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Operating Performance Comparisons between Laser Doppler Velocimetry and Time of Flight Techniques

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Operating Performance Comparisons between Laser Doppler Velocimetry and Time of Flight Techniques

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Abstract

Characterizing the aerodynamic diameter of aerosol particles in the atmosphere or generated from the respiratory drug delivery devices has been subject of research for a long time. This study presents the operating performance comparisons between two aerosol particle sizing instruments which incorporate real time characterization of both atmospheric and respiratory drug aerosols. The instruments were: the single particle aerodynamic relaxation time (ESPART) analyzer and the aerodynamic particle sizer (APS) spectrometer. The ESPART operates on the principle of laser-doppler-velocimetry, whereas the APS operates on the principle of time-of-flight technique. They are a class of instruments that measure the aerodynamic diameter of individual particles following a controlled acceleration in a well-defined flow field. Both instruments are capable of sizing several thousand particles in a second. The tested aerosols were generated from several commercially available respiratory drug delivery inhalers, nebulizers, and blow-off cup aerosol generators. They were 1) Qvar Metered Dose Inhaler (MDI), 2) Albuterol MDI, 3) Ventolin MDI, 4) PARI-LC Plus Nebulizer and NaCl solution (7mg/ml), 5) PARI-LC Plus Nebulizer and Polymer Microsphere solution in water, 6) Blow-off cup and Lactose Monohydrate submicronized powder, and 7) Blow-off cup and Mannitol powder. The results showed that both instruments demonstrated similar performance within ± 0.5% variation for the aerosols with count median aerodynamic diameter (CMAD) > 3.0 µm and mass median aerodynamic diameter (MMAD) > 4.0 µm. However, both instruments showed some different performances within ± 4% variation for the aerosols with CMAD and MMAD less than 3.0 µm and 4.0 µm, respectively. The ESPART was providing electrical charge and polarity of aerosols in addition to particle's aerodynamic diameter information.

1. Introduction

In the aerosol research community, various techniques are routinely employed in real-time particle count, aerodynamic size, and electrostatic charge spectrometry. Most common among these are laser-doppler-velocimetry (LDV), and time-of-flight (TOF). Each of these techniques has scientific evidences of robustness and they are widely adopted in aerosol studies. During recent two decades various commercial organizations and academic laboratories developed powerful equipments employing these techniques. Furthermore, there has been tremendous amount of interests and successes in real-time analysis of aerosols upon generation.

The major physical properties of any kind of aerosols are its inborn suspended particle’s size (diameter), shape, diffusivity, density, and electrostatic charge [1]. In order to use them for industrial or therapeutic purposes, understanding and controlling these physical properties are topics of much current interest. In fact, aerosol particle's size influences rest of the other physical properties. The gravitational force, terminal settling velocity, inertia force and electrostatic force that act on a particle are approximately proportional to the square of the particle diameter [2]. Therefore, one of the most commonly used terminologies in aerosol science and technology is the aerodynamic diameter (d_a) to represent the size of a particle. This is defined, for a particular particle, as the diameter of the spherical particle with density of 1000 kg/m^3 (the density of a water droplet) that has the same settling velocity as the particle. Mathematically it was derived from Stoke's Law and is defined by:

$$d_a = (\rho_p / \rho_0)^{0.5} d_p$$

where d_p is the particle diameter, ρ_p is particle density, and ρ_0 is the standard particle density 1000 kg/m^3. The aerodynamic diameter can be imagined of as the diameter of a water droplet having the same aerodynamic behaviors as the particle [3]. If a particle has an aerodynamic diameter of 1 µm, it behaves in an aerodynamic sense like a 1 µm water droplet regardless of its shape, density, or physical size. The aerodynamic diameter is the key property of a particle to characterize its deposition, Coulombic attraction/repulsion force, diffusivity, and velocity while airborne and suspended in the aerosol.

