

CHARACTERIZATION OF 6-METHYL-1,3,8-TRICHLORODIBENZOFURAN (MCDF) AS A 2,3,7,8-TCDD ANTAGONIST IN MALE RATS: INDUCTION OF MONOOXYGENASES

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ABSTRACT

Treatment of male Long Evans rats with doses of MCDF up to 200 $\mu\text{mol/kg}$ did not significantly induce hepatic microsomal aryl hydrocarbon hydroxylase (AHH) or ethoxyresorufin O-deethylase (EROD) activities, whereas administration of 2,3,7,8-TCDD (16 nmol/kg) caused up to a 10 to 40-fold induction of these enzymes. Cotreatment of the rats with 2,3,7,8-TCDD (16 nmol/kg) and MCDF (50 $\mu\text{mol/kg}$) resulted in the inhibition of the monooxygenase enzyme induction response over a 72 hour period. Treatment of the animals with 2,3,7,8-TCDD alone caused an initial decrease in the concentration of the cytosolic Ah receptor followed by an increase of these levels (~ 2 times higher than in control rats) after 72 hours. In contrast, MCDF treatment did not alter hepatic cytosolic Ah receptor levels and in the cotreatment studies (MCDF + TCDD), the effects of 2,3,7,8-TCDD on receptor levels was inhibited. Using [^3H]-2,3,7,8-TCDD (+ MCDF), the time-course accumulation of nuclear [^3H]-2,3,7,8-TCDD-receptor complexes was also investigated. Surprisingly, MCDF did not decrease occupied nuclear 2,3,7,8-TCDD-Ah receptor levels.