

II B. CENTER HIGHLIGHTS

Research Highlight #139

The pro-oxidant chromium (VI) inhibits mitochondrial complex I, complex II, and aconitase in the bronchial epithelium: EPR markers for Fe-S proteins

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Introduction: Human exposure to hexavalent chromium largely results from industrial use and release and can cause respiratory effects. Environmental exposure is of increasing concern because more than 10^5 tons of Cr are released annually and because of widespread contamination in water supplies. Hexavalent chromium (Cr(VI)) as chromate is a strong oxidant that readily enters cells.

Methods: EPR spectra were obtained at 10 K using the Bruker E500 ELEXSYS spectrometer and at three powers (20, 5, and 0.2 mW) for all samples. Additional spectra at more powers and temperatures were taken if there were unanticipated changes in the power saturation or in the temperature dependencies.

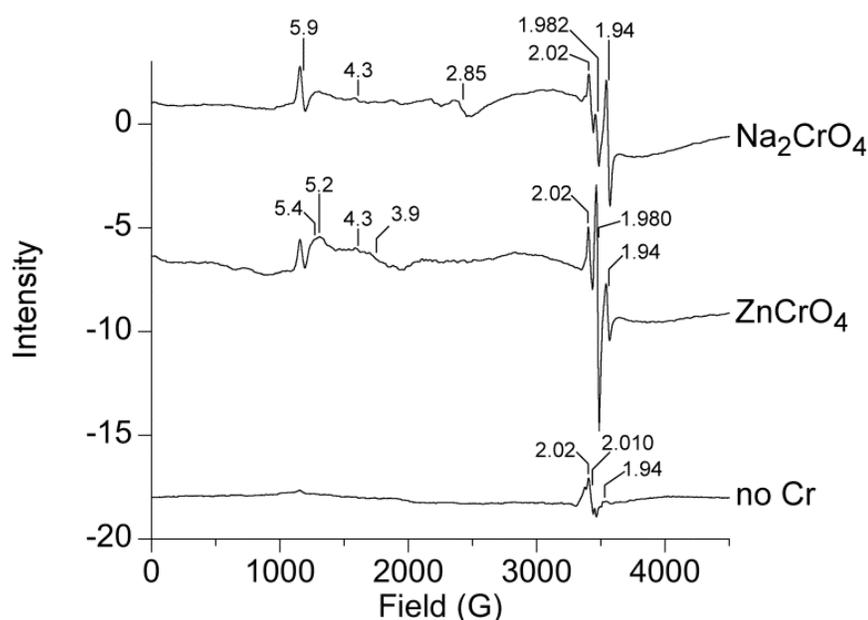


Figure 1: EPR spectra (at 10 K, 20 mW) of bovine bronchi (12 cm^2 of bronchial epithelium) treated *ex vivo* with Na_2CrO_4 or ZnCrO_4 (0.177 mg Cr/cm^2) or buffer (no Cr) for 3 hrs at 37°C , and washed with buffer. The bronchial epithelium was harvested by scraping, and the cell suspension was frozen in liquid nitrogen. Spectra at lower powers and with less Cr(VI).

Results: EPR studies of samples at 10 K showed a strong signal at $g = 1.94$ that is consistent with the inhibition of electron flow through complex I and/or complex II. A signal at $g = 2.02$ indicated that oxidation of the Fe-S center of aconitase occurred. The $g = 1.94$ signal was intense and remained after extracellular Cr(VI) was removed, whereas the $g = 2.02$ signal decreased after Cr(VI) was removed. Analogous EPR findings were noted in bovine airways treated *ex vivo* with Cr(VI) (see Fig. 1). EPR spectra simultaneously showed signals for Cr(V) and Cr(III), which verify Cr(VI) exposure and its intracellular reductive activation.

Implications: Overall, data support the hypothesis that Cr(VI) exposure has deleterious effects on a number of redox-sensitive core mitochondrial proteins. The $g = 1.94$ signal could prove to be an important biomarker for oxidative damage resulting from Cr(VI) exposure.