

US EPA ARCHIVE DOCUMENT

DATA EVALUATION RECORD

TRICHLORFON

Acute Toxicity in Rabbits (Oral Gavage)

CITATION: Markiewicz Z, Kurski B, Smigielska J. 1975. Changes in several blood clotting parameters in rabbits during experimental toxicity with Foschlor-20. Med. Weter. 31(4):231-233. (Translation).

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STUDY TYPE: Acute Toxicity in Rabbits (Oral Gavage).

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ACCESSION NUMBER: Not available.

MRID NUMBER: Not available.

LABORATORY: Institute of Noninfectious Diseases AR-T Olsztyn.

TEST MATERIAL: The test chemical was identified as Foschlor-20 (trichlorfon). Purity and formulation were not stated. Although the source of the test material was not stated, it was indicated as having been manufactured in Jaworznie.

PROTOCOL:

1. The animals were hybrid rabbits of both sexes. They were between 3 and 5 months of age and weighed an average of 2.5 kg. There were 15 animals per group.
2. Test compound was given in soy oil emulsion by oral gavage. Each animal served as its own control based on data collected before dosing. Dosing was as follows:

Group (No.)	Foschlor (mg/kg)	Atropine and toxogonin ^a
I (15)	500	+
II (15)	250	+
III (15)	250	-

^a 10 mg/kg atropine sulfate and 10 mg/kg toxogonin were given intravenously after 1 hour.

3. The following parameters were studied:
 - o Blood clotting was determined on days 1, 3, and 10.
 - o Prothrombin time was determined on days 1, 3, and 10.

- o Serum calcium was determined on days 1, 3, and 10.
- o Clinical examinations were conducted.
- o Histopathologic examination was performed on liver and lungs.

RESULTS:

Toxic signs developed in 10-15 minutes in animals of groups I and II. There was constriction of the pupils, general weakness, and tremors. At the highest dose, in 6 of 15 animals, there were clonic-tonic convulsions. Symptoms appeared later in group III animals. One animal in group I died at 4 days; 2 animals in group III died in a few hours.

In all groups mean blood clotting time was shorter compared to pretreatment times. After 10 days, shorter blood clotting times were observed in 85, 53, and 100 percent of animals in group I, II, and III, respectively. There was no dose related trend or effect of toxogonin and atropine on clotting time. Prothrombin was shortened in all treatment groups after 1, 3, and 10 days. Platelet counts were elevated in all treatment groups and after 10 days remained elevated in 64, 66, and 76 percent of the animals in group I, II, and III, respectively. Serum calcium level was not affected. The effects on blood clotting are summarized in Table 1.

Necropsy and histopathologic examinations showed hemorrhaging of the stomach and intestines, inflammation of the lungs, and degenerative changes in the liver. The primary site of toxicity was the liver, causing an increase in platelets and clotting factors I and VIII.

TABLE 1. Mean Group Values for Blood Clotting Parameters after Treatment with Foschlor-20

Parameter	Observation Time Days	Group		
		I	II	III
Clotting Time (min:sec)	Before treatment	3:10	2:00	2:33
	1	2:34	1:53	1:36
	3	2:15	1:54	1:55
	10	2:17	2:00	1:32
Prothrombin Time (sec)	Before treatment	50	38	64
	1	46	26	49
	3	32	29	44
	10	38	32	65
Platelet Count ($\times 10^3/\text{mm}^3$)	Before treatment	418	227	392
	1	452	425	483
	3	484	453	462
	10	399	203	450

CONCLUSIONS:

Treatment of rabbits with trichlorfon caused a decrease in blood clotting time and prothrombin time and an increase in platelet counts; atropine and toxogonin did not modulate these effects when administered simultaneously. Data for individual animals were not presented, although some ranges of values were presented in the narrative. Before treatment, prothrombin time ranged from 30 to 112 seconds and platelet counts ranged from 153 to 599 (10^3 per mm^3). An untreated control group was not included so normal variation of the clotting parameters over a 10-day time period was not available for comparison with variation in treated animals. It is the opinion of this reviewer that the data presented does not permit a clear conclusion on the possible modulating effect of administration of atropine and toxogonin on the toxic effects of trichlorfon.

CORE CLASSIFICATION: Supplementary Data.

The study is classified as Core Supplementary Data because of the extensive variation in the parameters measured, and the limited duration of the study.