with appropriate device selection/design – can be leveraged to intentionally tune deposition to enhance drug product performance.

Acknowledgements

The authors are grateful for the generous support of this work provided by the Research & Development Department at Kindeva (Lexington, KY, USA). Nasal cast model developed at Virginia Commonwealth University (VCU) by a team led by Laleh Golshahi, Associate Professor and Founder & CEO of 3DInhale.

References

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