Absence of Conversion of *o,p'*-DDT to *p,p'*-DDT in the Rat

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Several reports have appeared in the literature which described the in vivo and in vitro conversion of o,p'-DDT to p,p'-DDT (1). These observations were not consistent with experimental results previously obtained at this laboratory, when o,p'-DDT was administered to the rat and squirrel monkey, or with those of Lamont et al. (2) when o,p'-DDT was administered to mallard ducks. The conversion of o,p'-DDT to p,p'-DDT is of interest; p,p'-DDT has greater insecticidal activity, o,p'-DDT has been reported to have high estrogenic activity (3), and o,p'-DDD, a metabolite of o,p'-DDT, induces atrophy of the adrenal cortex in man (4) and the dog (5). Additionally, it has been suggested that many of the undesirable effects of technical DDT are due to the o,p'-component (6).

The experiment described in this communication was designed to parallel the studies of Klein et al. (1) except that ^{14}C ring-labeled o,p'-DDT (7) was incorporated in the experiment. The purpose of the experiment was to test the report observation that o,p'-DDT is converted to p,p'-DDT by measuring the ^{14}C activity of the p,p'-DDT found in the animals fed ^{14}C-labeled o,p'-DDT. If this conversion does take place, ^{14}C-p,p'-DDT would be recovered.

To study the storage and possible isomeric conversion of o,p'-DDT, 12 female Sprague-Dawley rats weighing 200-250 g each were fed 50 ppm o,p'-DDT in their diet for 12 weeks. No sign of toxicity developed in any animal. For each of the 3 days before the animals were to be sacrificed, ^{14}C-labeled o,p'-DDT (5 μCi, 1 mg) was administered orally in peanut oil to the 12 animals receiving o,p'-DDT. An additional 6 animals were included in the experiment as controls. The animals were sacrificed by decapitation and dissected immediately. Fat samples (5 g) were collected, prepared for residue analysis by the method of Mills, Onley, and Gaither (8), analyzed by gas-liquid chromatography (8), and the results

[1] Samples were counted with a Nuclear Chicago Mark I liquid scintillation system in vials containing 15 ml of 8g of Butyl PBD and 85 g of naphthalene per liter of p-dioxane.

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confirmed by thin layer chromatography (8). Radioactivity of individual residues was determined by liquid scintillation counting[1] of the individual components trapped in cool capillary tubes attached to the exit of the gas-liquid chromatograph. The absolute recovery of radioactivity was determined by combusting a portion of the fat and determining $^{14}CO_2$. All analytical manipulations were compared to those values obtained by combustion. Recoveries of radioactivity were determined after extraction, as well as after liquid-liquid partition, column, and gas chromatography. Recovery of ^{14}C from the fat was determined to be 85 ± 6%. Recoveries of ^{14}C ring-labeled o,p'-DDT and p,p'-DDT, injected into and collected from the gas-liquid chromatograph, were not significantly different and were determined to be 64 ± 11%.

The quantities of residues of p,p'-DDE and p,p'-DDT found in the fat of rats treated with o,p'-DDT were not different from those in the control, as shown in Table 1. The levels of o,p'-DDT in the fat of the animals receiving 50 ppm in their diet as well as ^{14}C-labeled o,p'-DDT were approximately five times those of the animals receiving only ^{14}C-labeled o,p'-DDT. No o,p'-DDE was detected. The lack of change in the storage of p,p'-DDE and p,p'-DDT suggested that o,p'-DDT was not isomerically converted. Increased concentration of o,p'-DDD found in both groups of rats treated with o,p'-DDT indicates that conversion from o,p'-DDT to o,p'-DDD did occur.

TABLE 1

Pesticide residue contents (ppm, mean ± S.E.) of fat from rats fed o,p'-DDT*

Pesticide found	Control (6 rats)	Treatment ^{14}C-o,p'-DDT† (6 rats)	50 ppm in diet‡ + ^{14}C-o,p'-DDT (12 rats)
p,p'-DDE	1.3±0.19	1.1 ± 0.14	1.2 ± 0.07
p,p'-DDT	3.6±0.48	2.7 ± 0.16	3.3 ± 0.34
o,p'-DDD	N.D.	0.25± 0.03	1.2 ± 0.07
o,p'-DDT	M.D.	2.1 ± 0.31	9.6 ± 0.62

* N.D. = None detectable at 0.1 ppm.
† Given orally for 3 days before sacrifice.
‡ Fed daily for 12 weeks.

The results of the radioassay of these fat samples are shown in Table 2. The lack of any ^{14}C activity in either p,p'-DDT or p,p'-DDE indicates that ^{14}C-o,p'-DDT was not converted to these compounds. The technique used would detect ^{14}C-labeled o,p'-DDT at 20 times back-

ground at the level of 0.05 ppm. The finding of radioactivity in the o,p'-DDD confirms that conversion of o,p'-DDT to o,p'-DDD did occur. The consistency of the specific activity of ^{14}C-labeled o,p'-DDT in the six rats administered only ^{14}C-labeled o,p'-DDT provided additional confidence in the comparison of results by gas-liquid chromatography and liquid scintillation counting. The nearly equal specific activities of ^{14}C-o,p'-DDT and ^{14}C-o,p'-DDD supported the observation that the o,p'-DDD residue was derived only from the ^{14}C-o,p'-DDT administered orally. The similarity of ^{14}C concentrations in the fat of rats which had been fed 50 ppm of o,p'-DDT for 12 weeks + 3 oral doses of ^{14}C-o,p'-DDT and those receiving only the 3 oral doses suggests that there was no difference in the animals' storage of o,p'-DDT or o,p'-DDD due to prior exposure. The low residues of o,p'-DDT found in this experiment are similar to those reported by Klein et al. and reaffirm the suggestion that o,p'-DDT is more rapidly metabolized than p,p'-DDT.

TABLE II

Radioassay (mean ± S.E.) of rat fat for residues of o,p'-DDT, o,p'-DDD, p,p'-DDT, p,p'-DDE (trapped after separation by gas-liquid chromatography)*

Pesticide found	Treatment: Control	^{14}C-o,p'-DDT† (6 rats)	50 ppm in diet‡ ^{14}C-o,p'-DDT (12 rats)†
p,p'-DDE	0	0	0
p,p'-DDT	0	0	0
o,p'-DDD			
DPM/mg	N.D.	3.0 ± 0.3	3.1 ± 0.4
Specific activity, mCi/mmole	N.D.	1.9 ± 0.2	0.41± 0.06
o,p'-DDT			
DPM/mg	N.D.	23 ± 2	25 ± 2
Specific activity, mCi/mmole	N.D.	1.8 ± 0.2	0.40 ± 0.05

* N.D. = None detectable; 0 = contained no radioactivity.
† Given orally for 3 days before sacrifice.
‡ Fed daily for 12 weeks.

This work supports the contention that o,p'-DDT is not converted to p,p'-DDT in the rat.

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