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Effect of Charge on the Deposition of Electrostatically Charged Inhalable Aerosol in Lung Model

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Abstract

Inhalable drugs are widely used for treating lung diseases such as asthma, emphysema, and cystic fibrosis. The aerosol particles in these inhalable drugs may be charged electrostatically. The deposition of these inhaled therapeutic aerosol particles in the different regions of the lung depends on the particle aerodynamic diameter, electrostatic charge distribution, particulate number density, breathing rate, aerodynamics of the lung, ambient temperature, and relative humidity (RH). The primary mechanisms for lung deposition of inhaled particles are impaction, gravitational settling, diffusion, interception, and electrostatic attraction. To simulate lung deposition, electrostatically charged aerosol particles are introduced through a throat section into a glass bead lung model. The E-SPART analyzer was used to measure aerosol deposition as a function of the particle charge and size. Experiments were carried out to determine the increase in deposition efficiency as a function of the net charge-to-mass ratio (Q/M) of aerosol particles. Using a fairly monodisperse aerosol of 5.0 μm count median aerodynamic diameter, it was found that the total deposition efficiency increased from 54% to 91% when Q/M increased from 0.5 to 9.67 μC/g. The data show that enhanced delivery of the therapeutic aerosol in the lung can be achieved by controlling the electrostatic charge on the inhaled aerosol particles.

Introduction

Inhalable drugs are widely used for treating lung diseases such as asthma, emphysema and cystic fibrosis. Localized delivery of drugs to the pulmonary tract has become an increasingly important and effective therapeutic method. Several studies show the clinical advantage of inhalation aerosols over systemic therapy for the treatment of lung disorders. Relatively small doses are required for effective therapy, since delivering small doses of active ingredients directly to the lung effectively targets the drug, thereby maximizing therapeutic effect. Lower dosage regimens may provide considerable cost savings, especially with expensive therapeutic agents. The efficiency of a therapeutic aerosol is mainly determined by the amount of drug reaching the target site, which in turn depends on the particle size, charge distribution, particulate number density, and the breathing rate, aerodynamics of the lung, and ambient temperature and relative humidity (RH). The primary mechanisms for inhaled particle deposition are impaction, gravitational settling, diffusion, interception and electrostatic attraction. Electrostatic charge has been shown to influence the deposition of inhaled particles within the lung (Balachandran et al., 1991; Melandri et al., 1983). It was found that with an increase in charge on the inhalable particles, there was an increase in the fraction of drug reaching the periphery of the pulmonary tract. Drug residence time and therefore duration of effect at the site of action is a function of the rate of pulmonary clearance and pulmonary absorption, which in turn are determined by several factors, including the physicochemical properties of the drug, such as molecular weight, dissolution rate, partition coefficient, and charge. The therapeutic effect and the duration of this effect are determined not only by the drug dose and its pulmonary clearance, but also by particle-to-particle interactions (Bailey et al., 1998; Balachandran et al., 1997). These pulmonary drugs are inhaled from dry powder inhalers, metered dose inhalers, spinning disk aerosol generators, atomizers, or nebulizers. The overall success of an aerosol delivery system is determined by its components, the mechanism of dispersion, and patient compliance. The challenges encountered with aerosol drug delivery include the control of particle size, distribution, and the reproducibility of dose uniformity.

The various sections of the experimental setup (Fig. 1) to study the deposition were the spinning disk aerosol generator, hollow cast larynx section, glass bead lung model, sampling chamber, and the particle analyzer E-SPART (Mazumder et al., 1991). A spinning disk aerosol generator is used to produce aerosol particles in the range of 1-25 μm. The ring electrode around the spinning disk of the aerosol generator charges the particles, and by varying the voltage the magnitude and polarity of charge of the particles can be changed. Aerosolizing a liquid solution produces the inhalable particles generated by the spinning disk aerosol

