UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 12 1983

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

TO: Henry Jacoby, PM 21
Registration Division (TS-767)

THRU: Edwin R. Budd, Section Head
Toxicology Branch, HED (TS-769)

Budd 7/11/83

SUBJECT: Review of A Dermal Absorption Study in Rats
Captan 50-WP T-11008. Stauffer Chemical Co.
August 27, 1982. Acc. No. 249333
TOX Chem. No. 159

This study has previously been reviewed by Dr. Zendzian for SPRD. His review is attached.

William R. Schneider, Ph.D.
Toxicology Branch
Hazard Evaluation Division (TS-769)

Attachment

1

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Subject: Captan, Dermal Penetration Study

To: Homer K. Hall, Chief
Chemical Review Branch #1
SPRD

11/18/82

From: Robert P. Zendzian, Ph.D.
Pharmacologist
Toxicology Branch, HED

Thru: William Butler, Head
Review Section III

William Burnam, Deputy Chief
Toxicology Branch

Attached is my review of Captan 50-WP: A Dermal Absorption Study in Rats by Joseph S. Ader, Ph.D., July 26, 1982. The study establishes an absorption role of 1.3%/hour of Captan from Captan 50-WP in the rat. This rate can be used as an upper limit for dermal absorption of captan in man since human skin is generally considered up to five times less permeable than rat skin. However, I suggest that we use the rat rate of 1.3%/hour and only consider differences in permeability if it does not provide an adequate margin of safety.

Also, care should be used in the method of utilization of this rate. Thus, if an individual is exposed to 80 grams during an 8-hour working day, we should not use 80 gm x 1.3% x 8 hr for calculating a total absorption. The absorption calculation should be based on an accumulation of 10 gm/hr during the working day.

2

Data Evaluation Report

Compound: Captan 50-WP

Citation: Captan 50-WP: A Dermal Absorption Study in Rats, T-11008 J. S. Adir & R. I. Freidenthal, July 26, 1982

Stauffer Chemical Co.
Environmental Health Center
Farmington, Connecticut 06032

Reviewed by:
11/18/82
Robert P. Zendzian, Ph.D.
Pharmacologist
Toxicology Branch, HED

Core Classification: Supplementary

Conclusion:

The study indicates a maximum dermal absorption rate of 1.3%/hour for captan in the 50% WP formulation. Problems in the experimental design which were demonstrated in this study make it impossible to utilize more fully the data generated. However, since the procedure itself is experimental, the results do not diminish the value of the hourly rate.

Materials:

1. Nonlabeled Compound
   Captan 50-WP
   Lot No.: DJF 0213-J
   EAC Code: 0139-05

2. Radiolabeled Compound
   ^{14}C labeled as *

3

Chevron Chemical Company
Lot No.: 49-173.395
Radiochemical Purity 88.8%
Specific Activity: 38.9 uCi/mg

3. Dosing Suspension

Captan was prepared as a suspension in water on the day of dosing, at nominal concentrations of 2.5 and 25 mg/ml captan each containing 88 uCi/ml. Aliquots of all solutions were assayed to insure homogeneity of captan and radio activity.

4. Test Animals

Sprague-Dawley derived Charles River adult male rats, 240-280 gm and 9-10 weeks of age were used for the study.

Methods

1. Experimental Design

Twenty-four hours prior to dosing, the hair on the rat's back was clipped and the skin washed with acetone. An "Elizabethan" collar was placed around the torso immediately behind the forelimbs, and the rats placed in individual cages. At time zero, 0.2 ml of the appropriate suspension was applied to the back by pipette. The residue in the pipette was measured and the exact quantity applied was determined. Animals were individually caged in metabolism cages. Four animals from each dose were sacrificed at 1, 2, 4 and 8 hours after dosing.

The skin of the application site, blood sample, total urine and feces and residual carcass were collected separately and analyzed for radioactivity.

Results

Data generated in the study are presented in Tables 1, 2 and 3 from the report.

Discussion

This study is, in essence, serving two purposes which can be mutually contradictory; 1) The determination of dermal penetration of captan and 2) the testing of a method for determining dermal penetration. As such, the study has provided usable quantitative information on the dermal penetration of captan but, because of problems with design, the data are not as complete as hoped for.

The study demonstrates a small but measurable absorption of captan through the rat's skin. The report concludes that "Under the conditions of this study, rats absorbed a maximum of 6.4-9.0% of the applied doses of captan within 2-4 hours of its application." While not disputing this conclusion, I believe

4.

that a more usable and defensible absorption rate of 1.3%/hour can be derived from the data. This figure minimizes the variability present in the data. The variability of the data points to correctable problems in the study which can be use to design better future studies on other compounds.

The major problem associated with this study can be called "falloff." The material is applied to the skin which remains uncovered for the duration of the exposure. The material dries and then can flake off. This falloff may contaminate the urine and feces collection or may be eaten by the rat. The longer the animal is maintained and the higher the dose, the more it is possible for this contamination to occur.

The data give some indication that this falloff and contamination has occurred. On Tables 1 and 2, several individual animal values of urinary excretion have been circled. These values are obviously considerably larger than the values of the remaining animals in their respective group. One can observe that most but not all of these animals also show a relatively high quantity of material in the carcass and a higher concentration in the blood. The animals showing a relatively high quantity of compound in urine, carcass and blood may be considered a result of ingesting falloff material while those showing high values only in urine may be considered a result of contamination by falloff. Since there are some high values that do not fit either pattern, one cannot be certain of this explanation, but the entire matter casts doubt on the accuracy of the data for 2, 4 and 8 hours. In addition, the material was applied as a water suspension which certainly would have dried by the end of the first hour, so that one can expect a different pattern of absorption during subsequent hours.

On this basis, the most useful data are those collected during the first hour. Summing the mean recovery in urine, feces, and carcass as indicataive of absorption and calculating percent of mean applied dose gives 0.9%/hr absorbed at 0.5 mg and 1.3%/hr absorbed at 5.0 mg. The higher value will be used for calculating dermal absorption of captan following exposure to the 50% WP formulation.

Captan tox review

Page _____ is not included in this copy.

Pages 6 through 8 are not included in this copy.

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 quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

X FIFRA registration data.

_____ The document is a duplicate of page(s) _____.

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.
