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DATA EVALUATION RECORD

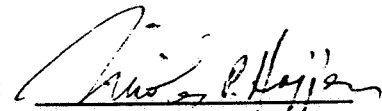
TRICHLORFON

Metabolism and Toxicity in Rats

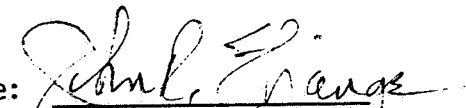
CITATION: Arthur BW, Casida JE, 1957. Metabolism and selectivity of O,O-dimethyl-2,2,2-trichloro-1-hydroxyethylphosphonate and its acetyl and vinyl derivatives. Agric. Food Chem. 5:186-192.

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DATA EVALUATION RECORD

STUDY TYPE: Metabolism and Toxicity in Rats, Certain Insect Species, and Pea Plants.

CITATION: Arthur BW, Casida JE, 1957. Metabolism and selectivity of 0,0-dimethyl-2,2,2-trichloro-1-hydroxyethylphosphonate and its acetyl and vinyl derivatives. Agric. Food Chem. 5:186-192.

ACCESSION NUMBER: Not available.

MRID NUMBER: 00005296.

LABORATORY: Department of Entomology, University of Wisconsin, Madison, Wisconsin.

TEST MATERIAL: Trichlorfon (purity not specified).

PROTOCOL:

1. [³²P]Trichlorfon was synthesized by a de novo procedure starting with phosphorus-32. The test material was purified on a silica gel column and had a specific activity of about 1 mCi/g (purity not specified). The non-radiolabeled trichlorfon used (source unspecified) was purified prior to use, but its purity was not specified.
2. The acute intraperitoneal toxicity of trichlorfon to white rats (source, age, sex, and strain not specified), and several potential target insects, e.g., housefly, following topical application was determined.
3. In vivo and in vitro metabolism studies were carried out:
 - (a) Houseflies were treated with 50 µg/g of [³²P]trichlorfon and the hydrolysis curve was obtained from fly homogenates.
 - (b) Pea plants were also treated at the same level as flies and the hydrolysis curve was obtained from pea plant homogenates.
 - (c) Approximately 80 µg of labeled trichlorfon was added to human serum, and the partitioning properties were used to determine hydrolysis in a chloroform/water extraction.

- (d) The metabolism of [³²P]trichlorfon in a female dog (strain not specified) following intraperitoneal injection at 150 mg/kg was studied.
4. The Fujiwara test (Nat. Ges. Rostoch 6:33-43, 1916), which shows maximum absorption at 360 and 530 nm, was used to assay for the trichloroethyl portion of trichlorfon or its metabolites.
 5. The rates of acid and alkaline hydrolysis of trichlorfon were determined.

RESULTS:

Rat erythrocyte cholinesterase was inactivated by trichlorfon, and the studies identified a dimethylphosphoryl cholinesterase as the inactive enzyme. In the female dog, less than one percent of the administered dose was excreted unchanged in the 2 days following treatment as determined by radiotracer and bioassay determinations. A trichloroethyl glucuronide metabolite was identified in the urine and accounted for about 65 percent of the administered dose. Blood samples indicated that trichlorfon was rapidly degraded, with only 0.4 percent of the administered dose detected as the parent compound. These findings were in agreement with the disappearance of toxicity signs and the recovery of the dog.

In houseflies, trichlorfon was hydrolyzed, but no other ³²p-containing metabolites were detected. There was no evidence of its conversion to the more active vinyl phosphate derivative or that in vivo detoxification can be used to explain relative susceptibility of flies to trichlorfon and the vinyl phosphate derivative.

Plant metabolism showed that trichlorfon was rapidly hydrolyzed, with about 80 percent hydrolyzed in 3 days. However, the vinyl phosphate was 65 percent hydrolyzed within 3 days.

In vitro metabolism in human plasma resulted in a rapid degradation of trichlorfon and its acetyl derivative (about 70 - 80 percent in 4 hours) compared with the vinyl phosphate derivative (about 10 percent in 4 hours), which correlates well with the relatively low toxicity of trichlorfon to mammals.

Trichlorfon was rapidly converted to the vinyl phosphate derivative under alkaline conditions, but was stable under acidic conditions (one percent hydrolysis in 24 hours).

CONCLUSIONS: The authors compared the toxicity of trichlorfon, its acetyl derivative (0,0-dimethyl-2,2,2-trichloro-1-acetoxyethylphosphonate) and 0,0-dimethyl-2,2-dichlorovinylphosphate. The authors concluded that there was a marked variation in the sensitivity between different species to the 3 chemicals, with the vinyl phosphate derivative being more toxic than the other two phosphonates.

The low mammalian toxicity of trichlorfon was associated with its rapid metabolism. Although trichlorfon is rapidly dehydrochlorinated in alkaline solutions to the vinyl phosphate analog, there was no evidence that of this conversion in mammals and houseflies in vivo.

CORE CLASSIFICATION/EVALUATION: Supplementary data.

The purity and source of the chemicals, and the source and strain of animals used were not specified. The limited analytical methods used in this 1957 study provide qualitative rather than quantitative data.