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HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
PEST 361

DATA EVALUATION REPORT

CAPTAN

STUDY TYPE: BIOAVAILABILITY- MOUSE

Prepared for

Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by

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Task Order No.97-015B

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This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464.

CAPTAN **Bioavailability Oral Study (no guidelines)**

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DATA EVALUATION RECORD

STUDY TYPE: Bioavailability - Mouse
(No guidelines)
DP BARCODE: D225683 SUBMISSION CODE: SSE04312
P.C. CODE: 081301 TOX. CHEM. NO.:

TEST MATERIAL (PURITY): Captan (89.4% [technical grade]; 99.0% [analytical grade]; 1,2-^{14}C-(cyclohexane)Captan repurified by flash column chromatography to 99.1%)

SYNONYMS: 3a,4,7,7a-tetrahydro-2-[(trichloromethyl)thiol]-1H-isoindole-1,3(2H)-dione; N-(trichloromethylthio)-4-cyclohexene-1,2-dicarboximide; N-trichloromethyl-thio-3a,4,7,7a-tetrahydrophthalimide; Merpan, Orthocide-406

CITATION: Provan, W. and H. Eyton-Jones (1996) The bioavailability of Captan to the duodenum of CD-1 mice following dietary administration. Central Toxicology Laboratory, Aldery Park, Macclesfield, Cheshire, UK SK10 4TJ. Study No. XM5010, XM5087, Report No. CTL/R/1260. January 24, 1996. MRID 43982202. Unpublished.

SPONSOR: Zeneca Agricultural Products, P.O. Box 15458, Wilmington, DE 19850-5458.

EXECUTIVE SUMMARY: In a study to assess the bioavailability of ingested Captan, groups of 30 (experiment 1) or 10 (experiment 2) CD-1 male mice were fed 400 or 3000 ppm radiolabeled Captan (99.1%; Batch No. 14264-13-1 [technical grade non-labeled Captan]) in the diet for up to 30 hours. Groups of six mice given Captan-free diet served as controls.

There were no treatment-related toxic effects reported. This preliminary nonguideline study provided cursory time-course information regarding the distribution of dietary radiolabeled Captan in the gastrointestinal tract of mice. Over the 30-hour treatment period, radioactivity in all regions of the gastrointestinal tract increased. For all time periods, maximum concentrations were associated with the stomach, caecum, and rectum. The highest levels in these regions were observed at 30 hours and represented

approximately 0.20, 0.35, and 0.175 μmol equivalents of Captan. The study authors correctly assumed that these regions contained the highest level of radioactivity due to the discreet, cyclic nature of motility in the regions thereby allowing accumulation of radioactivity. Slight fluctuations in intestinal contents were attributed to photoperiod effects on the feeding activity of the mice. The radioactivity recovered from the gastrointestinal tract of mice in the two exposure groups reflected the approximately 7-fold difference in the dose. High performance liquid chromatography analysis indicated that the radioactivity distal to the stomach was associated with metabolites of Captan rather than parent compound.

Because food intake and body burden of radioactivity were not provided it was not possible to determine the total intake of radiolabeled Captan necessary for determination of overall mass balance of administered radioactivity. The absence of these data do not necessarily invalidate the findings regarding the distribution of radioactivity in the gastrointestinal tract but do compromise a quantitative assessment of bioavailability and extent of gastrointestinal absorption of the test material.

COMPLIANCE: This nonguideline study is considered marginally acceptable for providing data regarding the bioavailability of Captan and/or metabolites in mice following dietary administration but is deficient in quantitatively assessing bioavailability of the test material. Signed and dated GLP Compliance (10/10/95) and flagging criteria statements (10/10/95) were present but no quality assurance statement was available. The study was not fully compliant with GLP standards.

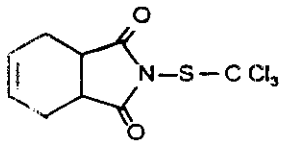
I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Captan

Description: off-white/beige solid
Lot/Batch #: 14264-13-1, CTL ref. No. Y01716/025 (technical grade); CTL ref. No. Y01716/012 (analytical grade)
Purity: Captan (89.4% [technical grade]; 99.0% [analytical grade]; 1,2-^{14}C-(cyclohexane)captan repurified by flash column chromatography to 99.1%)
Stability of compound: not stated
CAS #: 133-06-2

Structure:



Captan
(position of radiolabel not specified)

2. Vehicle and/or positive control

Powdered rodent chow (CT1 diet)served as the vehicle; no positive controls were used.

3. Test animals

Species: Mouse
Strain: CD-1
Age and weight at study initiation: 4-6 weeks and 28-30 g on delivery;
28-30 g
Source: Charles River, UK
Housing: after assignment to experimental group, housed singly in stainless steel, wire-bottom cages.
Diet: CT1 diet provided ad libitum (Special Diet Services, Ltd, Witham, Essex, UK) for controls and treatment group.
Water: filtered water provided ad libitum
Environmental conditions:
Temperature: 21±0.2°C
Humidity: not provided
Air changes: not provided
Photoperiod: 12 hr light/12 hr dark
Acclimation period: 4 days for acclimatization to powdered diet or 8 days for acclimatization to test diet

B. STUDY DESIGN

1. In life dates

Not provided

2. Animal assignment

Animals were assigned randomly to the test groups in Table 1.

also analyzed by HPLC following the same extraction procedures as used for the tissue samples.

