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DATA EVALUATION REPORT

Study Type: Metabolism (Absorption in Rats)

TOX Chem No.: 264

Accession No.: 071392

Test Material: Kryocide

Study No.: WT-12-82

Sponsor: Pennwalt Research Laboratories
Tacoma, WA

Testing Facility: Pennwalt Research Laboratories
Tacoma, WA

Title of Report: Kryocide Insecticide Absorption in the Rat

Author(s): Not specified

Report Issued: February 1, 1983

Conclusions:

The present study was inadequate in measuring absorption and/or excretion of Kryocide in the rat.

Classification: Core-Supplementary

1 of 6

Material and Methods:

Young adult Sprague-Dawley rats (source and sex not specified) weighing between 233 and 396 g each were used for this study. The test chemical Kryocide was mixed with the diet (ground laboratory chow) at an approximate feeding level of 5 percent (4.93%). The purity of Kryocide used in this study was not reported. A total of 11 rats were housed individually in metabolism cages allowing for separate collection of urine and feces. All animals were offered 20 g of the test diet/day and deionized water was available to all animals ad libitum. Food consumption was recorded daily and body weights were recorded on days 0, 3, 7, 14, and 28 on study. Urine and feces were collected three times a week throughout the study. Three mL of blood was drawn from each animal immediately prior to sacrifice. The animals were sacrificed at different intervals as follows: Three animals after exposure to the test chemical for 3 days; three animals after exposure to the test chemical for 7 days; three animals after 14 days of exposure; and two animals after exposure for 14 days and maintenance on untreated diet for another 14 days.

Kryocide (and/or metabolite) concentrations in the urine, feces, bone, and blood were determined for all animals by measuring the fluoride levels in these samples. Fluoride levels in the urine were determined by the method of Tiesl. Background levels were determined for each animal prior to feeding. The recovery from urine samples spiked with fluoride (at the range of 8 to 67 ppm) was reported by the authors to be higher than 98 percent. Fluoride levels in the feces were determined by a modification of the Palmer method for cryolite. Background levels were determined for each animal prior to treatment. The authors reported that "adequate" recoveries were obtained for free fluoride and fluoride from Kryocide when feces were fortified with fluoride or Kryocide. Fluoride levels in the bone were determined by the method of Singer and Armstrong. The authors reported that background fluoride levels in the bone were comparable to reported literature values. Fluoride levels in the blood were determined by using a combination of the methods of Gron et al., Singer and Armstrong, and Dabeka et al. Background levels were determined from blood samples obtained by closed heart puncture from various animals. Those levels were, according to the author, in agreement with reported literature values.

Results and Discussion:

The present study has investigated the absorption and excretion of Kryocide by male and female Sprague-Dawley rats. Results presented here indicate that approximately 80 percent of the administered dose was excreted in the feces and only less than 1 percent of the dose was excreted in the urine. Fluoride levels in the blood were found to be very low and with the exception

of three animals, these levels were similar to the untreated control levels. On the contrary, total fluoride levels in the bone were found to be fairly high (approximately 3000 ppm) compared to the untreated control levels (approximately 1000 ppm). Since the authors did not report the final weight of the bone for each rat (or the mean weight) it is not possible to estimate how much Kryocide has accumulated in the bone for each rat. Assuming, however, that approximately 10 percent of the rat body weight is bone, the total quantity of fluoride in the bone represents approximately 60 mg or 0.45 percent of the total dose or 6 percent of the daily dose. Thus, from the available data it can be estimated that approximately less than 10 percent of the daily dose is absorbed from the gastrointestinal tract and excreted within 24 hours in the urine and feces. The rest of the dose (90%) most probably is not absorbed and is excreted directly in the feces. These conclusions are also supported by the fact that no appreciable fluoride quantities were detected in the blood and that absorbed Kryocide, if not conjugated in the body, should be excreted in the urine rather than the feces based on its relatively low molecular weight (MW = 210).

Conclusions:

The present study is not adequate in estimating the absorption and/or excretion of Kryocide in the rat.

Classification:

This study is classified as Ccre-Supplementary for the following deficiencies:

1. The sex and source of rats used were not specified.
2. The purity of the test chemical, Kryocide, was not specified.
3. The sponsor did not provide any information for the selection of the dose level used.
4. The sponsor did not justify why all animals were offered 20 g of diet irrespective of their body weight.
5. The animals used in this study varied tremendously in body weight.
6. The sponsor did not run any specific tests (i.e., iv injections, bile duct cannulation, serial blood withdrawal, etc.) to show definitively that Kryocide absorption has taken place.

7. The analytical techniques used for estimating Kryocide concentrations in urine, feces, bone, and blood by measuring fluoride content were not fully substantiated.

8. From the way the data are presented (Table 3 of the original report) it is not clear how ppm of fluoride in urine or feces correlate with mg of Kryocide in the same excreta.

9. The sponsor did not provide the weight of bone in each animal so that the total amount of Kryocide stored in the bone could be estimated for each animal.

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