ACUTE ORAL EXPOSURE TO 2,3,7,8-TETRABROMODIBENZO-*p*-DIOXIN (TBDD)

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ABSTRACT

Oral exposure of graded doses of TBDD to male rats resulted in differential absorption and accumulation in liver and adipose tissue, with tissue distribution and excretion being dose-dependent.

INTRODUCTION

Polybrominated dibenzo-*p*-dioxins (PBDDs) and dibenzofurans (PBDFs) are of major concern because of potential occupational and environmental exposures and their structural similarity to the highly toxic chlorinated analogues. They are formed during the low temperature extrusion process in making plastics and during thermolysis or pyrolysis of plastics, carpets, textiles, and other materials containing brominated flame retardants. Little data exist regarding the actual environmental occurrence of PBDDs and PBDFs as well as the biological fate and potential hazards to man and the environment. 2,3,7,8-Tetrabromodibenzo-*p*-dioxin (TBDD) appears slightly less potent than the chlorinated analogue TCDD in the characteristic toxic responses of teratogenic effects, thymic atrophy, weight loss, and

chloracne in animals. We have undertaken to study the absorption and disposition of the TBDD in order to evaluate the potential for human risk.

METHODS

The absorption, excretion, and terminal tissue distribution of TBDD-derived radioactivity were characterized following acute oral administration of graded doses of [1,6-^{3}H]-TBDD in the male Fisher 344 rat. Groups of 4 rats (3 months old, 250-300 grams) were administered 0.001, 0.01, 0.1, or 0.5 μmoles ^{3}H-TBDD/kg (0.5, 5, 50, or 250 μgm/kg) by gavage at 5 ml/kg in 1:1:3::ethanol:Emulphor^{R}:water. Rats were housed in individual metabolism cages. Urine and feces were collected daily. At 72 hours following dosing, animals were killed by CO_2 asphyxiation and tissues collected. Radioactivity was determined in the excreta and tissues.

RESULTS AND DISCUSSION

Over the three-day period, feces was the major route of excretion. By 72 hours, 43% (0.001 μmole/kg), 39% (0.01 μmole/kg), 60% (0.1 μmole/kg), and 72% (0.5 μmole/kg) of the total dose was excreted. At termination, most of the body burden was found in the liver with 20% (0.001 μmole/kg), 31% (0.01 μmole/kg), 21% (0.1 μmole/kg), and 14% (0.5 μmole/kg) of the total dose and adipose tissue with 20% (0.001 μmole/kg), 16% (0.01 μmole/kg), 10% (0.1 μmole/kg), and 6% (0.5 μmole/kg) of the total dose.

Disposition of TBDD showed similar results to the highly toxic chlorinated analogue TCDD which is also distributed to the liver and adipose tissue and primarily excreted in the feces. TBDD demonstrated dose-dependent tissue distribution and excretion. Following oral exposure of graded doses, TBDD exhibited differential absorption. At the higher dose levels, absorption appeared non-linear. These results emphasize important considerations for high to low dose extrapolation of results from animal studies for purposes of human risk assessment of TBDD.

DISCLAIMER

This document has been reviewed in accordance with U.S. Environmental Protection Agency policy and approved for publication. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

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