Comparative Study on Tissue Retention of PCB Methyl Sulfone Metabolites in Different Mammalian Species.

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INTRODUCTION

Several PCB congeners with vicinal hydrogen atoms in the *meta* and *para*-positions in one of the two phenyl rings are biotransformed to PCB methyl sulfone metabolites. Instead of being readily excreted metabolic products, they have been shown to accumulate in mammals and are today known as environmental contaminants with similar lipophilic character as the parent compound. In fact, the $MeSO_2$-CBs have been detected in many mammals [1], as well as in humans [2]. Several studies have been made on the retention of $MeSO_2$-CBs in animals exposed to individual chlorinated biphenyls (CBs). Some 4-$MeSO_2$-CBs have shown to be specifically retained in the lung bronchial mucosa in mice [3]. On the other hand, the isomeric 3-$MeSO_2$-CBs were selectively detected in liver of several mammals, at higher concentration than in other tissues [1]. Recently, *in vivo* studies in rats showed that some 3-$MeSO_2$-CBs derived from the CBs with a 2,5-dichloro-substituted phenyl ring strongly induced PB-type enzymes in the liver [5]. It is therefore of great concern to further investigate the tissue retention of these persistent metabolites. In present study the concentration ratios of 3- and 4-$MeSO_2$-CB are compared among several species. Particularly, the concentration of these compounds in the liver and adipose tissues in wildlife and experimental animals have been studied.

EXPERIMENTAL

Samples of blood, blubber and liver of a grey seal (*Halichoerus grypus*), liver and muscle of otter (*Lutra lutra*), wild mink (*Mustela vison*) and experimental mink dosed

with to Clophen A50 and tissues of male rats dosed with 2,3,6,2',4',5'-hexaCB (CB-149) were analyzed for $MeSO_2$-CBs according to our conventional method [5]. Identification and determination were performed by GC/ECD and GC/MS/NICI using the authentic $MeSO_2$-CBs and the internal standards that have been prepared previously [6].

RESULTS AND DISCUSSION

Fig. 1 shows a gas chromatogram of $MeSO_2$-CBs present in grey seal blood. Of the 35 $MeSO_2$-CBs detected, at least 24 were identified as 3- or 4-$MeSO_2$-CBs derived from CBs with a 2,5-dichlorinated or a 2,3,6-trichlorinated phenyl ring. These isomeric pairs accounted for more than 95% of the total $MeSO_2$-CB concentration as determined by GC/ECD. The $MeSO_2$-CB composition was different depending on the tissues analyzed. In liver, the five components (filled peaks in Fig. 1) were selectively localized at one order of magnitude higher concentration than in the blubber. These components consisted all of stuctures with a 3-$MeSO_2$-2,5,6- trichlorophenyl ring in the molecule. The concentration of these $MeSO_2$-CBs was about 90 % of the total $MeSO_2$-CB level in the liver. On the other hand, in grey seal blubber a large number of 3- and 4-$MeSO_2$-CBs were detected and identified as metabolites of triCBs to heptaCBs. These $MeSO_2$-CBs were present in a similar concentration range.

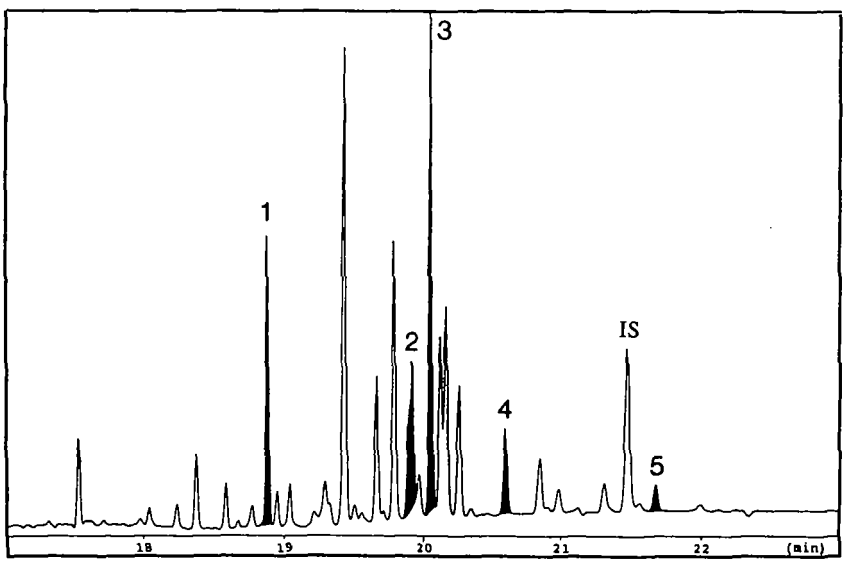

Fig. 1. GC/ECD of $MeSO_2$-CB fraction from blood of a grey seal. Filled peaks were identified as 3-$MeSO_2$-2,5,6,2',5'-pentaCB (peak 1), 3-$MeSO_2$-2,5,6,2',3',5'-hexaCB (peak 2), 3-$MeSO_2$-2,5,6,2',4',5'-hexaCB (peak 3), 3-$MeSO_2$-2,5,6,2',3',4'-hexaCB (peak 4) and 3-$MeSO_2$-2,5,6,2',3',4',5'-heptaCB (peak 5).

