Aerosol performance of the single-use Pulmospray™ soft mist inhaler for inhalation of high amounts of liquid formulations

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Background

Liquid formulations are popular for drug delivery in inhalation products. Many compounds are available as liquid formulation and delivery devices as Soft Mist Inhalers (SMI) or smart nebulizers have been employed to improve the delivery efficiency and usability. However, conventional SMI are limited to small dosages[1,2] and nebulizers require electricity, which is often not in-line with the target treatment setting or use environment, were single use or energy independent on-the-go devices are required (e.g. COVID-19, rescue).

Objective

In this study, we assessed the aerosol performance and lung deposition efficiency of the single-use, open system mechanical Pulmospray® soft mist inhaler for application of liquid volumes up to 1 mL.

Method

Pulmospray® Soft Mist Inhaler

The Pulmospray® is a single use, disposable soft mist inhaler (Figure 1) for delivery of up to 1 mL inhalation solutions to the lower respiratory tract. It includes the so-called Spray Nozzle Unit technology (SNU) that is used for generating the aerosol from the liquid solution. The SNU consists of a small silicone chip with a dimension of approximately 1 x 1 mm and approximately one hundred micro-nozzles of variable diameter (see Figure 3 for detail). The liquid solution flows through these nozzles to form a liquid jet that then breaks-up into small respirable droplets.

The device is used in combination with an off-the-shelf sterile syringe that is connected via a tube to the patient interface (mouthpiece). Prior to administration the syringe is filled with inhalation solution and manually actuated by means of the Respi Lever Drive™ synchronized with the patient inhalation. Upon actuation the patient inhales deep and slow through the mouthpiece that it designed to provide a guided inspiratory flowrate of not more than 20 l/min. Residual volume remaining in the device is approximately 0.13 mL.

Figure 1: *Pulmospray® Soft Mist Inhaler*

To assess the aerosol characteristics of the Pulmospray® SMI, cascade impaction testing (NGI) is performed (3 repetitions, 1 mL of 5.85% NaCl). Four device variants with different micro-nozzle sizes (1.6, 1.7, 1.8 and 1.9 µm) are tested. The content sampled on impactor stages and the UIP is assessed by Conductivity to determine Mass Median Aerodynamic Diameter (MMAD), Geometric Standard Deviation (GSD) and Fine Particle Fraction (<5 µm). The delivery rate of each device was assessed by using a spray time of 10 sec per actuation.

Aerosol Performance

The Median Aerodynamic Particle Diameter (MMAD) decreases proportionally with smaller nozzle pore size from 6.70 µm for the 1.9 µm nozzle down to 5.12 µm for the 1.6 µm nozzle as shown in Table 1. For all nozzle sizes tested, the aerosol clouded exhibits an approximated log-normal particle size distribution within a narrow band (GSD = 1.46 – 1.56). For small nozzle pores, Pulmospray® has a fine-particle fraction of nearly 50%, which is comparable to that of other soft mist inhalers[2]. The time to deliver 1mL of inhalation solution with Pulmospray® is between 1.5 min and 2.3 min for the 1.9 µm and 1.6 µm micro-nozzle, respectively.

Table 1: *Aerosol Characteristics of Pulmospray® Soft Mist Inhaler*

Nozzle Pore Size [µm]	**MMAD** [µm]	**GSD** [-]	**FPF <5µm** [%]	**Output Rate** [mg/min]	**Time to Deliver 1 mL dose** [min]
1.6	5.12	1.46	47.5	436	2.3
1.7	5.73	1.49	36.6	490	2.0
1.8	5.90	1.48	33.6	516	1.9
1.9	6.70	1.56	25.5	675	1.5

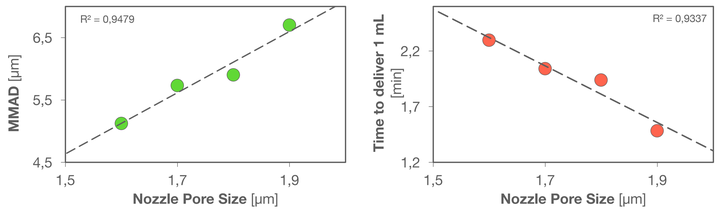

Figure 3: *Pulmospray® MMAD (left) and time for 1 mL delivery (right) versus Nozzle Pore Size.*

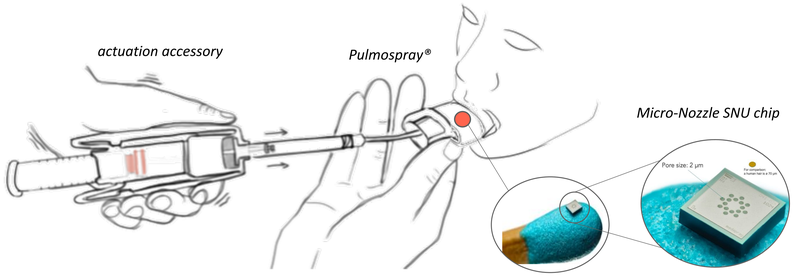

Figure 3: *Pulmospray® SMI with Respi Lever Drive actuation accessory; SNU containing the micro-nozzles*

Lung deposition Modelling

Regional lung deposition of drug delivered with Pulmospray® for different micro nozzles is estimated through numerical deposition modelling of the 5.85% NaCl inhalation solution. Here we use the ICRP deposition Model[4], which is a semi empirical algebraic deposition model. Deposition was calculated for an adult healthy subject anatomy (FRC=3300 mL). Unsteady airflow is modeled with a mean inspiratory flow rate of 20 L/min, a 3 sec. inhalation time, a 1:1 inhalation/exhaled ratio and a tidal volume of 1000 mL.

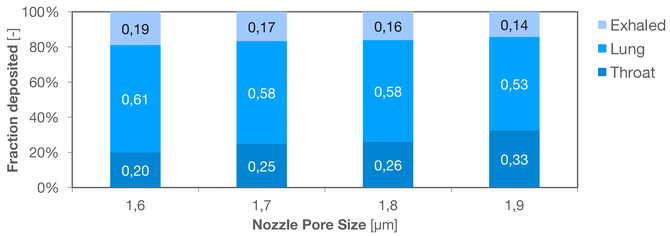

Figure 4: *Modelled lung deposition with Pulmospray® Nozzle Pore Size.*

The result of the deposition model are summaries in Figure 4 as fraction of dose delivered. Drug deposition to the whole lung varies between 53% and 61% for the 1.9 µm and 1.6 µm micro-nozzle, respectively and 8% reduced for a particle size of 5.12 µm compared to 6.7 µm. Total lung Deposition with the single-use Pulmospray® SMI is comparable to that determined for other SMIs (~57%) using functional respiratory imaging[2]. Total throat deposition is estimated as low as 20% for the smallest snozzle size and increases to up to 33% for the largest nozzle.

Conclusion

Results from this study indicate that the single-use Pulmospray® SMI allows a fast administration of 1 mL inhalation solution within ~2 min. The combined results from narrow particle size distribution (GSD), small nozzle pore size (MMAD) and the built-in flow limitation of the device allows efficient delivery to the lungs as indicated by other publications[3]. In conclusion, the single-use Pulmospray® SMI provides a viable solutions for fast and convenient drug delivery as it is often required for hospital use and/or the treatment of infectious diseases.

References

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