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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

July 17, 1987

SUBJECT: Azodrin - Dermal Absorption in Rats

TO: Judith Houswith PhD
Head
Review Section VI
Toxicology Branch

FROM: Robert P. Zendzian PhD
Senior Pharmacologist
Toxicology Branch
HED (TS-769)

Action Rquested

Review the following study;

Dermal Absorption of ^{14}C-Azodrin® insecticide in rats: Absorption over 7 days, B.C. Dickie & L.W. LeVan, Hazleton Laboratories America Inc. (Madison), HLA Study Nop. 6160-107, DuPont study No. AMR-629-86, 4/17/87; MRID 401868-01

Conclusions

Moderate quantities of monocrotophos were absorbed. For rats washed after 24 hours and followed for a total of 168 hours postdose, 15.01, 9.96 and 4.04 % of the respective doses of 0.2, 2.0 and 20 mg/rat were absorbed. This includes material in the skin. The study is aceptable.

Data Evaluation Report 006016

Compound Azodrin® (Monocrotophos)

Citation
Dermal Absorption of ^{14}C-Azodrin® insecticide in rats: Absorption over 7 days, B.C. Dickie & L.W. LeVan, Hazleton Laboratories America Inc. (Madison), HLA Study Nop. 6160-107, DuPont study No. AMR-629-86, 4/17/87; MRID 401868-01

Reviewed by Robert P. Zendzian PhD 7/17/87
Senior Pharmacologist

Core Classification Acceptable

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Materials

^{14}C-monocrotophos (stock solution in acetone) Tox Spl #923

Nonradioactive monocrotophos (>99% pure) WRC #55D, three samples from the same lot were received on 7/1/86, 8/28/86 and 12/2/86.

Albino male rats, Wistar strain, from Harlan Sprague Dawley

Experimental Design

"Rats selected for the study had a body weight range of 242 to 290 gm. Groups of 28 rats were dermally dosed and than patched with foam pads at each of the following dose levels: 0.2, 2.0 and 20 mg/rat. Subgroups of four animals/dose level were sacrificed at each of the following time intervals: 0.5, 1, 2, 4, 10, 24 and 168 hours (7 days post dose). ----- Animals at the 168-hour time point received a skin wash (soap and water) and were repatched at 24 hours."

Because of technical problems the five animals/dose at 168-hours groups were repeated using glass enclosures to protect the application site. Analysis was not performed on the origional groups.

Because of additional technical problems the following additional replacement groups of "five rats (having foam pads) that were dermally dosed with 2.0 mg/rat of the test material and sacrificed at 24 hours (Group 2); and 30 rats (having glass enclosures) that were dermally dosed with 20 mg/rat of the test material with five rats each sacrificed at 0.5, 1, 2, 4, 10 and 24 hours" were teated. Analysis were not performed on the origional groups.

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For all treatment groups, "Approximately 24 hours before dosing, the back and shoulders of each rat were clipped ---- and the clipped area was washed with acetone."

For the first set of experimental groups the application site was prepared as follows:
"Shortly before dosing, the dose area was marked onto the central portion of the clipped area using a 3 cm x 4 cm template and black fine-tip marker. A foam patch was made from 6 cm x 7 cm self-adhering foam pads 1 cm thick. The center section (4cm x 5 cm) of each pad was cut out to form a frame with sides approximately 1 cm wide. The foam pad was then placed on the animal's back with medical adhesive. Adhesive strips approximately 1 cm wide were secured with medical adhesive to the top (nonadhesive side) of the frames so that no gaps were present. Covers (approximatley 8 cm by 8 cm) were prepared from a fine cotton cloth."

Test material was applied in a volume of 200 ul. Dosing solution included 20% acetone to duplicate the use product.

"The animal was restrained until the test material dried (30 minutes), the backing on the adhesive strips removed and the fine cotton cloth was placed on the foam pad. Elizabethan collars were placed on every animal and each animal was housed in a stainless steel metabolism cage."

For the repeat of the 168 hour experimental groups the application site was prepared as follows:
"Shortly before dosing, a glass enclosure (2.5 cm x 5 cm inner surface)was glued to the middle of each animal's back using a cyanoacrylate-based glue. Medical silicone adhesive Type A was applied on the outside of the ring to seal it. An Elizabethan collar was placed around each animal's neck. The test material was applied within the glass enclosure and spread evenly on the skin using the dosing needle. After test material application, the animals were restrained manually for 30 minutes to allow the test material to dry. While rats were restrained, excreta was not collected. After the test material dried, rubber cement was applied to the top portion of the glass enclosure. A nonocclusive coton cover (approximastely 5 cm x 7 cm) was placed on top of the glass enclosure. The animals were placed in Nalgene® metabolism cages."

