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

005912

MAY 27 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Triphenyltin hydroxide (TPTH), Dermal Absorption Study in Rats

TO: Joanna Dizikes PM-64
Registration Division (TS-767)

FROM: Robert P. Zendzian PhD 5/28/87
Pharmacologist
Mission Support Staff
Toxicology Branch
HED (TS-769)

THROUGH: Reto Engler PhD, Head
Mission Support Staff

Theodore M. Farber PhD, Chief
Toxicology Branch
5/27/87

Compound; Triphenyltin hydroxide

Tox Chem #896E

Registration #083601

Registrant; American Hoechst

MRID #400730-01

Tox Project #7-0414

Action Requested

Review the following study;

An extended duration dermal absorption study in rats with 14C-triphenyltin hydroxide, E.M. Caine, WIL Research Laboratories, Inc. WIL-39033, Feb 6, 1987. MRID 400730-01.

Conclusions

Following a soap and water wash, sufficient triphenyltin hydroxide remained on the application site to allow absorption of up to 18.79, 13.1 and 4.7 percent of the applied dose of 20, 200 and 2000 ug respectively. This absorption occured over a period of 14 to 21 days following washing the skin. Two to three times as much material can be washed off the skin of the living rat than from the skin removed from a sacrificed animal.

Discussion

In 1986 the Registrant submitted a report of a dermal absorption study of TPTH in rats which was reviewed by the Agency (Zendzian 1986). That study showed that a large percent of the applied dose remained on/in the skin at the application site and was potentially available for absorption. It was recommended that a study be performed to determine if this material could be washed from the skin, with soap and water, and if the quantity remaining after the wash could be absorbed over subsequent days. This study was designed to and has provided that information. Unfortunately, the test compound in this study was applied in an emulsifiable concentrate and dilutions thereof while in the first study the test compound was applied as a suspension in water. Thus, the two studies are not comparable (complimentary). The registrant has since performed and submitted a study utilizing a suspension for applying the dose.

However, it should be noted that the data produced in this study may be used in quantitating the absorption of TPTH when exposure is to an emulsifiable concentrate or dilutions thereof for a period of 10 hours.

Reference

Memo, Zendzian, Triphenyltin Hydroxide, Review of Additional Data from Dermal Absorption Study. Mar 5, 1986

Attachments

DER

Date Evaluation Report

Compound TPTH (triphenyltin hydroxide)

Citation An extended duration dermal absorption study in rats with ^{14}C-triphenyltin hydroxide, E.M. Caine, WIL Research Laboratories, Inc. WIL-39033, Feb 6, 1987. MRID 400730-01.

Reviewed by Robert P Zendizan PhD 5/21/87
Pharmacologist

Core Classification Acceptable

Conclusions

Following a soap and water wash, sufficient triphenyltin hydroxide remained on the application site to allow absorption of up to 18.79, 13.1 and 4.7 percent of the applied dose of 20, 200 and 2000 ug respectively. This absorption occured over a period of 14 to 21 days following washing the skin. Two to three times as much material can be washed off the skin of the living rat than from the skin removed from a sacrificed animal.

Materials

^{14}C labeled triphenyltin hydroxide, (HOE 29664) uniformly labeled with ^{14}C in the phenyl rings. Batch 15101 II Specific activity 23.09 uCi/mg, radiopurity 99.1%.

[redacted]

Young adult Crl:CD®(SD)BR rats from Charles River Breeding Laboratories.

Experimental Design

"Three groups of male rats, 20 animals to a group, were treated dermally with a single dose of suspensions of ^{14}C labeled test material following an acclimation preiod. Each dose was applied witin a rubber ring cemented to a shaved area of skin on the back of each rat. After application of each dose, a circle of filter paper was cemented in place on the rubber ring to cover the application zone. Each rat was then placed in a metabolism unit which allowed an effective separate collection of urine and feces but not a collection of volatiles. After an exposure period of ten hours, the aplication sites were washed with a mild aqueous soap solution to remove unabsorbed test material. The application sites were covered again with paper. The rats were placed back into the metabolism units and the disposition of the applied ^{14}C was determined. At time points 10 or 24 hours, 7, 14 or 21 days after application of the test material, sub-groups of four rats were sacrificed. The amounts of test material planned to be administered to each group are summarized as follows:

