Influence of Fluid Physiochemical Properties on Aerosolization Performance of a Novel Soft Mist Inhaler

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INTRODUCTION

- Soft mist inhalers (SMIs) are propellant-free inhalers that are gaining interest in the delivery of drugs, especially proteins and biologics, due to the low shear stress [1] they produce during aerosolization and low carbon footprint [2].
- The effectiveness of the SMI inhalation therapy relies on many factors, including the device manufacture and physicochemical properties of the inhalation solution [3].
- The Aim of the study was to evaluate the influence of fluid physiochemical properties on droplet size distribution using the Pulmospray™ SMI device, (Resyca B.V, Enschede, Netherlands).
- Specifically, we will evaluate the following properties: (1) fluid viscosities, (2) ionic strength and (3) surface tension of different fluid mixtures and study their particle size distribution at two different inhalation flow rates.

EXPERIMENTAL METHODS

- A series of fluid mixtures with variable viscosities, ionic strengths and surface tension were prepared by mixing different WFI with concentrations of 0.3%, 0.6%, 0.9%, 9% w/v of NaCl, glycerol 0, 5%, 10%, 20% and 30% w/v, ethanol 5%, 10%, 20%, 30%, 40%, and 50% v/v and Span 20 (0.01% and 0.05% v/v).
- These fluids were characterized for their corresponding physiochemical properties and their effect on aerosol size distribution using the Pulmospray™ SMI device.
- In situ, real-time measurement of the droplet size distribution was performed by laser diffraction using a Spraytec particle sizer (Malvern Instruments, Worcestershire, UK).
- The flow rate through the Spraytec was set at 15 (low) or 30 (high) L/min and calibrated using a flow meter, with the device in-line during setup.

RESULTS

To vary the ionic strength of the solution, varying concentrations of NaCl from 0.3 to 9% w/v were evaluated (Figure 1).

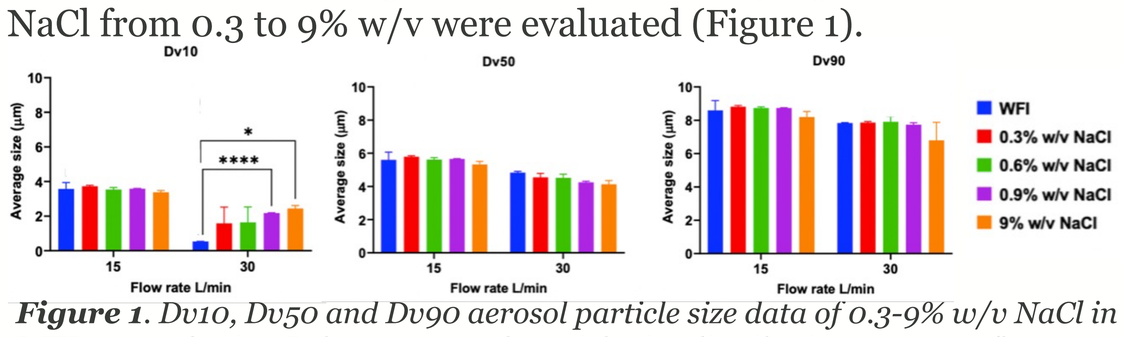

Figure 1. *Dv10, Dv50 and Dv90 aerosol particle size data of 0.3-9% w/v NaCl in WFI sprayed using Pulmospray and particle size distribution curves at flow rates of 15 and 30 L/min.*

To evaluate the effect of viscosity, varying concentrations of glycerol from 5-30 % w/v were tested (Figure 2).

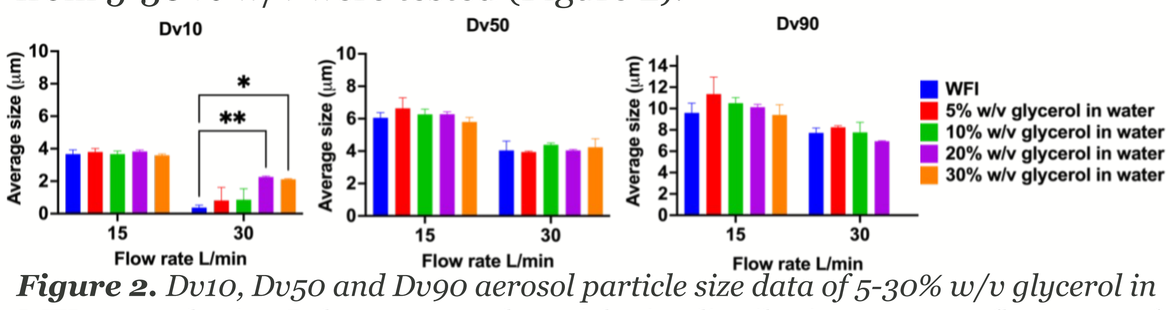

Figure 2. *Dv10, Dv50 and Dv90 aerosol particle size data of 5-30% w/v glycerol in WFI sprayed using Pulmospray and particle size distribution curves at flow rates of 15 and 30 L/min.*

To modify the surface tension of the solution, different ethanol concentrations were evaluated from 5 - 50 % v/v (Figure 3).

