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Isolation and Characterization of a Form of Cytochrome P-450 with High Specificity to Aflatoxin B_1 From 3-Methylcholanthrene-treated Hamsters

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S 9 fraction of PCB-treated hamsters was shown to be highly active in the induction of aflatoxin B_1 (AFB_1) mutagenicity. The potency of the activity of S 9 from various experimental animals is, in the descending order, hamster, rabbit, guniea pig, rat, mouse and suncus murinus. The activity of hamser S 9 is more inducible by the treatment with 3-methylcholanthrene (3-MC) than with phenobarbital and is present in hepatic microsomes, indicating that the enzymes responsible for the metabolic activation of AFB_1 might be cytochrome P-450s that could be induced by 3-MC. From hepatic microsomes of 3-MC-treated hemsters, 3 forms of cytochrome P-450 were isolated. These include 2 major forms (Form I and II) and one minor form (Form III). They are difierent in their physicochemical and catalytic properties. Of these, Form I, having its absorption maximum at 448.5 nm in its CO-complex of reduced form, low spin form of ferric ion and a molecular weight of 56,000, was shown to be highly active in the activation of AFB_1 mutagenicity and in the production of AFB_1-DNA adducts. The activity of Form I is more then 50 times higher in the induction of AFB_1 mutagenicity than cytochrome P-450s purified from the livers of 3-MC-treated rats. Form I could also activate the mutagenicuty of other AFB_1-related mycotoxins such as sterigmatocystin and O-methylsterigmatocystin.

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