Comparison of Three Aqueous Aerosol Inhalation Devices for Delivering Anti-tuberculosis Bacteriophage D29
1. Department of Mechanical Engineering, University of Alberta, Edmonton, AB, Canada; 2. Faculty of Pharmacy, University of Sydney, Sydney, NSW, Australia; 3. Department of Chemical and Materials Engineering, University of Alberta, Edmonton, AB, Canada; 4. Department of Biological Sciences, University of Pittsburgh, PA, USA; 5. Centenary Institute of Cancer and Cell Biology, and Sydney Medical School, Royal Prince Alfred Hospital, and University of Sydney, Sydney, NSW, Australia

Introduction
Antibiotic-resistance
Phage therapy is an alternative [1,2]

Materials and Methods

Results and Discussion

![Jet Nebulizer](image1)

**Table 1: Phage D29 deactivation due to aerosolization and rate active phage reach the respective devices.**

<table>
<thead>
<tr>
<th>Inhalation Device</th>
<th>Deactivation (%)</th>
<th>Active Phage Delivery Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jet Nebulizer</td>
<td>99.981 ± 0.005</td>
<td>7.1x10^6 ± 1.7x10^6 pfu/min</td>
</tr>
<tr>
<td>Vibrating Mesh Nebulizer</td>
<td>60 ± 11</td>
<td>3.3x10^6 ± 0.8x10^6 pfu/min</td>
</tr>
<tr>
<td>Soft Mist Inhaler</td>
<td>72 ± 14</td>
<td>4.6x10^6 ± 2.0x10^6 pfu/dose</td>
</tr>
</tbody>
</table>

* < 90% deactivation is acceptable

![Vibrating Mesh Nebulizer](image2)

**Figure 7: Schematic of the soft mist inhaler. The shear and pressurization was relatively harmful to D29.**

![Soft Mist Inhaler](image3)

**Figure 5: Droplet production with the jet nebulizer.**

**Figure 6: Vibriostat mesh nebulizer droplet production mechanism: (a) the structure surrounding the aperture plate, (b) close-up of a funnel-shaped orifice in the aperture plate illustrating the micropump action, which ejects droplets.**

**Figure 4: Mathematical prediction for phage nebulization cycle count with the jet nebulizer.**

**Figure 3: Tested inhalation devices & collection filter [6-9].**

Conclusions

- Ensure your inhalation device does not deactivate the phage before starting pulmonary experiments
- Titer reduction is inhalation device- and phage strain-dependent
- Jet nebulization can deactivate D29; deactivation is likely due to stresses during baffle impaction and renebulization
- Other phage readily survive jet nebulization [10]
- Vibrating mesh nebulizer is a good choice for starting animal studies with D29
- Soft mist inhaler may be useful for self-administration, being pocket-sized and multidose
- Phage therapy using inhalation devices is feasible, and promising

References

Acknowledgements
The authors thank Arlene Oatway for help with the transmission electron micrograph and Jim Finck for providing Aerogen nebulizers and equipment.

The authors thank Arlene Oatway for help with the transmission electron micrograph and Jim Finck for providing Aerogen nebulizers and equipment.

**Figure 2: Lytic cycle [5], and M. smegmatis plaque assay plate.**

**Figure 1: Morphological components of a tailed phage [4], and TEM of phage D29, which lyses M. tuberculosis.**


**Image from: http://d3hjf51r9j54j7.cloudfront.net/wp-content/uploads/sites/5/2008/01/spiriva_respimatw_image1_3.jpg**

**Image from: http://www.med.de/Bilder/Aerogen%20Solo%20Vernebler%20Aeroneb.jpg**

**Image from: http://www.nlm.nih.gov/medlineplus/Bacteriophage.html**


**Image from: http://www.nlm.nih.gov/medlineplus/Bacteriophage.html**

**Image from: http://www.nlm.nih.gov/medlineplus/Bacteriophage.html**

**Image from: http://www.nlm.nih.gov/medlineplus/Bacteriophage.html**

**Image from: http://www.nlm.nih.gov/medlineplus/Bacteriophage.html**

**Image from: http://www.nlm.nih.gov/medlineplus/Bacteriophage.html**

**Image from: http://www.nlm.nih.gov/medlineplus/Bacteriophage.html**