A Novel Contact-Triggered Vibrating-Mesh Nebulizer: Aerodynamic Performance and Drug Distribution of Suspension Drug Delivered with MicroBase µSMI

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Introduction

Although traditional vibrating mesh nebulizers overcome many of the disadvantage of small volume jet nebulizer, which include being noisy, bulky, exhibiting poor portability, and being inefficient [1]. They are prone to mesh clogging, require inconvenient cleaning/disinfection processes, and are expensive [2]. During repetitive nebulization, the microscopic holes in the vibrating mesh module may be easily obstructed by suspension-based formulations, dust, or other particles bigger than the aperture size. The more often such a nebulizer is used, the more likely the holes of the mesh will be blocked. A contact-triggered vibrating mesh nebulization system, MicroBase µSMI (Figure 1), which utilizes a cost-effective disposable medical cup, was developed to overcome the limitations of traditional vibrating mesh systems. In this study, we compared the aerosol characteristics of a suspension-type drug formulation delivered with MicroBase µSMI to those obtained using a series of commercially available vibrating mesh nebulizers.

Methods

The nebulization performance of MicroBase µSMI, Aerogen® Solo, Philips InnoSpire Go, and PARI eRapid® were compared using previously reported methods with minor modifications [3]. In brief, a unit dose of budesonide (Pulmicort Respules® , 1 mg/2 mL, AstraZeneca) was filled into each nebulizer. The resulting budesonide aerosols were characterized using a next generation impactor (NGI, Model 170, Copley Scientific) at a constant flow rate 15 L/min and an operating temperature of 5℃. The amount of budesonide on each stage was determined using a validated high performance liquid chromatography (HPLC, Waters Alliance System) method. The distribution of budesonide nebulized by MicroBase µSMI and the other commercial nebulizers was also analyzed using a breathing simulator (BRS 1100, Copley Scientific) and delivered dose aerosol capture system with quantitative drug recovery. The BRS was set to generate an adult breathing pattern (total volume = 500 mL, frequency = 15 cycles/min, inhalation:exhalation ratio = 1:1). All experiments were performed three times. The mean and standard deviation are reported in Table 1. Student's t-tests comparisons resulting in $p < 0.01$ were considered statistically significant.

Results

Traditional vibrating mesh medication cups are comprised of a container, mesh, and vibrating module in constant, direct contact with one-another (Figure 2A) during nebulization. In contrast, the MicroBase µSMI separates the container and mesh from the vibrating module (Figure 2B) and nebulization does not occur until the mesh/medication cup contacts the vibrating module (Figure 2B).

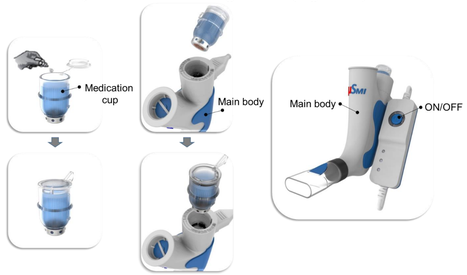

Figure 1. Design and assembly of MicroBase µSMI.

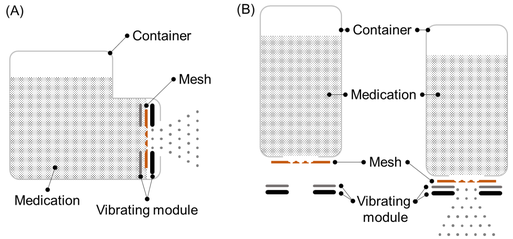

Figure 2. A) Illustration of traditional vibrating-mesh and B) contact-triggered vibrating-mesh medication cup.

