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DATA EVALUATION REPORT

Study Type: Dermal absorption in rat Tox. Chem No. 323EE

Accession No.: 265795

Test Material: propiconazole

Synonyms: tilt, CGA 64 250

Study Number: ABR-86064

Sponsor: Ciba Geigy

Testing Facility: Biochemistry Dept. Agricultural Division
Ciba Geigy Corp. Greensboro, N.C.

Title of Report: Dermal absorption of ^{14}C propiconazole

Author: T. Murphy, K. Brown, D. Doornheim

Report Issued: 9/30/86

Conclusions:
Three groups of 4 male rats/group were treated with dermal application of ^{14}Cpropiconazole. One group was treated for 24 hours and immediately sacrificed, a second group was treated for 10 hours, the skin washed with soap and water rinse followed by 72 hours of depletion time; and a third group was treated for 24 hours followed by 72 hours depletion time after a soap and water rinse. Dose levels used were 0.1, 1.0 and 10.0 mg/rat. For the 24 hour exposed rats the percent absorbed was 57.1, 27.1 and 30.1% for the low, mid and high dose groups respectively. The rate of excretion of the radioactivity was inversely related to the dose administered. For the 10 hour exposure (72 hour depletion) animals the dose absorbed was 42.4, 21.5, and 31.0% of the administered radioactive dose for the low, mid and high dose groups respectively. For the 24 hour exposure (72 hour depletion) animals the dose absorbed was 54.7, 29.8, and 29.8% of the dose administered for the low, mid and high dose groups respectively. Both groups of animals which had depletion times excreted the bulk of the radioactivity within 24 and/or 48 hours, mainly in the urine. Results suggest that the radioactivity remaining in skin after 72 hours is somehow bound and is not available for further absorption.

Core Classification: acceptable

A. Materials:

1. Test Compound: ^{14}C- propiconazole, labelled in triazine ring.

Specific Activity: 28.2 uCi/mg with a purity of 95% for the low and mid dose groups and,
Specific activity for high dose group was 2.01 uCi/mg purity wasn't specified.

Dosing solution: Dermal application of ^{14}C propiconazole made at doses of 0.1, 1.0, and 10.0 mg/rat, equivalent to 0.01, 0.1 and 1.0 mg/c^2 for 10-hour exposure. 50 ul of solution was used for the low and mid dose groups and 100 ul was used for high dose animals.
From a 3 EC Formulation suspended in H_2O

2. Test Animals:

Species: rat, male

Strain: Harlan Sprague Dawley

Age: not specified

Weight: 200-250 gms

Source: Madison Wisconsin

Study Design:

The number of animals used per group was not given in the study text however, the raw data in back indicate that 4/group were used. The study design was the same for this study as the previous one, ABR 86053, except for the following absorption and depletion phases. 10 hour animals had non-occlusive bandages removed and treated area was washed and the animals were kept in metabolism cages for an additional 72 hours to measure the depletion of radioactivity. 24-hour animals had non-occlusive bandages removed at 24 hours and treated area was washed and the animals were kept for an additional 72 hours. A third group of animals was treated for 24 hours and sacrificed with no depletion phase. After washing treated areas the 10-hour animals had urine and feces collected at 24, 48 and 72 hours post treatment and the 24-hour exposure animals had urine and fecal collections at 24, 48, 72 and 96 hours post dosing. At sacrifice the treated skin was rinsed a second time.

Results:

1. For the 24 hour exposure period the total radioactivity recovery ranged from 82.8 to 105.3% of the administered dose. As seen in the last study, the percent absorbed decreased with increasing dose. After 24 hours exposure, 57.1, 27.1 and 30.1% were absorbed for the low, medium and high dose groups respectively. Again, as seen in the last study, a large percentage of the radioactivity was removed with the soap and water rinse. 39.2, 37.2 and 65.2% were removed by soap and water from the low, mid and high dose groups

respectively. The major route of excretion was urine. Data are presented on appended page 1.

2. Data from the 10 hour exposure (72 hour depletion) animals are on appended page 2. Total recoveries ranged from 86.6 to 108.0% of the administered dose. Total absorption for the 82 hour period was 48.3, 25.2 and 37.0% for the low, medium and high doses respectively. Urine again was the major route of excretion with the bulk of the radioactivity being excreted within 24 hours after exposure. (see appended pages 4, 5 and 6.)
After 10 hours of exposure, 48.4, 38.2 and 46.2% of the applied dose was removed in the first soap and water wash. The second wash accounted for only a very small percent of the total radioactivity.

3. The 96 hour animals, ie. those treated for 24 hours of exposure with a 72 hour depletion time have summary data on appended page 3. Total recoveries were 101.7, 95.3 and 90.9% for the low, medium and high dose groups respectively. Appended pages 7, 8 and 9 have bar graphs for both urine and fecal radioactive output for the 4 time periods of collection. Most of the radioactivity was excreted in the 24 and/or 48 hour time periods. Again, the main route of excretion was urine.

Discussion:

For the 24 hour exposure rats the percent absorbed was 57.1, 27.1 and 30.1% for the low mid and high dose groups respectively. The rate of excretion was inversely proportional to dose for the 10 hour exposed (72 hour depleted) animals. The dose absorbed was 42.4, 21.5 and 31.0% of the administered radioactivity for the low, mid and high dose groups respectively. For the 24 hour exposed (72 hour depleted) animals the dose absorbed was 57.4, 29.8 and 29.8% of the administered dose for the low mid and high dose groups respectively. Both groups of animals that had depletion times, excreted the bulk of the radioactivity within 24 and/or 48 hours, mainly in urine. Results suggest that the radioactivity remaining in skin after 72 hours is somehow bound and is not available for further absorption.

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The next 9 page(s) is/are not included in this copy of the TILT reviews.

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___ Identity of product inert ingredients

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