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THE EFFECT OF SOME PESTICIDES ON CELL PROLIFERATION AND ABNORMAL MITOSES IN RAT LIVER

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Some organohalogen pesticides have been classified as rodent non-genotoxic hepatocarcinogens and/or liver tumor promoters. The early hepatic changes produced by this type of carcinogens have in common an association with cell proliferation proposed to be the useful endpoint in screening of non-genotoxic, potentially carcinogenic substances. We studied the effect of organohalogen pesticides, bromopropylate [isopropyl 4,4-dibromobenzylate] and DDT [1,1-(2,2,2-trichloroethylidene)-bis-(4-chlorobenzene)] on DNA synthesis, mitotic activity including histological changes in rat liver. Males Wistar rats (Pzh:Wis) weighing 200±10g were used. Bromopropylate and DDT were administered orally either in a single or in repeated doses (given at 24h intervales) of 125, 250, 500mg/kg b.w. and 12 or 24mg/kg b.w. respectively. DNA synthesis was measured by [^{3}H]thymidine incorporation into nuclear DNA. The number of mitoses was counted in 2000 hepatocytes and expressed per 1000 hepatocytes. Histological hepatic changes were determined by microscopy in preparations stained with haematoxylin and eosin.

In the case of both pesticides, DNA synthesis and mitotic activity increased significantly in a dose-dependent manner after single administration of compounds. After prolonged administration of bromopropylate and DDT, DNA synthesis and number of mitotic figures tended to decline, though differences between two higher doses of bromopropylate (500 and 250mg/kg b.w.) and control animals were still significant. Histological and cytological analysis showed the presence of dose-dependent abnormal mitotic figures (and c-mitoses) in hepatocytes of the bromopropylate and DDT treated rats. In particular after administration of higher doses of compouds, mitotic spindle exibited disturbances. Therefore, it is possible that both pesticides selectively affect functions of the mitotic spindle resulting in abnormal mitosis.