EVALUATION OF THE AERONEB GO® NEBULIZER PERFORMANCE WITH PULMOZYME® (2.5mg/2.5ml)

STUDY REPORT

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1. Study Objective

The objective of this study was to measure the inhalable mass and the particle size of Pulmozyme® (Roche, Neuilly sur seine, France) generated by the Aeroneb Go® nebulizer (Aerogen, USA).

2. Measurement method

The experimental set up defined by EN13544-1 European standard and the mass measurement method defined in the article (2) were used in this study.

2.1 Tested Materials

-3 Aeroneb Go® nebulizers (Aerogen, Gallway, Ireland), each nebulizer was tested 2 times (n=6)
- Pulmozyme® 2.5mg/2.5ml (Roche, Neuilly sur seine, France) Batch B1307

2.2 Inhaled Mass (IM)

2.2.1 Experimental setup (Figure 1)

Nebulizers were connected to a piston pump (Harvard, U.S.A.) set at a frequency of 15/min, 500 ml tidal volume, and a 50/50 inspiration/expiration ratio.

A filter holder containing a non-absorbent Pari filter (Pari, Starnberg, Germany) for Pulmozyme® collection was positioned between the nebulizer and the piston pump (Harvard, USA). Filters were changed every 5 minutes until the end of nebulization. Pari filters were weighed before aerosol collection and after aerosol collection and filter drying. The duration of the nebulization was defined by the time of nebulization generation until the end of aerosol generation.

2.2.2 τ calculation

All measurements were performed at a hygrometry of humidity levels ranging from 35% to 55%. The scale (Precisa 40SM-200A, Sartorius, Bradford, U.K.) had a 0.01 mg precision. The output measurements took into account the absolute dryness of the filters and the relative mass of the drug in the aerosol collected. The drying of filters before and after aerosol collection was obtained by keeping them during 24 hours each time in the scale room.

The relative mass of the RhDnase (τ) in total solute mass (drug + excipients=Pulmozyme®) collected on the filters was measured as follows. 3 Pari filters (Pari filter, Pari, Germany) were weighed. 1 mg of RhDnase (1 ml of the Pulmozyme® at a concentration of 1mg/ml) was placed with a pipette onto each of three Pari filters. All filters were dried in the scale room during a 24-hour period. The difference between the weight of each filter after solution pipetting and drying and its weight before pipetting was calculated (Δ). The value of τ was calculated by determining the ratio between the RhDnase mass deposited on the filter (1 mg for RhDnase) and Δ (τ = 1 mg/ Δ)

2.2.3 Rhdnase mass calculation

The nebulized Pulmozyme® mass was measured under the nebulization conditions described in the *Experimental Set-up* section above, by weighing filters both before aerosol collection and after aerosol collection and filter drying (Pulmozyme mass).

The RhDnase mass was calculated as the product of Pulmozyme® mass mass and the proportion of RhDnase contained in Pulmozyme® mass (Rhdnase mass = Pulmozyme® mass X τ).

2.3 Particle size measurement (Figure 2)

To determine the particle size of the Pulmozyme aerosol produced by the Aeroneb Go nebulizer, we used a device that takes measurements by means of the laser diffraction method (Mastersizer-X).

The mouthpiece of the nebulizer was positioned at a distance of 1 cm from the lens and 2 cm from the laser beam. The aerosol was sprayed across the laser beam and toward a vacuum pump positioned 5 cm beyond the beam and set at an output rate of 25 l/min.

The Mastersizer-X acquired data during all the aerosol generation. The data inversion calculation was computed by the Mastersizer-X software for calculate the mass median mass aerodynamic diameter (MMAD).

