

Particle Solubility and Delivery of Inhaled Manganese to the Rat Brain: Manganese Sulfate and Manganese Tetroxide Pharmacokinetics Following Repeated (14-Day) Exposure

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ABSTRACT

Dissolution rate can influence the pulmonary clearance of a metal and thus affect its delivery to the brain and other organs. The goal of this study was to determine the exposure-response relationship for the relatively soluble sulfate (MnSO_4) and insoluble tetroxide (Mn_3O_4) forms of inhaled manganese in adult male CD rats. Rats were exposed 6 hr/day for 7 days/week (14 exposures) to either MnSO_4 or Mn_3O_4 at 0, 0.03, 0.3, or 3 mg Mn/m^3 . End-of-exposure olfactory bulb, striatum, cerebellum, bile, lung, liver, femur, serum, and testes manganese concentrations and whole-body ^{54}Mn elimination rates were then determined. Increased whole-body ^{54}Mn clearance rates were observed in animals from the high-dose (3 mg Mn/m^3) MnSO_4 and Mn_3O_4 exposure groups. Elevated manganese concentrations in the lung were observed following MnSO_4 and Mn_3O_4 exposure to ≥ 0.3 mg Mn/m^3 . Increased olfactory bulb and femur manganese concentrations were also observed following MnSO_4 exposure at ≥ 0.3 mg Mn/m^3 . Elevated striatal, testes, liver, and bile manganese concentrations were observed following exposure to MnSO_4 at 3 mg Mn/m^3 . Elevated olfactory bulb, striatal, femur, and bile manganese concentrations were observed following exposure to Mn_3O_4 at 3 mg Mn/m^3 . Animals exposed to MnSO_4 (3 mg Mn/m^3) had lower lung and higher olfactory bulb and striatal manganese concentrations when compared with levels achieved following similar Mn_3O_4 exposures. Our results suggest that inhalation exposure to soluble forms of manganese results in higher brain manganese concentrations than those achieved following exposure to insoluble forms of manganese.