In Vitro Evaluation of Regional Drug Deposition in Nasal Airways of Children Using Realistic Anatomical Replicas

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Overview and Objectives

- To study the effect of age on drug delivery efficiency of nasal spray drug products
- To address the complexity in controlling administration parameters in children using in vitro methods in lieu of clinical studies
- This study describes an in vitro investigation of the regional drug deposition in children from 2 to 11 years old (20 nasal airway replicas, 50% male and 50% under 6 years old) with a commercially available nasal spray product (FLONASE® SENSIMIST™ ALLERGY RELIEF)

Methodology

Nasal Sprays In Vitro Characterization

The volumetric droplet size distribution of the FLONASE SENSIMIST ALLERGY RELIEF nasal spray and its plume characteristics were measured at 30 and 60 mm from the spray tip using Spraytec (Malvern Instruments, Inc., USA) and Proveris SprayVIEW™ system.

Nasal Airway Models Development

- ✓Reviewed the computerized tomography (CT) scans based on Lund MacKay Score
- ✓ Generated the 3-D models using Mimics Innovation Suite 21.0
- ✓Segmented the models to posterior and anterior regions with nozzle tip positioner in 3-Matics 13.0
- ✓Rapid prototyping the final pieces in high clarity rigid plastic

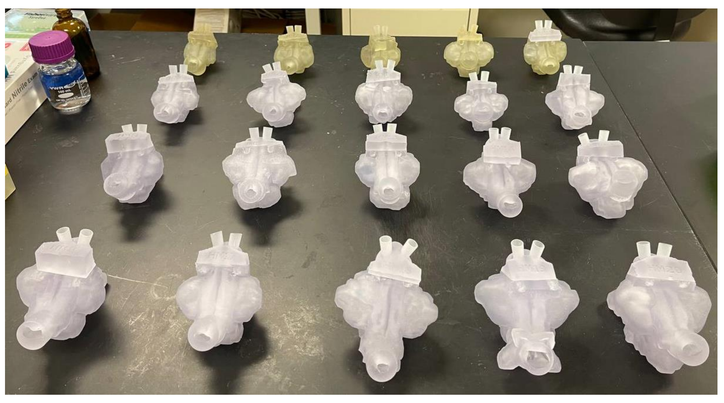

Figure 1. Twenty rapid prototyped nasal models of children 2-11 years old.

In Vitro Drug Deposition Study

- ✓A "gentle" breathing pattern was generated using the ASL 5000 breathing simulator. More details are given in [1].
- ✓With one nostril blocked, one shot of FLONASE SENSIMIST ALLERGY RELIEF (27.5 ug Fluticasone Furoate) nasal spray was sprayed in the other nostril at the beginning of the inhalation.
- ✓Drug content in each piece was quantified using a validated HPLC method. More analytical details are given in [1].

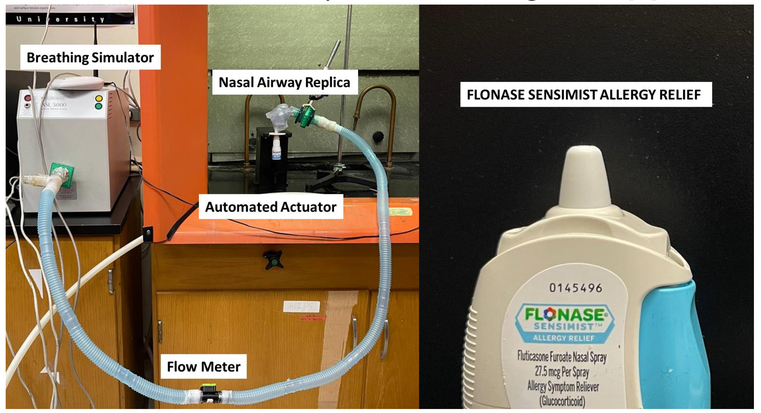

Figure 2. Experimental setup of the deposition study (Left) and the FLONASE SENSIMIST ALLERGY RELIEF (Right).

Results

Dv50 and plume characteristics of FLONASE SENSIMIST ALLERGY RELIEF nasal spray at 30 and 60 mm from the spray tip were measured and can be found in Table 1.

Table 1. Median volumetric diameter and plume characteristics of the nasal spray product based on three replicates (mean ± SD).

Actuation Distance (mm)	30	60
D_{v50} (µm)	66.1 ± 0.8	54.1 ± 1.2
Plume Angle (º)	N/A	36.9 ± 2.1
Plume Width (mm)	N/A	39.7 ± 2.2
Ovality	1.2 ± 0	1.2 ± 0.1
Area (mm^2)	398.3 ± 39.5	1115 ± 86.2

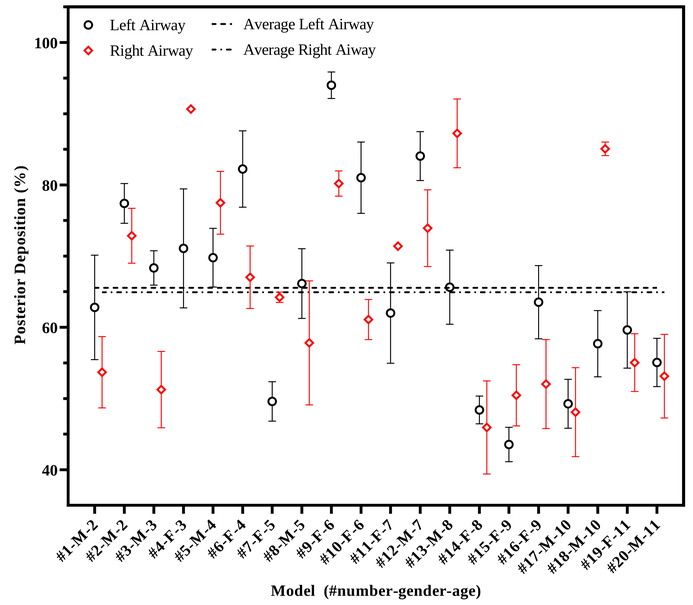

Figure 3. Posterior deposition of Fluticasone Furoate in all 20 pediatric nasal airway models based on three replicates (mean ± SD). The x-axis shows the model number, subjects' gender (M: Male and F: Female) and age.

Summary

- We observed a wide range of deposition (44 – 94%) from the 20 models and their 40 nasal cavities.
- There was no significant difference in posterior drug deposition in the left and right nasal cavities of children.
- ANOVA test revealed significant differences in drug deposition values in children vs. adults (p = 0.0265) with the same nasal spray [1].
- For adults, the experimental range was 42 – 92% and 29 – 92% in the left and right sides of the nasal airways [1]. However, for children, the observed range of deposition was narrower (left side: 44 – 94%, right side: 46 – 91%), showing more consistent intranasal drug delivery in children.

References

[1] Manniello, M. D., Hosseini, S., Alfaifi, A., Esmaeili, A. R., Kolanjiyil, A. V., Walenga, R., ... & Golshahi, L. (2021). In vitro evaluation of regional nasal drug delivery using multiple anatomical nasal replicas of adult human subjects and two nasal sprays. International Journal of Pharmaceutics, 593, 120103.

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