

Effect of benzo[a]pyrene on DNA synthesis and DNA polymerase activity of rat liver nuclei

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When benzo[a]pyrene (B[a]P) was administered intraperitoneally to rats 48 hr before they were killed, the DNA-synthesizing capability of isolated rat liver nuclei was decreased as compared with control animals. B[a]P also inhibited in vitro DNA synthesis in nuclei purified from control animals; this effect was enhanced by NADPH. DNA polymerases solubilized from purified nuclei of B[a]P-treated animals were less active than those of control animals. DNA polymerase β was more inhibited than DNA polymerase α . Purified rat liver nuclei devoid of cytoplasmic contamination possess an NADPH-dependent B[a]P hydroxylase activity. The observed inhibition of DNA synthesis in nuclei isolated from B[a]P-treated rats was increased by NADPH. Moreover, there was an increased inhibition of DNA polymerase activity by nuclear membranes obtained from B[a]P-treated animals when the incubations were performed in the presence of NADPH. Also, the derivative B[a]P-trans-9,10-dihydrodiol was a potent inhibitor