A Personalized Approach to Respiratory Drug Delivery:

µMIST® Spray Technology Electrically Controls & Adjusts the Location of Drug Deposition in the Respiratory Tract.

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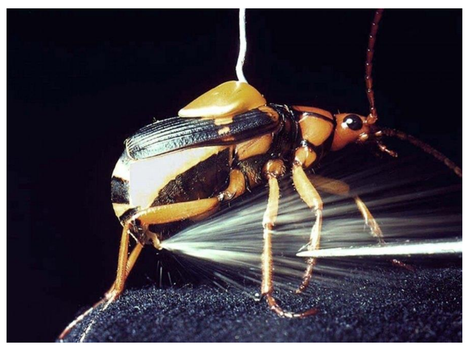
BACKGROUND & AIM

The growing use of inhaled bronchodilators, antibiotics and new drug candidates has increased the demand for novel drug delivery systems (DDS) that can maximise respirable doses and deliver drugs to specific regions in the respiratory tract to reduce the required effective dose and minimise systemic side effects [1]

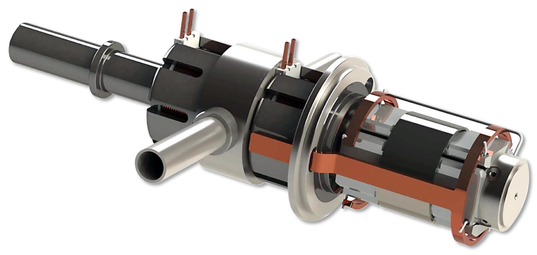
This is particularly relevant for novel therapies, under development, which require use of potent drugs associated with adverse side effects such as inhaled delivery chemotherapy agents [2,3]

Swedish Biomimetics 3000 uMIST Technologies are developing a hand-held respiratory DDS, designed to enable precise and adjustable control over the location of drug deposition, using a technology named the µMIST® spray platform.

This study provides proof-of-concept results for the fine-tuned delivery of salbutamol, a model inhalable drug, to different areas of the respiratory tract, in an artificial lung model using the µMIST® spray platform.



A)



B)

Fig 1 A) Bombardier Beetle defence mechanism B) uMIST Technologies spray doser (EP32)

The µMIST® spray platform is a biomimetic technology, inspired by the Bombardier Beetles natural defence mechanism, that employs a unique form of rapid vaporization.

- **Patented, electrically powered spray technology**
- **Eco-friendly, aerosol-free, VOC-free**
- **Compact spray doser, hand-held system manufactured**

- **Droplet size electrically controlled (<5 to 200µm) using 1 nozzle type**
- **Unprecedented narrow distribution spray profiles (StD <0.5µm)**

THIS RESEARCH:
Demonstrate the ability to finely tune and control the location of drug deposition in the respiratory tract

ACTIVE CONTROL OF DRUG DEPOSITION IN THE LUNG

Methodology: Salbutamol sulphate (Ventolin Nebules, GSK, 2.5 mG) was selected as a model inhaled API to assess deposition in an artificial lung model. Drug deposition studies were conducted at Intertek Melbourn Laboratories (UK) using a Next Generation Impactor (Anderson Impactor, Copley Scienitifc, UK) shown in Fig 2B. 2.5 mL volumes were dispensed in the fluid-feed chamber, and ejected at 28 mL/hr (set to match state-of-the-art nebulizers on the market) using the uMIST® spray platform which was set to generate MMADs of 5, 6 & 7-µm respectively.

