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TITLE: EXTRAPULMONARY TRANSLOCATION OF ULTRAFINE CARBON PARTICLES FOLLOWING WHOLE-BODY INHALATION EXPOSURE OF RATS

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ABSTRACT: Studies with intravenously injected ultrafine particles have shown that the liver is the major organ of their uptake from the blood circulation. Measuring translocation of inhaled ultrafine particles to extrapulmonary organs via the blood compartment is hampered by methodological difficulties (i.e., label may come off, partial solubilization) and analytical limitations (measurement of very small amounts). The objective of our pilot study was to determine whether ultrafine elemental carbon particles translocate to the liver and other extrapulmonary organs following inhalation as singlet particles by rats. We generated ultrafine C-13 particles as an aerosol with count median diameters (CMDs) of 20-29 nm (GSD 1.7) using electric spark discharge of C-13 graphite electrodes in argon. Nine Fischer 344 rats were exposed to these particles for 6 h. in whole-body inhalation chambers at concentrations of 180 and 80 $\mu\text{g}/\text{m}^3$; 3 animals each were killed at 0.5, 18, and 24 h postexposure. Six unexposed rats served as controls. Lung lobes, liver, heart, brain, olfactory bulb, and kidney were excised, homogenized, and freeze-dried for analysis of the added C-13 by isotope ratio mass spectrometry. Organic C-13 was not detected in the C-13 particles. The C-13 retained in the lung at 0.5 h postexposure was about 70% less than predicted by rat deposition models for ultrafine particles, and did not change significantly during the 24-h postexposure period. Normalized to exposure concentration, the added C-13 per gram of lung on average in the postexposure period was similar to 9 ng/g organ/ $\mu\text{g}/\text{m}^3$. Significant amounts of C-13 had accumulated in the liver by 0.5 h postinhalation only at the high exposure concentration, whereas by 18 and 24 h postexposure the C-13 amount of the livers of all exposed rats was about fivefold greater than the C-13 burden retained in the lung. No significant increase in C-13 was detected in the other organs which were examined. These results demonstrate effective translocation of ultrafine elemental carbon particles to the liver by 1 d after inhalation exposure. Translocation pathways include direct input into the blood compartment from ultrafine carbon particles deposited throughout the respiratory tract. However, since predictive particle deposition models indicate that respiratory tract deposits alone may not fully account for the hepatic C-13 burden, input from ultrafine particles present in the GI tract needs to be considered as well. Such translocation to blood and extrapulmonary tissues may well be different between ultrafine carbon and other insoluble (metal) ultrafine particles.