Placental Transfer of Hexachlorobenzene in the Rat

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Hexachlorobenzene (C_6Cl_6, HCB) has gained prominence as an environmental contaminant through its use as a fungicide and as an industrial chemical (KOEMAN et al., 1969; ACKER and SCHULTE, 1970; JOHNSON et al., 1974). Although there is considerable information on the metabolism, distribution and biochemical effects of this compound in adult rats (MEHENDALE and MATHEWS, 1973; GRANT et al., 1974; KUIPER-GOODMAN et al., 1974) no information is available on the accumulation of HCB by the rat fetus *in utero*. This study reports on the transplacental passage and subsequent fetal tissue distribution (brain and liver) of HCB in the rat.

Methods

Study 1. The fetuses for this study were obtained from an experiment designed to determine the teratogenicity of hexachlorobenzene (KHERA, 1974). Nulliparous Wistar rats (200-250 g) were paired overnight with males. The morning when sperm were observed in vaginal smears was considered to be day 1 of pregnancy. The mated females were randomly assigned to experimental groups and administered HCB (BDH, England. Purity not less than 99.5%) in corn oil at 80 and 120 mg/kg body weight. The amount of corn oil administered was 1.0 ml/100 g body weight. The females were dosed daily at the above levels from day 6-16 of pregnancy and were killed on day 22 of gestation. The fetuses were removed by cesarian section, weighed and stored frozen pending HCB analysis. Ten pups from 4 litters were analyzed in the 80 mg/kg group and 15 pups from 6 litters analyzed in the 120 mg/kg group.

Study 2. The same experimental design was used as in Study 1 except that the HCB levels tested were 5, 10, 20, 40 and 80 mg/kg. Fetuses were removed by cesarian section on day 22, 4 pups/litter were dissected to remove brain and liver. These along with the remaining

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TABLE 1

HCB Residue Data[1]

HCB Administered[2]	Study 1		Study 2				
	HCB Residue in fetus		HCB Residue				
	ppm	ug/fetus	Maternal Liver (ppm)	Fetal Liver (ppm)	Fetal Brain (ppm)	Whole Fetus (ppm)	Whole Fetus (ug)
5	—	—	9.3±2.9	1.8±0.1	1.1±0.1	1.5±0.1	7.5±0.6
10	—	—	9.6±0.4	3.9±0.3	2.1±0.2	2.3±0.1	11.9±0.7
20	—	—	21.7±0.9	6.2±0.6	3.9±0.3	5.4±0.1	27.9±0.6
40	—	—	51.6±2.2	16.5±2.5	8.4±1.1	10.9±0.8	53±3.2
80	17.5±1.5	83.0±9.8	86.0±0.8	35.8±4.1	17.5±2.3	18.9±0.3	90.5±1.6
120	30.7±9.7	169±65	—	—	—	—	—

1 Figures represent the mean ±S.E. See methods for number of animals.

2 The amount of HCB administered in mg/kg body weight.

whole pups(at least 20 per dose level) and the maternal liver (two per dose level) were frozen pending HCB analysis.

HCB analysis of tissues was carried out using a GLC-EC technique described previously (VILLENEUVE et al., 1974a). Results are expressed as ppm wet tissue and ug per total tissue.

Results

Fetuses from an earlier investigation reporting the non-teratogenicity of HCB (KHERA, 1974) were analyzed and found to contain significant residues of HCB (Table 1). When the study was repeated using additional dose levels (Study 2) the residue data (Table 1) confirmed that HCB crosses the placenta and accumulates in the fetus in a dose-dependent manner. At all doses the maternal liver had the highest HCB residue followed by fetal liver, whole fetus and fetal brain. This is in direct contrast to the results obtained in the rabbit (VILLENEUVE et al., 1974b) where the fetal liver contained 2-4 times the level of the corresponding maternal organ, which in turn was 10-15 times higher than fetal brain levels. In both species no fetopathic effects were observed at any dose level. In view of these and earlier findings it is concluded that the presence of HCB in fetal and maternal tissues caused no apparent adverse effect on fetal development.

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