Antagonism of DDT Storage in Guinea Pigs by Dietary Dieldrin

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Tissue storage of organochlorine pesticides is one aspect of major importance in the toxicology of such compounds in most organisms. However, the toxicologic implications of multiple exposure to various organochlorine pesticides is complicated by their propensity to interact antagonistically in some species. When DDT and dieldrin are fed simultaneously to rats, there is a decrease in dieldrin storage and, if the dieldrin dosage is sufficiently high, a modest increase in DDT storage (1). The theorized mechanism for the antagonism of dieldrin storage by DDT is induction of dieldrin-metabolizing liver microsomal enzymes (2).

This phenomenon is apparently subject to wide species variability. DDT antagonized dieldrin storage in pigs (3) and trout (4), but not in sheep or hens (3). In dogs, DDT enhanced dieldrin storage after aldrin consumption (5). Conversely, dieldrin stimulated DDT storage in trout (4) and dogs (5). This report describes the DDT-dieldrin interaction in guinea pigs.

Methods

Adolescent male Hartley guinea pigs weighing 200 to 300 grams were individually caged and were fed experimental diets ad libitum for 14 days. The basal diet was ground Purina Guinea Pig Chow. Pesticides dissolved in petroleum ether were added to the diets before mixing. Chromatographically pure samples of p,p'-DDT, HEOD (dieldrin), and the gamma isomer of hexachlorocyclohexane (lindane) were fed. Storage of pesticides in peritoneal fat was determined by gas liquid chromatography (1). Liver microsomal enzyme activity was measured via O-demethylation of p-nitroanisole (6), oxidative cleavage of EPN (6), and oxidation of aniline (7) in the 10,000 x g supernatant fluid on the day of kill. The assayed products in the enzyme procedures were p-nitrophenol (PNP) from p-nitroanisole and EPN, and p-aminophenol (PAP) from aniline.

Results

DDT, dieldrin, and lindane were fed to guinea pigs at 25 ppm of the diet. From the results summarized in Table 1 it can be seen that lindane and DDT were stored at low levels and only moderately stimulated the activity of liver microsomal enzymes. No DDE was detected. Dieldrin was stored at a much higher level and markedly induced enzyme activity.

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TABLE 1

Activity of hepatic microsomal enzymes and pesticide storage in guinea pigs fed DDT, lindane, or dieldrin for 14 days.[a]

Treatment	N	Pesticide storage (ppm in fat)	O-demethylase (μmoles PNP/hr/ g liver)	EPN detoxication (μmoles PNP/hr/ g liver)	Aniline oxidase (μmoles PAP/ 30 min/ g liver)
Control	5	-	1.40 ± .13	.92 ± .06	.36 ± .04
DDT (25 ppm)	5	21 ± 2	1.68 ± .16	1.18 ± .14	.49 ± .09
Lindane (25 ppm)	5	12 ± 4	1.86 ± .16	1.04 ± .09	.55 ± .03[c]
Dieldrin (25 ppm)	4	542 ± 114	3.40 ± .46[c]	1.51 ± .19[b]	.82 ± .11[c]

a Values are mean ± SE
b Significantly different from control at .05 level
c Significantly different from control at .01 level

The DDT-dieldrin interaction was studied in guinea pigs placed on a 2 X 2 factorial arrangement of 1 ppm dieldrin and 50 ppm DDT. An extra group was fed 50 ppm dieldrin. From the results summarized in Table 2 it can be seen that dieldrin storage was unaffected by DDT. However, DDT storage was slightly reduced by concurrent dieldrin exposure. There was no detectable storage of DDE. Microsomal enzyme activity was not markedly altered by DDT but was significantly elevated in those animals fed the high level of dieldrin. A decrease in body weight gain (0% gain compared to 13% in controls) significant at the .05 level was noted in animals fed 50 ppm dieldrin.

The indication in the above data that DDT storage in guinea pigs is antagonized by dieldrin was verified in a later experiment. Control guinea pigs were fed 50 ppm DDT in comparison to a group fed a diet containing both 50 ppm DDT and 25 ppm dieldrin (Table 3). This level of dieldrin had no effect on body weight gain. Storage of DDT in body fat was reduced 76% by concurrent dieldrin consumption. Microsomal enzyme activity was significantly elevated in dieldrin-fed animals.