The mass median aerodynamic diameter (MMAD), geometric standard deviation (GSD), fine particle fraction (FPF, < 5 µm), and fine particle dose (FPD, < 5 µm) of budesonide aerosols generated by MicroBase µSMI and captured in the NGI are 5.26 µm, 1.78, 44.33%, and 0.26 mg, respectively (Table 1). Judged using the same metrics, this is comparable to the aerosol performance of the commercially available Aerogen Solo, Philips InnoSpire Go, and PARI eRapid, except the FPF of MicroBase µSMI is lower than that of the Philips InnoSpire Go, and both FPF and FPD of MicroBase µSMI are higher than PARI eRapid (Table 1).

	MMAD (µm)	GSD	FPF (<5 µm, %)	FPD (<5 µm, mg)
MicroBase µSMI	5.26 ± 0.11	1.78 ± 0.02	44.33% ± 1.67%	0.26 ± 0.01
Aerogen Solo	5.10 ± 0.30	1.98 ± 0.07	47.28% ± 4.99%	0.30 ± 0.04
Philips InnoSpire Go	4.88 ± 0.04	1.71 ± 0.02	50.77% ± 0.92%*	0.21 ± 0.02
PARI eRapid	5.91 ± 0.22	1.83 ± 0.03	35.77% ± 1.96%*	0.10 ± 0.01*

* $p < 0.01$

Table 1 - NGI-derived aerodynamic performance of MicroBase µSMI and comparator nebulizers using a budesonide suspension.

Table 2 shows the distribution of budesonide nebulized by MicroBase µSMI and the other commercial nebulizers, along with the calculated respirable dose, determined during the BRS studies. The inhaled dose (often termed the delivered dose) of MicroBase µSMI is significantly higher than that of the other three nebulizers, and reached 0.51 mg. In other words, these in vitro experiments suggest that more than half of the loaded dose is likely to be delivered into a patient's lungs with only 0.37 mg retained in the device and 0.08 mg lost to the atmosphere during a nebulization treatment. In comparison, the existing platforms suggested an inhaled dose of between 0.15 and 0.33 mg. Our in vitro studies suggest the lower inhaled dose is attributable to either high residual dose loss in the device (PARI eRapid, 0.78 mg) or a higher exhaled dose (Aerogen Solo, 0.29 mg).

Respirable dose is used as a surrogate for the amount of medication that could be potentially delivered into lower respiratory duct of a patient [4]. It is calculated as the product of the inhaled dose and FPF (derived from NGI experiments). Therefore, either increasing inhaled dose or FPF could improve respirable dose. As shown in Table 2, the respirable dose of MicroBase µSMI (0.23 mg) is similar to Aerogen Solo (0.15 mg), and significantly higher than Philips InnoSpire Go (0.11 mg) and PARI eRapid (0.05 mg).

	Inhaled Dose (mg)	Residual Dose in Device (mg)	Residual Dose in Ampoule (mg)	Exhaled Dose (mg)	Respirable Dose[a] (mg)
MicroBase µSMI	0.51 ± 0.03	0.37 ± 0.05	0.04 ± 0.01	0.08 ± 0.03	0.23 ± 0.02
Aerogen Solo	0.33 ± 0.02*	0.31 ± 0.07	0.07 ± 0.01	0.29 ± 0.06*	0.15 ± 0.03
Philips InnoSpire Go	0.22 ± 0.02*	0.61 ± 0.09	0.06 ± 0.01	0.11 ± 0.06	0.11 ± 0.01*
PARI eRapid	0.15 ± 0.01*	0.78 ± 0.02*	0.06 ± 0.01	0.01 ± 0.01	0.05 ± 0.01*

* $p < 0.01$

[a] Respirable Dose = Inhaled Dose × FPF

Table 2 - BRS-derived dose delivery performance of MicroBase µSMI and comparator nebulizers using a budesonide suspension.

Conclusions

A new nebulization technology, contact-triggered vibrating-mesh nebulization, was developed - MicroBase µSMI. In this study, we demonstrated in vitro aerodynamic characteristics similar to other commercial nebulizers; and projected that a higher inhaled dose might be achievable using MicroBase µSMI.

Bibliography

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