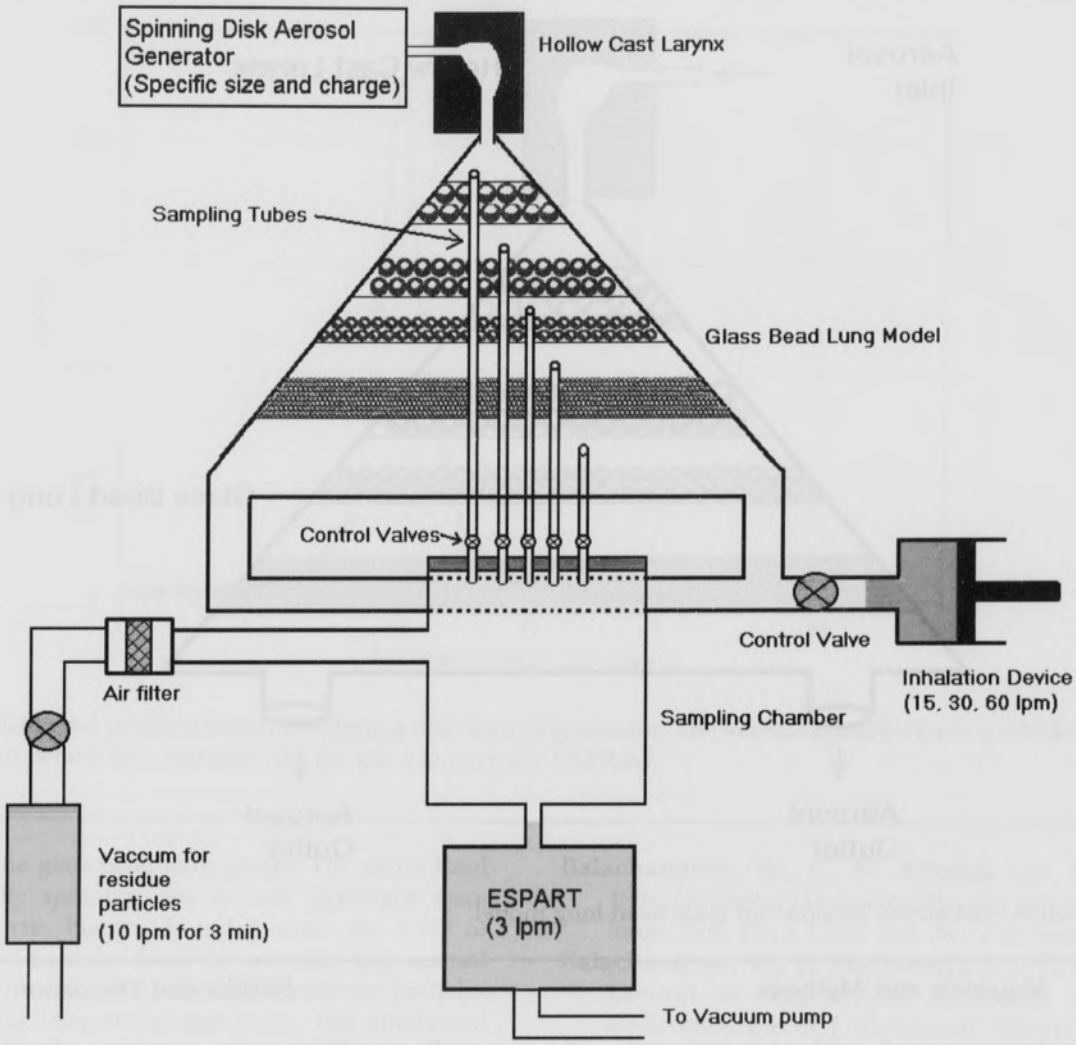

Fig. 1. Shows the site-specific deposition system to study the effect of charge on drug particles in surrogate lung models.

generator. The liquid solution is injected as a continuous stream at a constant flow rate onto a spinning disk. Due to the high velocity of the spinning disk liquid droplets are produced, which form an aerosol cloud. The droplets are charged through induction charging. The airflow stream carries this cloud.

The inhalable charged particles enter the hollow cast throat section and the glass bead lung model (Fig. 2), where they are deposited. A multi-layer granular bed filter was designed to approximate the deposition characteristics of the bronchial and alveolar regions of the human lung. The sizes of the beads were selected to correspond to the sizes of different bronchial orders as given in the Olson model of the lung (Gao, 1994). The cross sectional area of the filter increases as bead size decreases so that the calculated Reynolds number through the beads is equal to that specified in the Olsen model for the corresponding bronchial and trachobronchial orders. The airflow velocity decreases by a factor of 250 in an actual human lung as air reaches the lower regions of the lung. This is a result of the increase in total cross-sectional area due to the large number of airways. The particles in the different regions can be analyzed for the aerodynamic diameter and charge-to-mass ratio (Q/M) distributions using the E-SPART. From the different regions of the glass bead lung model, the particles enter the sampling chamber connected to the E-SPART particle analyzer, which measures the size and charge distributions of particles in the aerodynamic diameter range of 1-25 μm.

