Characterization and Quantification of Manganese Aerosols for Pre-Clinical Study of Manganism

Calista-Mehitabel Okine[1], Muwu Xu[2], Ignacio Javier Novoa Cornejo[1], Justin Helman[3], Meng Wang[2], Vijaya Prakash Krishnan Muthaiah[1].

[1] Department of Rehabilitation Sciences, School of Public Health and Health Professions, State University of New York at Buffalo, Buffalo, NY, United States.
[2] Department of Epidemiology and Environmental Health, School of Public Health and Health Professions, State University of New York at Buffalo, Buffalo, NY, United States.
[3] Department of Pediatrics, Jacob School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY, United States.

Introduction

Manganese is essential for human health, but prolonged exposure to high levels of manganese can lead to a neurological disorder called **Manganism**. This health condition shares similar symptoms with **Parkinson's disease**, making it difficult to diagnose.

In pre-clinical studies, it is crucial to accurately measure and characterize manganese aerosols to understand the potential risks associated with inhalation exposure to manganese.

Objective

Welders are subjected to chronic occupational exposure to high levels of manganese (Mn) resulting in Manganism.

Towards investigating the pathomechanism of Manganism, currently, we are establishing a pre-clinical study platform.

Our objective is to characterize the Mn aerosol to simulate real-world exposures of Mn toxicity, which occurs through inhalation. As a prelude to in vitro and in vivo investigation, we characterized the Mn aerosols in this specific study and optimized the exposure rate to be implemented in our pre-clinical study.

Methods

For this project, we aerosolized the Mn particles from the Manganese Chloride solution at a 2.5 or 5 L/min flow rate to achieve 5mg/m^3 with ten puffs of Mn fumes every 5 mins, which repeats every 25 mins up to 8 h.

In this study, we measured the particle concentrations of manganese using an ultrasonic personal air sampler (UPAS) and condensation particle counter (CPC).

Further, we characterized the particle size and dispersion of Mn aerosols of different flow rates using scanning electron microscopy (SEM) with x-ray microanalysis (XRM) to analyze their effects on a cellular level.

Fig 1A: CHTechUSA. (n.d.). E-STEP. CHTechUSA. https://chtechusa.com/products_tag_smoke_E-STEP.php

Fig 1B: MyUwell. (n.d.). Valyrian III. Retrieved April 22, 2023, from https://www.myuwell.com/products/mod&kit/valyrian-III.html

Results

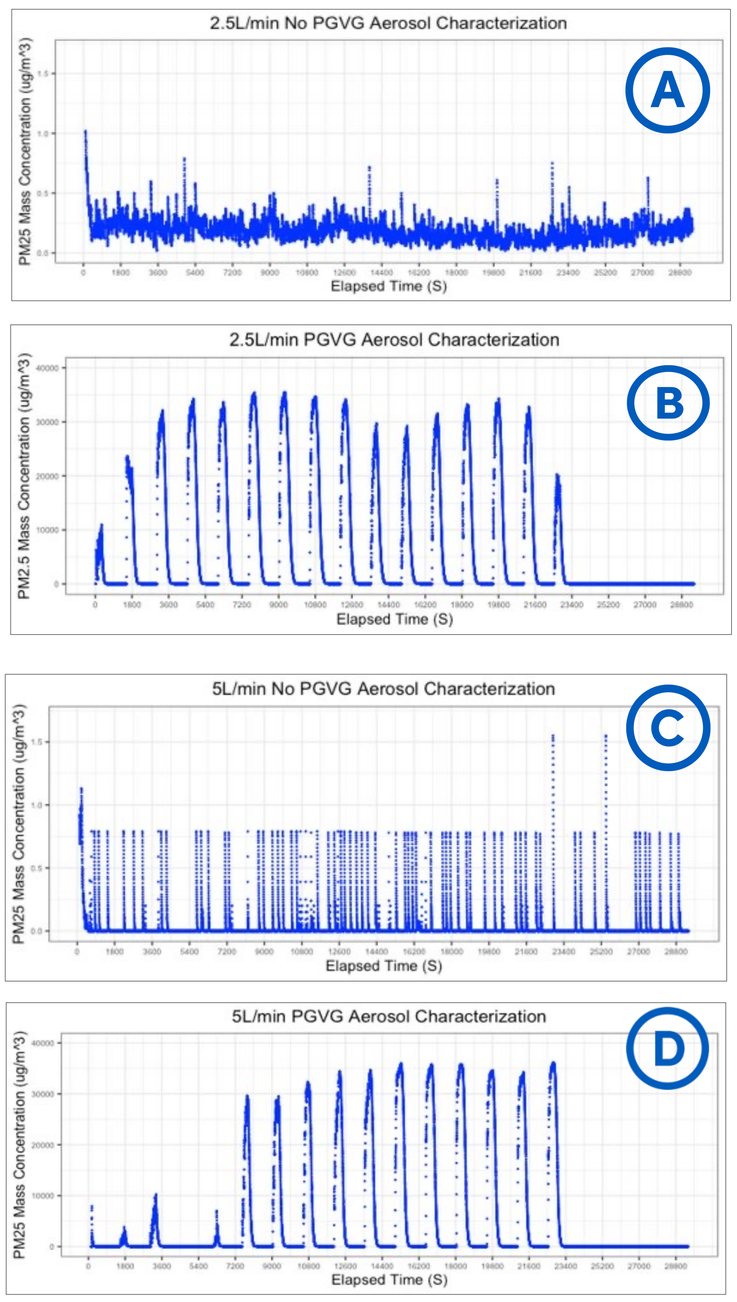
The general population manifesting sub-clinical signs of Mn toxicity had environmental air exposures >0.1 µg/m^3.