Discussion

A question of importance in organochlorine pesticide exposures is the ability of organisms to adapt. The guinea pig apparently possesses this ability to a greater degree than other mammals studied. The ability of rats and other species to adapt to DDT was observed but generally unappreciated for many years (8). Rhesus monkeys fed DDT are similar to guinea pigs in that they do not accumulate DDE but their retention of DDT is similar to most other mammals (9). More recently Morello (10) has noted that in rats DDT stimulates its own metabolism. Even in humans there are now indications that DDT storage can be reduced through enhanced metabolism (11).

The ability of organochlorine pesticides to induce liver microsomal enzymes in guinea pigs is apparently related to tissue storage levels of these pesticides. The lack of a DDT effect on dieldrin storage in guinea pigs may be due to an insufficiency of DDT at the sites of this activity in the body.

The limited storage of DDT in guinea pigs and absence of DDE would suggest that this species may possess an efficient DDT-metabolizing system. The relationship in dieldrin-fed guinea pigs of increased microsomal enzyme activity and decreased DDT storage suggest that the storage level might be reduced through stimulated activity of DDT-metabolizing enzymes. On the other hand, there is the possibility that the reduced storage of DDT in guinea pigs is due to a species difference in absorption or translocation of the chemical.

TABLE 2

Activity of hepatic microsomal enzymes and pesticide storage in guinea pigs fed various combinations of DDT and dieldrin for 14 days.[a]

Treatment	N	DDT		Dieldrin		O-demethylase (μmoles PNP/hr/ g liver)	EPN detoxication (μmoles PNP/ hr/g liver)	Aniline oxidase (μmoles PAP/ 30 min/g liver)
		Consumed (mg/Kg BW)[b]	Stored (ppm)	Consumed (mg/Kg BW)[b]	Stored (ppm)			
Control	7	-	-	-	-	1.14 ± .10	.75 ± .03	.35 ± .09
Dieldrin (1 ppm)	4	-	-	.85 ± .01	8 ± 2	1.74 ± .24	.88 ± .17	.25 ± .03
DDT (50 ppm)	4	39 ± 3	28 ± 5	-	-	1.51 ± .24	.86 ± .10	.37 ± .06
Dieldrin (1 ppm) DDT (50 ppm)	4	40 ± 2	20 ± 2	.81 ± .03	8 ± 1	1.87 ± .30	.96 ± .19	.38 ± .05
Dieldrin(50 ppm)	4	-	-	35 ± 9	361 ± 63	4.12 ± .36[c]	1.54 ± .13[c]	.76 ± .04[c]

a Values are mean ± SE
b BW is body weight at start of experiment
c Significantly different from control at the .01 level

TABLE 3

Activity of liver microsomal enzymes and storage of pesticides in guinea pigs fed DDT and DDT plus dieldrin for 14 days.[a]

Treatment	N	DDT		O-demethylase (μmoles PNP/hr g liver)	EPN detoxication (μmoles PNP/hr g liver)	Aniline oxidase (μmoles PAP/ 30 min/g liver)
		Consumed (mg/Kg BW)[b]	Stored (ppm)			
DDT (50 ppm)	4	72 ± 6	26 ± 2	1.41 ± .13	.75 ± .07	.38 ± .06
DDT (50 ppm) Dieldrin (25 ppm)	4	81 ± 3	6 ± 1[d]	3.17 ± .19[d]	1.01 ± .12	.64 ± .05[c]

a Values are mean ± SE
b BW is body weight at start of experiment
c Significantly different from control at .05 level
d Significantly different from control at .01 level

The different nature of the DDT-dieldrin interaction in guinea pigs as compared to rats and other species is troublesome to the extrapolation of pesticide interaction data from species to species. But it does provide more varied material from which to choose models of human responses to pesticides. Additionally, and perhaps more importantly, it adds to our awareness of the importance in solving environmental problems of not limiting studies to effects of a single substance on a single species, but rather engaging in studying interactions of various substances and species.

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