Toxicity and Tissue Levels in the Rat and Guinea Pig Following Acute Hexachlorobenzene Administration

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Introduction

Hexachlorobenzene (HCB, C_6Cl_6) is used both as an agricultural and industrial chemical. Like many other organohalogens, concern has been raised over its bioaccumulation and persistence in the environment. This has prompted considerable research to determine both its short and long term biological effects (Ockner and Schmid, 1961; Medline et al., 1973; Somers et al., 1973, Vos et al., 1971, Grant et al., 1974a; Villeneuve, 1974; Villeneuve and Hierlihy, 1974, Villeneuve et al., 1974a; Villeneuve et al., 1974b; Khera, 1974). Although some studies reported the acute toxic effects of HCB (Melis, 1956, Savitkii, 1965), there is very little information relating tissue levels in animals which died from HCB intoxication. The present work was initiated to determine the extent of toxicity and tissue accumulation of HCB in both sexes of two species.

Methods

Eleven male (270-300 g) and eleven female (198-210 g) Wistar rats (Woodlyn Farms, Ontario) as well as 7 male (628-800 g) and 7 female (520-604 g) guinea pigs (Connaught Laboratories, Willowdale, Ontario) were dosed daily (p.o.) with hexachlorobenzene (British Drug House, England purity greater than 99.5%) in corn oil for 16 days at 500 mg/kg body weight. All animals which survived the treatment were killed 24 hrs after the last dose by decapitation. Liver and brain tissues were excised and

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stored frozen pending HCB analysis. Animals which died during the 16 day period were immediately dissected to obtain the liver and brain which were also 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 of wet weight tissue.

Results

Table 1 summarizes the data obtained from the rat study. Of the 11 males administered HCB, 8 died during the dosing period. Female rats were less affected by HCB with only 5 dying while on test. Both males and females which died during dosing lost the same amount of weight; however, it took more doses to achieve this weight loss in females. No significant difference was noted in either brain or liver levels of HCB in both sexes that died during dosing. For animals killed after 16 doses, the males gained weight while the females lost weight, but not as much as those which died during dosing. There was no difference in amounts of HCB in the brain and liver in male and female animals killed after 16 days.

TABLE 1

Toxicity and tissue residue levels of rats dosed p.o. with 500 mg HCB/kg body weight/ day.

Group[1]	No. Animals	No. of[2] Doses	WT. Gain[2] (g) during dosing period	HCB content (PPM)[2] Brain	Liver
M-D	8	13.3±0.5	-33.5±5.0	131±14	605±86
F-D	5	15.6±0.2**	-32.4±3.0	132±22	779±218
M-K	3	16.0	24.0±1.0	83±14	449±100
F-K	6	16.0	-14.5±5.7**	117±17	326±40

1 M refers to male, F to female, D to those animals which died during dosing and K those animals which were killed after 16 doses.
2 Represents the mean ±S.E.M.
* Denotes significant difference (P=0.05) from opposite sex
**Denotes significant difference (P=0.01) from opposite sex

Table 2 summarizes the data obtained in the guinea pig study. All animals died during dosing. The number of doses each animal recieved were the same but males lost more weight than females. Furthermore male brain and liver accumulated more HCB than the female tissues.

TABLE 2

Toxicity and tissue residue levels of guinea pigs dosed p.o. with 500 mg HCB/kg body weight/day.

Group[1]	No. Animals	No. of[2] Doses	WT. Gain2 (g) during dosing period	HCB content (PPM)[2] Brain	Liver
M-D	7	12.1±1.2	-193±14	11.3±1.8	220±41
F-D	7	9.0±1.2	-110±17**	5.59±1.1*	117±17*

1 M refers to male, F to female
2 Represents the mean ± S.E.M.
* Denotes significant difference from other group (P=0.05)
** Denotes significant difference from other group (P=0.01)

Tissue accumulation of HCB was greater in the rat than in the guinea pig. However, the rat was less susceptible to the toxic effects of HCB as measured by mortality and body weight loss. The most important difference between the rat and guinea pig is the greater susceptibility exhibited by the latter species, a fact which has been reported previously by Melis (1955). An interesting feature with the rat toxicity data is that it is directly contrary to findings on long term chronic feeding studies (Grant, 1974b). He found females to be more susceptible to the toxic effects of HCB than males. A probable explanation is that female rats acquire porphyria when exposed to HCB to a greater extent than male rats (Grant, 1974b). The chronic toxicity thus tends to be associated with the development of porphyria, while in a short term acute study like ours, porphyria would be expected to play little part.

In summary, the comparative effects of acute HCB administration in the rat and guinea pig have been noted. Male rats appear to be more susceptible to the toxic effects of HCB than female rats but this difference is not

reflected by different brain or liver residue levels. HCB is more toxic but accumulates to a much lesser degree in the guinea pig.

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