In addition, particles also acquire electrostatic charges during generation by the diffusion of ions in aerosol streams which is caused by the collisions resulted from Brownian motion of the ions and particles [3]. Acquisition of charges by a particle as a function of time and the charge state of the particle can be calculated in a simplified and dimensionless form with the following equation [4,5].

$$q = \frac{n e^2}{2\pi \varepsilon d_p k T} \qquad (1)$$

where q is called the particle charge, n is the number of elementary charge units, e is the electronic charge (1.6 x 10^{-19} Coulomb), ε is the permittivity of air, d_p is the particle diameter, k is the Boltzmann's constant, and T is the absolute temperature. If we know the density of particle, ρ, then the charge on an individual particle can be described in terms of its average charge-to-mass ratio, q/m, which can be calculated by the following equation.

$$\frac{q}{m} = \frac{3 n e^2}{\pi^2 \varepsilon \rho d_p^4 k T} \qquad (2)$$

There are numerous instruments to characterize both aerodynamic size and electrostatic charge of aerosols. This study compares the aerosol characterizing performances of two widely used aerosol particle analyzer instruments. One is called the Electronic Single Particle Aerodynamic Relaxation Time (ESPART) analyzer (US Patent 4633714 of the University of Arkansas at Little Rock, Arkansas, USA), and the other is called the Aerodynamic Particle Sizer Spectrometer (APS) (TSI Incorporated, Shoreview, Minnesota, USA) [6,7].

The ESPART incorporates the methodology of LDV principle, which measures simultaneously both aerodynamic diameter of and electrostatic charge (magnitude and polarity) of aerosol particles generated by various aerosol generation methods [8]. The LDV method characterizes each aerosol particle in real time. Opto-electronic measurements including LDV are non-intrusive, fast response times, and high data measurements accuracy [9].

The APS adopts the TOF measurement technique to determine aerodynamic diameter of individual aerosol particle measured in an accelerating flow field with a single, high-speed timing processor; coincidence detection achieved using a patented, double crest optical system; particle size binning based on internally stored calibration curve [10,11]. The present investigation had two specific objectives, which were the characterizations and comparisons of aerodynamic properties of aerosols generated by several different methods.

2. Materials and Methods

The tested aerosols were generated from several commercially available respiratory drug delivery inhalers, nebulizers, and blow-off cup aerosol generators. They were 1) Qvar Metered Dose Inhaler (MDI) (3M, Northridge, California, USA), 2) Albuterol MDI (Warrick Pharmaceuticals, Reno, Nevada, USA), 3) Ventolin MDI (Allen and Hanburys Respiratory Care, Victoria, Australia), 4) PARI-LC Plus Nebulizer (PARI, Midlothian, Virginia, USA) and sodium chloride solution (7mg/ml), 5) PARI-LC Plus Nebulizer and Polymer Microsphere solution in water (Duke Scientific, Freemont, California, USA), 6) Blow-off cup and Lactose Monohydrate submicronized powder (Gallade Chemical Inc., Santa Ana, California, USA), and 7) Blow-off cup and Mannitol powder (Aceto Corp., Lake Success, New York, USA).

2.1. ESPART Analyzer Instrument

The Electronic Single Particle Aerodynamic Relaxation Time (ESPART) analyzer measures aerodynamic size and electrostatic charge every single particle in real time [8]. It was designed and developed in the Aerosol Drug Delivery Research Lab of the University of Arkansas at Little Rock, Little Rock, Arkansas, USA [6]. Figure 1 illustrates its working principle. The suction pump of the ESPART draws aerosol at the rate of 1 L/min. The flow is directed downwards through a sensing volume of focused beams of laser radiation. During sampling each particle traverses through converging laser beams. It also experiences AC electric excitation which makes it oscillate horizontally. The photomultiplier is used to measure the intensity of the scattered light generates by each particle as it passes through the sensing volume. The electronic signal and data processor analyzes the phase lag of the particle motion with respect to the AC electric field driving the particle. The aerodynamic diameter is derived from the phase lag value. The direction and amplitude of the electrical migration velocity of the particle with respect to the electric field provides the polarity and magnitude of its electrostatic charge.

The ESPART analyzer operates in two modes. In mode 1, it measures the aerodynamic diameter of each particle whether the particle is charged or uncharged. Acquired aerosol data in this mode represents total (charged and uncharged) particles. In mode 2, it measures the aerodynamic diameter and the electrostatic charge of each charged particle. In mode 2, it ignores the uncharged particles purposely (i.e., by design). In this study mode 1 and mode 2 data were obtained in completely separate experimental runs.

The ESPART collects and stores raw data by using LabView™ application software (National Instruments, Austin, Texas, USA). Acquired data can be analyzed and mined by the Aerosol Particle Data Analyzer (APDA) software (developed in C Language at the Aerosol Drug Delivery Research Lab of the University of Arkansas at Little Rock, Little Rock, Arkansas, USA). APDA data can be cleaned and transferred to spreadsheets (Excel) which allows generating graphs and tables.

