Characterization of Vibrating Mesh Aerosol Generators

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ABSTRACT

The fate of inhaled aerosol particles within the respiratory tract is determined by factors such as the particle size distribution, breathing pattern, and airway geometry. Thus, matching the aerosol therapy device to the patient is crucial to achieving a high target site dose and minimizing side effects. High output efficiency and minimal residual volume have been reported for vibrating mesh nebulizers, which generate a high percentage of particles in the respirable fraction. Using custom-made plates, this work aimed to investigate and identify the major operating parameters of these devices and their effects on the characteristics of the aerosol output.

Each plate contained between 279 and 4606 tapered apertures that ranged from 3 to 12 μm in diameter and were uniformly sized per plate. To investigate the effect of coagulation during droplet generation, the distance between the apertures was varied from 75 to 450 μm . The resonance frequency of the piezoelectric element was scanned, and the aperture plates were then vibrated at a fixed frequency (100–300 kHz), causing the ejection of liquid droplets. The nebulizers were mainly evaluated using a 0.9% sodium chloride solution. A syringe pump injected the solution into the vibrating mesh plates. The aerosol output was carried, dried, and introduced into the mixing chamber by a dilution air flow of 160 L min^{-1} . An aerosol size spectrometer was employed to measure both the number concentration and the size distribution of the output.

The droplet size increased with the aperture diameter. The distance between apertures did not affect the number concentration or the size distribution of the generated droplets. The droplet size decreased as the resonance frequency increased, but the extent was less than we expected. Each mesh possessed an optimal vibration frequency, which varied according to the size and the number of the apertures, for consistently maximizing the aerosol output. The optimal feeding rate increased with the number of apertures and the applied electric current, but the aerosol size distribution remained the same. Additionally, our results using a cotton wick to deliver the solution from the reservoir to the vibrating mesh indicate that fibrous sorbent materials can potentially replace the syringe pump.

Keywords: Nebulizer; Aerosol generation; Vibrating mesh; Piezoelectric element.

INTRODUCTION

Respiratory and lung diseases, including asthma attacks, chronic obstructive pulmonary disease (COPD), reduced lung function, and pulmonary cancer, which are caused by a series of carcinogenic chemicals that enter the body through inhalation, are becoming more prevalent as the world economy develops (Wan *et al.*, 2013; Neiderud, 2015;

Maji *et al.*, 2017). With the projected increase in urbanization, there is likely to be a marked increase in asthma cases (Robinson *et al.*, 2011). It is estimated that there may be an additional 100 million persons with asthma by 2025 (Masoli *et al.*, 2004). In the United States, morbidity caused by COPD is 4%, making COPD the fourth leading cause of death, exceeded only by heart attacks, cancer, and stroke (Hurd, 2000). According to the Global Burden of Disease Study, COPD, by 2020, is also listed in the 10 leading causes of disability-adjusted life-years (Murray and Lopez, 1997).

Nebulizers have been utilized to deliver medications through inhalation for decades (Dhand, 2001; Ibrahim *et al.*, 2015). Aerosol therapy with small molecules has been employed for treating lung diseases such as asthma, chronic obstructive pulmonary disease, and cystic fibrosis (Labiris and Dolovich, 2003; Lannefors, 2006; Sims, 2011). The aerosol therapeutic paradigm has been expanded into

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the delivery of macromolecules into the systemic circulation through the lung for the treatment of systemic disease, such as diabetes mellitus (Newhouse, 1999; Dhand, 2001). In the future, many other medications are likely to be administered in this way (Newhouse and Corkery, 2001).