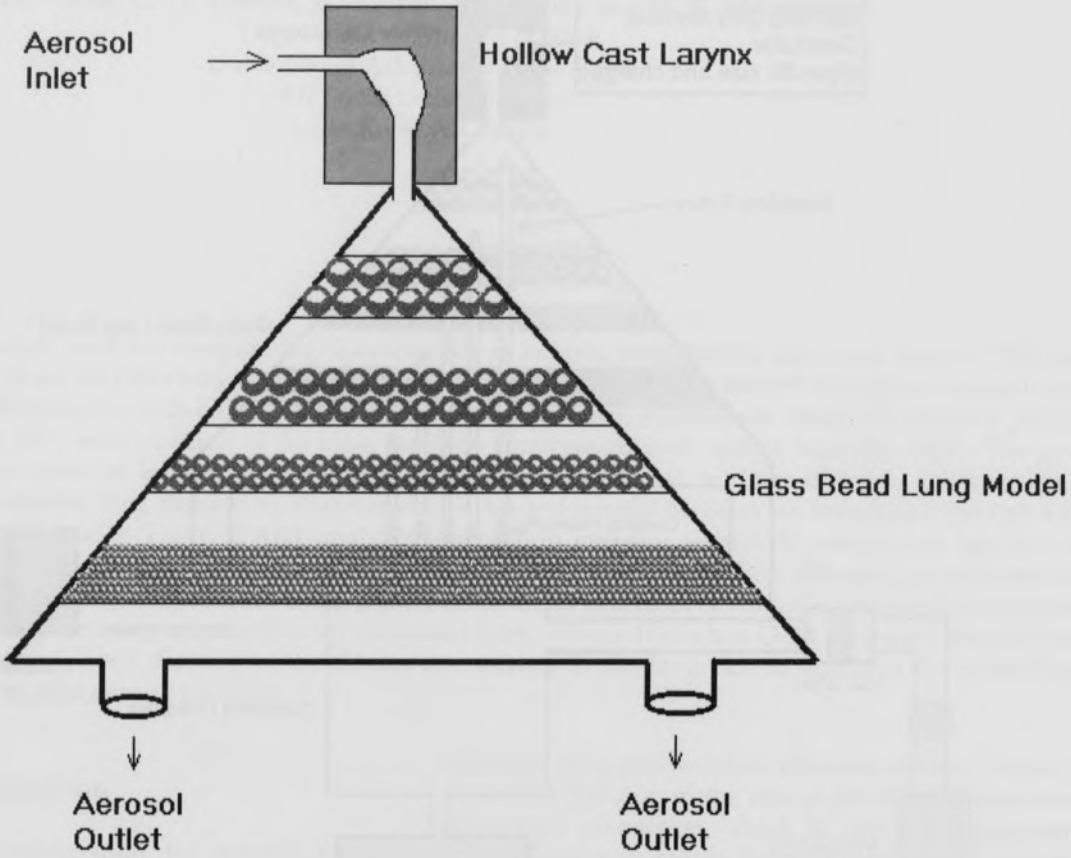

Fig. 2. Shows hollow cast larynx section and glass bead lung model.

Materials and Methods

To generate the test aerosol, a solution of 2% emery oil and 98% alcohol was prepared. Changing the percentage of emery oil in the alcohol solution controlled the particle size. The liquid solution was fed to the spinning disk aerosol generator to produce inhalable aerosol particles of specific size. By applying voltage on the ring electrode, the particles acquired charge. When +30 volts were applied on the ring electrode, particles with an average Q/M of −4.21 μC/g were obtained. When −30 volts are applied, particles with a Q/M of + 9.67 μC/g were obtained. Test aerosols with well-characterized size and charge distributions entered the hollow cast larynx section where the large particles deposited (Wesley et al., 2000; Schlesinger et al., 1977). The particles then entered the glass bead lung model. The particles, depending on their size and charge, deposited in the various sections of the model. The particles from the different sections of the glass bead lung model were sampled to determine the particle size and charge distribution. The E-SPART sampled the particles from the sampling chamber at a rate of 3 lpm.

