***In vivo* Metabolism of 3,3',4,4'-Tetrachlorobiphenyl in Rats: Occurrence and Liver-Specific Retention of Methylsulfonyl Metabolite**

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Introduction

Methylsulfonyl (MeSO₂) metabolites of polychlorinated biphenyls are environmental contaminants that accumulate in tissues of mammals and human. These metabolites are known to be derived from chlorobiphenyls (CBs) with 2,5- or 2,3,6-chlorine substitution, although there is little information on the formation of MeSO₂-CB from CBs with 3,4-chlorine substitution. We report the identification and tissue distribution of sulfur-containing metabolites in rats dosed with 3,3',4,4'-tetraCB (TCB), which is one of the most toxic coplanar CBs.

Methods

Male Wistar rats were given a single ip dose of TCB (80 μ mol/kg) and feces were collected daily for four days. The rats were killed 96 h after the dosing, and blood, liver, lung, kidney and adipose tissue were analyzed for metabolites. These samples were purified by gel permeation chromatography (Bio-Beads S-X3) and fractionated to acidic and neutral metabolites for GC/MS analysis.

Results and Discussion

Fecal metabolites in acidic fraction consisted of four components identified as 4-hydroxy-3,3',4'-triCB, 4-hydroxy-3,3',4',5-tetraCB, 5-hydroxy-TCB and hydroxy-methylthio-triCB (unknown

structure). In neutral fraction, four sulfur-containing metabolites were isolated and identified as 5-methylthio-TCB, 6-methylthio-TCB, 5-MeSO₂-TCB and 2-MeSO₂-5-methylthio-3',4,4'-triCB by GC/MS comparison with authentic samples. Excreted amounts of fecal metabolites during the 4 d after dosing were estimated to be about 4.2, 0.5 and 0.3% of the dose for the hydroxy metabolites, the sulfur-containing metabolites and unchanged compound, respectively.

A large amount of 5-MeSO₂-TCB was retained in liver (122 ± 31 ng/g wet weight). This metabolite was also found at low levels (3.4 ± 0.8 ng/g) in adipose tissue, but was not detected in blood, lung or kidney (detection limit, 0.2 ng/ml or g). The concentration ratio of 5-MeSO₂-TCB/unchanged compound ranged from 0.13 to 0.34 in the liver, whereas it was from 0.0001 to 0.0002 in the adipose tissue. These results indicate the liver-specific retention of 5-MeSO₂-TCB in rats, and were also confirmed by evaluating the tissue distribution in rats ip dosed with 5-MeSO₂-TCB (2 μ mol/kg).

In conclusion, TCB was biotransformed to 5- and 6-methylthio metabolites, probably *via* 5,6-epoxide in rats. The distribution pattern of MeSO₂-CB derived from TCB was different from that of MeSO₂-CB derived from 2,5-chlorine substituted congeners. Further studies are needed to learn the toxicity of MeSO₂ metabolite of TCB.