The following samples were collected for analysis;

1. Total urine
2. Total feces
3. Cage rinse (combined with urine)
4. Blood
5. Skin wash (washes at sacrifice were performed on excised skin)
6. Skin at application site (frozen before assay)
7. Carcasses

Results

Results are summerized in Tables 1 and 2.

Discussion

The data produced in this study indicate that there is a significant difference in tne ability to wash test material off the skin depending on whether the animal is alive during the wash or whether the animal is killed, the skin removed and then washed. In the 24 hour exposure groups, the animals are killed, the skin is removed and then it is washed. In tne 168 hour exposure groups, the skin is washed at 24 hours and the animals retained for another 124 hours before sacrifice. These latter animals show a significantly lesser removal of test compound by washing the skin then occured in the animals killed at 24 hours and then washed.

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Table 1. Summary of mean recovery as percent of dose. Data from various tables in the report.

Group# and Dose (mg/rat)	Exposure Duration (hour)	Recovery of radioactivity in							Total Absorbed[1]	Total Not Absorbed[2]	Total[3]
		Skin Wash	Cloth Cover	Foam Pad	Skin	Urine	Feces	Carcass			
1	0.5	89.51	0.66	0.63	2.18	NS	NS	0.48	2.66	90.97	93.45
(0.2)	1	87.07	0.59	4.29	3.57	<0.10	0.01	0.41	4.09	91.95	96.04
	2	85.74	3.84	0.48	4.08	<0.10	NS	0.40	4.58	90.05	94.62
	4	83.25	3.84	0.47	4.34	0.18	0.03	0.44	4.98	87.55	92.53
	10	81.64	3.48	3.57	3.87	0.52	0.04	0.70	5.12	88.68	93.80
	24	78.13	4.56	2.16	4.77	2.94	0.11	1.27	8.74	85.54	94.28
	168*	60.70	13.40	NA	3.06	11.0	0.45	0.55	15.01	74.10	89.11
2	0.5	85.37	0.83	3.22	2.03	NS	NS	0.92	2.94	89.42	92.37
(2.0)	1	81.81	1.33	3.94	1.08	0.15	0.01	0.88	2.12	87.08	89.20
	2	86.51	4.43	0.32	1.06	<0.10	0.01	0.61	1.78	91.26	93.04
	4	88.12	2.33	2.78	1.42	<0.10	0.01	0.40	1.93	93.24	95.17
	10	84.60	2.76	3.59	3.14	0.59	0.04	0.43	4.19	90.95	95.14
	24	76.38	4.78	1.89	2.01	4.19	0.12	0.99	7.31	83.04	90.35
	168*	73.27	12.38	NA	4.20	5.0	0.39	0.40	9.96	85.65	95.61
3	0.5	96.85	1.40	NA	0.55	NS	NS	0.34	0.89	98.24	99.13
(20)	1	92.49	2.38	NA	1.12	<0.10	0.3	0.34	1.59	95.33	96.92
	2	92.38	1.12	NA	1.38	<0.10	0.1	0.34	1.83	95.61	97.43
	4	90.33	2.40	NA	0.99	0.18	0.4	0.34	1.55	94.77	96.33
	10	85.20	2.34	NA	1.85	0.36	0.5	0.34	2.59	93.20	95.79
	24	85.20	5.88	NA	1.29	1.81	0.07	0.35	3.52	91.90	95.42
	168*	72.94	12.80	NA	0.84	2.4	0.35	0.49	4.04	85.74	89.78

* Application site washed at 24 hours postdose
1. Sum of recovery in skin, urine, feces and carcass
2. Sum of recovery from cloth cover, foam pad and skin wash
3. Sum of absorbed and not absorbed.
NS No sample
NA Not Applicable, glass rings

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Table 2. Concentration of Radioactivity in Blood (ug-Equivalents/g)

Group# and Dose (mg/rat)	Exposure Duration (hour)	Mean Concentration
1 (0.2)	0.5	0.003
	1	0.003
	2	0.003
	4	0.004
	10	0.009
	24	0.012
	168*	<0.002
2 (2.0)	0.5	0.094
	1	0.083
	2	0.062
	4	0.038
	10	0.051
	24	0.112
	168*	<0.021
3 (20)	0.5	<0.191
	1	(0.251
	2	0.211
	4	0.379
	10	0.288
	24	0.389
	168*	<0.191

* Application site washed at 24 hours post dose

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