CASWELL FILE

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

005913

MAY 27 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Triphenyltin Hydroxide, Dermal Absorption in Rats

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

FROM: Robert P. Zendzian PhD 5/26/87
Pharmacologist
Mission Support Staff
Toxicology Branch
HED (TS-769)

THROUGH: Reto Engler PhD, Head 5/26/87
Mission Support Staff

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

Compound; Triophenyltin Hydroxide Tox Chem #896E

Registration 083601 Registrant; Hoechst

Accession #401983-01 Tox Project #7-0698

Action requested

Review the following study;

An extended duration dermal absorption study in rats with ^{14}C-triphenyltin hydroxide, E.M. Caine, WIL Research Laboratories, Inc. WIL-39037, May 11, 1987. MRID 401983-01.

Conclusions

The study is acceptable.

Washing the application site at 10 hours removed 40.8 - 47.7 % (low dose), 49.7 - 69.3 % (intermediate dose) and 71.2 - 79.8 % (high dose) of the applied dose. Quantity absorbed increased with time to a mixiumum of 34.0% (low dose), 15.7 % (intermediate dose) and 15.5 % (high dose). Maximum absorption occured 7 - 14 days after dosing. Quantity remaining in the washed skin decreased with time after washing; 47.0 to 0.4 % (low dose), 31.9 to <0.2 % (intermediate dose) and 12.9 to <0.1 (high dose).

1

Date Evaluation Report

005913

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-39037, May 11, 1987. MRID 401983-01.

Reviewed by Robert P. Zendizan PhD 5/26/87
Pharmacologist

Core Classification Acceptable

Conclusions

Washing the application site at 10 hours removed 40.8 - 47.7 % (low dose), 49.7 - 69.3 % (intermediate dose) and 71.2 - 79.8 % (high dose) of the applied dose. Quantity absorbed increased with time to a mixiumum of 34.0% (low dose), 15.7 % (intermediate dose) and 15.5 % (high dose). Maximum absorption occured 7 - 14 days after dosing. Quantity remaining in the washed skin decreased with time after washing; 47.0 to 0.4 % (low dose), 31.9 to <0.2 % (intermediate dose) and 12.9 to <0.1 (high dose).

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, Batch 15101 IV specific activity 4.589uCi/mg radiopurity 99.1% both batches.

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, in water, 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

The distribution of applied ^{14}C labeled triphenyltin hydroxide is presented in Table 1. The quantity absorbed increased with the dose and with time after application although the percent of dose absorbed decreased with the dose. The percent of the dose that was removed from the skin at the 10 hour wash and at the terminal wash is presented in Table 2. The quantity of test compound and the percent of dose that could be removed at the 10 hour wash increased with the dose. The percent of dose that could be washed from the skin at termination was somewhat similar for each dose although the quantity increased with the dose. This is the only study of this type avaible at this time and it is not known if the agreement in percent of dose is reflective of a general principle or unique to this compound.

Table 1. Distribution of applied ^{14}C labeled triphenyltin hydroxide. Data from table 3 of the report.[a]

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	in animal	washed skin	Average TPTH equivalents absorbed[b] (% dose)
I	10 hr	25.66	49.8	0.2	<0.1	1.7	47.0	1.9
	24 hr	26.00	51.5	0.6	0.3	2.5	40.8	3.4
	7 day	25.48	43.6	4.4	18.9	3.2	7.3	26.5
	14 day	25.35	46.6	6.3	24.5	3.2	3.1	34.0
	21 day	25.20	40.8	6.0	20.5	0.2	0.4	28.1
II	10 hr	278	55.1	0.4	<0.1	<0.1	31.9	0.8
	24 hr	278	56.4	0.3	<0.1	<0.1	28.5	1.3
	7 day	281	61.6	2.4	10.2	10.2	1.0	15.7
	14 day	282	67.1	3.2	10.1	10.1	0.4	13.7
	21 day	281	69.2	2.6	10.0	10.0	<0.2	12.9
III	10 hr	2598	85.4	<0.1	<0.1	<0.1	8.4	<0.01
	24 hr	2589	81.6	<0.1	<0.1	0.2	12.9	0.26
	7 day	2587	77.9	1.2	5.0	2.6	2.6	8.8
	14 day	2584	71.3	2.9	12.2	0.4	<0.1	15.5
	21 day	2592	75.9	1.8	7.9	0.1	<0.1	9.8

a. Concentration in muscle under the application site and in the blood were generally below the limit of detection.
b. Totals urine, feces and in animal.

Table 2. Percent of dose removed from the skin at the 10 hour, live, wash and at the terminal, sacrifice, wash.

Rat Group	Time of Sacrifice (hr/day)	Average amount TPTH applied (ug)	Site Wash (% Dose) 10 hour	Sacrifice	Total[a]
I	10 hr	25.66	47.7	5.1	49.8
	24 hr	26.00	47.2	4.3	51.5
	7 day	25.48	43.6	<0.4	43.6
	14 day	25.35	46.6	<3.1	46.6
	21 day	25.20	40.8	0.1	40.8
II	10 hr	278	49.7	5.3	55.1
	24 hr	278	52.8	3.6	56.4
	7 day	281	61.6	0.04	61.6
	14 day	282	67.0	0.01	67.1
	21 day	281	69.3	<0.03	69.2
III	10 hr	2598	76.7	8.0	85.4
	24 hr	2589	79.8	1.8	81.6
	7 day	2587	77.9	0.04	77.9
	14 day	2584	71.2	<0.03	71.3
	21 day	2592	75.9	<0.03	75.9

a. totals are not exact, determined separately from components.