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Absorption of some Organochlorine Compounds by the Rat Small Intestine—*In Vivo*

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Although there are many reports on the properties and effects on the flora and fauna of DDT, HCB, lindane and PCBs (BROOKS 1974, HUTZINGER et al. 1974, TURNER and GREEN 1974, BOOTH and McDOWELL 1975, ENGST et al. 1977) little is known about the absorption of these compounds into the body after oral administration. In particular, the role of the lymphatic system in the absorption of these compounds is not clear, in spite of the known importance of this system in the absorption of long-chain fatty acids, cholesterol and some other dietary components (CODE 1968).

Compounds that enter the body via the intestinal lymphatic system, bypass the liver; accordingly they are not subjected initially either to the detoxifying reactions of the liver or to excretion via the biliary system. In effect, compounds transported in the above manner can be distributed to all parts of the body in their unmetabolised form.

This paper reports studies to compare the absorption in blood or lymph of DDT, HCB, lindane or a mixture of three PCBs from rat intestinal loops.

MATERIALS AND METHODS

Organochlorines used in the intestinal loops

All the organochlorines used in this work were analytical grade samples obtained from commercial sources.

DDT - 1,1,1-trichloro-2,2-di-(4-chlorophenyl) ethane.
HCB - hexachlorobenzene.
Lindane - 1,2,3,4,5,6-hexachlorocyclohexane.

The PCB used was an equimolar mixture of the following three isomers:

2,5,2^1,5^1-tetrachlorobiphenyl

2,4,5,2^1,5^1-pentachlorobiphenyl

2,3,4,5,6,2^1,5^1-heptachlorobiphenyl.

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Preparation of intestinal loops

Male Wistar rats (300-350 g) were used. Intestinal loops were prepared as described by TURNER et al. (1977). In addition, the intestinal lymphatic duct was cannulated at a point just before it enters the cisterna chyli. The polythene cannulae were secured with tissue glue (Ethicon Bucrylat, Ethicon, Hamburg, Germany). To avoid losses of lymph fluid it was necessary to close off the accessory lymph duct which was sometimes well-developed. Blood transfusions were carried out as described by TURNER et al. (1977).

Injection of loops

The prepared loops were injected with 0.4 ml of a solution of the appropriate organochlorine compound dissolved in rat bile. The rat bile was pooled from several male rats with cannulated bile ducts, stored at -18 °C in aliquots suitable for use in preparing the solutions of the organochlorine compounds.

Two concentrations of the organochlorine compounds were used, 0.05 µmole and 0.10 µmole/0.4 ml bile. The PCBs were injected as an equimolar mixture, i.e., either 0.05 µmole or 0.10 µmole of each compound. Before the injection of the organochlorines, mesenteric venous blood and lymph from the intestinal lymphatic duct were collected for 3-4 minutes to provide control samples for analysis. After injection of the compound, blood and lymph were collected for a further 30 minutes. The volumes of all blood and lymph samples were measured and the samples then deep-frozen until analysis.

Analyses

DDT, HCB and lindane levels were determined by the method of HUNNEGO and HARRISON (1971) and PCBs by the method of DOGUCHI and FUKANO (1975).

RESULTS AND DISCUSSION

The results are summarised in Table I. From the table it can be seen that lindane was rapidly absorbed. This may be a consequence of its greater water solubility compared with the other organochlorine compounds used. Lindane has a solubility in water of 7.3 ppm at 25 °C (GUNTHER et al. 1968) compared with the other compounds which have solubilities less than 50 parts per billion (HUTZINGER et al. 1974). With the PCB compounds there was a decrease in absorption as the chlorine content of the molecule increases; thus, about 10% of the tetrachloro-compound was absorbed, about 4% of the pentachloro-compound and only 0.9% of the heptachloro-compound. There is also a decrease in water solubility of these compounds as the chlorine content increases (HUTZINGER et al. 1974).

TABLE I

The absorption of lindane, HCB, DDT and a mixture of three PCBs from rat intestinal loops *in vivo*.

Nmole of compound in loop	% absorbed from intestine/30 min			Ratio blood/lymph concentrations		
	Experiment			Experiment		
	1	2	3	1	2	3
Lindane						
50	42.6	29.6	40.9	151	1477	2045
100	53.0	42.3		5296	1057	
HCB						
50	7.0	6.8	11.5	116	170	576
100	10.5	8.2	10.2	260	115	1019
DDT						
50	2.5	4.1	6.5	131	25	3.1
100	1.8	3.2	2.0	15	1.1	16
PCB*						
50-tetra-	8.7	8.1	12.0	33	202	298
penta-	3.9	3.6	5.3	6.0	15	32
hepta-	1.1	0.8	1.0	0.9	2.6	3.6
100-tetra-	6.9	9.5		345	474	
penta-	2.9	3.7		11	60	
hepta-	0.8	0.8		0.8	2.4	

* 2,5,2^1,5^1-tetrachlorobiphenyl

2,4,5,2^1,5^1-pentachlorobiphenyl

2,3,4,5,6,2^1,5^1-heptachlorobiphenyl

The more lipid-soluble compounds were also absorbed into the lymphatic system whereas the least lipid-soluble compound (lindane) was only detected in traces in the lymph of some of the rats. The blood/lymph ratio of DDT was lower than that for lindane or HCB. The highly chlorinated biphenyls were more readily absorbed by the lymphatic system than the less chlorinated biphenyls. In fact in two animals the proportion of PCB in the lymph was greater than that in the blood. Different blood/lymph ratios of individual PCB compounds may account in part for the variations reported between gas chromatograms of standard Arochlor mixtures and the chromatogram profiles obtained from tissue extracts (HUTZINGER et al. 1974). It is generally assumed (HUTZINGER et al. 1974) that different rates of metabolism of the various chlorinated biphenyls account for the differences in the gas chromatogram profiles. The demonstration in this work that

highly chlorinated biphenyls are absorbed via the lymphatic system as well as via the blood system means that careful interpretation of gas chromatogram profiles is needed. Compounds entering the lymphatic system avoid the "first pass" effect encountered by substances absorbed directly into the bloodstream. Therefore, whereas the highly chlorinated PCBs may be distributed to the tissues and stored in the fat, less chlorinated compounds, with a high blood'lymph ratio, could be extensively metabolised by the liver before reaching the tissues.

Under "natural" conditions, when the organochlorine compounds are mixed with food, it is likely that there would be a much greater absorption into the lymphatic system of mammals than indicated in the present work, since the organochlorines would dissolve in the dietary lipids and be incorporated in bile-salt micelles.

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