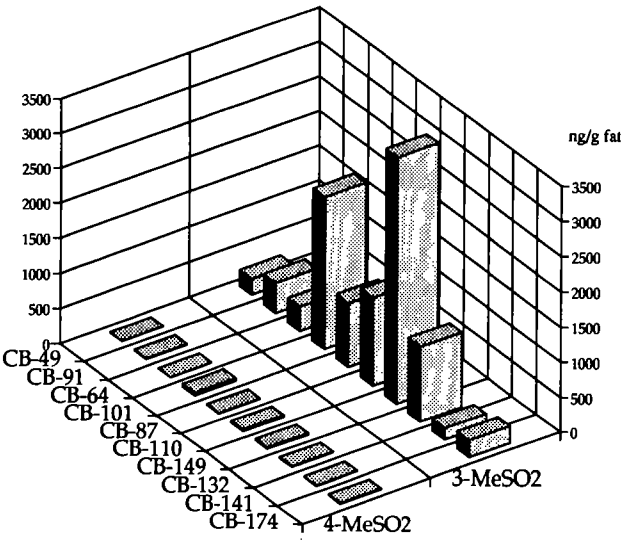

Fig. 2. Levels of 3- and 4-$MeSO_2$-CB congeners in otter liver.

Differences in tissue distribution among $MeSO_2$-CB congeners were most obvious in the liver from otter. In the otter analyzed, all of the 3-$MeSO_2$-CBs, most probably derived from the ten parent compounds, among which CB-87, -101, -110, -132, -149 showed the highest concentrations in the liver (cf. Fig.2). The total concentrations of 3-$MeSO_2$-CB in the four liver samples studied were estimated to be 0.4 -33 μ g/g extracted lipid, corresponding to 1/10 - 8/10 of the total PCB levels. In contrast, all the isomeric compounds with the $MeSO_2$-group in 4-position, except for the pair formed from CB-101, were more abundant in the muscle, although the levels were low (0.01-0.3 μg/g).

Liver-specific retention of 3-$MeSO_2$-CB was also observed in wild mink, although it was less specific than in the otter. One of the major components in the liver was 3-$MeSO_2$-2,5,6,2',4',5'-hexaCB, which was also the most abundant sulfone in otter and seal liver. In minks dosed with Clophen A50, the composition of $MeSO_2$-CBs were compared in blood, liver and muscle. 3-$MeSO_2$-2,5,2',3',4'-pentaCB and 3-$MeSO_2$-2,5,6,2',3',4'-hexaCB dominated in the liver, whereas 3-$MeSO_2$- 2,5,2',4',5'-pentaCB and 4-$MeSO_2$- 2,3,6,3',4'-pentaCB were more strongly retained in the muscle. The ratios of 3- and 4-$MeSO_2$-derivatives of CB-149 (present in Clophen A50 at about 4.5 %) were 1:1 in the blood, 3:1 in the liver and 1:2 in the muscle.

CB-149 was administered i.p. to male rats and several tissues were analyzed for the $MeSO_2$-CB. At 7 days after the dosing, all tissues were found to contain 3- and 4-$MeSO_2$-CB, together with the parent CB. However, the 3-$MeSO_2$-CB that shows a

strong retention in wild species didn't show any retention in rat liver under the experimental conditions used. In contrast, the 4-$MeSO_2$-CB was localized selectively in the lung.

In conclusion, liver-specific retention of 3-$MeSO_2$-CB was observed in the three mammalian species studied. With regard to the structural requirement for the uptake to liver, it is suggested that otter and mink favors strongly the components with 3-$MeSO_2$-2,5-dichloro- or 3-$MeSO_2$-2,5,6-trichloro substitution, whereas grey seal requires the latter composition only. These highly selective distribution may reflect the presence of specific binding site in the liver. Recent studies, as mentioned above, have shown that some 3-substituted $MeSO_2$-CBs had a strong inducing capacity of PB-type enzymes in hepatic microsome of rats [4].

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