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Tissue Distribution of Co-Planar and Non-Planar Tetra- and Hexa- Chlorobiphenyl Isomers in Guinea Pigs after Oral Ingestion

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Food ingestion is the most important route for the uptake of lipophilic organochlorine contaminants. Uptake and transfer of the contaminants from the digestive tract to target organs can be used for risk evaluation. The bioconcentration and migration of polychlorobiphenyls (PCBs) is highly structure - dependent (Safe 1989). Bioconcentration is correlated with lipophilicity on the basis of the n-octanol/water partition coefficient in its logarithmic form - logKow (McLachlan 1993; Gobas et al. 1994). However, some factors e.g. diffusion through cell membranes, accumulation in specific organs and tissues, uptake and depuration kinetics and metabolism can also influence the bioconcentration (Franke et al. 1994).

Individual PCB compounds of commercial PCB preparation are taken up by organisms to markedly different extents (Borlakoglu et al. 1991; Storrhansen and Spliid 1993; Bernhoft and Skaare 1994; Nims et al. 1994) Ness et al. 1994). Until now little is known about the distribution of non-planar and co-planar PCBs in different tissues. Co-planar PCBs have dioxin - like toxicity.

The purpose of this study was to examine differences in the bioconcentration of two pairs of tetra- and hexa- chlorobiphenyls, corresponding to the co-planar and non-planar conformations, from the digestive tract and their distribution in different tissues of guinea pigs.

MATERIALS AND METHODS

Guinea pigs were orally administered a single dose of a total of 18 mg (6 mg PCB-54, 3 mg PCB-80, 7 mg PCB-155 and 2 mg PCB-169) of PCBs per kilogram body weight in olive oil (0.4 mL/kg body weight). Six adult female guinea pigs 10 months old, 700-800 g in weight were used. During the experiment faeces were collected daily and analysed for PCB content. Animals were sacrificed the 7th day after PCB administration. Levels of individual PCB compounds were measured in faeces and in various tissues

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of guinea pigs. To an aliquot of a homogenized individual sample of faeces, brain, muscle, abdominal adipose tissue, liver, blood, or kidney, dilute sulphuric acid (1:1) was added. The hexane sample extract was cleaned-up with concentrated sulphuric acid and purified by alkaline hydrolysis (KOH-ethanol), and by chromatography on micro columns (id 0.5 cm, 5 cm high) of silica (eluted with hexane) and Florisil (eluted with 1% dichloromethane in hexane). The hexane eluate was then analysed by high resolution gas chromatography (HRGC) with ^{63}Ni electron capture detection (ECD). HRGC-ECD was performed on a Hewlett-Packard 5890 instrument using a split-splitless injector and a 60 m x 0.25 mm (id) fused silica capillary column coated with SPB5 (Supelco), using hydrogen carrier gas. Individual PCB compounds, no. -54, -80, -155, and -169 were synthesized in our laboratory. Quantitation was performed with external standards. Recoveries were in the range of 80 - 102 %, depending on the component. IUPAC numbers were used for the assignation of PCB components (Ballschmiter and Zell 1980).

RESULTS AND DISCUSSION

The results are summarized in Table 1. The bioconcentration and the distribution patterns of four individual PCBs were different between faeces and tissues (Fig. 1).

Absorption in gastrointestinal tract of the studied PCBs calculated as a mass balance from the input (oral intake) and output (faeces collected during 7 days) was over 99 %. This is in agreement with the values of 96-98 % found for the intestinal absorption of some PCB compounds in human infants (McLachlan 1993). The lower retention of lower chlorinated and non-planar PCBs (e.g. PCB-54) and the higher retention of planar and highly chlorinated PCBs (e.g. PCB-169) with longer residence times in faeces was observed. This can be explained by a higher resorption of the less lipophilic compounds (1ogKow for PCB-54 and -169 were 5.21 and 7.42, respectively), and/or a lower resistence of PCB-54 to degradation in the digestive tract. PCB-54, with unsubstituted meta-para positions in the biphenyl molecule, was the most labile, and PCB-169 with a substituted meta-para position, was the most stable of the PCB compounds studied towards metabolism. These results suggest that the more highly toxic co-planar PCB (PCB-169) was associated to a greater degree with nonassimilated material in faeces than was the non-planar hexachloro substituted isomer (PCB-155).

The amount of toxic PCB ingested expressed in TEQ (2,3,7,8-TCDD toxic equivalents for PCB no. -77 and -169 were 0.0005 and 0.01 respectively from Ahlborg et al. 1994; TEQ of PCB-77 was used for PCB-80) was 0.060 µM/kg bw and surpassed the LD_{50} (30 days post exposure) dose for the guinea pig of 0.006 µM/kg bw (McConnell 1989). A deterioration in the animals was observed. Seven days after ingestion, the highest TEQs due to co-planar PCBs were present in fat and liver tissues, and the lowest in brain and blood (Table 1). The total PCB levels increased in the following

Table 1. Distribution of individual PCB compounds in guinea pig tissues after oral ingestion

