Inhalation Sciences

Exposure of the Tracheally Intubated Rat to Aerosolized Lunar Dust Surrogate JSC1A-vf

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Background

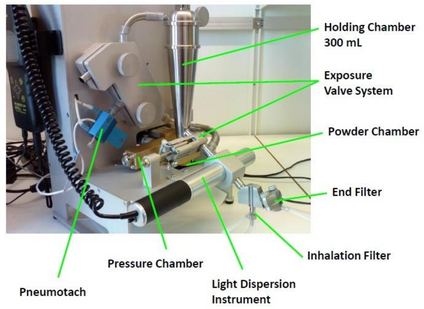
Exposure to inhaled mineral dusts is a long-known cause of acute as well as chronic disease in humans. The causative exposures can either be episodic high-level exposures or more chronic low-level background exposures. One particular example of the former scenario is the risk of high level exposures to mineral dusts during manned missions to the moon or other extraterrestrial bodies. However, there has been a paucity of methods for studying biological effects in laboratory animals following controlled inhalation exposures to higher concentrations of respirable particles.

The purpose of the current research was to expose the tracheally intubated rat via inhalation to high concentrations of the aerosolized lunar dust surrogate JSC1A-vf (Courtesy of Dr. John James, NASA).

Materials and Methods

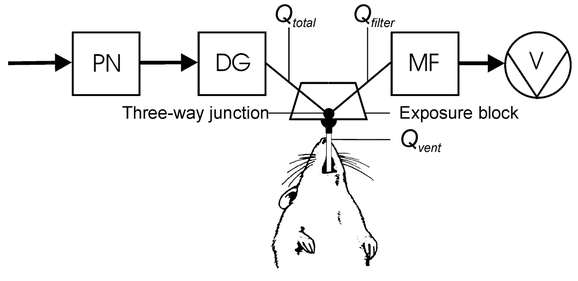
Aerosols of JSC1A-vf with a Mass Median Aerodynamic Diameter (MMAD) of 2.5 µm, at aerosol concentrations of approximately 2.5 mg/L were generated with the Dustgun aerosol generator.

The Dustgun Aerosol Generator



Rats under light anesthesia were intubated with an endotracheal catheter. Two groups of animals were exposed one at a time to target lung burdens of 1 and 3 mg JSC1A-vf, respectively. The PreciseInhale dosing system was used for active control of the exposures. The control was based on local aerosol concentration measured with a light dispersion instrument in the breathing zone, combined with the ventilation pattern of the individual animals. Immediately after exposures, the animals were euthanized and lungs were harvested for analysis of the mineral dust content. The analysis was based on the dust silica component, using tissue digestion and a spectrophotometric method.

The Exposure Model: Tracheally Intubated Rat



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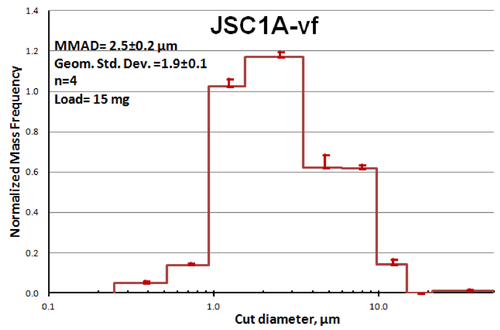
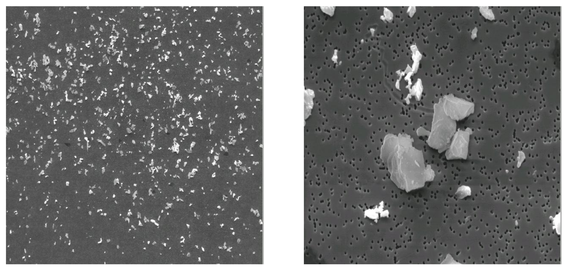
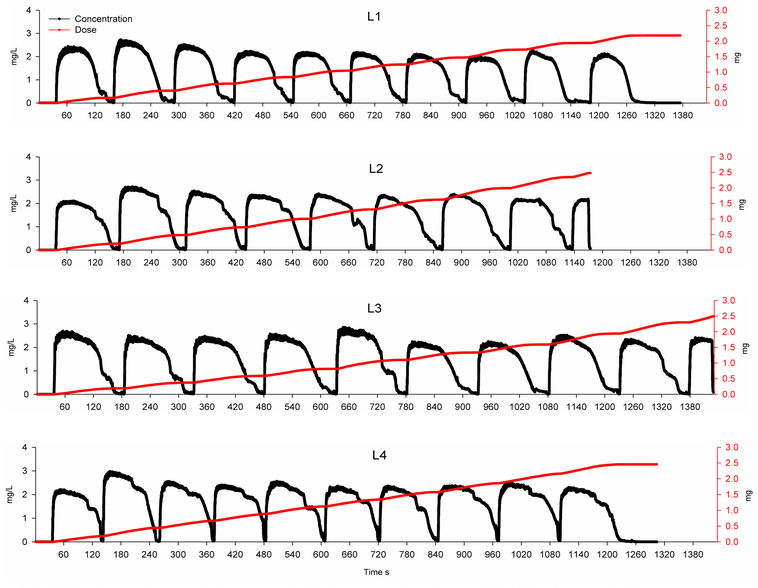
Aerosol Particle Size Distribution



