

P066 Lipid Oxidation Products as Markers of Oxidative Stress:
Validation Studies in Animal Models.

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Oxidation products of lipids in plasma and urine of rats were measured as part of a comprehensive, multilaboratory validation study searching for non-invasive biomarkers of oxidative stress. The goal of the study is to find the most sensitive, selective and specific markers of oxidative stress that are applicable to different oxidative insults and stored specimens. The study was organized and sponsored by NIEHS/NIH, RTP, NC, USA.

This is the second report of the worldwide Biomarkers of Oxidative Stress Study (BOSS) using the acute CCl₄ poisoning as a rodent model for oxidative stress. The time (2, 7, and 16 h) and dose (120 and 1200 mg/kg ip)-dependent effects of CCl₄ on concentrations of lipid hydroperoxides, TBARS, malondialdehyde (MDA) and isoprostanes were investigated with different techniques. Comparisons about the sensitivity of a given assay were carried out as well.

It was found that plasma concentrations of MDA and isoprostanes (measured by GC/MS) and urinary concentrations of isoprostanes (measured with an immunoassay) were increased in CCl₄ treated rats in a time- and dose-dependent manner. All other products were not changed by CCl₄ or showed only high-dose and/or single time point effects. In addition, measures of oxidation products of proteins (protein carbonyls, methionine sulfoxidation, tyrosine oxidation products) and DNA (strand breaks, 8-OHdG, M1G) were not changed in a time-and dose-dependent manner by CCl₄. Therefore, at this time, there are no good markers of oxidative damage to DNA or proteins with CCl₄ poisoning.

It is concluded that measurements of free radical mediated lipid peroxidation products - MDA and isoprostanes concentrations in plasma (by GC/MS) and urinary isoprostanes (by immunoassay or GC/MS) are promising candidates for general biomarkers of oxidative stress.