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THE EFFECTS OF PHTHALATES AND CLOFIBRATE ON THE OXIDATIVE DAMAGE AND ACTIVITIES OF METABOLIZING ENZYMES IN THE RATS

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The phthalates have been shown to produce hepatic peroxisome proliferation and certain peroxisome proliferators (PPs) are also known to increase the incidence of liver tumors in rodents. In this study we investigated the correlation between oxidative injury, changes in peroxisomal and microsomal enzymes and tumor formation in PP-treated rats. The oxidative damage was measured by using 8-hydroxydeoxyguanosine (8-OHdG) in DNA and malonedialdehyde (MDA) in rat liver. The promoting effect of PPs was investigated by using diethylnitrosamine-initiated preneoplastic foci model in rats. The rats were orally treated with phthalates or clofibrate following dosages for 14 days; di-2-ethylhexyl phthalate (DEHP), dibutyl phthalate, butylbenzyl phthalate : 50, 200 and 1000 mg/kg, clofibrate : 100 mg/kg in corn oil. In rats treated with PPs the relative liver weights were significantly increased, but relative weights of adrenal gland markedly decreased. Both phthalates and clofibrate markedly increased the activity of carnitine acetyl CoA transferase and palmitoyl-CoA oxidation, but significantly decreased activities of microsomal enzymes such as 1A1, 1A2, 3A4 and UDP-glucuronosyltransferase. Treatment with phthalates or clofibrate dramatically enhanced the MDA contents in livers and 8-OHdG in hepatic DNA. In 3-months rat liver GST-P foci bioassay, DEHP and clofibrate formed much more foci than control.