Scanning Electron Micrograph of Aerosolized JSC1A-vf



Aerosol Concentration and the Cumulative Dose Inhaled[1]



[1] **Individually registered in four rats (L1-L4) exposed to 1 mg of JSC1A-vf aerosol. The instrument signal was corrected for a Substance Correlation Factor of 0.169.**

Results

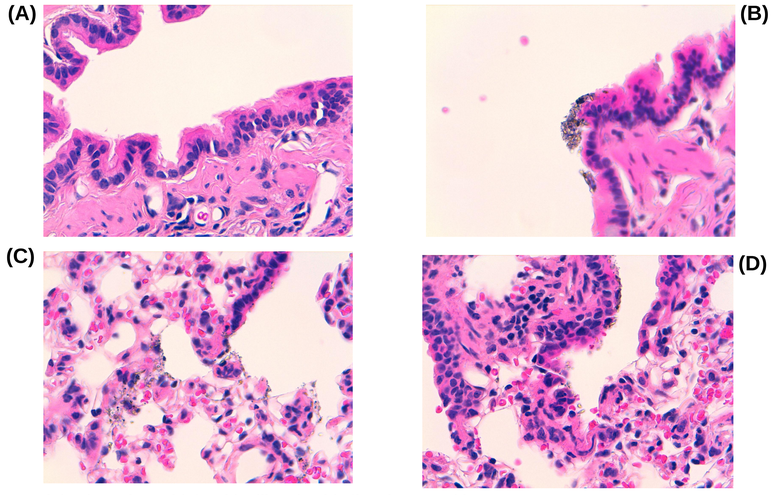
The two exposure levels were reached within about 20 min and one hr exposure time, respectively. The maximum standard deviation from the target lung burden was ±17%. Light microscopy investigation of exposed lungs demonstrated a distribution of inhaled dust throughout the lungs with a markedly denser deposition in the bronchial tree compared to the alveolar region.

***In Vivo* exposures of the endotracheally intubated rat to aerosolized JSC1A-vf: Characteristics of the exposures (mean ± SD; n=4)**

Experiment	Number of Exposure Cycles	Target Dose[1] (mg)	Inhaled Aerosol Dose[2] (mg)	Mcutoff[3] (mg)	Achieved Dose[4] (mg)	Achieved Dose; % of Target
Low dose	10±1	1.0	2.4±0.1	1.0±0.1	1.2±0.0	116±4
High dose	28±2	3.0	7.4±0.1	3.0±0.0	2.8±0.5	89±15

[1] **The projected deposited dose of aerosolized JSC1A-vf in the lung.**
[2] **Cumulative for all exposure cycles.**
[3] **The deposited dose at cutoff, expressed as the logged inhaled aerosol dose multiplied by the fractional aerosol deposition Fdep= 0.40.**
[4] **The attained dose of aerosolized JSC1A-vf deposited in the lung.**

Light microscopy images of the control lung (A), and lungs exposed to aerosolized JSC1A-vf (B-D).



(A) A large bronchiole with ciliated epithelium in control lungs.
(B) Inhaled particles on the ciliated epithelium of a large bronchiole.
(C) Inhaled particles on the epithelium of a terminal bronchiole and alveoli.
(D) Inhaled particles on the epithelium of a small bronchiole.
Hematoxylin & eosin, magnification 63X.

Conclusions

By providing a high dose-rate method for inhalation exposures, the aerosol technology may constitute a useful alternative to intratracheal instillation as a method for enablling high-level episodic exposures in toxicological studies.
Compared to nose-only inhalation exposures, where typically 2/3 of the administered dose deposits in the nasal airways, the intratracheal inhalation method provides a lung-specific dose of the study aerosol.

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