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DATA EVALUATION RECORD

TRICHLORFON

METABOLISM

CITATION: Dedek W, Lohs K. 1970. The alkylating effect of trichlorfon in warm-blooded animals. II. Distribution of ^{14}C in organs and liver proteins in rats following application of ^{14}C-trichlorfon. Z. Naturforsch. 25(10):1110-1113 [English translation].

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DATA EVALUATION RECORD

STUDY TYPE: Metabolism in rats.

CITATION: Dedek W, Lohs K. 1970. The alkylating effect of trichlorfon in warm-blooded animals. II. Distribution of ^{14}C in organs and liver proteins in rats following application of ^{14}C-trichlorfon. Z. Naturforsch. 25(10):1110-1113 [English translation].

ACCESSION NUMBER: Not available.

MRID NUMBER: Not available.

LABORATORY: Research Institute for Chemical Toxicology, German Academy of Sciences, Berlin.

TEST MATERIAL: [$^{14}CH_3O$]Trichlorfon.

PROTOCOL:

The purpose of this study was to investigate the methylating properties of trichlorfon in rats in vivo. [$^{14}CH_3O$]Trichlorfon (specific activity, 1.35 mCi/g, purity not specified) was administered intravenously or intraperitoneally to male rats. The maximum tolorated dose was reported to be "approximately 50 mg (body weight 180 g)." [This is not clearly defined in this translation and might be 50 mg/180 g, equivalent to 278 mg/kg]. The animals (number per dose unspecified) received the following doses: 20 or 40 mg/rat intravenously and sacrificed after 17 and 3 h, respectively; 40 or 50 mg/rat intreperitoneally and sacrificed after 2 and 4 h, respectively. Samples from various organs were extracted with acetone to remove unmetabolized trichlorfon and acetone soluble metabolites and the extracts were tnen radioassayed. Total radioactivity in organ samples was determined following freeze drying, combustion, and radioassay of resulting $^{14}CO_2$. Moist or freeze-dried organ samples were directly dissolved with Soluene TM-100 (Packard) in toluene. Proteins were also isolated from liver tissue and precipitated at 0-4°C, and the unprecipitated protein samples were subsequently desalted by dialysis. The water-soluble and water-insoluble portions were precipitated separately with acetone, vacuum dried, dissolved in Soluene TM-100, and the ^{14}C activity determined.

RESULTS:

The radioactivity found in the tissues examined (liver, lungs, kidneys, heart, spleen, blood, and brain) did not exceed 10 percent of the total administered dose. The results also indicated a decrease in radioactivity present in these organs and tissues with time. The acetone extract of tissues contained approximately 1 percent of the total radioactivity present in the organs. The remaining radioactivity was therefore considered to be bound to proteins. The radioactivity bound to liver proteins (globulins and albumins) was determined, and the results are presented in Table 1.

TABLE 1. ^{14}C In Liver Tissue and Five-Times Reprecipitated Liver Proteins

Substance		^{14}C ("Ipm"/mg)[a]
Liver tissue		2460
Homogenate residue		750
Protein, water-insoluble globulin	1.	290
	2.	355
	3.	295
	4.	310
	5.	300
	6.	300
Protein, water-soluble albumin	1.	670
	2.	540
	3.	635
	4.	960[b]
	5.	1080[b]
	6.	580

[a]Probably denotes dpm/mg tissue.

[b]Values imprecise since weight less than 0.5 mg.

CONCLUSIONS:

The authors concluded that the methyl moiety of [$^{14}CH_3O$] trichlorfon was enzymatically conjugated to liver proteins in treated rats. Alkylation of these proteins would be similar to the enzymatic methylation of glutathione, which had been previously reported in the literature. They presumed, therefore, that some effects of trichlorfon and other organophosphorous insecticides could not be exclusively attributed to cholinesterase inhibition, but also to protein alkylation.

CORE CLASSIFICATION: Supplementary Data.

The methods used in this study were not clearly stated. The radiolabeled trichlorfon was probably mixed with non-radiolabeled materials to achieve the stated doses. However, the source and purity of the non-radioactive material was not stated. The number of animals used per dose, and the exact dose levels used were not stated.