Evidence for Conversion of DDT to TDE in Rat Liver: I. Liver/Body Fat Ratios of TDE

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The origin of TDE (DDD) found in the livers of animals orally exposed to DDT (1, 2, 3, 4) is in question. Some studies indicate it is the product of hepatic metabolism of DDT (3, 4, 5); others that it is the result of bacterial action on DDT in the intestinal tract (6, 7). It is reasonable to assume that both mechanisms operate in the intact animal, but the relative contribution by each is not known.

A consideration of the pathway for absorption of DDT compounds from the intestinal tract should permit an in vivo assessment of the relative contribution by action of intestinal microflora and by hepatic conversion to the TDE found in animal tissues. Rothe et al. (8), using C^{14}-labeled DDT, showed that DDT and derived compounds are absorbed from the intestinal tract primarily, if not solely, by the lymphatic system and not by the hepatic portal vein.

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Thus, DDT compounds are transported from the intestines to the general circulation of the body and not directly to the liver. TDE absorbed from the intestinal tract would therefore be expected to deposit in similar concentration in body fat depots and in liver lipids unless some mechanism for withdrawal of TDE from the general circulation of the body operates much more actively in liver than in fat depots. In any event, TDE formed from DDT in the gut and TDE administered orally should give similar liver/adipose tissue TDE ratios. In the absence of absorption differentials, TDE absorbed from the gut should give a liver/adipose tissue TDE ratio approaching unity. TDE produced in the liver should result in a ratio greater than 1, with the magnitude of the ratio depending upon the extent of hepatic conversion of DDT to TDE. This paper presents data on DDT and TDE concentrations in liver and body fat lipids of rats fed DDT and rats fed TDE.

Materials and Methods

The data presented for DDT ingestion were obtained from rats employed in other studies concerned with oral exposure to DDT conducted in this laboratory (9). The rats were female Sprague-Dawley-derived animals produced in this laboratory. They were fed diets containing 20 or 200 ppm technical DDT for approximately 22 weeks.

TDE administration was conducted for the specific purpose of comparing the liver/adipose tissue TDE ratios obtained for the above animals with the ratios resulting from TDE absorbed from the intestinal tract. The animals employed for TDE ingestion were

females from the same colony as the females described above. These animals were fed 100 ppm p,p'TDE for 7 and 14 days. Longer feeding periods were not employed because Haag and Kampmeier (10) found that longer periods of TDE ingestion by rats (up to 12 weeks) did not qualitatively change the storage sites of TDE.

The technical DDT used was commercial grade. Analysis showed that it contained 80% p,p'DDT, 17% o,p DDT, 3% p,p'DDE, and no detectable TDE. The p,p'TDE was prepared in this laboratory. It contained 0.38% o,p TDE and no detectable contamination by other isomers or metabolites; p,p'DDT, if present, was less than 0.11%.

The determination of lipid content of tissues and the extraction and cleanup for DDT compound analysis were performed by the method of Stanley and LeFavoure (11). An Aerograph 600-C gas chromatograph with an electron capture detector was used for quantitation. The column packing for determination of p,p'DDT in the presence of high concentration of p,p'TDE was 3% SE-30 on Chromport XXX 80/90. All other determinations were made using a mixed column with a 3:2 ratio of 3% QF-1 and 3% SE-52 on 60/80 Gas Chrom Q. Breakdown of DDT to TDE did not occur in the gas chromatographic procedure under the operating conditions employed.

Results and Discussion

The data presented in Table 1 demonstrate that oral exposure of rats to DDT results in liver lipid TDE concentrations 25 to 40 times greater than those in body fat. Since DDT compounds absorbed from the intestinal tract bypass the liver on their entry into the

organism (8), the above results could not be produced by TDE absorbed from the gut unless TDE were preferentially extracted from the general circulation by the liver. That this is not the case is shown by data obtained after TDE ingestion (Table 1); TDE concentrations in body fat exceed those in liver lipids.

There is no reason to assume that TDE introduced into the gut by the oral route would give a different storage pattern than TDE produced in situ by the intestinal microflora. Animal organs cannot distinguish molecules of a chemical by their origin unless they are in some manner not equivalent. In the absence of evidence to the contrary, it is reasonable to assume that ingested TDE and TDE of microbial origin are equivalent. Thus, high concentrations of TDE in the liver in combination with low levels in body fat after oral exposure to DDT strongly support the hypothesis of hepatic metabolism of DDT to TDE. The low values of TDE in body fat, which may reflect TDE of intestinal origin, indicate that the contribution by intestinal microflora to TDE found in animal tissues is small compared to that made by the liver.

The data relating to DDT ingestion presented in Table 1 (TDE content low in body fat and high in liver lipid, with the latter exceeding the DDT value in liver by 2 to 4 times) are consistent with the few other published reports on the same subject (3, 4). The data relating to TDE ingestion (Table 1) are also in agreement with reports of body fat as the major storage depot for ingested TDE in rats (10) and dogs (12).

TABLE 1

p,p'DDT and p,p'TDE Concentrations in Tissues of Rats Fed DDT or TDE

Animal Number	Level and Duration of Feeding	Perirenal Fat		Liver		TDE Liver/Body Fat Ratio
		DDT	TDE	DDT	TDE	
1	200 ppm Tech DDT 22 weeks	570	6	39	172	29
2	200 ppm Tech DDT 22 weeks	500	5	84	200	40
3	20 ppm Tech DDT 22 weeks	77	3	46	74	25
4	20 ppm Tech DDT 22 weeks	170	3	21	80	27
5	100 ppm p,p'TDE 7 days	2	200	7	130	.65
6	100 ppm p,p'TDE 14 days	3	230	3	140	.61
7	100 ppm p,p'TDE 14 days	2	190	2	140	.74

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