Intranasal Powder Administration of a Spray Dried Tuberculosis Vaccine Candidate Characterized using the Alberta Idealized Nasal Inlet

Brynn Murphy[1], Maximilian Aisenstat[2], Mani Ordoubadi[2], Scott Tavernini[1], Kelvin Duong[1], Jing Zheng[3], Randy Whittal[3], Dominic Sauvageau[4], Christopher Fox[5], Warren Finlay[1], Reinhard Vehring[2], Andrew Martin[1]

[1]Aerosol Research Laboratory of Alberta, University of Alberta, Edmonton, AB, CA; [2]Particle Engineering Research Group, University of Alberta, Edmonton, AB, CA; [3]Mass Spectrometry Facility, University of Alberta, Edmonton, AB, CA; [4]Chemical and Materials Engineering, University of Alberta, Edmonton, AB, CA; [5]Access to Advanced Health Institute (AAHI), Seattle, WA, United States

Introduction

Intranasal vaccine delivery is advantageous for generating an immune response as it is non-invasive and may provide effective protection by mimicking the natural entry route for many pathogens.

The objectives of this study were to determine the *in vitro* deposition profile of a spray dried tuberculosis (TB) vaccine powder delivered by the Aptar Pharma Unidose Powder System (UDSp) using the Alberta Idealized Nasal Inlet (AINI) [1], and to develop an effective coating method for the AINI to mitigate particle bounce and re-entrainment.

Figure 1. *A transparent view of the UDSp device (Aptar Pharma)*

Materials and Methods

Powder Composition

- Trehalose, Adjuvant, and Vaccine powders were spray dried using a custom research dryer [2].
- To target nasal delivery, ID93 (antigen) + GLA-SE (adjuvant) and vaccine powder feedstock concentrations, and spray drying process parameters were modified from a previous inhalable version [3].
- Devices were filled with 10 mg, 20 mg, or 40 mg Trehalose powder, or 20 mg of Adjuvant or Vaccine powders, according to manufacturer instructions.

Table 1. *Particle compositions of Trehalose, Adjuvant, and Vaccine powders*

Component	Particle (% w/w)		
	Trehalose Powder	Adjuvant Powder	Vaccine Powder
Trehalose	100	81	81.4
Squalene	0	14	14
DMPC	0	3	3.1
Tris (Buffer)	0	1	1
Vitamin E	0	0.4	0.4
GLA	0	0.04	0.08
ID93 Antigen	0	0	0.03

AINI Coating

Two coatings were applied to the inner surfaces of the AINI, and evaluated using the Trehalose powder:

(1) 20% Tween 20 in glycerol (v/v)

(2) 1 ml Brij solution (3 g Brij in 20 ml Ethanol): 5 g glycerol

Experimental Apparatus

- Devices were automatically actuated using manufacturer-supplied actuation parameters.
- Devices were oriented 45° from the inlet plane of the vestibule.
- A pre-separator was included to collect large non-inhalable particles (cut size of 14.9 µm @ 30 L/min).
- An inhalation flowrate of 7.5 L/min through the AINI was achieved by drawing 30 L/min through the pre-separator and supplying 22.5 L/min to the mixing inlet.
- Particles penetrating the pre-separator were collected on a breathing filter; a cotton swab and crystallization disk collected any fraction of the dose that escaped out of the nostril during testing (the 'Residual' dose).
- Deposited trehalose in each AINI region was assayed using Liquid Chromatography – Mass Spectroscopy (LCMS).

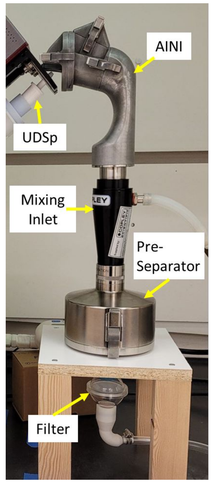

Figure 2. *The experimental setup.*

Results

Coated versus Uncoated AINI

- High pre-separator recovery when uncoated indicates particle bounce and re-entrainment occurred.
- Reduced pre-separator recovery when coated indicates coatings mitigated bounce and re-entrainment.
- Similar results observed for 10 mg and 20 mg doses in the coated versus uncoated AINI.
- Brij coating selected for further experiments.