Aerosol deposition in the respiratory tract has been known to be a strong function of particle size (Stahlhofen *et al.*, 1980; Varghese and Gangamma, 2006; Patterson *et al.*, 2014; Lin *et al.*, 2018). Therefore, size distribution of the atomized droplets is critical to the nebulizer's performance. A nebulizer is a device used to convert liquid into aerosol droplets. There are three types of nebulizers: jet nebulizer, ultrasonic atomizer, and vibrating mesh nebulizer. The main principle of a jet nebulizer is to pass air/gas through a small hole in the nebulizer to suck and atomize the liquid solution or suspension into polydisperse droplets. It was the first aerosol generator to be used for medication starting in the 1950s. The main problems of a jet nebulizer include it being bulky, not easy to carry, and noisy (Mercer, 1973; Alvine *et al.*, 1992; O'Callaghan and Barry, 1997). Ultrasonic nebulizers, invented in 1964, use a piezoelectric crystal vibrating at a high frequency (1.2–2.4 MHz) to generate polydisperse aerosol particles. The size of the generator was greatly reduced since the air compressor was replaced by an ultrasonic generator. Traditional ultrasonic nebulizers are quieter but have problems of residual formulation due to dead volume, inability to aerosolize viscous solutions, settling of suspensions, and degradation of heat-sensitive materials (Maehara *et al.*, 1986; Taylor and McCallion, 1997; Watts *et al.*, 2008).

Vibrating mesh technology revolutionized nebulizer design. Vibrating mesh nebulizers have been recently introduced into the market. The first mesh was introduced in the 1980s by Omron Healthcare (Vecellio, 2006). These devices have now been applied to many other fields of specialization. Among these are veterinary medicine, cosmetics, disinfection, agriculture, and thermal comfort. These devices can operate with batteries and are small enough to be carried around (Waldrep and Dhand, 2008).

Vibrating mesh aerosol generators, also referred to as “mesh nebulizers,” use a vibrating plate with multiple apertures to generate droplets. During operation, upward and downward movement of the aperture plate creates a micro-pumping action that extrudes liquid through the apertures to form liquid jets. Each jet continues to be intact to a certain length and then breaks to droplets. The breakup of a high-speed liquid jet injected through a circular nozzle into a stagnant gas (hereinafter referred to as “atomization”) is a complicated multi-parameter two-phase problem. Although several theoretical models have been proposed to predict the droplet size distribution, the mechanism that controls atomization has not yet been determined. Based on the maximum instability theory (Rayleigh, 1878), the relationship between the droplet diameter d_d and the undisturbed jet diameter d_j was obtained as follows:

$$d_d = 1.89d_j \quad (1)$$

Thus, the droplet size can be determined if d_j is known.

However, due to d_j being largely a theoretical abstraction, a more general model for predicting the mean droplet diameter has been suggested as follows (Balabel and Wilson, 2013):

$$d_m = ad_o^{3/2}/p^{1/3} \quad (2)$$

where d_m is the mean diameter, d_o is the nozzle diameter, p is the jet pressure at the nozzle outlet, and a is an experimental parameter.

A good aerosol generator should be efficient, stable, and reproducible. Mesh nebulizers have most of the features of ideal aerosol generators—stability, portability, convenience, energy efficiency, and ease of use—when compared with other nebulizers (Pitance *et al.*, 2010; Pritchard *et al.*, 2018). Vibrating mesh nebulizers are becoming more popular in medications mainly for producing predominant respirable fractions capable of reaching into the peripheral lung, and low residual volume. However, published experimental data on the performance characteristics of these miniature electronic nebulizers are still very limited, probably due to the confidentiality practice of the pharmaceutical industry. Thus, the main purpose of the present study is to thoroughly explore the characteristics of a typical vibrating mesh aerosol generator from the perspective of aerosol generation. Therefore, the feasibility of using vibrating mesh technology to tailor the particle size distributions to suit specific requirements was challenged.