2.2. APS Spectrometer Instrument

The Aerodynamic Particle Sizer (APS) Spectrometer accelerates the aerosol sample flow (1 L/min) through an accelerating orifice. The aerodynamic size of a particle determines its rate of acceleration, with larger particles accelerating more slowly due to increased inertia. As particles exit the nozzle, they cross through two partially overlapping laser beams in the detection area. Light is scattered as each particle crosses through the overlapping beams. An elliptical mirror, placed at 90 degrees to the laser beam axis, collects the light and focuses it onto an avalanche photo detector (APD). The APD then converts the light pulses into electrical pulses. The configuration of the detection area improves particle detection and minimizes Mie scattering oscillations in the light-scattering-intensity measurements. Figure 2 illustrates working principle of the APS.

The use of two partially overlapping laser beams results in each particle generating a single two-crested signal. Peak-to-peak time-of-flight is measured with 4-nanosecond resolution for aerodynamic sizing. The amplitude of the signal is logged for light-scattering intensity. The smallest particles may have only one detectable crest and are binned separately. In uncorrelated mode, these particles are displayed in the smallest size channel (less than 0.523 micrometer). Particles with more than two crests, indicative of coincidence, are also binned separately but are not used to build aerodynamic-size or light-scattering distributions.

The APS uses the Aerosol Instrument Manager software, a 32-bit program designed for use with Windows operating systems. The Aerosol Instrument Manager Software controls instrument operation, plus it provides file management capabilities and numerous choices for data display. Graphs and tables allow viewing channel data as well as raw data, giving the highest resolution possible. One can view all data types—time-of-flight, light-scattering, or correlated data—with the Aerosol Instrument Manager software. An export function allows easy transport of data files to spreadsheet or other applications for customized data handling.

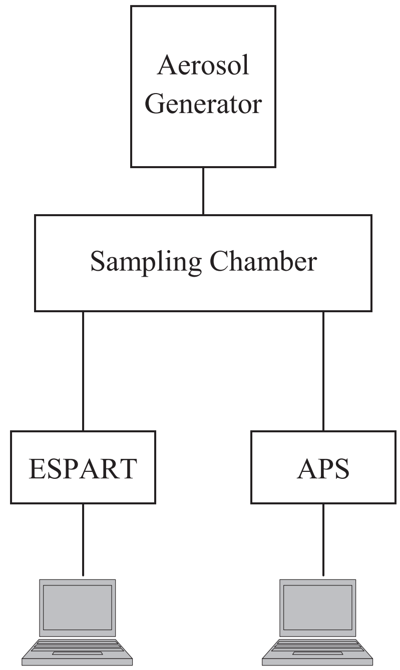


Figure 3: The Simplified Schematic of the Experimental Setup.

A simplified schematic of the experimental setup is shown in Figure 3. During each experiment, the aerosol sampling chamber was cleaned and evacuated before each run of the experiment. Aerosols were generated and filled the sampling chamber before starting the simultaneous characterization by the ESPART and the APS. Both instruments measured aerosols for five minutes continuously. Thus it was unlikely that variation of aerosol quantity generated by each individual method affected the measurements, and comparisons. The procedure was repeated for ten consecutive runs. The aerodynamic size data was acquired for both instruments, and the charge-to-mass ratio data was measured for the ESPART only since the APS does not support measurement of this property.

3. Results and Discussion

It is necessary to point out that for some aerosol characterization methods other than LDV and TOF, sample preparation of the atomizing solution is required. For example, compendial methods that are based on either the multistage liquid impinger or cascade impactor require preparation of ultraviolet spectrophotometer detectable concentration of sample solution which takes repetitive dilution of the tested samples. Such solution preparation procedure takes long time. Nevertheless laboratory experimentalists need a relatively simple and fast measurement method, which both the ESPART and APS instruments are capable to perform.

Table 1 summarizes the aerodynamic diameters (count median aerodynamic diameter and mass median aerodynamic diameter), and electrostatic charge statistics of all tested aerosols determined by the LDV technique (ESPART Analyzer).

Table 2 summarizes the aerodynamic diameters (count median aerodynamic diameter and mass median aerodynamic diameter) statistics of all tested aerosols determined by the TOF technique (APS Spectrometer).

Figures 4 and 5 present the count median aerodynamic diameter (CMAD) and mass median aerodynamic diameter (MMAD) of aerosols generated by various methods.

It was observed that the CMAD and MMAD in the generated aerosols are consistent with findings that were reported by other investigators [12, 13]. The results showed that both instruments demonstrated similar performance within ± 0.5% variation for the aerosols with count median aerodynamic diameter (CMAD) > 3.0 μm and mass median aerodynamic diameter (MMAD) > 4.0 μm. However, both instruments showed some different performances within ± 4% variation for the aerosols with CMAD and MMAD less than 3.0 μm and 4.0 μm, respectively.

