

DATA EVALUATION RECORD

TRICHLORFON

Chronic Oral (Intragastric) Toxicity in Rats

CITATION: Sasinovich LM, Ya L, Voronina YS, Kagan S, Nesterova MF.
1973. The effects of chlorofos on the functional condition of the liver
and kidneys in animal experiments. Farmikol. Toksikol. (Kiev) 8:125-128
(translation).

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STUDY TYPE: Chronic oral (intragastric) toxicity in rats.

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ACCESSION NUMBER: Not available.

MRID NUMBER: Not available.

LABORATORY: Not available.

TEST MATERIAL: Trichlorfon, purity not stated.

PROTOCOL:

1. The test compound was identified as chlorofos (trichlorfon). The purity of the compound was not stated.
2. The test animals were as follows:
 - o Species/Strain--white rats (strain not specified)
 - o Number/Sex--200 (sex not specified)
 - o Age at Initiation--(sexually mature)
3. The compound was administered intragastrically. The vehicle and the concentration of the formulation used in administering the test compound was not specified.
 - o Dosage:
 - Low --8.5 mg/kg/day for 9 months (1/100 LD₅₀)
 - High --42.5 mg/kg/day for 2 months (1/20 LD₅₀)
4. The following parameters was measured:

Hepatic and renal function was studied at 2 weeks and at 1, 2, 3, 6, and 9 months.

a. Liver function:

- o Detoxification - Quick and Pytel test
- o Galactose clearance
- o Serum proteins
- o Enzymatic activity of liver homogenates: aspartate amino transferase, alanine amino transferase, alkaline phosphatase, and cholinesterase

b. Renal function:

- o Urine volume - spontaneous and water or saline-loaded animals
- o Urinary protein (Lowry)
- o Blood urea nitrogen
- o Extraction time for indigo carmine

c. General health

d. Animal weight gain

e. Kidney and liver weight at sacrifice

f. Kidney and liver levels of chlorofos and metabolites by thin layer chromatography and enzymatic assay

RESULTS:

The results are summarized in Table 1. Administration of chlorofos produced changes indicative of functional disturbances in the liver. Changes occurred at the low dose and some were present at 2 months and the animals studied for 9 months. There were phasic changes in excretory function of the kidneys; for example, increased excretion of indigo carmine at 2 and 3 months which was lower at six months but not different than controls at 9 months. Urea nitrogen did not differ from controls. There was a slight decrease in renal cholinesterase at the low dose after 2 months and at the high dose after 2 weeks. At the high dose there was 60 percent inhibition of renal cholinesterase at 2 months. Levels of chlorofos and the metabolite DDVF in the liver ranged from 0.07 to 0.25 mg/kg and in the kidneys ranged from 0.05 to 0.18 mg/kg.

CONCLUSIONS:

Trichlorfon was administered to rats daily by the intragastric route at 8.5 mg/kg for 9 months or at 42.5 mg/kg for 2 months. There was weight loss at the high dose but no toxic signs at the low dose. There were minimal effects on liver function and serum enzymes. Kidney cholinesterase was inhibited 60 percent at the high dose after 6 months and was only slightly reduced at the low dose. There were no numerical data or statistical analysis of any parameter. Therefore it is impossible to validate any conclusions which were presented.

CORE CLASSIFICATION:

Supplementary (Jm, 07.30.83)

The study is Core ~~Invalid~~ since only summary data were presented. No quantitative data were presented to support the summary conclusions.

TABLE 1. Results of Chlorofos (Trichlorfon) Administration

Parameter	Low Dose	High Dose
Toxic signs	None	Weight loss 2 mo Bristled hair 2 mo
Detoxification	No effect	No effect
Hexobarbital sleeping time	Increased 9 mo	Decreased 2 mo
Fasting blood glucose	No effect	No effect
Hyperglycemic coefficient	Elevated 9 mo	
Enzyme effects		
Serum alanine amino transferase	Slightly decreased (9 mo)	No effect
Liver alkaline phosphatase	Decreased (2,9 mo)	No effect
Serum alkaline phosphatase	Decreased	Decreased
Serum and RBC cholinesterase	Some inhibition	Marked inhibition
Liver cholinesterase	42 percent inhibition	43 percent inhibition
Serum proteins		
3 months	Decreased albumin gamma globulins	Increased beta and
9 months	Normal	Normal
Kidney cholinesterase	Decreased after after 2 weeks	Slightly reduced at 9 mo Decreased after 2 60 percent inhibition at 2 mo