METHODS

The vibrating mesh aerosol generator is made of a vibrational piezoelectric element and a stainless steel plate. The thickness of the stainless steel plate is 40 μm , with a surface area of 36 mm^2 and weight of 0.012 g. The major operating parameters and ranges are listed in Table 1. As shown in Fig. 1(A), the aperture is a micro-tapered hole with a cone angle, α , of 60° at a rough estimate. The wider portion of the aperture is on the liquid side, and the narrower end is on the side the droplets emerge. The number of apertures on each plate ranges from 279 to 4606. The size of the apertures (the narrower end) ranges from 3 to 12 μm and is uniform on each plate. The distance between apertures is varied from 75 to 450 μm to investigate the potential coagulation after the solution is atomized. The frequency, voltage, and current supplied to the vibrating piezoelectric unit are also varied to determine the optimal combination for aerosol generation. These nebulizers are mainly evaluated with 0.9% sodium chloride solution. A syringe pump (KDS 200; KD Scientific Inc., Holliston, MA, USA) and cotton wicks are employed to deliver the solution to the vibrating mesh plate. There are three ways to deliver the solution to the vibrating mesh, as shown in Fig. 1(B). They are (1) upward, with a mesh placed horizontally and solution fed from below; (2) downward, with solution fed from above the mesh; and (3) sideward, with vibrating mesh standing vertically and solution fed from the side.

It is difficult to characterize a droplet size distribution in

Table 1. Operating parameters of the vibrating mesh nebulizer.

Parameter	Code	Range
Mesh configuration		
Aperture size (μm)	D_{apt}	3–9
Aperture distance (μm)	L	75–450
Number of apertures	N	279–4606
Total aperture area (mm^2)	A	10^{-3} – 10^{-1}
Driving mode		
Frequency (kHz)	Freq	150, 200, 300
Current (mA)	C	10–600
Voltage (V)	V	0–100
Orientation and delivery methods		
Orientation	U	$\uparrow, \downarrow, \rightarrow$
Delivery method	M	Syringe pump and cotton wick

Fig. 1. Schematic diagram of the experimental system set-up.

a reproducible manner because of evaporation after aerosolization. Therefore, the generated aerosol particles, after passing through a radioactive source, 10 mCi ^{241}Am , are introduced into a mixing acrylic chamber by the filtered air flow of 160 L min^{-1} to completely dry the aerosol (Fig. 1). An aerosol size spectrometer (welas digital 3000; Palas GmbH, Karlsruhe, Germany) is employed to measure the number concentration and size distribution of aerosols. The particle detection range was set from 0.2 to $10 \mu\text{m}$. Polystyrene latex spheres (Duke Scientific Corp., Palo Alto, CA, USA) are used to calibrate the size accuracy

of the welas. Thus, the particle size measured by the spectrometer is then an “equivalent PSL diameter.” The sampling flow rate of the welas is 5.0 L min^{-1} and periodically checked using an electronic bubble meter (Giliblator; Gilian Instrument Corp., Wayne, NJ, USA). The temperature and relative humidity (RH) inside the mixing chamber are monitored with a thermo hygrometer (HygroLog HL-NT2-DP; Rotronic AG Bassersdorf, Switzerland) to assure that all droplets are dried. The information of size distribution provided by the aerosol size spectrometer is then employed to back-calculate the original droplet size

distribution. The dry particle diameter, d_p , depends on the volume fraction of the solute, F_v , and the droplet diameter, d_d , according to the equation (Hinds, 1999):

$$d_p = d_d(F_v)^{1/3} \quad (3)$$

For example, a particle size distribution with a count median diameter (CMD) of 0.6 μm would result from a 0.9% saline droplet distribution with a CMD of 2.9 μm .

RESULTS AND DISCUSSION

The piezoelectric plate can be activated only under some specific resonance frequencies, which is determined by the electrical impedance, as shown in Fig. 2. The phase angle and impedance are shown as a function of frequency. The phase angle and impedance show impulsive rise at resonance frequencies of 150, 200, and 300 kHz when the aerosol generation is actuated. The voltage decreases with increasing frequency, but it shows abrupt drop at these particular frequencies when the current is fixed at 140 mA.