Figure 6 presents the net electrostatic charge or charge-to-mass ratio and polarity of generated aerosols measured by the ESPART. However, the APS does not support measurement of this property by design.

In this study, it was logical to recognize certain limitations. The data obtained from LDV or TOF method should be used with caution, however. Most notable issue is the lack of direct relationship with the mass of drug substance present and the vulnerability of the measurements to coincidence effects when sampling concentrated aerosols, may severely limit the significance of data from some aerosol drug delivery systems such as metered dose inhaler. Moreover when measuring particles smaller than 0.5 μm or larger than 20 μm, data accuracy has to be compromised to a great extent due the design constraints, therefore present study purposely avoided investigating the behavior of particles outside the size range of 0.5 to 20 μm.

4. Conclusions

This study evaluated the performance in characterizing aerosol particles' aerodynamic diameters of two real-time measurement techniques. Both the LDV-ESPART and TOF-APS are powerful instruments which are capable of providing quantitative and aerodynamic information on laboratory generated aerosols. Former also provides the real-time electrical properties. Since there is no lengthy sample preparation involved in techniques employed by these instruments, they are very user friendly tools in situations where aerosol properties data and quick determination of results are essential.

5. References

[1] S. Suarez, and A.J. Hickey, "Drug Properties Affecting Aerosol Behavior," Respiratory Care Journal, Vo. 45, No. 6, June 2000, pp. 652-666.

[2] U.S. EPA, "Basic Concepts in Environmental Sciences," United States Environmental Protection Agency, Research Triangle Park, NC. Available at www.epa.gov/cgi-bin, accessed on in March 15, 2009.

[3] W.C. Hinds, "Aerosol Technology: Properties, Behavior and Measurement of Airborne Particles," John Wiley and Sons Inc., New York, February 1998.

[4] P.A. Lawless, "Particle Charging Bounds, Symmetry Relations, and An Analytic Charging Rate Model for the Continuum Regime," Journal of Aerosol Science, Vo. 27, No. 2, March 1996, pp.191-215.

[5] R.A. Fjeld, D. Wu, and A.R. McFarland, "Evaluation of Continuum Regime Theories for Bipolar Charging of Particles in the 0.3-13 µm Diameter Size Range," IEEE Transactions for Industrial Applications, Vol. 26, No. 3, 1990. pp. 523-528.

[6] M.K. Mazumder, and R.E. Ware, "Aerosol Particles Charge and Size Analyzer," US Patent # 4633714, 1987.

[7] TSI, Inc., "Catalog for Model 3321 Aerodynamic Particle Sizer Spectrometer," Available at www.tsi.com, accessed on July 27, 2008.

[8] M.K. Mazumder, J.D. Wilson, D.L. Wankum, R. Cole, G.M. Northrop, L.T. Neidhardt and T.B. Martonen, "Dual Laser Doppler System for Real-time Simultaneous Characterization of Aerosols by Size and Concentration," In Lung Dosimetry, ed. Crapo JD, San Diego: Academic Press, 1989, pp. 211-234.

[9] J.W. Czarske, "Laser Doppler Velocimetry Using Powerful Solid-state Light Sources," Measurement Science and Technology. Vol. 17, July 2006, pp. R71-R91.

[10] D. Leith and T. M. Peters, "Concentration Measurement and Counting Efficiency of the Aerodynamic Particle Sizer 3321," Journal of Aerosol Science, Vol 34, No. 5, May 2003, pp. 627-634.

[11] S.W. Stein, P.B. Myrdal, B.J. Gabrio, D.R. Oberreit, and T.J. Beck, "Evaluation of a New Aerodynamic Particle Sizer Spectrometer for Size Distribution Measurements of Solution Metered Dose Inhalers," Journal of Aerosol Medicine, Vol. 16, June 2003, pp. 107-119.

[12] J.P. Mitchell, and M.W. Nagel, "Time-of-Flight Aerodynamic Particle Size Analyzers: Their Use and Limitations for the Evaluation of Medical Aerosols," Journal of Aerosol Medicine, Vol. 12, Winter 1999, pp. 217-240.

[13] M.W. Nagel, K.J. Wiersema, S.L. Bates, and J.P. Mitchell, "Size Analysis of a Pressurized Metered Dose Inhaler-Delivered Solution Formulation by an Aerosolizer LD-Time-of-Flight Aerosol Particle Size Spectrometer," Journal of Aerosol Medicine, Vol. 15, March 2002, pp. 75-85.

