AirLife™ Misty Fast™ disposable small-volume nebulizer (SVN)

Competitive analysis

Introduction

Delivering nebulized medication to the lungs depends on a variety of clinical and device-related variables. Patient breathing patterns, type and dilution of the drug nebulized, nebulizer flow rates, and device selection and orientation all have the potential to affect the amount of drug delivered to the patient.

In vitro *(bench)* testing can provide the end user with useful information regarding nebulizer performance. Various test methods have been used previously; however, the quantification of inhaled drug mass through the use of a simulated breathing patient has become an increasingly well-accepted evaluation method that allows for more accurate drug dose estimation.

Study conducted

Vyaire conducted a study comparing the performance of five conventional small-volume nebulizers *(SVN)* using cascade impaction to characterize the aerosol quality and a simulated breathing patient to estimate the mass of drug delivered to the patient. The study was designed to closely simulate typical clinical conditions in the acute care setting and resulted in the following:

- The AirLife™ Misty Fast™ SVN delivers efficacious drug *(drug within respirable range of 1–5 microns)* significantly faster than the other SVNs tested.
- The rate of inhaled efficacious drug is significantly higher for the AirLife Misty Fast SVN than the other SVNs tested.
- The inhaled respirable mass per breath of the AirLife Misty Fast SVN is greater than other SVNs tested.

Particle size testing

Cascade impaction was used to analyze the particle size characteristics. Cascade impaction was chosen for the following reasons:

- Cascade impaction measures aerodynamic diameter directly, which accounts for the density and irregular shape of drug particles. It is believed that aerodynamic diameter more accurately predicts the behavior of aerosol as it is delivered into the patient's lungs.[1]
- There is more historical data on particle size measurement using cascade data than any other method. Relative comparison of previous devices tested using cascade impaction can be readily made.
- Cascade impaction is one of the USP methods for characterization of particle distributions.[2]

Testing was conducted using a Next Generation Impactor *(NGI)* with seven collection stages per USP 36 *(U.S. Pharmacopeia)*. Particle size testing was conducted with the collection stages at both "chilled" and "ambient" conditions. Both test methods aim to reduce the effect of evaporation during testing to better represent the direct drug output of the nebulizer made available to the patient. The chilled test reflected the USP 362 recommended methods of testing where the impactor was controlled to a temperature of 5 ± 1.5 °C with a vacuum flow of 15 LPM. The ambient test was conducted at room temperature with room air controlled to 50 ± 5 % relative humidity with a vacuum flow of 28.3 LPM. Ambient data at an extraction flow of 28.3 LPM was presented for comparative reasons with prior testing of nebulizers.

Testing of samples was concluded one minute after the onset of sputter. The onset of sputter plus one minute is the recommended treatment time due to the majority of drug being provided to the patient without unnecessarily prolonging the therapy. Clinical evidence also suggests that very little drug is inhaled after the onset of sputter, therefore leading the recommendation to be one minute after the onset of sputter.[3]

Inhaled drug mass testing

A simulated breathing patient was attached to the SVN with a collection filter in-line to capture the drug substance that would be delivered to the patient. A breath profile of 500 mL Vt, 15 breaths per minute, and an I:E ratio of 1:1 was used per USP 36. The nebulizer drug output characteristics are shown in the table below:

SVN	AirLife Misty Fast		Hudson MicroMist™		AirLife Misty Max 10™		Salter NebuTech™		WestMed VixOne™	
NGI setting	Chilled	Ambient	Chilled	Ambient	Chilled	Ambient	Chilled	Ambient	Chilled	Ambient
Respirable output rate	165 ± 6	177 ± 9	115 ± 14*	116 ± 10*	112 ± 8*	97 ± 12*	117 ± 17*	164 ± 21*	142 ± 17*	142 ± 11*
Inhaled respirable output rate	76 ± 3	70 ± 2	48 ± 3*	48 ± 2*	48 ± 3*	41 ± 2*	49 ± 8*	49 ± 8*	58 ± 2*	55 ± 2*
Inhaled respirable mass per breath *(µg)*	**5.1 ± 0.2**	**4.6 ± 0.2**	**3.2 ± 0.2***	**3.2 ± 0.1***	**3.2 ± 0.2***	**2.7 ± 0.1***	**3.3 ± 0.6***	**3.3 ± 0.5***	**3.9 ± 0.1***	**3.7 ± 0.1***
Respirable fraction 1–5 µm	57 ± 2	52 ± 2	50 ± 3*	49 ± 2*	59 ± 3**	51 ± 2**	34 ± 6*	34 ± 5*	55 ± 2*	52 ± 2**
MMAD	3.3 ± 0.1	2.4 ± 0.2	4.0 ± 0.3*	1.8 ± 0.1*	3.3 ± 0.2**	1.4 ± 0.3*	5.5 ± 0.6*	4.7 ± 0.4*	3.8 ± 0.2*	2.2 ± 0.3*
GSD	2.1 ± 0.0	2.6 ± 0.1	2.1 ± 0.0**	3.2 ± 0.2*	2.1 ± 0.1**	2.5 ± 0.5**	2.2 ± 0.1*	2.1 ± 0.1*	2.1 ± 0.0**	2.9 ± 0.3*

Note: Data presented as mean ± standard deviation.