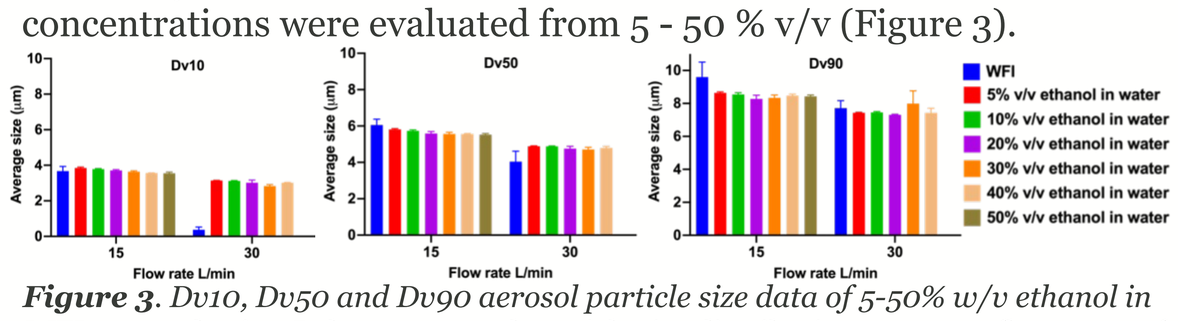

Figure 3. *Dv10, Dv50 and Dv90 aerosol particle size data of 5-50% w/v ethanol in WFI sprayed using Pulmospray and particle size distribution curves at flow rates of 15 and 30 L/min.*

To investigate the impact of surface tension, Span 20 was used at a concentration of 0.01 and 0.05 % v/v in WFI while keeping the other factors such as osmolality and viscosity constant (Figure 4).

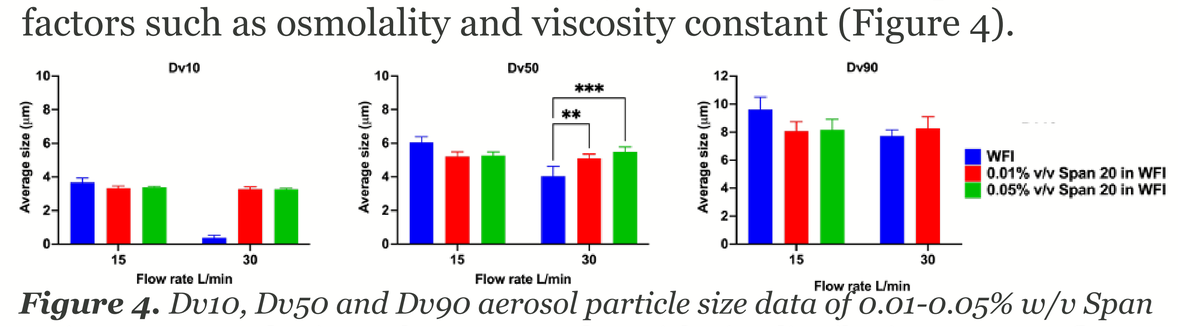

Figure 4. *Dv10, Dv50 and Dv90 aerosol particle size data of 0.01-0.05% w/v Span 20 in WFI sprayed using Pulmospray and particle size distribution curves at flow rates of 15 and 30 L/min.*

DISCUSSION

- Results demonstrate that reliable aerosol generation over a wide range of viscosity and surface tension can be achieved with the Pulmospray™ device without a significant effect on the quality of the generated aerosol.
- Irrespective of physicochemical properties, median diameter (Dv50) ranges between 5 – 6µm for flow rates of 15L/min and between 4 – 5µm for flow rates up to 30L/min, indicating an aerosol quality suitable for efficient inhalation.
- In general, the Pulmospray™ device produces smaller aerosol droplets at higher flow rates compared to lower flow rates across the different solution mixtures.
- This is attributed to the mechanisms of aerosol generation relying on the combination of airflow through the device interacting with the fluid properties and the physical droplet generation by Rayleigh breakup [2].
- The characteristic of aerosol generation and resulting lung deposition from the Pulmospray™ SMI is independent of the physiochemical properties of the inhalation solution and the inhalation flow rate.

CONCLUSION

- In conclusion, the single-use Pulmospray™ SMI device is an efficient inhaler for the delivery of drug products to the lungs with varying physiochemical properties of the inhalation solution and inspiratory flow rates.

ACKNOWLEDGEMENT

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