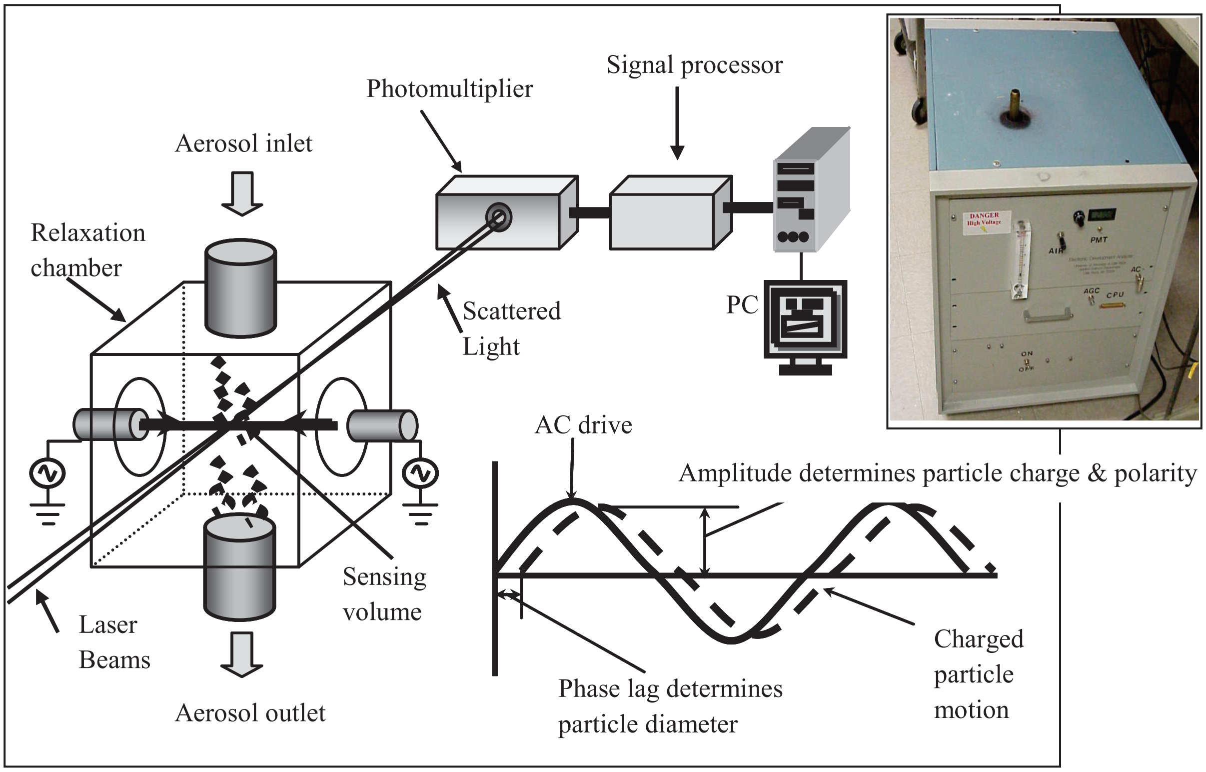


Figure 1: Operation of the Electronic Single Particle Aerodynamic Relaxation Time (ESPART) Analyzer. Inset shows the ESPART unit. (Reference 8).