Therefore, our 5 mg/m3 of Mn fumes exceeds the threshold limit value (TLV) of 0.02 mg/m^3.

In our set-up, mass accumulation of Particulate Matter (PM2.5) Concentration of Respirable Mn Dust within animal cage measured by Ultrasonic Personal Air Sampler reached 4 mg/m^3 with 2.5L/min flow rate.

We also found that the particle count reached up to 2x10^5 /Cm^3.

Fig 2. PM2.5 concentration in the airflow with Manganese (Mn) (2A) with and without (2B) Propylene Glycol/Vegetable Glycerine (PG/VG) – as measured by Ultrasonic Personal Air Sampler (UPAS); A/B 2.5 - L/min; C/D – 5 L/min



Mn Aerosol Exposure Set-up

10 puffs of Mn with or without PG/VG for 5 min for each 30 mins up to 8 hours at 2.5 L or 5 L airflow/min.
(Fig 1A – In vivo set-up and Fig 1B – Invitro set-up)

Fig 3. PM2.5 Particle count of Mn aerosols at 2.5 L/min As measured by Condensation particle counter (3007).

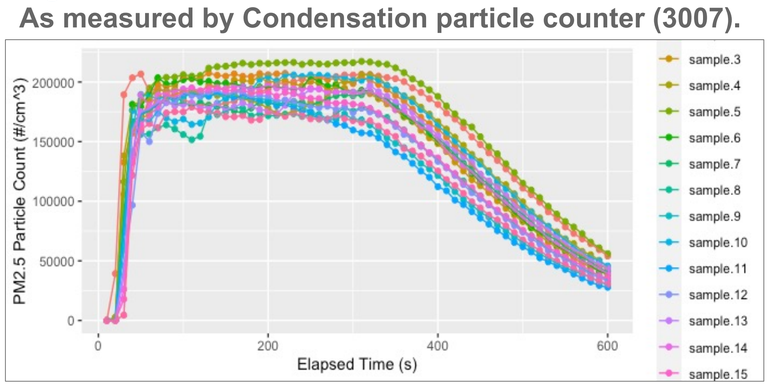
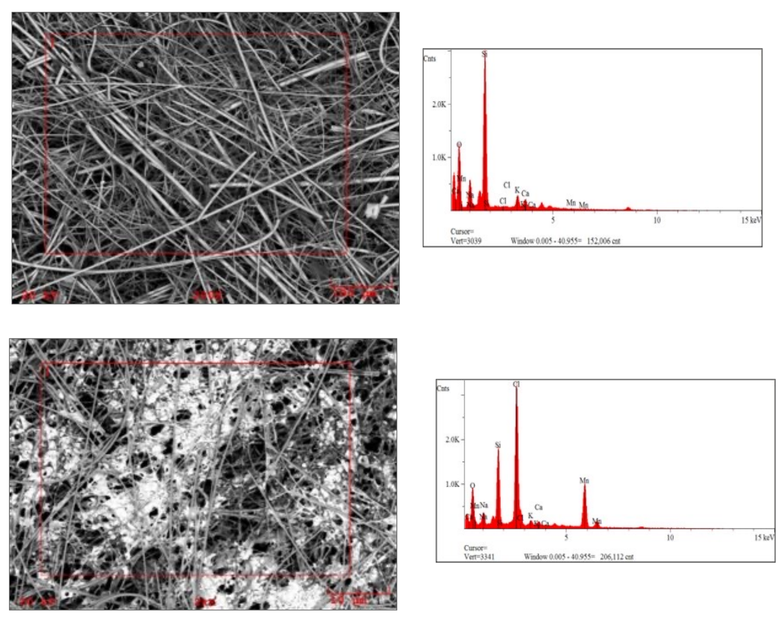


Fig 4. Elemental analysis of Mn aerosols by Scanning Electron Microscopy – X-ray Microanalysis (SEM-XRM) A/B – Negative control with spectra' C/D Positive control with Spectra; E – Spectral Analysis of Positive Control



Elt.	Line	Intensity (c/s)	Atomic %	Conc.	Units	
O	Ka	410.60	59.567	39.083	wt.%	
Na	Ka	157.82	3.943	3.717	wt.%	
Si	Ka	1,093.56	10.071	11.599	wt.%	
Cl	Ka	2,285.55	16.592	24.122	wt.%	
K	Ka	73.55	0.585	0.937	wt.%	
Ca	Ka	58.95	0.462	0.759	wt.%	
Mn	Ka	860.44	8.781	19.783	wt.%	
			100.000	100.000	Wt.%	Total

Inference

The Minimum Risk Level (MRL) for Mn has been estimated as 0.3 µg/m^3 in respirable dust based on health effects resulting from chronic inhalation exposure to Mn.

ACGIH sets the Time Weighted Average-Threshold Limit Value (TWA-TLV) as 0.02 mg/m^3 for Mn dust and 5 mg/m^3 for total welding fumes in the respiratory fraction of factory workers.

We estimated our dose of Mn fumes to the level of Total Welding Fume as 5 mg/m^3

With 2.5L/min flow rate we achieved close to 4 mg/m^3. In this study, we will use 2L/min flow rate to achieve 5mg/m^3 with 10 puff of Mn fumes for every 5 mins which repeats for every 25 mins up to 8 h

The outcome of these characterization parameters will be incorporated to investigate the cellular pathomechanism of manganese toxicity.

References

Dorman, D.C., et al., *Application of pharmacokinetic data to the risk assessment of inhaled manganese.* Neurotoxicology, 2006. **27**(5): p. 752-764.

University at Buffalo The State University of New York

Department of Rehabilitation Sciences, School of Public Health and Health Professions, State University of New York at Buffalo, Buffalo, NY, United States

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