Figure 1 : Experimental set up for inhaled mass measurement

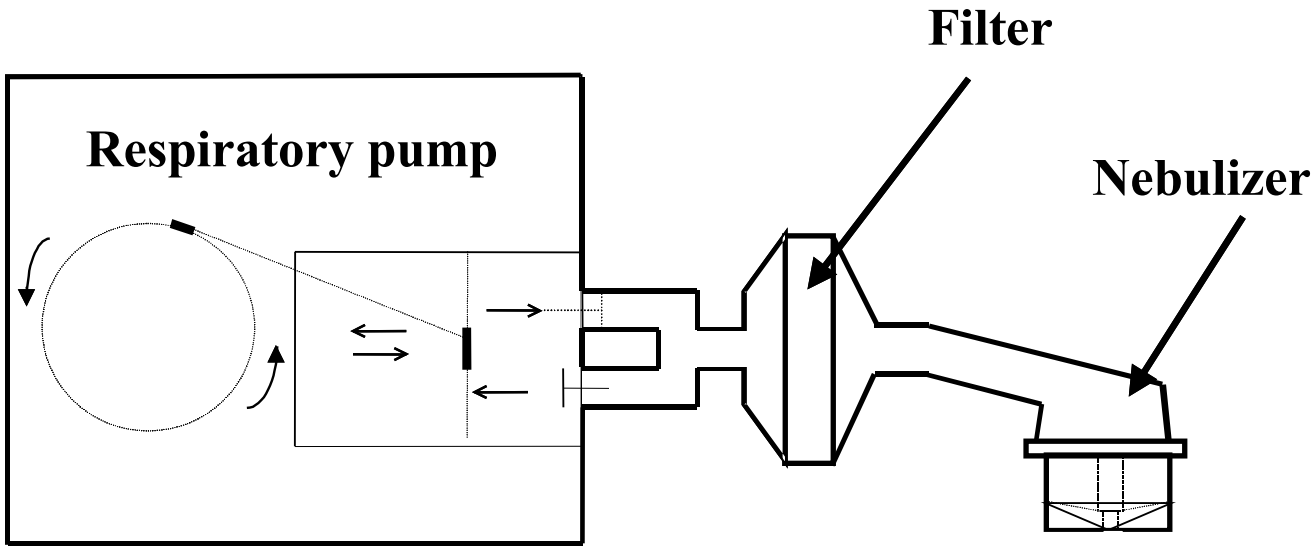
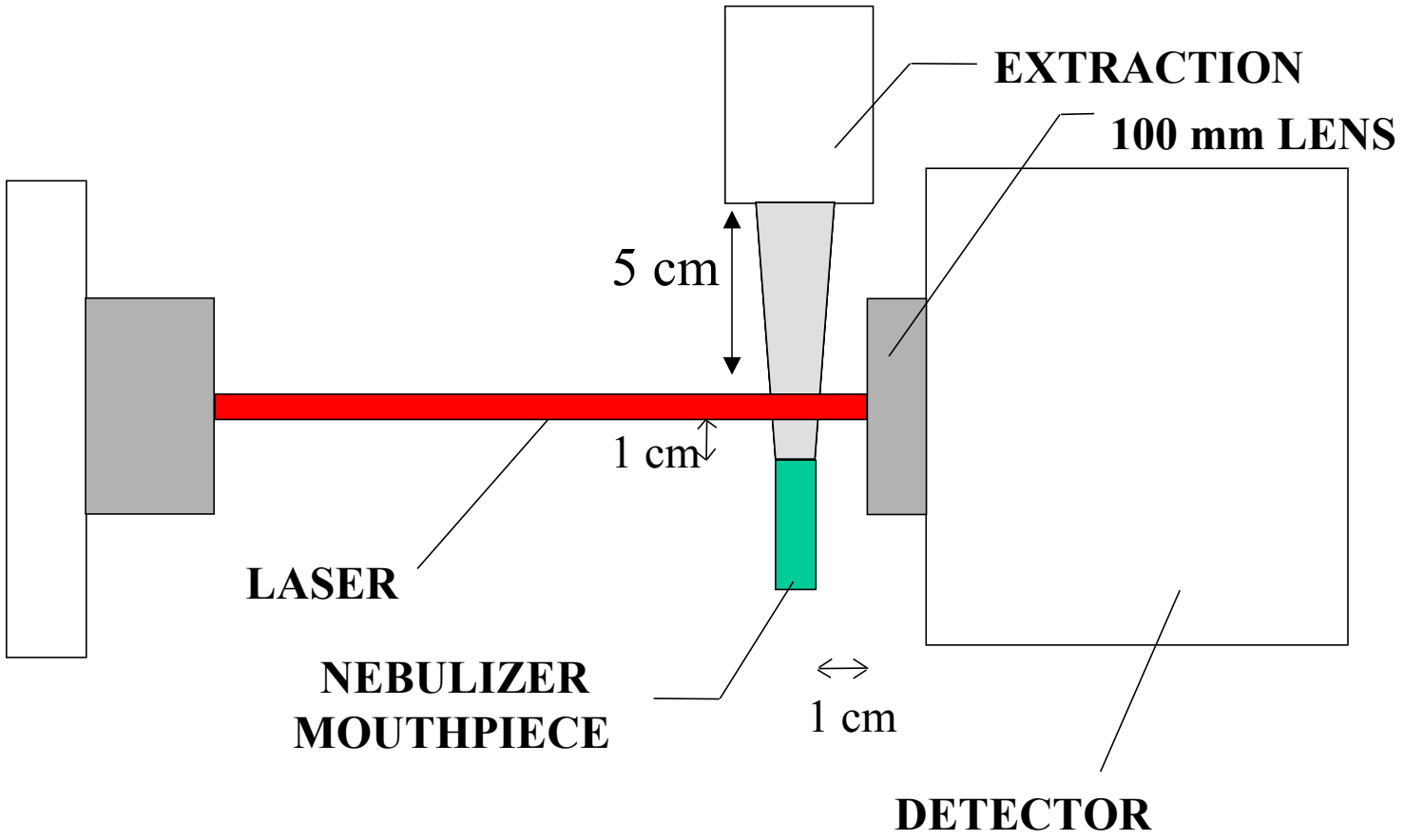