Results and Discussion

Figures 3-8 show the particle size distributions (PSDs) of the aerosol particles from the glass bead lung model. Lognormal distribution was selected empirically to fit the wide range and skewed shape of aerosol size distributions. Keeping all variables such as airflow and liquid solution flow rate constant, the aerosol cloud was fed from the aerosol generator through the three layers of the glass bead model and its PSD was measured. When the particle number density was high, there was mutual repulsion between the particles, and they deposited on the glass beads and the wall. However, if the particle number density was low, the image force acting on the particle due to the presence of glass beads and the wall was the principal force responsible for particle deposition.

Figure 3 shows the PSD of particles coming from the spinning disk aerosol generator as measured by the E-SPART. The number of particles was found to decrease from 18136 to 8184 (Fig. 4) when measured for 5 min at the inlet and outlet. Thus the efficiency of deposition was found to be only 54%, and the remaining 46% of the particles

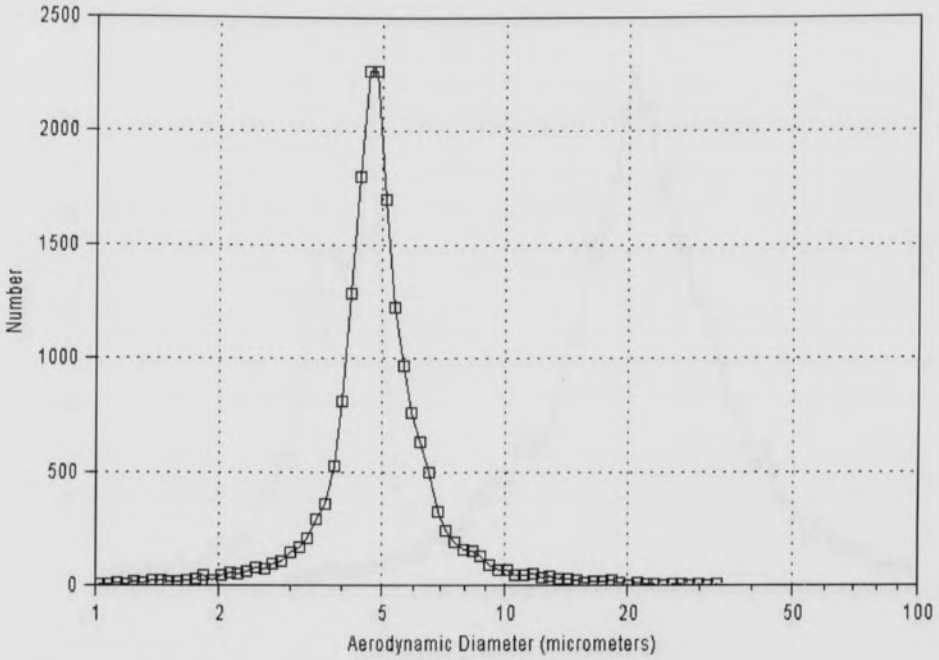

Fig. 3. PSD of uncharged particles from the spinning disk aerosol generator. The aerosol particles have a CMAD = 4.8 μm and MMAD = 5.5 μm, which was measured by the particle analyzer ESPART.

passed through the glass bead lung model. The aerosolized particles from the spinning disk aerosol generator were fairly monodisperse. Figures 5 and 6 show the PSD of positively charged particles from the spinning disk aerosol generator and from the model. The PSD after the particles passed through the lung model was wider. The number of particles was found to decrease from 14998 to 1294, increasing the deposition efficiency to 91%. Similarly, it was found that for negatively charged particles the particle count fell from 15727 to 1036, resulting in an efficiency of 93%.

Conclusions

The particle deposition was found to be dependent on the distribution of particle charge and size. Due to the image forces or the mutual repulsion of the particles, the deposition is found to increase. By controlling the charge and particle size distributions of the drug particles, it may be possible to control their deposition in the various regions of the lung.