II. **RESULTS**

A. OBSERVATIONS

1. Toxicity

There were no treatment related signs of toxicity reported

2. Mortality

There were no treatment-related deaths reported.

B. BODY WEIGHT AND WEIGHT GAIN

The treatment phase of the experiment was only 30 hours. No information was provided regarding body weight changes.

C. FOOD CONSUMPTION AND COMPOUND INTAKE

1. Food consumption

No information was provided regarding food consumption.

2. Compound consumption

No information was reported regarding compound intake.

D. URINALYSIS

With the exception of analysis for Captan-derived radioactivity and metabolites (data not provided in study report), urinalysis was not performed.

E. TISSUE AND SAMPLE ANALYSIS

The authors reported that the radioactivity associated with the gastrointestinal tract was very low compared to that ingested. For the 3000 ppm group, recovery was 12.7% at 6 hours but declined to 2.2% at 30 hours of exposure. Recovery of radioactivity over the 30-hour exposure period exhibited variations consistent with photoperiod-dependent feeding (e.g., greater levels of radioactivity following nocturnal feeding). Higher levels of radioactivity consistently detected in the stomach, caecum, and rectum are consistent with the discreet, cyclic motility associated with these regions of the gastrointestinal tract. Throughout the

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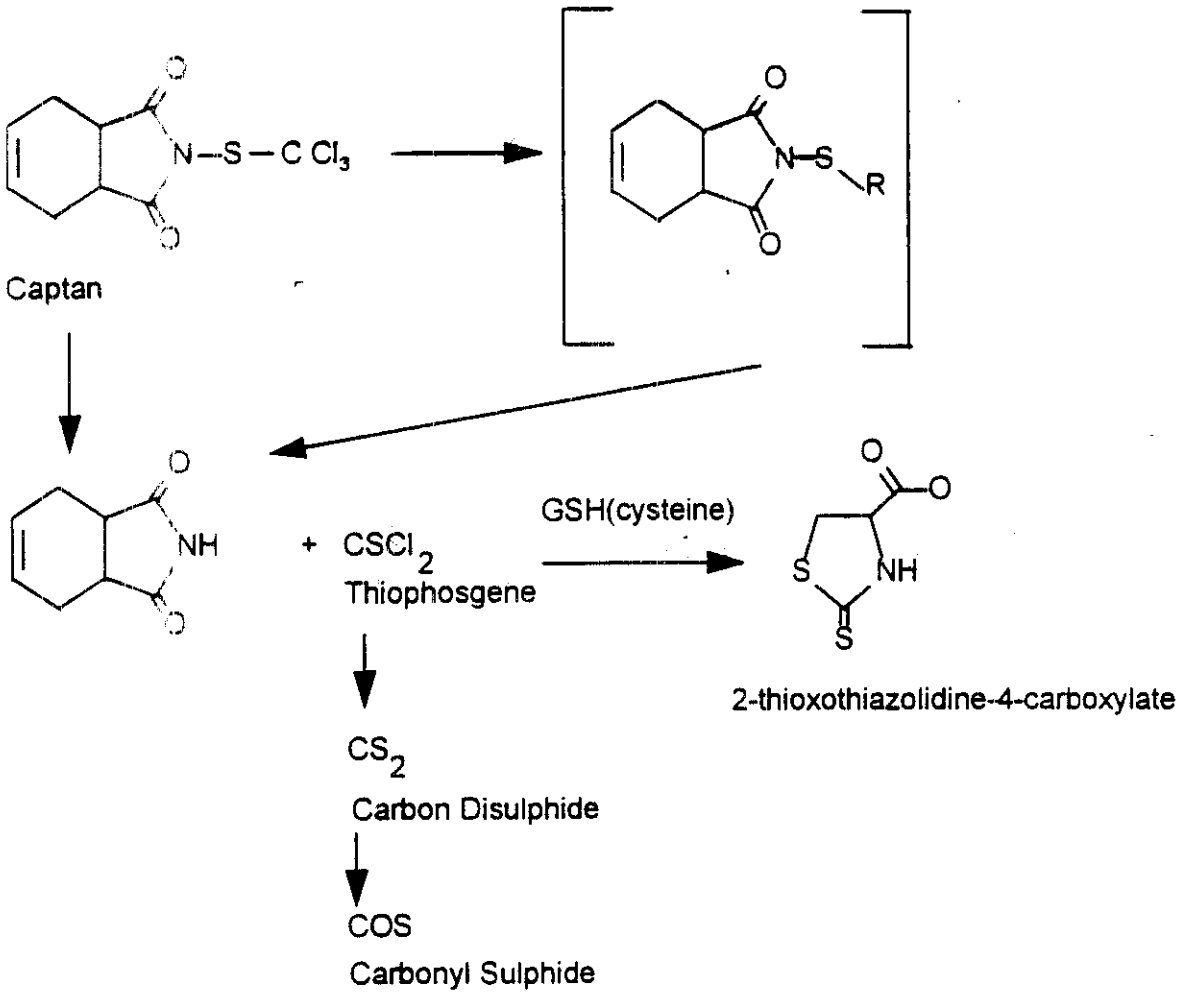

Figure 1. Breakdown products of Captan. Data taken from Figure 8. P. 26, MRID43982202

13544

R148180

Chemical: Captan

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HED File Code: 13100 Other Tox Documents
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