The effect of aperture size on the CMD of generated droplets is shown in Fig. 3. Notice that the droplet size distribution is back-calculated from the dried particle size distribution measured by the aerosol size spectrometer. Consistent with previous studies (Balabel and Wilson, 2013; Zhao *et al.*, 2015), the CMD of generated droplets increases

linearly with increasing aperture size. For drug delivery purposes, it would be ideal to generate all sub-micrometer-sized droplets to have higher aerosol penetration into the deep lung. However, an aperture size smaller than 2 μm is difficult to make, due to technical limitations at present.

The distance between apertures, aperture distance, might have an effect on generated droplet size distribution if the distance is too close because of higher probability of droplet coagulation. Fig. 4 shows that the generated droplet size is not affected by aperture distance ranging from 80 to 450 μm , with aperture size of 5 μm , frequency of 300 kHz, and solution feeding rate of 0.1 mL min^{-1} . There is a slight increasing trend as the aperture decreases, but the difference is still not significant.

The maximum droplet generating rate is determined by gradually increasing the solution feeding rate of a syringe pump. Fig. 5 shows that for an aperture size of 4 μm , 1911 apertures, and an aperture distance of 120 μm , the number concentration of droplets increases steadily with increasing solution feeding rate until the maximum droplet concentration of $7 \times 10^4 \text{ count cm}^{-3}$ is reached, when the solution feeding rate is 0.7 mL min^{-1} . It is likely that the 1911 apertures on the plate are not fully used for droplet generation if the feeding rate is lower than 0.7 mL min^{-1} , and the aerosol cloud rises vertically, as shown in Fig. 5(a). When the solution feeding rate exceeds 0.7 mL min^{-1} , the number concentration of droplets decreases sharply because the piezoelectric

Fig. 2. Resonance frequency (log scale), impedance, and voltage of a typical mesh.

Fig. 3. CMD of droplets as a function of mesh aperture size.

Fig. 4. CMD of droplets as a function of aperture distance.

element is overloaded with solution. Excess solution flows beyond the edge of the vibrating plate, resulting in partial and unstable vibration of the stainless steel plate. The aerosol cloud moves downward unstably, as the feeding rate exceeds the maximum, as shown in Fig. 5(b).

The effect of solution feeding rate on the size distribution of generated droplets is shown in Fig. 6. As can be seen, the droplet size distribution remains unchanged as the solution feeding rate increases to 0.7 mL min^{-1} , the maximum feeding rate. If the feeding rate exceeds 0.7 mL min^{-1} , the number concentration of particles and both the CMD and the geometric standard deviation (GSD) increase slightly.

The maximum feeding rate should increase with increasing number of apertures on the vibrating plate. Fig. 7 shows that as the number of apertures increases from 379 to 4606, the maximum feeding rate increases linearly from 0.1 to 2.0 mL min^{-1} , with aperture size of $3 \mu\text{m}$ and operation frequency of 300 kHz . The maximum feeding rate also increases with increasing total aperture area, as shown in Fig. 8. The linear regression analysis shows a high coefficient of determination of 0.96.

Droplet generation can only be actuated when the frequency is set to 150, 200, or 300 kHz , as shown in Fig. 2. Higher operating frequency makes smaller droplets, as expected and shown in Fig. 9. The droplet size should decrease to 0.63 times of CMD as the frequency doubles from 150 to 300 kHz (Mercer, 1973). However, the CMD decreases only 0.86 times, probably due to the measurement error and counting efficiency of the aerosol size spectrometer, which are functions of particle size. The maximum solution feeding rate is expected to increase with increasing operating frequency. However, the frequency of 200 kHz does not follow the linear increasing trend, as shown in the lower plot of Fig. 9. In addition, the maximum feeding rate under 300 kHz is 3 times more than that under 150 kHz . Therefore, more data are apparently needed to clarify how operating frequency affects the maximum solution feeding rate.