PCB IUPAC no.	structure	log Kow[a]	oral intake (ng/g body wt.)	PCB contents[b] in samples (ng/g wet wt.)							
				faeces[c]		adipose tissue	liver	muscle	kidney	brain	blood
				day 1	day 7						
54	2,2',6,6'	5.21	6,000 (33)[d]	427 (24)	17 (4)	79 (0.6)	2 (0.1)	16 (1.3)	8 (0.8)	10 (9)	1 (5)
80	3,3',5,5'	6.48	3,000 (17)	380 (19)	84 (20)	5,246 (42)	517 (31)	493 (41)	371 (37)	46 (43)	7 (37)
155	2,2',4,4',6,6'	6.41	7,000 (39)	555 (28)	97 (24)	2,877 (23)	101 (6)	282 (23)	165 (16)	30 (28)	4 (21)
169	3,3',4,4',6,6'	7.42	2,000 (11)	596 (29)	213(51)	4,387 (35)	1,048 (63)	417 (35)	472 (47)	20 (19)	7 (37)
		Total PCB	18,000	2,006	411	12,589 /14,800/[e]	1,668 /35,500/	1,208 /19,800/	1,036 /22,500/	106 /22,500/	19
		TEQ[f]	21.50	5.98	2.17	46.49	10.74	4.42	4.90	0.22	0.07

a from Hawker and Connell (1988)
b arithmetic mean of 6 samples
c mixture of faeces samples from 6 animals
d weight percent (in parentheses) in PCB mixture
e lipid adjusted
f toxic equivalents (2,3,7,8-TCDD=1), (ng/g wet wt)

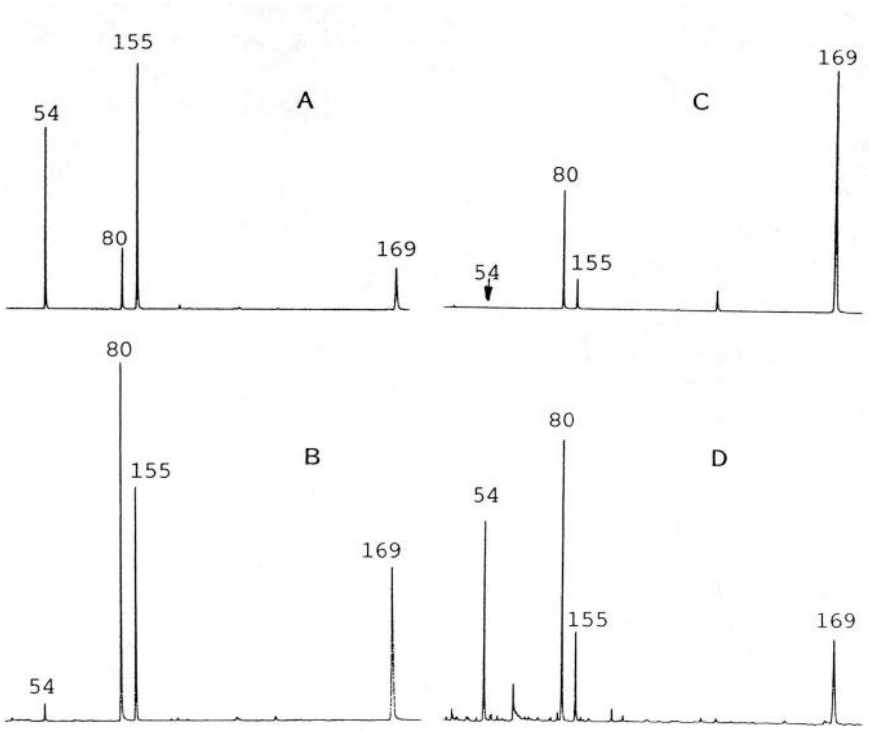

Figure 1. Gas chromatograms (EC detector) of PCB mixture ingested (A), of PCBs extracted from fat (B), liver (C), and brain (D) of guinea pigs. PCBs are assigned with IUPAC numbers.

order: blood < brain < kidney < muscle < liver < abdominal adipose tissue. Adjusted to lipid weight, the sum of PCBs increased in the order brain < blood < adipose fat < muscle < kidney < liver.

The migration of PCBs through blood to different organs or receptors might be governed by the structure of the targets. In the PCB pattern of liver tissue the major contribution was the metabolically stable highly chlorinated toxic co-planar PCB-169, with a minor contribution of lower chlorinated non-planar PCB-54. That indicats persistence to degradation of higher chlorine substituted co-planar PCBs (e.g. PCB-169, substituted in both para and all meta positions). The most outstanding observation was the difference between the brain and liver PCB congener patterns (Fig. 1). The liver/brain ratios of PCBs no. -54, -155, -80, and -169 were 0.2, 11.2, 3.3, and 52.4, respectively, and could have resulted from different stabilities and transformation processes of individual PCB compounds. In brain tissue the lipid composition, and lower permeability of the blood-brain barrier (Borlakoglu et al. 1990; Bernhoft and Skaare 1994) influenced the low PCB level. The minimal metabolism occurring in brain (Borlakoglu et al. 1990) could explain the relatively high amount of metabolically labile PCB-54 found in brain compared with all other tissues.

There are indications that the blood-brain barrier can distinguish between co-planar and non-planar PCB isomers. From the data in Table 1 the ratios of co-planar PCB-169 to non-planar PCB-155 in adipose and brain tissues were 1.5 and 0.7, respectively. From the low PCB-169/PCB-155 ratio in brain we could speculate that in brain tissue co-planar PCB isomers were less bioconcentrated than non-planar ones.

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