PROTEIN OXIDATION DIFFERENCES OF HEXAVALENT AND TRIVALENT CHROMIUM J.S. Ishmael and R.J. Keller, Occupational and Environmental Health Program, Department of Pharmacology and Toxicology, University of Arkansas for Medical Sciences, 4301 W. Markham, Little Rock, AR 72205

Chromium is a documented carcinogen that is used commonly in industries such as leather tanning, electroplating and stainless steel welding. The Occupational Safety and Health Administration (OSHA) has recently prioritized the re-evaluation of the chromium exposure standard because of its carcinogenic effects. Industrial exposures to chromium occur from hexavalent chromium (Cr (VI)), a known pulmonary carcinogen, and the trivalent form (Cr (III)). Trivalent chromium, however, is not considered a lung carcinogen. The mechanistic reasons for the differences in carcinogenic potential between Cr(VI) and Cr(III) are not known but may be related to differences in their ability to generate reactive oxygen species (ROS). Chromium is known to catalyze the formation of reactive oxygen species that may have a role in disease, aging, and oxidative stress. The generation of ROS is known to play a role in lipid peroxidation, DNA damage, and protein oxidation. The purpose of this study is to compare the ability of hexavalent and trivalent chromium to form reactive oxygen species which may be related to differences in their toxicity.

Both hexavalent and trivalent chromium were used in increasing concentrations ranging from 0.1mM to 1.2mM to oxidize proteins under physiological conditions resulting in protein carbonyl formation. Oxidized proteins were reacted with 2,4-dinitrophenylhydrazine to form hydrazones that were measured spectrophotometrically. Hydrazone concentration is proportional to carbonyl content and is an accurate measurement of ROS production.

We measured carbonyl content and while Cr(VI) shows an increase in protein oxidation, Cr(III) did not. Hexavalent chromium carbonyl production ranged from .008 to .029 mmol carbonyl/mg protein while trivalent chromium did not increase carbonyl production. When only 0.4mmol hexavalent chromium was used and held constant, protein oxidation increased over time with carbonyl content increasing from .001 to .006 mmol carbonyl/mg protein in a one hour time span. Hexavalent chromium was effectively reduced to trivalent chromium in the presence of reducing agents and ROS production halted. Our data shows that hexavalent chromium produces ROS as shown through protein oxidation while Cr(III) does not. The results of our work show that the valence state of chromium is essential in metal catalyzed reactive oxygen species production.

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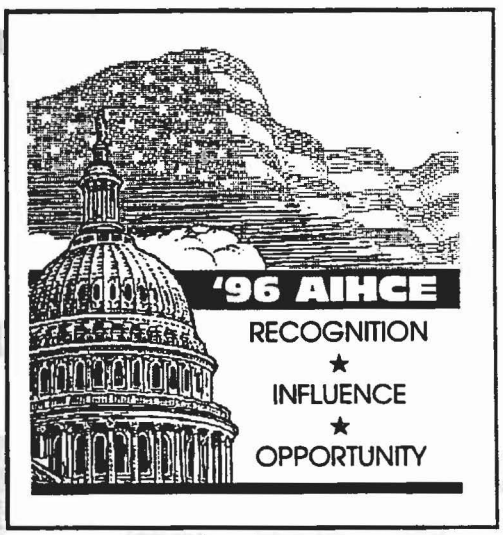

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