Reviewed by: Marcia van Gemert, Ph.D. Management 3/2/87
Head, Section III, Tox. Branch (TS-769C)
Secondary Reviewer: Theodore M. Farber, Ph.D.
Chief, Toxicology Branch (TS-769C) 3/17/87

DATA EVALUATION REPORT

Study Type: Metabolism in rats

Tox. Chem No. 323EE

Accession No.: 265794

Test Material: CGA 64 250

Synonyms: Tilt, Technical

Study Number: 9/81

Sponsor: Ciba Geigy

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

Title of Report: The major metabolic pathways of CGA 64 250 in the rat

Author: W. Mucke

Report Issued: March 13, 1981

Conclusions: This is an extension of the previously reviewed study where ^{14}C- CGA 64 250 was given in a single gavage dose and was extensively metabolized in the rat with no detectable parent compound in urine and about 5% found in feces after 3 days.
The major metabolic pathways in this study have been proposed for CGA 64 250 based on NMR and mass spectroscopy analyses. A major metabolic pathway is through cleavage of the dioxalone ring with subsequent dechlorination and conjugation.

Core Classification: minimum

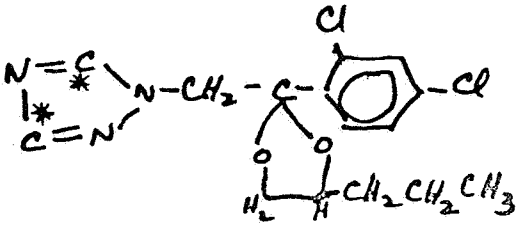
Quality Assurance Statement accompanied the report and was signed.

A. Materials:

1. Test Compound: Radiolabelled compounds used.

A. Triazole [3,5-^{14}C] CGA 64 250 (triazole labelled)

Structure:



Specific Activity: 59.6 uCi/mg

[redacted]

Purity: > 98%

This material was diluted with unlabelled CGA 64 250 with the following characteristics:

[redacted]

purity: 98.9%

to yield a specific activity of 23.1 uCi/mg

2. Test Animals:
Species: rats, male
Strain: Tif: RAI f(spf)
Weight: 167-186 gms
Age: not given
Source: Ciba Geigy Farms, Stein, Switzerland

3. Dosing solution: Given by gavage, dissolved in water/ethanol/ polyethylene glycol 200 (50/30/20 v/v)
Triazole labelled CGA 64 250 - 5.5 mg/ml
phenyl labelled CGA 64 250- 5.78 mg/0.9 ml

4. Animal assignments and study procedures:
20 male rats were treated orally with a single dose of 31.4 mg/kg triazole labelled CGA 64 250 and urine and fecal excretion of radioacctivity were determined.

Results:
The major results of this study are given in the previously reviewed metabolism study # 35/79 dated Aug. 31, 1979. This study gives some of the proposed metabolic pathways apparent from NMR and mass spectroscopy analyses.
A summary of the excreted radioactivity is on appended page 1.
Approximately 52.3% of the total radioactivity was excreted in urine by 3 days, 43.3% in feces giving a total excreted of 95.6%.

Information which may reveal manufacturing processes has been deleted

Structures of the relevant metabolites identified are on appended pages 2 and 3. A schematic diagram of the process followed for isolating the urinary and fecal metabolites can be found on appended pages 4 and 5. The proposed metabolic pathways can be found on appended page 6. The study text stated that there were further metabolites in the urine, but their comparatively small amounts led to the conclusion that they are minor metabolic pathways. In addition, the metabolic profile of both urine and feces appear similar, aside from the fact that a small amount of parent CGA 64 250 remains in feces and urine contains some conjugated phenolic metabolites.

Discussion:
The major metabolic pathways have been proposed for CGA 64 250 based on NMR and mass spectroscopic analysis. A major metabolic pathways are through oxidation of the propyl side chain or through cleavage of the dioxalone ring with subsequent dechlorination and conjugation.

TILT CGA-64250 Reviews

---

p. 4-9

The next 6 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.