Literature Cited

Bailey, A., A. Hashish, and **T. Williams.** 1998. Drug Delivery by Inhalation of Charged Particles. J. Electrostat. 44:3-10.

Balachandran, W., C. N. Ahmad, and **S. A. Barton.** 1991. Deposition of electrically charged drug aerosols in lungs. Inst. Phys. Conf. Ser. No. 118: Section 1:57-62.

Balachandran, W., E. Machowski, and **C. Hudson.** 1997. Control of drug aerosol in human airways using electrostatic forces. J. Electrostat. 40&41:579-584.

Gao, S. 1994. Development of Two-Component Packed granular filters with triboelectric enhancement. Ph.D. Dissertation. Department of Applied Science. University of Arkansas.

Mazumder, M. K., R. E. Ware, T. Yokoyama, B. J. Rubin, and **D. Kamp.** 1991. Measurement of particle size and electrostatic charge distributions on toners using E-SPART analyzer. IEEE Trans. Ind. Appl. Vol. 27 4:611-619.

Melandri, C. T. G., V. Prodi, T. De. Zaiacomo, M. Formignani, and **C. C. Lombardi.** 1983. Deposition of Charged particles in the human Airways. J. Aerosol Sci. Vol. 14 5:657-669.

Schlesinger, R. B., D. E. Bohning, and **T. L. Chan.** 1977. Particle deposition in a hollow cast of the human trachobronchial tree. J. Aerosol Sci. Vol. 8:429-445.

Wesley H. and **H. Warren.** 2000. Effect of entry conditions on monodisperse aerosol deposition in the mouth and throat region. Respiratory Drug Delivery VII, 557-559.

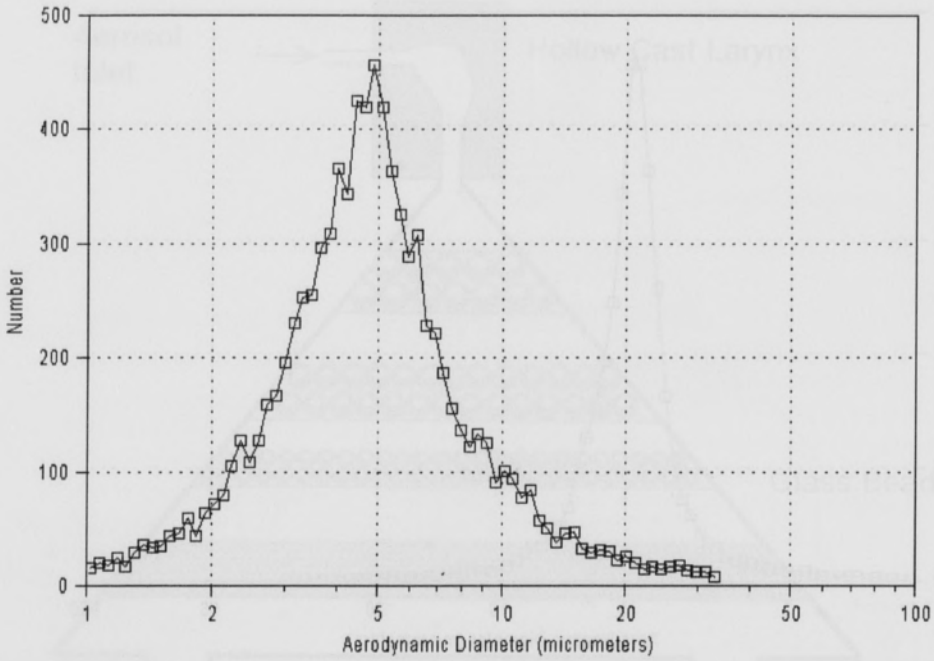

Fig. 4. PSD of uncharged particles collected after the aerosol passed through the first three sections of the lung model. Particle CMAD = 4.5 μm and MMAD = 6.9 μm.