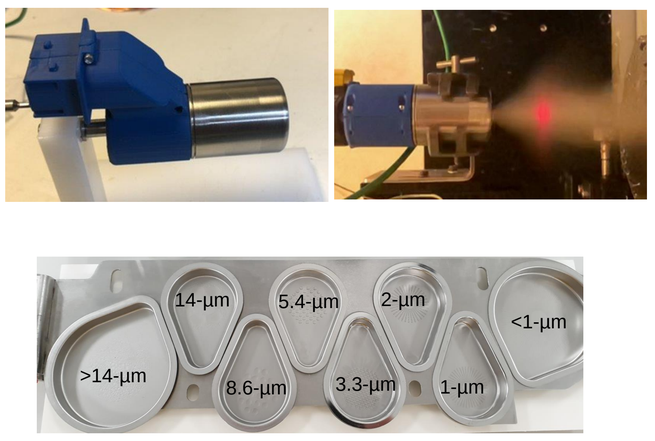


Figure 2 – Test rig set-up A) Spray doser B) NGI assembly

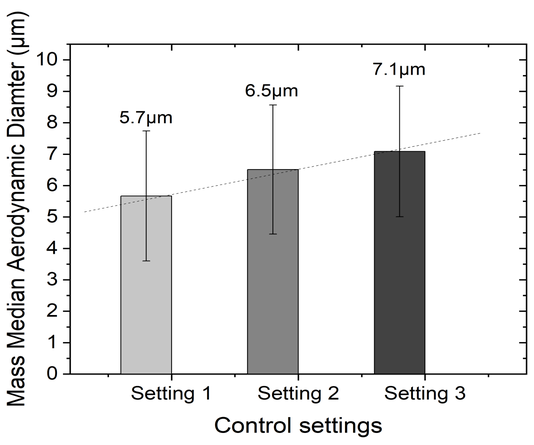


Figure 3 – Preliminary drug deposition study. Data shows MMAD (n=3 ± StD) achieved using different device settings set to generate MMADs of 5, 6 & 7-µm.

Results:

- Delivery of salbutamol sulphate was successfully controlled using the uMIST® spray platform. As shown in Figure 3, the MMAD was controlled and adjusted between 5.7, 6.5 and 7.1-µm.
- A mass flow rate of 1.2 mL/min -set to match fastest nebulizers in industry- delivered a standard 2.5 mL treatment in 2-mins.

PRELIMINERARY COMPATBILITY TESTS

High performance liquid chromatography (HPLC) was used for early-stage drug analysis to determine drug retention post-spray (Intertek, UK). Results indicated that current spray settings (temperature and residency time in heat chamber) induced slight degradation of salbutamol sulphate, with approximately 95% drug retention observed. Next steps will aim to increase drug retention to 99% -the accepted standard- by optimizing spray doser settings.

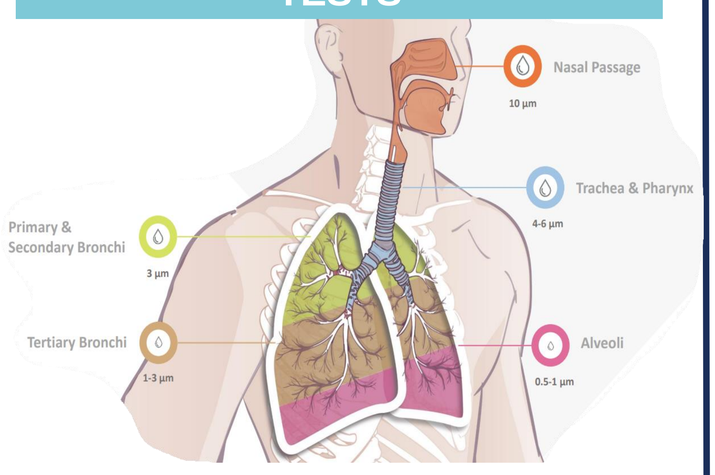


Figure 4- Anatomy of respiratory tract and deposition of particles.

THE VISION

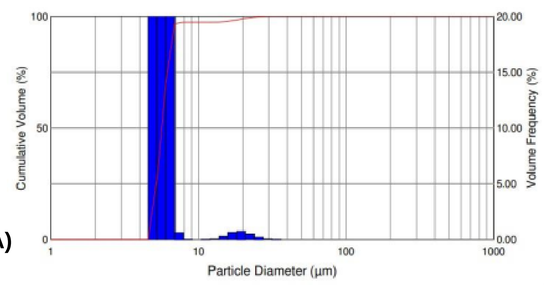
Results demonstrate a new proof-of-concept in respiratory drug delivery. Preliminary studies demonstrate that the µMIST® platform has the potential to fine-tune particle size, micron-to-micron, to enable precise drug delivery to the intended site of action.

