

6-Methyl-1,3,8-trichlorodibenzofuran (MCDF) as an Antiestrogen in Human and Rodent Cancer Cell Lines: Evidence for the Role of the Ah Receptor

T. ZACHAREWSKI, M. HARRIS, L. BIEGEL, V. MORRISON, M. MERCHANT, AND S. SAFE¹

Department of Veterinary Physiology and Pharmacology, Texas A&M University, College Station, Texas 77843-4466

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6-Methyl-1,3,8-trichlorodibenzofuran (MCDF) is a relatively nontoxic analog of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. Treatment of aryl hydrocarbon (Ah)-responsive MCF-7 human breast cancer cells with 100 nM MCDF resulted in the inhibition of 17 β -estradiol-induced proliferation and the secretion of the 34-, 52-, and 160-kDa proteins. After treatment of the cells with 17 β -[³H]estradiol, 100 nM of MCDF caused a decrease in the accumulation of the radiolabeled nuclear estrogen receptor (ER) complex in these cells. In parallel experiments, the antiestrogenic effects of MCDF were also determined in Ah-responsive wild-type Hepa 1c1c7 cells and Ah-nonresponsive class 1 and class 2 mutant cells. Treatment of the wild-type cells with 17 β -[³H]estradiol and 100 nM MCDF caused a decrease in the accumulation of radiolabeled nuclear ER complex in these cells whereas no significant effects were observed in the mutant cells as determined by velocity sedimentation analysis. Comparable results were obtained using ER antibodies to measure the decrease in immunoreactive nuclear ER. In addition, both actinomycin D and cycloheximide inhibited the MCDF-mediated decrease of nuclear ER levels in the Hepa 1c1c7 wild-type cells. Although 100 nM MCDF did not induce cytochrome P-450-dependent monooxygenases in the MCF-7 or Hepa 1c1c7 cell lines, incubation of nuclear extracts from the MCF-7 cells treated with 100 nM MCDF with a synthetic consensus dioxin responsive element (an oligonucleotide duplex of 26 bases) gave a retarded band in a gel-retardation assay. The data suggest that the antiestrogenic effects of MCDF does not require the induction of the *CYP1A1* gene expression but may involve the induction of other genes.