

DISTRIBUTION OF pp'DDT IN CERTAIN BRAIN REGIONS OF RATS
TREATED WITH DIAZINON

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The effect of diazinon, given intraperitoneally, on the distribution of pp'DDT was determined in certain brain regions of rats. pp'DDT concentration expressed per gram of wet weight was highest in the corpus striatum (2575 ng/g) followed by those in the cerebellum (1850 ng/g) and in the cortex (990 ng/g). Pretreatment with diazinon increased pp'DDT accumulation in various brain regions by about 20 per cent (corpus striatum 2995 ng/g; cerebellum 2240 ng/g and cortex 1245 ng/g) and reduced cholinesterase activity by 50-70 per cent.

The effects of pp'DDT have been reported to be directly related to the concentration of the compound in the brain (1, 2). In immature rats which tend to be insensitive to pp'DDT, less compound enters the brain than in adult rats, which are more susceptible to its effects (3, 4). Acetylcholinesterase activity in the brain has also been said to influence the entry of certain chemicals and drugs in the brain or to modify their effects (5, 6). The role of acetylcholinesterase inhibition on pp'DDT accumulation in various brain regions has not been determined. We now report on pp'DDT concentration in various brain regions in rats pretreated with diazinon, which is known to inhibit acetylcholinesterase activity in the brain and in other body tissues (7).

MATERIAL AND METHODS

Experimental animals were adult male albino rats, 150 ± 10 g. The animals were maintained on a 12 h light/dark schedule at a temperature of 25 ± 1 °C as reported elsewhere (8). pp'DDT (dissolved in peanut oil) was injected intraperitoneally in a dose of 25 mg/kg, 30 min after the administration of diazinon (10 mg/kg, i.p.). Control animals were given peanut oil. All the animals were decapitated one hour after

treatment with pp'DDT. The cortex, cerebellum and corpus striatum were dissected (9) and the level of acetylcholinesterase activity was determined by the method of *Ellman and co-workers* (10). pp'DDT was extracted with hexane and assayed by gas liquid chromatography (GLC) according to the procedure described by *de Faubert Maunder and co-workers* (11). The corpus striatum and cerebellum (both hemispheres) were pooled for each determination; the volumes of reagents or chemicals used were adjusted accordingly for each sample. Samples were analysed by gas liquid chromatography (Varian Aerograph Series 2400) using electron-capture detectors (^3H) at the following operating conditions: detector temperature: 200 °C; injector temperature: 190 °C; column temperature: 180 °C; gas flow: 40 ml/min; gas pressure: 65 psi; carrier gas: pure nitrogen passed through silica gel and molecular sieve to remove moisture and oxygen; column: glass spiral column, 1.8 m x 0.32 cm ID, coated with 1.5% OV-17 + 1.95% OV-2100.

The sensitivity of the method was 0.002 ppm for pp'DDT. The data were analysed statistically using Student's t-test. Significant differences between the means calculated as p values are given in Table 1.

RESULTS

Changes in the level of acetylcholinesterase activity in different brain regions (cortex, corpus striatum and cerebellum) in pp'DDT and diazinon treated rats are given in Table 1. The results indicate that more pp'DDT was present in the corpus striatum than in the other brain regions. Pretreatment with diazinon reduced acetylcholinesterase activity and increased pp'DDT concentration in all the brain regions (Table 1).

