A Single-Pass "Bubbling" Aerosol Generator for Inhalation Studies

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ABSTRACT

Inhalation exposure studies of pathogens require stable and reliable aerosol generators. When fragile biological particles are aerosolized, the organisms' structural and biological integrity must be preserved. Air jet as well as ultrasonic nebulizers induce significant stress and reduced viability due to forceful agitation, high shear force and repeated "recycling" of the carrier media. Recently, an aerosol generator which produces particles from a bubbling liquid was reported. This technique promised low shear force but a significant part of the fluid was still being recycled.

We describe an improvement in particle generation from a bubbling liquid by eliminating fluid reuse. In this device, a thin film of liquid is pumped to the top surface of a porous stainless steel disk. Air is forced through the disk from below and breaks the liquid film into bubbles that subsequently burst, releasing particles to the air. The particles are captured by eight air streams of dry air moving parallel to the disk. These streams originate from radial ports situated above the disk. The few particles not captured by the drying streams are collected at the bottom of the glass vessel and play no further role in aerosolization process.
We aerosolized *P. fluorescens* bacteria and polystyrene latex particles (1 micron) and determined that the particle concentration increased when the air flow through the porous disk was increased from 2 to 5 L/min. The variation of drying air streams from 10 to 30 L/min also produced increased aerosol concentrations. Distance between the drying air streams and the porous disk had little effect on particle output.

Generation of particles for one hour demonstrated stability of the aerosol concentration. Since organisms go through the aerosolization process only once, no significant decrease in bacterial viability is expected during prolonged generation.

GOAL OF THE STUDY

To develop and analyze a novel, liquid fed aerosol generator that utilizes bursting bubbles and has the potential for stable aerosol concentration with minimal damage to bacteria during prolonged use.

EXPERIMENTAL SETUP & PROCEDURES

1. **INTRODUCTION**. Inhalation studies, instrument calibration and evaluation of pathogen collection methods require stable and reliable aerosol generators. Also, when aerosolizing fragile biological particles one has to preserve the organisms' structural and biological integrity. Commonly used jet nebulizers have been shown to induce significant stress to biological particles due to their high shear force and repeated "recycling" of the microorganism suspension. One of the recent advances in this field was the introduction of an aerosol generator which produces particles from a bubbling liquid. This technique had low shear forces, but a significant part of the suspension was still repeatedly reused. Here we present a significant improvement in particle generation from a bubbling liquid by eliminating suspension reuse.

2. **"BUBBLING" AEROSOL GENERATOR**. In our new aerosol generator (Figure 1), a thin liquid film is formed on the top of a porous stainless steel disk by a liquid suspension delivered at a rate ranging from 0.17 to 2 ml/min. Air, forced through the disk, breaks the liquid film into bubbles that subsequently burst releasing particles into the air. In the initial version of the device, the particles released from the bubbles were captured by eight air streams of dry air moving parallel to the porous disk. These streams originated from circular ports situated above the porous disk. Particles not captured by the drying streams (they constitute a small fraction) were collected at the bottom of the glass vessel and played no further role in aerosolization process. After initial tests, we realized that particle aerosolization from the bubbling liquid can be very efficient, even without the use of eight streams of drying air inside the generator, when and if sufficient amount of air is forced through the porous disk. Thus, in all the tests presented here, the additional drying air was not employed.

3. **TEST PARAMETERS AND PROCEDURES.** In our tests, particles and fragments of liquid bubbles aerosolized using the "bubbling" aerosol generator entered a dry air stream of Q_{DRY}=50 L/min; thus, the liquid carrier is evaporated and only particles of interest remain in the air stream. The concentration of aerosolized particles was measured using on Optical Particle Counter (model 1.108, Grimm Technologies Inc., Douglasville, GA). In some tests, a Collison nebulizer (BGI Inc., Waltham, MA) was operated at 50 psi in parallel to the bubbling generator to compare performance of the two generators.

   Test parameters:
   - Air flow rate through the porous disk, Q_{BUB}: 2, 5, 10, and 20 L/min
   - Pore size of the porous disk: 0.2, 0.5, 1.0, 2.0, 5.0, and 10.0 µm
   - Liquid supply flow rate, Q_{LIQ}: 0.17, 1.0, 2.0 mL/min
   - Biological test particles: *Pseudomonas fluorescens* vegetative cells
   - Non-biological test particles:
     - Monodisperse Polystyrene Latex (PSL): 0.93, 2.93, and 5.09 µm
     - Polydisperse Sodium Chloride (NaCl) particles from saline solution

Figure 1. Left picture shows the assembled "bubbling" aerosol generator while the right panel shows the porous disk and liquid delivery system. Drying air may be added tangentially if needed.

RESULTS

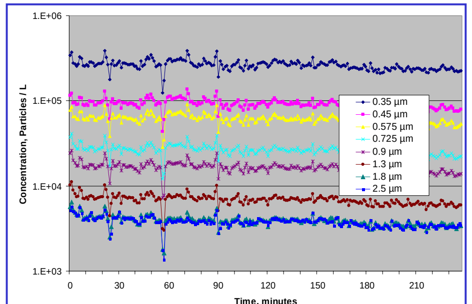

Figure 2. Stability of particle output by the "Bubbling" Aerosol Generator, when a polydisperse NaCL aerosol is made. Disk pore size = 0.5 µm, Liquid supply rate Q_{LIQ} = 0.17 mL/min, Bubbling air flow Q_{BUB} = 7L/min.