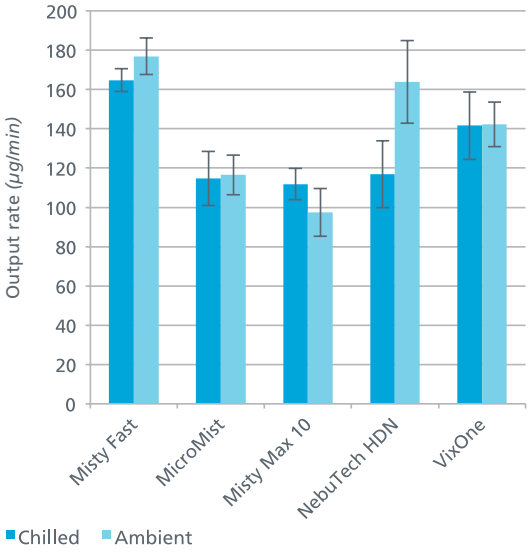
All tests were conducted with 3 mL doses of albuterol sulfate, 0.083% at a nebulizer drive flow rate of 8 LPM. Samples were assayed with a UV spectrophotometer *(wavelength of 277 nm)*. Comparisons were made using student's T-test for means.

* Difference between the AirLife Misty Fast SVN and other SVNs is statistically significant *($p < 0.05$)*.

** Difference between the AirLife Misty Fast and other SVNs is not statistically significant *($p > 0.05$)*.

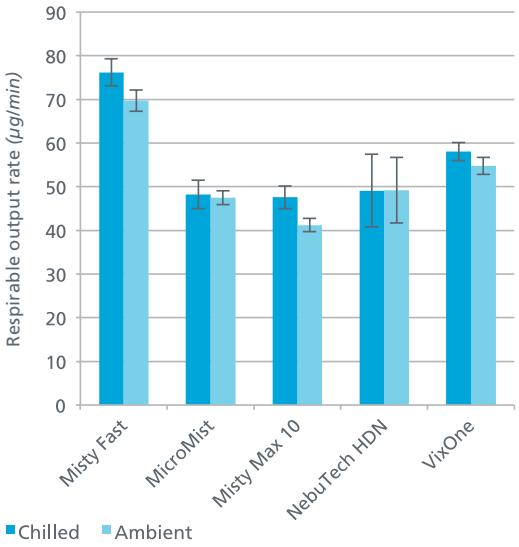
Respirable output rate

The respirable output rate is the rate of drug delivered by the nebulizer within the desired respirable range. Determined by dividing the respirable mass by the treatment time, the respirable output rate measures the nebulizer's efficiency in delivering the drug within the desired respirable range *(particles between 1–5 microns)*.



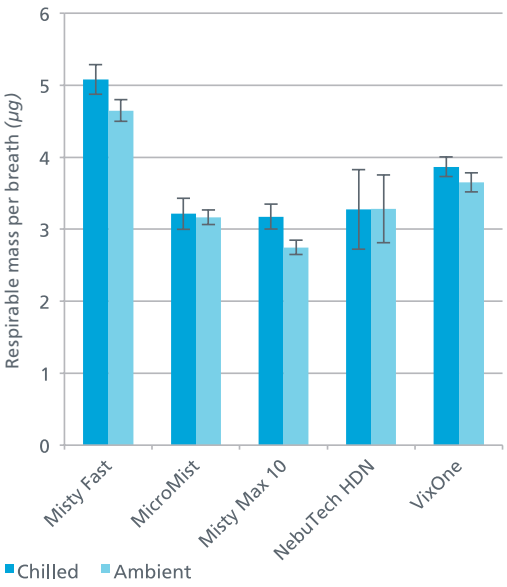
Inhaled respirable output rate

The respirable output rate is the rate of drug delivered by the nebulizer to a simulated breathing patient within the desired respirable range. Determine inhaled respirable output rate by multiplying the drug delivery rate on a breathing patient by the respirable fraction of the desired particle size range of 1–5 microns.



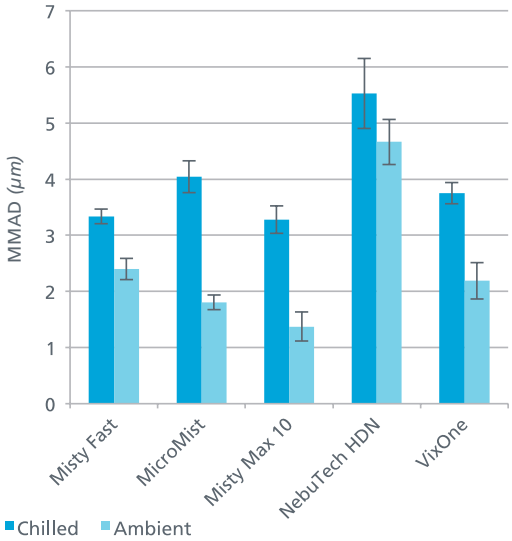
Inhaled respirable mass per breath

The inhaled respirable mass per breath is the drug mass delivered per breath to a simulated patient within the respirable range of particle sizes *(1–5 µm)*. This is determined by dividing the inhaled respirable output rate by the breath rate of the simulated patient. The inhaled respirable mass per breath is a measure of the nebulizer's efficiency in drug delivery within the respirable range per patient breath.