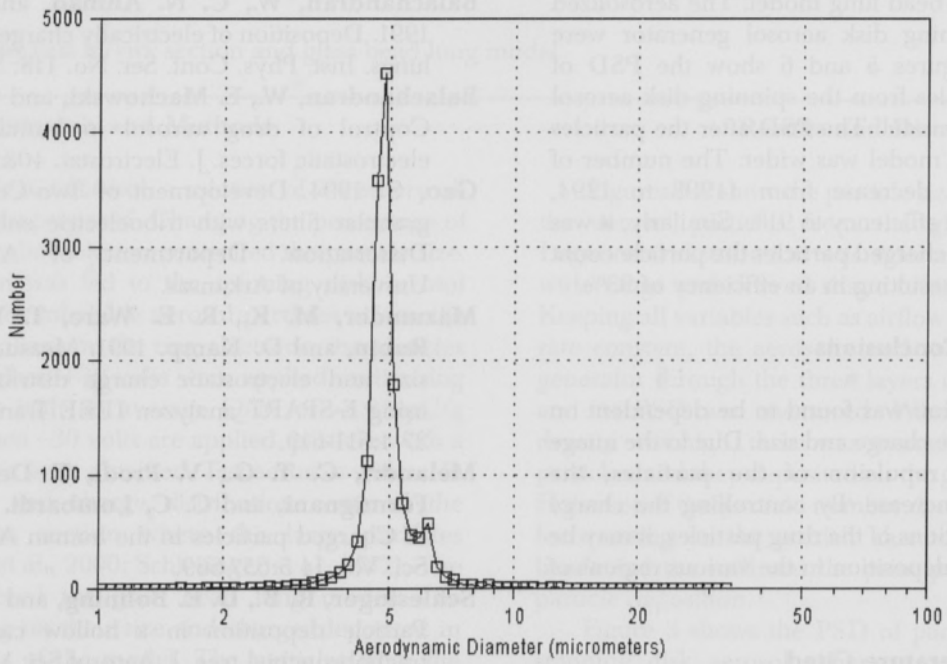

Fig. 5. PSD of positively charged particles collected from the spinning disk aerosol generator. Particle CMAD = 4.8 μm and MMAD = 4.9 μm.

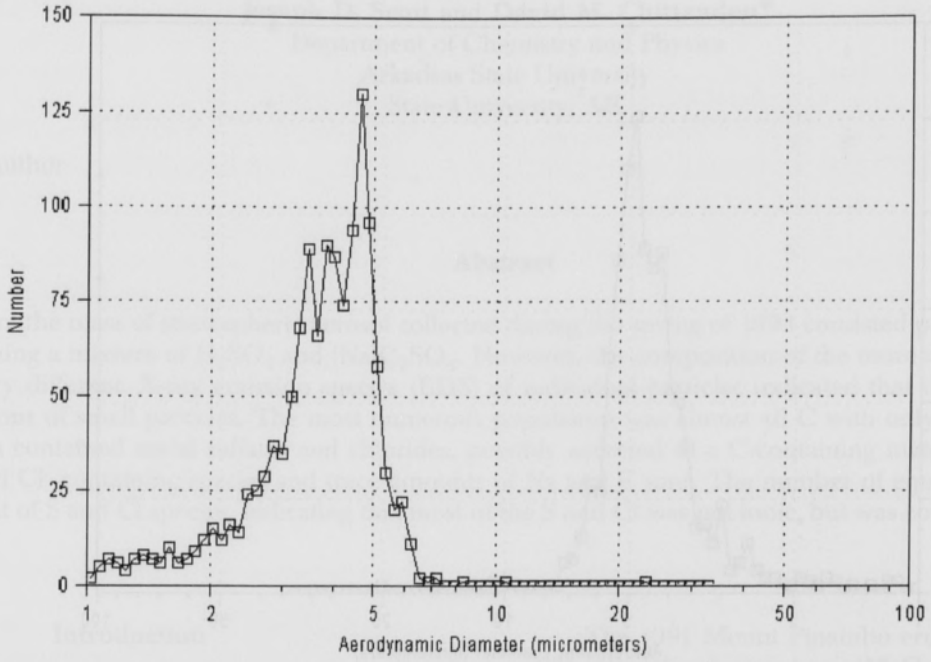

Fig. 6. PSD of positively charged particles collected after the aerosol passed through the first three sections of the lung model. Particle CMAD = 3.9 μm and MMAD = 4.6 μm.