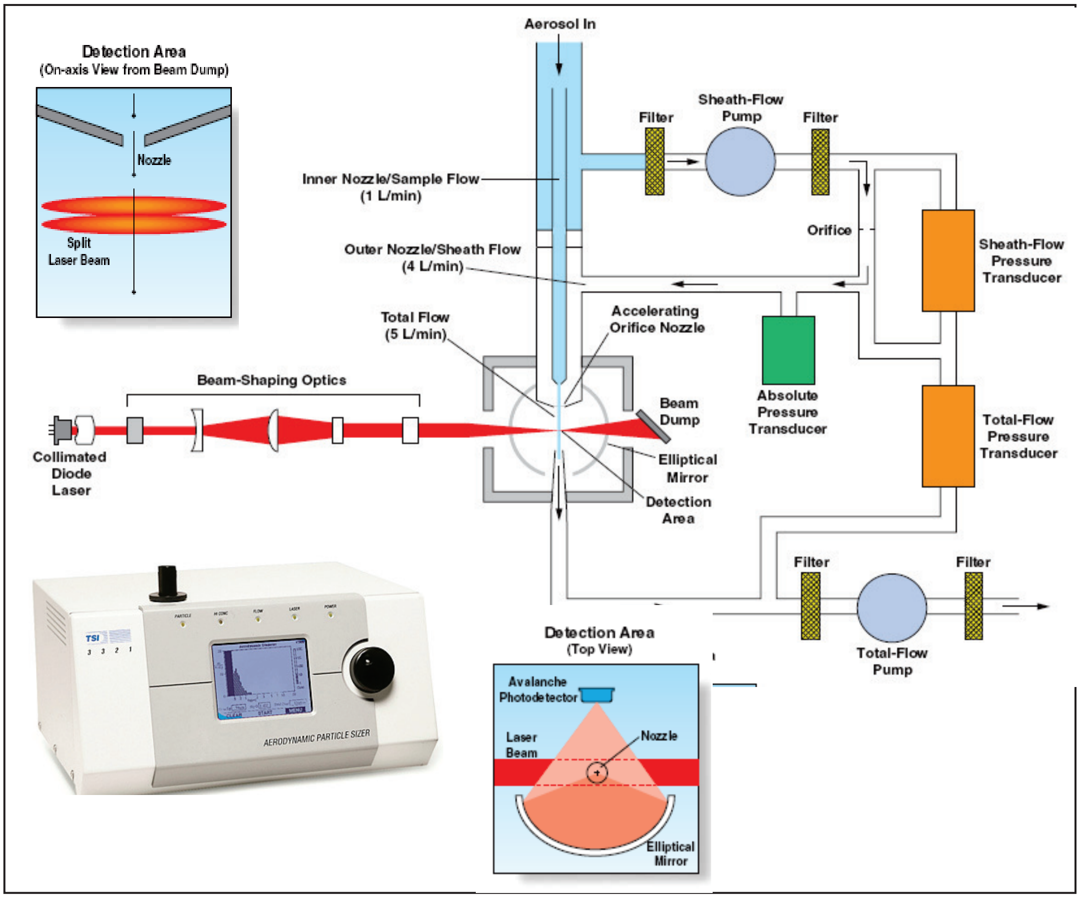


Figure 2: Operation of the Aerodynamic Particle Sizer (APS) Spectrometer Unit. Inset shows the APS unit. (Reference 7).

Table 1. Summary of the Tested Aerosols' Aerodynamic Size and Electrostatic Charge Properties Determined by the Lased Doppler Velocimetry Technique (ESPART Analyzer).

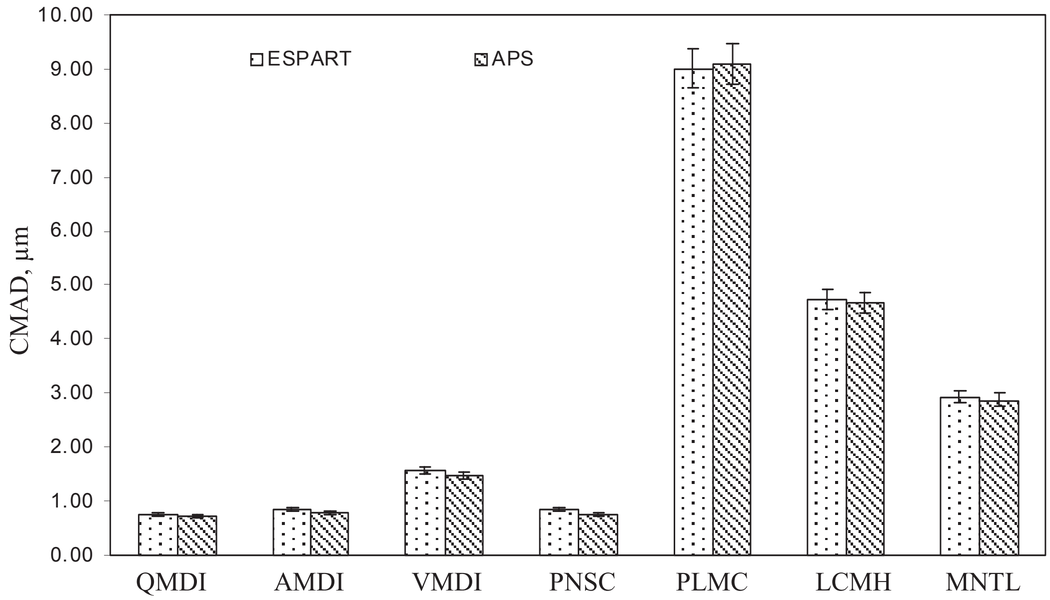
Aerosol	Total (charged & uncharged) Particles (St. Dev.)	Charged Particle (St. Dev.)	CMAD (μm) (St. Dev.)	MMAD (μm) (St. Dev.)	Net Charge to mass ratio (μC/g)
QMDI	6764 (8)	360 (4)	0.75 (0.01)	1.67 (0.04)	- 2.829 ± 0.07
AMDI	6514 (18)	1856 (16)	0.83 (0.03)	3.90 (0.06)	+ 4.072 ± 0.06
VMDI	5905 (5)	2971 (3)	1.56 (0.01)	2.71 (0.04)	+ 3.492 ± 0.05
PNSC	2238 (10)	301 (4)	0.83 (0.01)	1.51 (0.02)	- 0.774 ± 0.02
PLMC	2058 (11)	369 (2)	9.00 (0.04)	9.71 (0.02)	- 1.329 ± 0.04
LCMH	2032 (25)	1928 (6)	4.72 (0.06)	5.62 (0.07)	+ 3.265 ± 0.03
MNTL	1923 (13)	276 (11)	2.92 (0.01)	5.68 (0.09)	+ 2.503 ± 0.06

