Reviewed by: Marcia van Gemert, Ph.D. Marcia Gemert 2/24/87
Read, Section III, Tox. Branch (TS-769C)
Secondary Reviewer: Theodore M. Farber, Ph.D.
Chief, Toxicology Branch (TS-769C)

W.H. Burns 3/17/87

DATA EVALUATION REPORT

Study Type: Metabolism: Balance study in rats Tox. Chem No. 323EE

Accession No.: 265794

Test Material: CGA 64 250

Synonyms: Tilt

Study Number: 24/79

Sponsor: Ciba Geigy

Testing Facility: Dept. of Research and Development, Plant Protection Ciba Geigy Agricultural Division, Basle Switzerland

Title of Report: Distribution, Degradation and excretion of CGA 64 2500 in the rat.

Author: H. Hambock

Report Issued: July 18, 1979

Conclusions:
2 animals/sex were given a single dose of 0.5 mg/kg or 25 mg/kg ^{14}C CGA 64 250. Urine, feces and expired CO_2 were collected at 24 hour intervals for 6 days post dosing, after which animals were killed and tissues collected for analysis. Administered ^{14}C appeared to be rapidly excreted in the urine. Very little radioactivity was recovered from expired CO_2. Most tissue residue levels were extremely low, except for liver and kidneys in males and females and ovaries in females. Urinary metabolite pattern of the 0-24 hour urines appeared similar for both sexes and both doses. There were 4-10 polar metabolites detected in urine with no detectable intact parent compound found (cis or trans).

Core Classification: Supplementary, only 2 animals/sex were used metabolite data were missing, and purity and batch of the unlabeled compound were not defined.

A. Materials:

1. Test Compound: ^{14}C-labelled CGA 64 250, labelled in the triazole ring

Specific activity: 59.6 uCi/mg

[redacted]

Purity: 98%

Unlabelled CGA 64 250: purity and batch were not given

Information concerning manufacturing process has been deleted

2. Test Animals:

Species: rat

Strain: Tif RAI f (SPF)

Age: not given

Weight: not given

Source: Ciba Geigy Ltd. animal farm, Stein, Switzerland

Study Design:

Animal assignments and study procedures:

2 animals/sex were given a single oral dose of 0.5 mg/kg or 25 mg/kg one animal/sex served as control. ^{14}C CGA 64 250 and kept in metabolism cages with food and water ad libitum. Urine, feces and expired CO_2 were collected after a 17 hour fast at 24 hour intervals for 6 days at which time they were killed and samples of liver, fat, kidneys, muscle, blood, spleen, heart, lungs, testes, ovaries, brain and carcass were analyzed for radioactivity. Body weights were taken at the start and end of the experiment.

Dosing solution:

^{14}C CGA 64 250 was dissolved in ethanol/polyethylene glycol 200/ water 30/20/50 (v/v) to yield a solution of either 0.103 mg/ml or 4.75 mg/ml. 1 ml/solution was given by gavage. Procedures for measurement of radioactivity, and thin layer chromatography are on appended pages 1-5.

Results:

Excretion pattern:

Administered ^{14}C CGA 64 250 appeared to be rapidly excreted in the urine. Data are tabulated on appended page 6. Within 24 hours most of the radioactivity had been eliminated (74-84%). There did not appear to be a signiticant sex or dose-related difference

in pattern of excretion. However, with data from so few animals to analyze, that statement is close to conjecture. There was very little radioactivity recovered in expired air. At the end of 144 hours only about 0.4% of the administered radioactivity remained in the rats.

Tissue residues:

Tissue residue levels of radioactivity are on appended page 7. Most tissue levels of radioactivity in the 0.5 mg/kg group were undetected. At the 25 mg/kg dose most tissue levels were extremely low, except for liver and kidney in males and females and ovary in females. Residue patterns did not appear to be influenced by sex.

Urinary metabolite pattern:

Thin layer chromatography of the 0-24 hour urines revealed the same metabolite pattern for males and females, both low and high dose animals. According to the study text, without any documentation R_f values or other confirmatory data, at least 4-10 metabolites polar were detected. There appeared to be very little unchanged CGA 64 250 in urine (either cis or trans) at a limit of detection of 3%.

Discussion:

2 animals/sex were given a single oral dose of 0.5 mg/kg or 25 mg/kg ^{14}C CGA 64 250. Urine, feces and expired CO_2 were collected at 24 hour intervals for 6 days post dosing, after which animals were killed and tissues collected for analysis. Administered ^{14}C appeared to be rapidly excreted in urine. Very little radioactivity was recovered from expired CO_2. Most tissue residue levels were extremely low except for liver and kidneys in males and females, and ovaries in females. Urinary metabolite pattern of the 0-24 hour urines appeared similar for both sexes and both doses. There were 4-10 polar metabolites detected in urine with no detectable intact parent compound found (cis or trans).

TILT CGA-64250 Reviews

---

p. 4-10

The next 7 page(s) is/are not included in this copy of the TILT reviews.

The material not included contains the following type of information:

___ Identity of product inert ingredients

___ Identity of product impurities

___ Description of the product manufacturing process

___ Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commerical/financial information

___ A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

X Detailed methods and results of a registrant submission.

___ Duplicate pages.

The information not included generally is considered confidential by product registrants. If you wish to obtain the information deleted, please contact the individual who prepared this response to your request.