Comparison study

Methodology: The spray profiles and aerosol outputs of µMIST® spray platform and PARI Boy Sprint Adult (Pari, Germany) and were analysed using a Malvern Laser Diffraction Analyzer (Malvern Panalytical, UK) using saline solution (0.9%). Key aim was to compare the spray profile of µMIST® spray platform with a current industry standard.

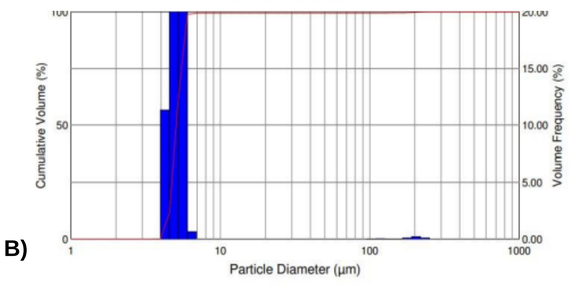
- The bandwidth of the µMIST® spray profile was similar to that of the PARI nebulizer, a current industry standard.
- The PARI nebulizer, at maximum compressor flow, provided an aerosol output rate of 0.38 mL/min (23mL/hr).
- The µMIST® spray platform provided an aerosol output of 1.2 mL/min (70mL/hr), whilst achieving a similar spray profile to PARI with narrow bandwidths.
- Standard treatment time of ≈2-min *versus* ≈7-min for µMIST® spray platform and PARI and respectively.

A)



Title	Average	Standard Deviation	Max	Min
Dv(10.0) (µm)	4.81	0.04	5.08	4.73
Dv(50.0) (µm)	5.64	0.07	5.89	5.44
Dv(90.0) (µm)	6.67	0.05	6.80	6.43
Transmission (%)	50.42	6.24	65.27	35.43
D[3][2] (µm)	5.69	0.08	5.94	5.44
Dv(50.0) (µm) : Avg	5.66	0.02	5.71	5.63

B)



Title	Average	Standard Deviation	Max	Min
Dv(10.0) (µm)	4.50	0.21	5.42	4.05
Dv(50.0) (µm)	6.22	14.65	194.30	4.41
Dv(90.0) (µm)	7.20	17.79	232.71	5.04
Transmission (%)	77.65	4.16	86.50	60.67
D[3][2] (µm)	5.18	1.69	29.84	4.45
Dv(50.0) (µm) : Avg	5.81	0.54	6.69	5.07

Figure 4 – Spray characterisation profiles of A) PARI Boy Sprint Adult and B) µMIST® spray platform using saline solution providing aerosol outputs of 0.38 mL/min and 1.2 mL/min respectively.

Conclusions & next steps

- Drug stability studies are currently under development with the aim of improving post-spray drug retention by reducing residency time in heat chamber.
- Next steps, optimise spray doser for drug compatibility and assess spray efficacy and compatibility with therapeutic biologics.
- **The technology presents itself as a promising solution for novel drug candidates that have optimal locations for pharmacological sites of action.**

[1] Maselli DJ, Keyt H, Restrepo M: *Inhaled Antibiotic Therapy in Chronic Respiratory Diseases*. Int J Mol Sci. 2017; 18(5): pp 1062-1065.

[2] Goel A, Baboota S, Sahni JK, Ali J: *Exploring targeted pulmonary delivery for treatment of lung cancer*. Int J Pharm Investig 2013; 3(1): pp 8-14.

[3] Mangal S, Gao W, Li T: *Pulmonary delivery of nanoparticle chemotherapy for the treatment of lung cancers: challenges and opportunities.* Acta Pharmacol Sin 2017; 38: pp. 782–797.