QMDI - Qvar Metered Dose inhaler, AMDI - Albuterol Sulphate Metered Dose Inhaler,
VMDI - Ventolin Metered Dose Inhaler, PNSC - PARI-LC Plus Nebulizer Sodium Chloride
PLMC - Polymer Microsphere, LCMH - Lactose Monohydrate, MNTL – Mannitol
CMAD - Count median aerodynamic diameter, MMAD - Mass median aerodynamic diameter

Table 2. Summary of the Tested Aerosols' Aerodynamic Size Properties Determined by the Time of Flight Technique (APS Spectrometer).

Aerosol	Total (charged & uncharged) Particles (St. Dev.)	CMAD (µm) (St. Dev.)	MMAD (µm) (St. Dev.)
QMDI	6928 (9)	0.72 (0.01)	1.54 (0.04)
AMDI	6636 (8)	0.78 (0.01)	3.71 (0.02)
VMDI	6249 (13)	1.48 (0.02)	2.49 (0.05)
PNSC	2463 (8)	0.76 (0.03)	1.51 (0.02)
PLMC	2456 (6)	9.10 (0.04)	9.69 (0.01)
LCMH	2299 (17)	4.67 (0.05)	5.54 (0.10)
MNTL	2272 (9)	2.88 (0.04)	5.76 (0.08)

QMDI - Qvar Metered Dose inhaler, AMDI - Albuterol Sulphate Metered Dose Inhaler,
VMDI - Ventolin Metered Dose Inhaler, PNSC - PARI-LC Plus Nebulizer Sodium Chloride
PLMC - Polymer Microsphere, LCMH - Lactose Monohydrate, MNTL – Mannitol
CMAD - Count median aerodynamic diameter, MMAD - Mass median aerodynamic diameter