Mass median aerodynamic diameter (MMAD)

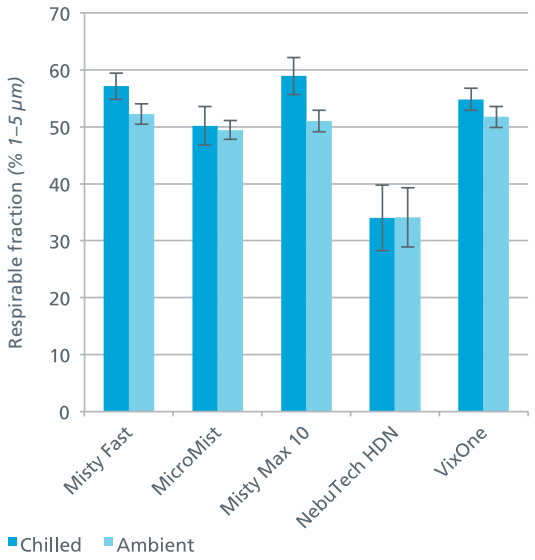
MMAD measures the central tendency of the size distribution of aerosol particles. It is the diameter, in micrometers, of which 50% of the mass of aerosol is larger and 50% is smaller.



Respirable fraction

Respirable fraction is the percent of aerosol generated by mass that falls within the desired respirable range. This is calculated as the ratio of drug mass within the desired respirable range to the total drug mass delivered for the duration of treatment.

It has been reported that particle sizes in the range of 1–5 µm are best for reaching the lung periphery.[3]



Products tested

All nebulizers were randomly pulled from production lots. Catalog numbers chosen were of similar configuration: nebulizer, T-piece, mouthpiece, oxygen tubing and 6" flextube. A minimum of 16 samples were used for each nebulizer tested for NGI and inhaled drug mass testing:

- The AirLife Misty Fast small-volume nebulizer *(cat. no. FN2438)*
- Hudson MicroMist *(cat. no. 1883)*
- AirLife Misty Max 10 nebulizer *(cat. no. 002438)*
- Salter Labs NebuTech HDN *(cat. no. 8960)*
- WestMed VixOne *(cat. no. 0210)*

Particle size

A next-generation seven-stage cascade impactor *(NGI)* with USP inlet was used and assayed with a spectrophotometer *(277 nm)*. Particle size characterization was performed using 3 mL of 0.083% albuterol solution and a nebulizer flow rate of 8 L/min. All cascade tests sampled nebulizer aerosol through the manufacturer's supplied T-piece and mouthpiece.

All particle size tests ran for one minute after the noted onset of sputter time. This treatment time was chosen because evidence suggests that after the onset of sputter, very little additional drug is inhaled. Clinicians have adopted the recommendations to stop nebulizer therapy at, or one minute after, the onset of sputter.[3]

Inhaled drug mass

The test set-up consisted of a filter placed between nebulizer mouthpiece and a simulated breathing patient. The filter captured the inhaled aerosol exiting the mouthpiece, and the drug mass deposited onto the filter was quantified with a UV spectrophotometer *(277 nm)*.

A simulated breathing patient was created by using an Ingmar ASL 5000 Adult/Neonatal Breathing Simulator. The output of the lung was verified with a TSI Certifier FA Plus Ventilator Test System 4080. An adult breathing patient was simulated in accordance with the USP 36 standard: 500 mL Vt, 15 BPM, 1:1 I:E ratio.[4]

A commonly used dosing of albuterol *(3 mL, 0.083% albuterol)* was nebulized. All nebulizers were run at a flow rate of 8 L/min. A new collection filter was replaced at each one-minute period to allow inhaled drug delivery rate quantification. All filters associated with a nebulization run were assayed, and the resultant drug amounts were totaled to obtain the inhaled drug substance delivered for the duration of the drug treatment.

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1. Kacmarek, Robert, Stoller, James, and Albert Hueur. "Egan's Fundamentals of Respiratory Care." 9th ed. St. Louis: Mosby Elsevier, 2009 Page 845.
2 U.S. Pharmacopeia *(USP)*, 36 *(General Chapter 601)*: Aerosols, nasal sprays, metered-dose inhalers, and dry powder inhalers.
3 Arzu, A., Hess, D., Myers, T., Rau J. A guide to aerosol delivery devices for respiratory therapists, 2nd edition. AARC, 2009, 1–69.
4 U.S. Pharmacopeia *(USP)*, 36 *(General Chapter 1601)*: Products for nebulization–characterization tests, November 2012.

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