Influence of Filled Dose

- Similar pre-separator recovery for 10 mg and 20 mg doses indicates that bounce was well controlled at lower filled doses.
- Higher pre-separator recovery for 40 mg dose indicates that some bounce still occurred, likely due to coating overload.
- Reduced recovery from vestibule for 40 mg may indicate site of coating overload.
- Increased filter deposition at lower doses may be caused by more efficient deagglomeration, better dispersion at lower doses.

Trehalose, Adjuvant, and Vaccine Powder Comparison

- Highest recovery from turbinates for all three powders.
- Higher recovery from vestibule, with increased variability, for Adjuvant and Vaccine powders.
- Majority of dose recovered from posterior AINI sections for all three powders.
- Low filter recovery indicates low anticipated lung dose for all three powders.

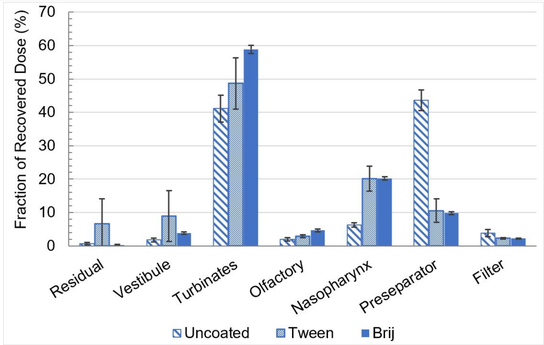

Figure 3. *Mean recovered trehalose from 40 mg doses of Trehalose powder in the uncoated, Tween-coated, and Brij-coated AINI.*

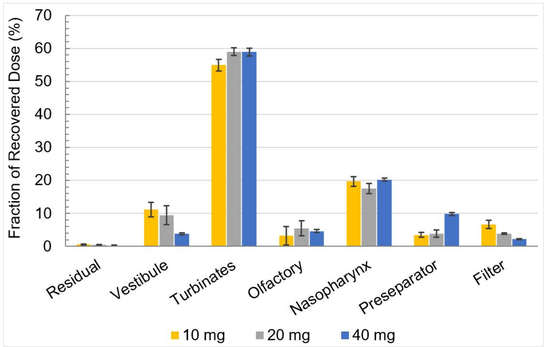

Figure 4. *Mean recovered trehalose for 10 mg, 20 mg, and 40 mg doses of Trehalose powder in the Brij-coated AINI.*

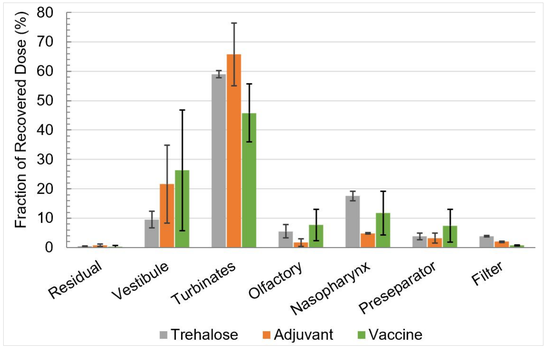

Figure 5. *Mean recovered trehalose from 20 mg doses of Trehalose, Adjuvant, and Vaccine powders in the Brij-coated AINI.*

Conclusions

- Coating AINI surfaces using the methods examined here provided effective mitigation of particle bounce.
- Coating overload may cause some bounce to occur at doses greater than 20 mg.
- Coating and use of the pre-separator are recommended when using the AINI with nasal powders, regardless of the dose.
- Delivery of spray dried powders for intranasal vaccine administration shows promise for the tuberculosis vaccine candidate studied here, and merits further exploration.

References

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