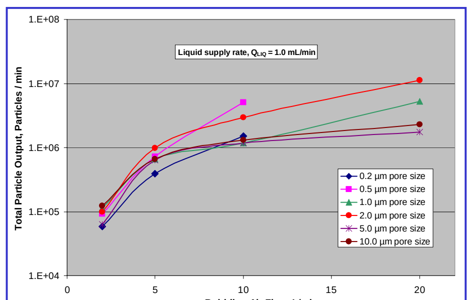

Figure 3. Performance of the "Bubbling" Aerosol Generator when aerosolizing 0.93 µm PSL particles at various air flow rates to the Bubbler while examining the effect of disk's pore size on the bubble generation at a single (fixed) liquid supply rate.

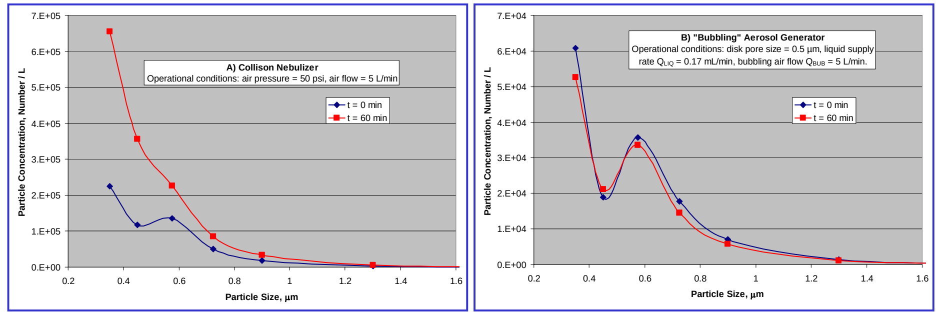

Table 1. Changes in viability of *Pseudomonas fluorescens* bacteria over time when aerosolized using a Collison Nebulizer versus the "Bubbling" Aerosol Generator.

	Collison Nebulizer		"Bubbling" Aerosol Generator	
	t = 0 min	t= 90 min	t = 0 min	t= 90 min
Concentration of viable bacteria in the liquid suspension, $C_{LIQ} = N_{CFU} / mL_{LIQ}$	1.53×10^9	1.37×10^9	1.04×10^9	1.16×10^9
Concentration of total aerosolized bacteria, $C_{AIR} = N_{BACTERIA} / L_{AIR}$	1.77×10^5	3.26×10^5	5.67×10^5	6.35×10^5
Ratio of viable liquid-borne vs. total airborne bacterial concentration, C_{LIQ} / C_{AIR}	8.60×10^3	4.19×10^3	1.83×10^4	1.83×10^4
Change in C_{LIQ} / C_{AIR} over time, %	NA	**- 51.3**	NA	**0**

Figure 4. Changes in bacterial size distribution over time when aerosol is produced by A) Collison nebulizer or B) "Bubbling" Aerosol Generator. **Table 1** illustrates changes in bacterial viability when aerosol is produced by two different methods.

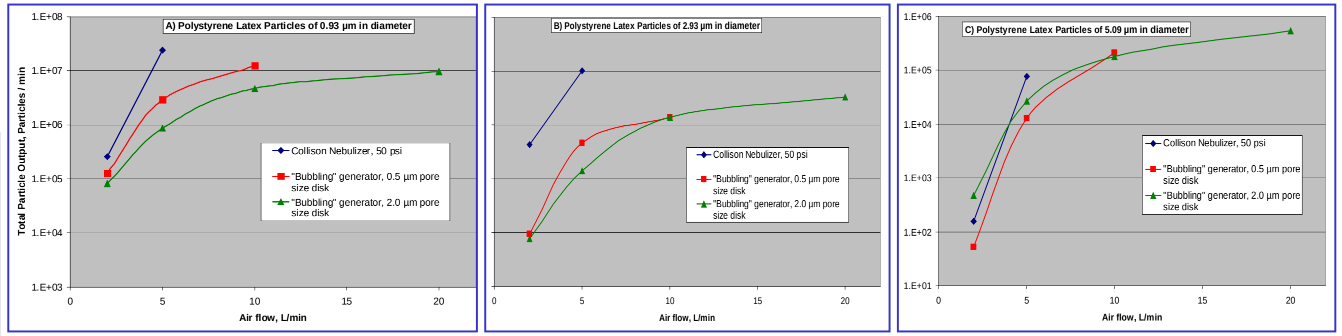

Figure 5. Comparison of the Collison nebulizer and the "Bubbling" Aerosol Generator when generating Polystyrene Latex (PSL) particles of different sizes. "Bubbling" generator's liquid supply Q_{LIQ} = 1.0 mL / min. Collison nebulizer operated at 50 psi.

DISCUSSION AND CONCLUSIONS

- The "Bubbling" aerosol generator produces a stable particle concentration with minimal changes with time of operation.
- Continuous aerosolization of *P. fluorescens* bacteria for 90 minutes with the "bubbling" generator did not result in changes of bacterial size distribution while the size distribution of the bacteria when aerosolized by a Collison nebulizer showed significant changes.
- Viability of *P. fluorescens* bacteria aerosolized using "bubbling" generator did not change during continuous aerosolization for 90 minutes; in contrast, the viability of the bacteria aerosolized by a Collison nebulizer decreased by more than 50%.
- The concentration of particles produced by the "bubbling" aerosol generator increases with increasing air flow through the disk and the increasing liquid delivery rate.
- Disks with porosity of 0.5 and 2.0 µm were identified as those resulting in best performance.
- The "bubbling" generator aerosolizes particles of 3µm and larger with the same or better efficiency as the Collison nebulizer.
- **This work demonstrates that the "Bubbling" Aerosol Generator has sufficient stability to produce constant aerosol concentrations over time with little change in particle size distribution and minimal damage to sensitive microorganisms; it is applicable for use in inhalation studies where extended delivery of stable and undamaged biological aerosols is required. Other applications are being investigated.**

ACKNOWLEDGEMENTS

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