Group Reference	Dosage Level (mg/kg)	Suspension Used	Planned amount of ^{14}C to be administered/rat (nCi)	(uG)
I	0.1	1-2	400	20
II	1.0	4-1	5000	200
III	10.0	7-1	4500	2000

Amounts of TPTH equivilants were determined in;

1. skin wash after 10 hr exposure
2. skin wash after sacrifice.
3. urine
4. feces
5 washed skin
6. blood
7. muscle beneath the application site
8. carcass
9. paper cover and ring

Results

Distribution of the applied doses is presented in Table 1. The study clearly shows that a significant protion of the material remaining on the skin after washing is absorbed. Table 2 presents data showing that there is a significant difference in the amount of test material that can be removed from the skin depending upon the condition of the skin. The 10 hour animals in each dose group were sacrificed, the skin and site protective appliance removed as a unit and the skin then washed. The application site on all the other animals was washed at 10 hours and the animals retained for 1 to 21 additional days. Two to three times as much material was washed from the skin of the living animals as from the skin removed from sacrificed animals.

Discussion

In the first dermal absorption study on triphenyltin hydroxide the animals were sactificed at the end of the exposure periods. Data showed that a major portion of the applied dose remained on the skin following the skin wash and was potentially available for further absorption. This study was designed to determine what portion of that material could be absorbed following the skin wash.

Table 1. Distribution of applied ^{14}C labeled triphenyltin hydroxide. Data from tables 18, 19, 20, 25, 26, 27, & 31 of the report.

Rat Group	Time of Sacrifice (hr/day)	Average amount TPTH applied (ug)	Average amount of TPHT removed wash process (% of dose)	Average TPTH equivalents in (% of Dose) urine	feces	carcass	washed skin	Average TPTH equivalents absorbed[b] (% dose)
I	10 hr	18.8	14.3*	0.1	<0.1	<1.41	91.8	<1.61
	24 hr	18.8	56.7	0.1	<0.1	<1.51	41.8	<1.61
	7 day	19.0	55.8	3.4	2.7	1.63	22.6	7.73
	14 day	18.5	51.7	7.1	8.7	1.49	2.2	17.29
	21 day	18.3	52.6	7.4	8.9	<2.49	2.0	18.79
II	10 hr	211.2	21.5*	<0.1	<0.1	<0.2	77.2	<0.4
	24 hr	211.0	61.0	0.1	<0.1	0.4	24.5	0.6
	7 day	212.2	51.9	3.5	5.6	2.1	10.3	11.2
	14 day	209.2	53.4	4.7	7.8	0.6	0.4	13.1
	21 day	211.5	56.1	4.0	7.2	0.3	<0.2	11.5
III	10 hr	1955.3	39.3*	<0.1	<0.1	<0.1	57.4	<0.3
	24 hr	1953.8	81.0	<0.1	<0.1	0.2	7.8	<0.4
	7 day	1954.8	80.3	0.6	0.8	1.3	3.8	2.7
	14 day	1954.8	76.5	1.3	3.2	0.2	0.1	4.7
	21 day	1960.5	78.6	1.4	2.8	0.1	0.03	4.3

* The application site was washed only once after sacrifice.
a. Concentration in muscle under the application site and in the blood were below the limit of detection.
b. Totals urine, feces and carcass.

Table 2. Effect of status of skin, on live rat or from dead rat, on washing off the test material.

Rat Group	Time of Sacrifice (hr/day)	Average amount TPTH applied (ug)	Site Wash (% Dose) 10 hour	Sacrifice	Total[b]
I	10 hr	18.8	a	14.1	14.3
	24 hr	18.8	52.3	4.2	56.7
	7 day	19.0	54.5	1.4	55.8
	14 day	18.5	51.6	<0.4	51.7
	21 day	18.3	52.7	<0.4	52.6
II	10 hr	211.2	a	21.6	21.5
	24 hr	211.0	59.0	2.0	61.0
	7 day	212.2	51.0	0.9	51.9
	14 day	209.2	52.6	<0.03	53.4
	21 day	211.5	56.0	<0.03	56.1
III	10 hr	1955.3	a	39.3	39.3
	24 hr	1953.8	78.7	2.3	81.0
	7 day	1954.8	78.4	1.9	80.3
	14 day	1954.8	76.5	<0.004	76.5
	21 day	1960.5	79.7	<0.004	78.6

a. application site was washed only after sacrifice.
b. totals are not exact, determined separately from components.