Figure 2 : Particle size measurement set-up



3. Results

3.1 Inhaled mass

Nebulizer	RhDnase Inhaled mass (µg)
Aeroneb Go 1a	857
Aeroneb Go 1b	815
Aeroneb Go 2a	832
Aeroneb Go 2b	806
Aeroneb Go 3a	822
Aeroneb Go 3b	657
mean	798
standard deviation	71

Table 1 : RhDnase inhaled mass results

3.2 Nebulization time

Nebulizer	Nebulization time (min)
Aeroneb Go 1a	4.1
Aeroneb Go 1b	3.8
Aeroneb Go 2a	4.8
Aeroneb Go 2b	5.1
Aeroneb Go 3a	4.3
Aeroneb Go 3b	4.2
mean	4.4
standard deviation	0.5

Table 2 : Nebulization time results

3.3 MMAD

Nebulizer	MMAD (µm)
Aeroneb Go 1a	5.0
Aeroneb Go 1b	5.1
Aeroneb Go 2a	4.3
Aeroneb Go 2b	4.1
Aeroneb Go 3a	4.4
Aeroneb Go 3b	4.2
mean	4.5
standard deviation	0.4

Table 3 : Mass Median Aerodynamic Diameter (MMAD) results

4. Conclusion

The RhDnase inhaled mass of the nebulized Pulmozyme® (2500µg/2.5ml) with the Aeroneb Go® nebulizer was 798µg ± 71µg.

The Mass Median Aerodynamic Diameter (MMAD) of the Pulmozyme® nebulized by Aeroneb Go® was 4.5µm ± 0.4µm.

The duration to nebulize the Pulmozyme® with Aeroneb Go® was 4.4min ± 0.5min.

References

1. European standard EN13544-1

2. Vecellio L, Grimbert D, Bordenave J, Benoit G, Furet Y, Fauroux B, Boissinot E, De Monte M, Lemarie E, Diot P. 2004. Residual gravimetric method to measure nebulizer output. J Aerosol Med. 17:63-71

Tours, 2006/08/30

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