

## **EFFECTS OF NANO-SIZED MIXED METAL PARTICLE EXPOSURE RESPIRATORY AND CENTRAL NERVE SYSTEM**

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### **ABSTRACT**

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Exposure to nano-sized mixed metal particle such as welding fume at high concentration can lead to develop pneumoconiosis or other related diseases. Among such diseases, the process of pulmonary fibrosis and manganism resulting from mixed metal particle has not been studied extensively. Accordingly, the current study investigated the inflammatory and genotoxic responses in the lung and the movement of manganese into specific brain regions. As such, rats were exposed to mixed metal particle at concentrations of  $65.6 \pm 2.9$  (low dose) and  $116.8 \pm 3.9$  mg/m<sup>3</sup> (high dose) total suspended particulate for 2 hr per day in an inhalation chamber for 30 days. Animals were sacrificed after the initial 2 h exposure, and after 15 and 30 days of exposure. The rats exposed to the nano-sized mixed metal particles exhibited a statistically significant ( $P < 0.05$ ) decrease in body weight when compared to the control during the 30-day exposure period, yet an elevated cellular differential count and higher levels of albumin, LDH, and  $\beta$ -NAG, but not elevated TNF- $\alpha$ , and IL-1 $\beta$  in the acellular bronchoalveolar lavage fluid. In addition, the DNA damage resulting from 30 days of mixed metal particle exposure was confirmed by a Comet assay and the immunohistochemistry for 8-hydroxydeoxyguanine (8-OH-dG). In addition, to investigate the movement of manganese after nano-sized mixed metal particle-exposure, primates were exposed to the mixed metal particles for 2 hrs per day in an inhalation chamber

system that is equipped with an automatic fume generator. Magnetic resonance Imaging (MRI) studies were conducted before the initiation of exposure and thereafter every month. During the exposure, the primate blood chemistry and hematology were monitored and the concentrations of metal components in the blood were measured every 2 weeks and compared with ambient manganese concentrations. The blood Mn concentration showed a significant increase from 3 months of exposure and reached a plateau at 100 days of exposure, showing at least more than 60 days of exposure period were required to build up blood Mn concentration. As building up Mn concentration in the blood, the decreases of MRI T1 relaxation time in the basal ganglia were detected and maintained continuously, indicating inverse relationship between blood Mn concentration and MRI T1 relaxation time (or direct relationship with MRI T1 high signal).