INDUCTION OF OXIDATIVE STRESS IN LIVER TISSUE OF RAT AFTER EXPOSURE TO 2,3,4,7,8-PENTACHLORODIBENZOFURAN (PeCDF)

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Introduction

2,3,4,7,8-Pentachlorodibenzofuran (PeCDF) is one of the most toxic environmental contaminant which produce a wide range of toxicities and biochemical effects in experimental animals[1-3]. Several mechanisms have been proposed for the toxicity of PeCDF[1,4]. Above all, oxidative stress is being considered as one of the important ones. Previous studies have shown that subchronic administration of PeCDF to laboratory animals induces the production of the reactive oxygen species[4]. In this study we have determined the potencies of PeCDF as inducer of oxidative stress in the hepatic tissue of rats after acute exposure with low dose.

Methods and Materials

PeCDF was dissolved in ethanol at concentration of 0.6 μM, and it was injected intravenously to 6-weeks old Sprague-Dawley male rats at the dose of 100 ng/kg body weight. After 3, 8 hr, the rats were euthanized using ether. Livers were removed, snap-frozen in liquid nitrogen, and stored at –80 °C until measurement of oxidative stress.

We employed the histochemical detection as oxidative stress measurement for tissue. Briefly, sections from frozen tissue were treated with 2', 7'-dichlorofluorescin (DCFH) as a probe for assessing the oxidative stress. The oxidation of DCFH to a fluorescent product (dichlorofluorescein; DCF) is currently used to evaluate oxidant stress. The oxidative stress was characterized by the increase in fluorescence of histological sections as assessed with a fluorescence microscope.

Furthermore, the content of thiobarbituric acid reactive substances (TBARS) in the liver homogenate, glutamate pyruvate transaminase (GPT) in the serum and 8-hydroxy-2'-deoxyguanosine (8-OHdG) in the liver were measured.

Results and Discussion

Measurements of the fluorescent product DCF in liver tissue showed increase in PeCDF treated rat tissues compared with control (ethanol treated) rat. No significant increases in lipid peroxidation, as indicated TBARS, were observed, relative to ethanol treated groups. But these results were due to a low sensitivity of TBARS method. Because 8-OHdG was increased by immunohistochemistry in the nuclei of hepatocyte after treated with PeCDF. And significant increase in GPT was observed at 3 hr after treated with 100 ng/kg of PeCDF. GPT is a kind of an index of an

inflammation. The results of the study suggest that acute exposure to PeCDF induce significant oxidative damage in the hepatic tissue of rats. Thus, the toxicity of PeCDF may be caused in part by free radical-mediated oxidative stress.

References

1. Johnson KL, Cummings AM, Birnbaum LS.(1997) Promotion of endometriosis in mice by polychlorinated dibenzo-p-dioxins, dibenzofurans, and biphenyls., Environ. Health Perspect., 105, 750-755.
2. Brewster DW, Elwell MR, Birnbaum LS.(1988), Toxicity and disposition of 2,3,4,7,8-pentachlorodibenzofuran (4PeCDF) in the rhesus monkey (Macaca mulatta)., Toxicol. Appl. Pharmacol., 93, 231-246.
3. Birnbaum LS, Harris MW, Crawford DD, Morrissey RE.(1987), Teratogenic effects of polychlorinated dibenzofurans in combination in C57BL/6N mice., Toxicol. Appl. Pharmacol., 91, 246-255.
4. Hassoun EA, Li F, Abushaban A, Stohs SJ.(2000), The relative abilities of TCDD and its congeners to induce oxidative stress in the hepatic and brain tissues of rats after subchronic exposure., Toxicology, 145, 103-113.