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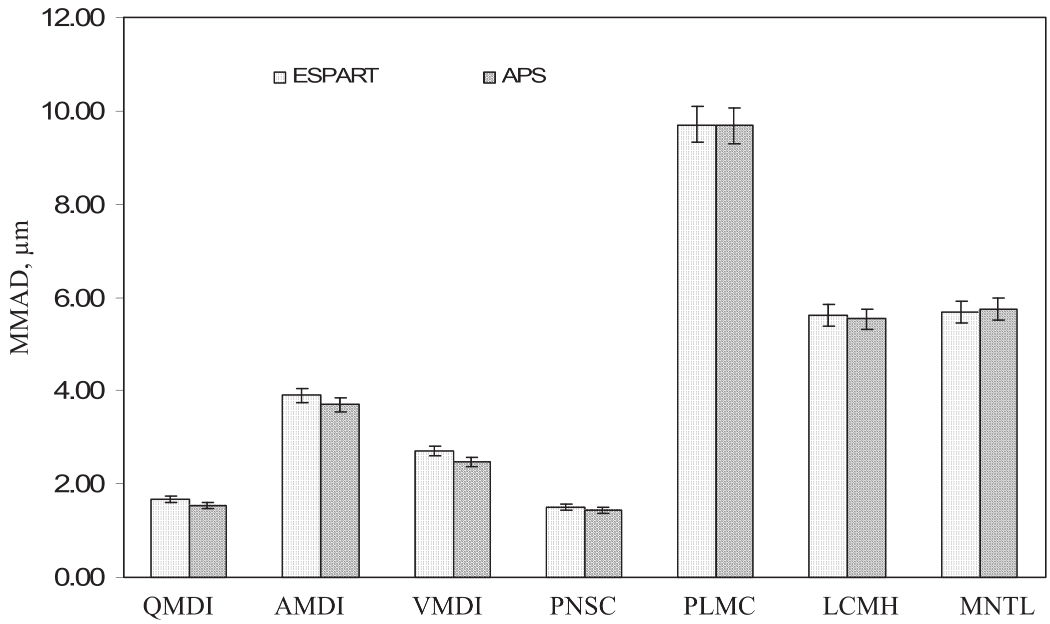
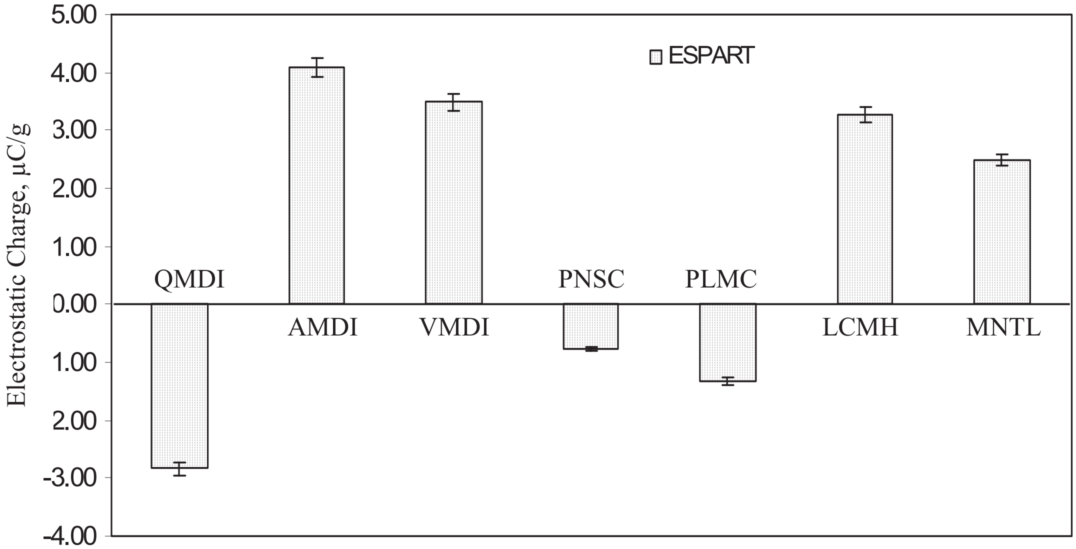
VMDI - Ventolin Metered Dose Inhaler, PNSC - PARI-LC Plus Nebulizer Sodium Chloride
PLMC - Polymer Microsphere, LCMH - Lactose Monohydrate, MNTL - Mannitol

Figure 4: Analyzed results of tested aerosols' count median aerodynamic diameter (CMAD), which were measured simultaneously by the Electronic Single Particle Aerodynamic Relaxation Time (ESPART) Analyzer and the Aerodynamic Particle Sizer (APS) Spectrometer.



QMDI - Qvar Metered Dose inhaler, AMDI - Albuterol Sulphate Metered Dose Inhaler,
VMDI - Ventolin Metered Dose Inhaler, PNSC - PARI-LC Plus Nebulizer Sodium Chloride
PLMC - Polymer Microsphere, LCMH - Lactose Monohydrate, MNTL - Mannitol

Figure 5: Analyzed results of tested aerosols' mass median aerodynamic diameter (MMAD), which were measured simultaneously by the Electronic Single Particle Aerodynamic Relaxation Time (ESPART) Analyzer and the Aerodynamic Particle Sizer (APS) Spectrometer.



QMDI - Qvar Metered Dose inhaler, AMDI - Albuterol Sulphate Metered Dose Inhaler,
VMDI - Ventolin Metered Dose Inhaler, PNSC - PARI-LC Plus Nebulizer Sodium Chloride
PLMC - Polymer Microsphere, LCMH - Lactose Monohydrate, MNTL - Mannitol

Figure 6: Analyzed results of tested aerosols' net electrostatic charge (charge-to-mass ratio) in micro-coulomb per gram measured by the Electronic Single Particle Aerodynamic Relaxation Time (ESPART) Analyzer. Aerodynamic Particle Sizer Spectrometer does not support characterization of this property by design.