Moreover, power increases with increasing current when

Fig. 5. Effect of liquid feeding rate on aerosol number concentration.

Fig. 6. Effect of liquid feeding rate on aerosol size distribution.

Fig. 7. The maximum feeding rate as a function of number of apertures.

the impedance and the operating frequency are fixed. Experimental results show that the droplet size distribution is not affected by changing the current, as shown in Fig. 10.

However, the maximum solution feeding rate increases with increasing operating current, as shown in the lower plot. Nevertheless, the maximum solution feeding rate

Fig. 8. The maximum feeding rate as a function of total aperture area.

increases only 30%, from 0.35 to 0.45 mL min⁻¹, while the current increases from 80 to 240 mA. Thus, from the perspective of energy consumption, this vibrating mesh aerosol generator should be operated under low current.

The effect of orientation of the vibrating mesh on droplet generation is an interesting issue to explore. The size distribution of droplets generated on different orientations is

almost identical with CMD of 0.45 μm and GSD around 2.1, with aperture size of 4 μm , 1911 apertures, aperture distance of 120 μm , and solution feeding rate of 0.4 mL min⁻¹. The aerosol number concentration and the maximum feeding rate are also not affected by the orientation of the vibrating plate. This finding is not totally in line with previous results (Skaria and Smaldone, 2010), in which the Omron NE-U22 generated larger droplets when placed horizontally, while the present study examined the sideward case.

Fibrous sorbent material, such as cotton wicks, was also employed to deliver the solution to the vibrating mesh, as shown in Fig. 12. Both delivery methods generate droplets of about the same size distribution, with CMD of 0.4 μm , and GSD of 1.7, when the aperture size is 3 μm , the aperture distance is 120 μm , and the number of apertures is 1911. Thus, the capillary force induced by cotton wicks works essentially the same as the syringe pump. However, the solution feeding rate produced by a piece of cotton wick is constant, about 0.09 mL min⁻¹, which is much lower than the maximum feeding rate of about 0.7 mL min⁻¹ when syringe pump is employed. Both size and properties of the sorbent materials are likely to influence the solution feeding rate, but that is not within the scope of the present study.

CONCLUSIONS

The operating parameters of a vibrating mesh nebulizer, specifically, the mesh configuration (the size, distance, and

Fig. 9. Effect of frequency on aerosol size and max feeding rate.

Fig. 10. Effect of current on aerosol size and max feeding rate.

Fig. 11. Effect of orientation on aerosol size distribution.

Fig. 12. Effect of delivery method on aerosol size distribution.

number of apertures), driving mode (frequency and current), solution feeding rate, orientation, and delivery method, were thoroughly examined to investigate their effects on the number concentration and the size distribution of generated droplets. The vibrating meshes tested in this work actuated the aerosol generation at resonance frequencies of 150, 200, and 300 kHz. The droplet size was roughly proportional to the nozzle diameter, and the droplet output increased with the size and number of the apertures, the applied frequency, and the current. The size distribution of the generated droplets did not exhibit significant effects from coagulation regardless of the distance between the apertures, which ranged from 75 to 450 μm . Although the tested vibrating meshes functioned in any orientation, currently available mesh nebulizers are designed to operate with a liquid reservoir; hence, incorrect orientation may inhibit the transportation of the nebulizing solution, thereby preventing the generation of droplets.

In our study, an optimal solution feeding rate was found for each mesh, which depended on the size and the number of the apertures. The aerosol output linearly increased with the feeding rate until this optimal rate was reached. Upon exceeding the optimal rate, the output exhibited a rapid and unstable decrease due to the mesh being overloaded, with excess solution simply overflowing the mesh.

Finally, the solution can be delivered to the piezoelectric plate by a fibrous sorbent material, such as a cotton wick, via capillary action. However, because of the difficulty in controlling the structural and surface properties of porous materials, the rate of transportation will likely vary. Moreover, cleaning and maintenance become critical issues when using such materials.

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