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Distribution and Excretion of 2,2′, 4,4′,6-Pentachlorobiphenyl in the Rat

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Polychlorinated biphenyls (PCB's) have been used extensively throughout the industrialized world for more than 40 years. Today PCB's are recognized as ubiquitous and persistant environmental contaminants (PEAKALL 1975). The biological properties of PCB's, and chlorinated hydrocarbons in general, are becoming better understood through studies of individual compounds (HAY 1978) and by such techniques as pharmacokinetic modeling (ANDERSON et al. 1977). This work describes the distribution and elimination of 2,2',4,4',6-pentachlorobiphenyl (2,2',4,4',6-PCB) in the rat. It has been pointed out that PCB's which are chlorinated in the 3,4-positions are not metabolized as readily as those compounds, which are not substituted in those positions; therefore 2,2',4,4',6-PCB should be a good model compound for those PCB's of relatively high chlorine content and long biological half-life.

MATERIALS AND METHODS

Five male (87-104 g) and five female (86-89 g) Sprague Dawley rats were acclimated to laboratory conditions in individual metabolism cages. All animals were fasted for 18 hours before receiving a Sesame oil solution of 5 µg 2,2',4,4',6-PCB per gram bodyweight by gavage. After dosing standard rat chow and water were available ad libitum. The dosing solution was prepared by adding 5.12 mg ^{14}C-labeled 2,2',4,4',6-PCB (specific activity 0.298 mCi/mmole), obtained from Gesellschaft fuer Strahlen- und Umweltforschung mbH, Institut fuer Oekologische Chemie, Birlinghoven, to a 5 ml volumetric flask and adding Sesame oil to the mark. Each animal received between 0.42 ml and 0.51 ml depending on bodyweight

Urine and feces were collected separately every 24 hrs from each cage. Urine volume was measured, an aliquot withdrawn and radioactivity determined by scintillation counting in a Packard 2425 Tri-Carb. Radioactivity in the feces was determined by oxidizing weighed samples of the homogenized feces in a Packard 306 sample oxidizer followed by scintillation counting of the generated $^{14}CO_2$.

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After eight days the animals were sacrificed. Organ and tissue samples were taken at necropsie and stored at -18°C until they could be oxidized to determine radioactivity.

RESULTS AND DISCUSSION

The concentrations of 2,2',4,4',6-PCB found in various tissues are listed in Table 1.

TABLE I

Concentration of 2,2',4,4',6-Pentachlorobiphenyl in Tissues of Sprague-Dawley Rats after a Single Oral Dose

Tissue	µg/g 2,2',4,4',6-PCB Males	Females
Heart	0.34	0.37
Lung	0.86	1.06
Duodenum	0.36	0.36
Liver	1.44	1.66
Abdominal Fat	27.4	27.7
Subcutaneous Fat	21.7	24.4
Lymph Nodes	8.07	6.11
Kidney	0.70	0.91
Testes	0.20	
Ovaries		11.74
Adrenal	4.49	6.51
Sciatic Nerve	7.62	3.12
Blood Plasma	0.13	0.13
Red Blood Cells	0.06	0.05
Muscle	0.20	0.33
Hair	0.26	0.40
Skin	0.43	0.47
Thymus	0.23	0.32

Fat levels in both males and females are high as are the levels found in lymph nodes. Adrenal and sciatic nerve also bear significantly high levels. Of particular interest are the relative levels found in ovaries and testes. The ovaries exhibit a concentration of 2,2',4,4',6-PCB over 50 times greater than the concentration found in the testes. High concentrations of other PCB's have been observed in the ovaries of rhesus monkeys (FELT et al. 1977) and rats (FELT et al. 1978 a,b). Also of interest are the fairly high levels observed in skin and hair. The importance of skin as a pharmacokinetic compartment for PCB's in the rat has been pointed out (LUTZ et al. 1977) and further confirmed in this study. The levels of 2,2',4,4',6-PCB which we observe in the hair do not vary appreciably with sampling site and are not significantly lowered

by washing the hair with a detergent solution or with acetone prior to sample oxidation.

The elimination of 2,2',4,4',6-PCB in rats follows a biexponential rate expression with an α phase half-life of 0.90 ± 0.1 and 0.95 ± 0.1 days for females and males respectively. The β phase half-lives are 4.2 ± 0.1 and 3.8 ± 0.1 days for females and males respectively. The method of calculating the half-lives has been described elsewhere (FELT et al. 1977). In 7 days, the males excreted 46.6 % and the females 38.3 % of the administered dose. The majority of the excreted radioactivity was found in the feces: 83 % in males and 81 % in females. Figure 1 shows the total excretion curves.

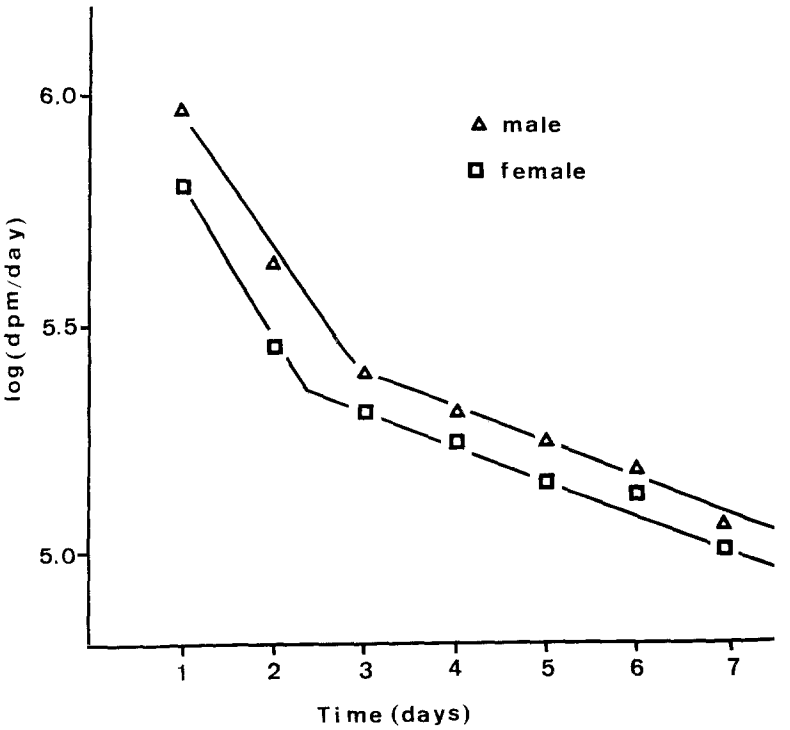

Figure 1: Total Excretion of 2,2',4,4',6-Pentachlorobiphenyl by Male and Female Rats

The metabolism of 2,2',4,4',6-PCB by rats has been reported (LAY et al. 1975, GOTO et al. 1975) and was not examined in detail here. However, chromatographic examination of 2,2',4,4',6-PCB metabolites confirms that hydroxylation is the predominant metabolic pathway.

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