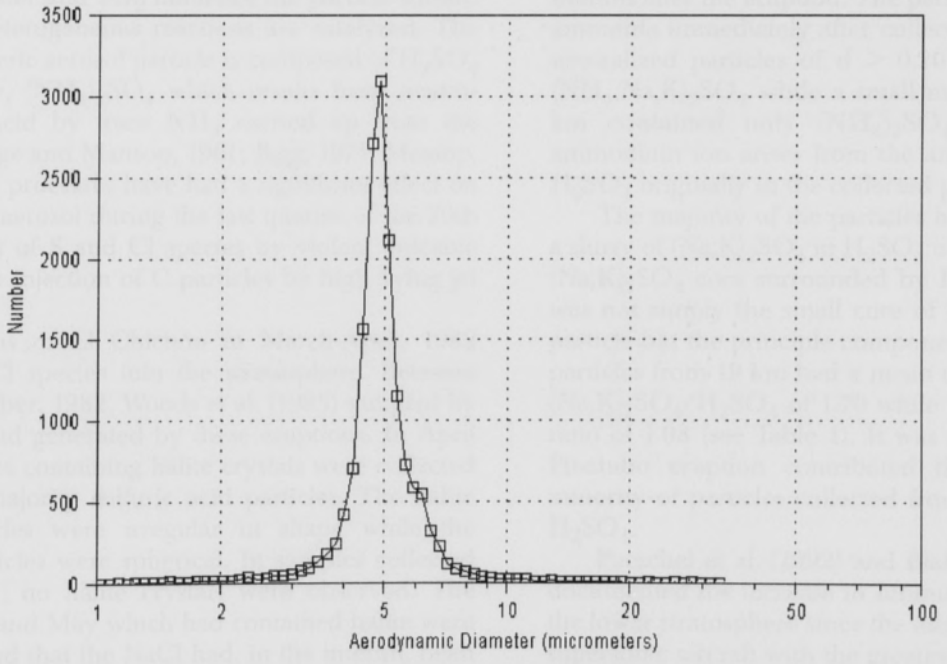

Fig. 7. PSD of negatively charged particles collected from the spinning disk aerosol generator. Particle CMAD = 4.9 μm and MMAD = 5.1 μm.

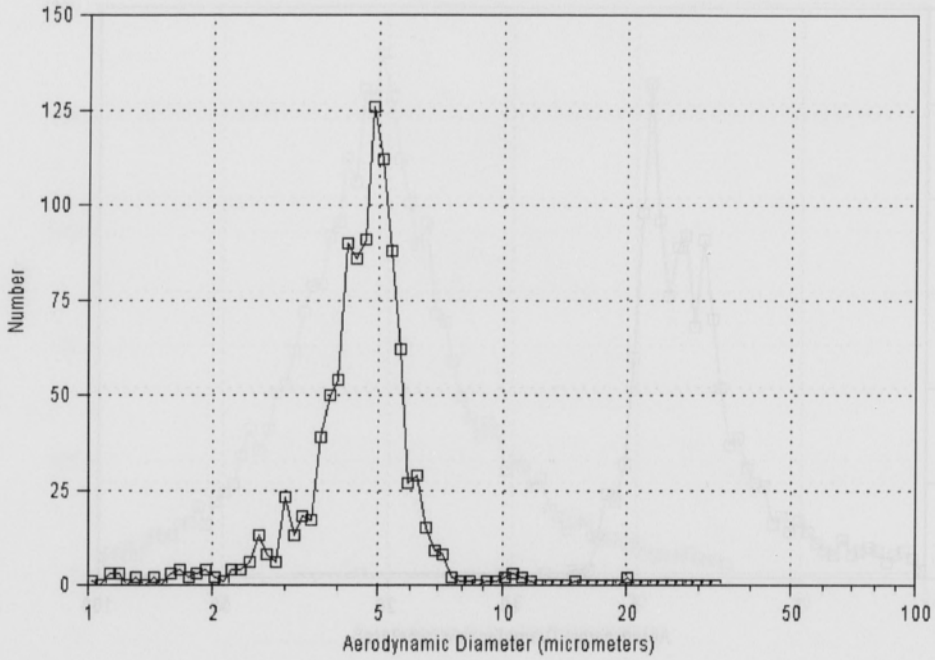

Fig. 8. PSD of negatively charged particles collected after the aerosol passed through the first three sections of the lung model. Particle CMAD = 4.7 μm and MMAD = 5.1 μm.