DISCUSSION

As expected, the organophosphorus compound diazinon induced remarkable inhibition of acetylcholinesterase activity in various brain regions (Table 1). The pp'DDT content of the cortex, corpus striatum and cerebellum is given in Table 1. It is of interest to note that pp'DDT accumulation was significantly greater in the corpus striatum than in the other brain regions both in normal and in diazinon treated animals. It was previously reported that the tremor appearing early during acute DDT poisoning was related to pp'DDT accumulation in the cerebellum (12, 13) which is involved in the regulation of motor function. As the corpus striatum is a brain area important for regulation of motor activity, its neurochemical changes or lesions being associated with certain motor dysfunctions (14-17), pp'DDT accumulation in this brain region is likely to be responsible for certain toxic effects as well. It was also previously reported that pretreatment of animals with physostigmine, an inhibitor of acetylcholinesterase of natural origin, caused greater penetration of certain chemicals and drugs (e.g. barbiturates) through the blood brain barrier (5, 6) resulting in their enhanced effects or accumulation in the brain. This is consistent with our finding that

Table 1
 Effect of diazinon on pp'DDT accumulation in certain brain regions of rats. pp'DDT (25 mg/kg, i.p.) was given 30 min after treatment with diazinon (25 mg/kg, i.p.). The animals were killed one hour after treatment with pp'DDT. Each group consisted of six animals.

Treatment group	Cortex		Corpus striatum		Cerebellum	
	Acetylcholinesterase mean \pm S. E.	pp'DDT (ng/g) mean \pm S. E.	Acetylcholinesterase mean \pm S. E.	pp'DDT (ng/g) mean \pm S. E.	Acetylcholinesterase mean \pm S. E.	pp'DDT (ng/g) mean \pm S. E.
1. Controls	6.18 \pm 0.47	N. D.	38.71 \pm 2.74	N. D.	33.12 \pm 1.85	N. D.
2. pp'DDT	5.92 \pm 0.30	990 \pm 22 ^{a,b} (860-1210)	40.01 \pm 2.90	2575 \pm 38 ^{a,b} (2450-2740)	32.71 \pm 2.41	1850 \pm 32 ^{a,b} (1725-2010)
3. Diazinon	3.38 \pm 0.18 ^a	N. D.	12.01 \pm 1.41	N. D.	16.12 \pm 1.72 ^{a,d}	N. D.
4. Diazinon + pp'DDT	3.42 \pm 0.22 ^a	1245 ^b \pm 31 (1050-1425)	12.65 \pm 1.84	2995 \pm 34 ^{b,c} (2860-3210)	16.72 \pm 1.82 ^{a,d}	2240 \pm 35 ^{b,d} (2050-2435)

N. D. = Not detected;

Figures in parentheses indicate the range of values.

The pp'DDT concentration is expressed as ng/g brain tissue. Acetylcholinesterase activity is expressed as micromoles of substrate (acetylthiocholine) hydrolysed/min/g.

a. Significantly different from group 1 values, $p < 0.01$.

b. Significantly different from group 2 values, $p < 0.05$.

c. Significantly different from the values for different brain regions in the same group (3&4) $p < 0.01$

d. Significantly different from the values for different brain regions in the same group (3&4) $p < 0.05$.

acetylcholinesterase inhibition in diazinon treated animals was accompanied by a greater accumulation of pp'DDT in certain brain regions (Table 1).

As the toxic effects of pp'DDT have been reported to be directly related to the concentration of the compound in the brain (1, 18), which increases with acetylcholinesterase inhibition in diazinon treated animals (Table 1), they are likely to be enhanced by previous exposure to acetylcholinesterase inhibitors.

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Sažetak

RASPODJELA pp'DDT U NEKIM DIJELOVIMA MOZGA U ŠTAKORA TRETIRANIH DIAZINONOM

Određivan je učinak intraperitonealno davanog diazinona na raspodjelu pp'DDT u nekim dijelovima mozga u štakora. Koncentracija pp'DDT po gramu težine mozga bila je najviša u korpusu strijatumu (2575 ng/g), zatim malom mozgu (1850 ng/g) i kori velikog mozga (990 ng/g). Prethodni tretman diazinonom povećao je akumulaciju pp'DDT u regijama mozga štakora za oko 20% (korpus strijatuma 2995 ng/g, mali mozak 2240 ng/g, kora velikog mozga 1245 ng/g). Aktivnost acetilkolinesteraze mozga smanjila se za 50 do 70%.

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