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RANGE FINDING TESTS ON 3,4-EPOXY CYCLOHEXYLETHYL TRIMETHOXYSILANE		
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MELLON INSTITUTE OF INDUSTRIAL RESEARCH

SPECIAL REPORT

611-1
32

Range Finding Tests on 3,4-Epoxy Cyclohexylethyl Trimethoxysilane

Union Carbide Chemicals Co., U.C.C.

Industrial Fellowship 274-25

Summary

Stomach Intubation, rat - LD₅₀ = 12.3 ml./kg.
Skin Penetration, rabbit - LD₅₀ = 6.30 ml./kg.
Inhalation, rat
Concentrated vapor generated at approx. 22°C.
8 hours killed 0 of 6.
Uncovered Skin Irritation, rabbit - minor, Grade 3.
Eye Injury, rabbit - none

Epoxy cyclohexylethyl trimethoxysilane has slight acute toxicity by both the peroral and skin penetration routes. The inhalation of concentrated vapor generated at room temperature presents no hazard to life. Rabbit eyes were unharmed by the instillation of excess amounts of the undiluted chemical while the uncovered rabbit skin responded to such contact with irritation no greater than marked capillary injection.

Methanol and trimethoxysilane have both been studied previously by this laboratory. The following table affords comparison of these two materials with epoxy cyclohexylethyl trimethoxysilane.

<u>Material</u>	<u>Peroral LD₅₀ ML./kg.</u>	<u>Skin Penetration LD₅₀ ML./kg.</u>	<u>Inhalation of Concentrated Vapor</u>	<u>Uncovered Skin Irritation</u>	<u>Eye Injury</u>	<u>Report Number</u>
Methanol	15.4	20	8 hrs. killed 5/6 4 hrs. killed 0/6	None	Minor	14-68
Trimethoxy- silane	9.33	6.30	15 min. killed 6/6 (62.5 ppm. for 4 hrs. killed 5/6, 31.25 ppm. for 4 hrs. killed 1/6)	Minor	Moder- ate	25-22
Epoxy Cyclo- hexylethyl Trimethoxy- silane	12.3	6.30	8 hrs. killed 0/6	Minor	None	This Report

Sample

An eight-ounce sample of 3,4-epoxy cyclohexylethyl trimethoxysilane was received from the Silicones Division, Long Reach Plant, Sistersville, West Virginia on April 25, 1962, for toxicological study at the request of R. C. Maier.

Single Peroral Doses

Epoxy cyclohexylethyl trimethoxysilane has an acute LD₅₀ of 12.3 (9.98 to 15.3) ml./kg. when administered undiluted by stomach intubation to male albino rats.

Carworth Farms-Elias non-fasted rats, five to six weeks of age and 90-120 grams in weight were dosed at levels differing by a factor of 2.0 in a geometric series. The rats were reared in our own colony and maintained from time of weaning on Rockland rat diet (complete). The method of moving average for calculating the median-effective dose (LD₅₀) was applied to the 14-day mortality data.

The animals became prostrate soon after dosing and most deaths occurred shortly thereafter. Gross examination at autopsy disclosed congested lungs, kidneys, stomachs and intestines, and pale mottled livers with prominent acini.

Skin Penetration

By rabbit skin penetration, the LD₅₀ is 6.30 (4.66 to 8.52) ml./kg. undiluted. Only moderate erythema of the skin resulted from these covered applications.

Male albino New Zealand strain rabbits, three to five months of age and averaging 2.5 kg. in weight were immobilized during the 24-hour skin contact period. Thereafter, the sheeting used to retain the dose in contact with the clipped skin of the trunk was removed and the animals were caged for the remainder of the 14-day observation period. The rabbits were procured locally and maintained on Rockland rabbit ration. The moving average method of calculating the LD₅₀ was used.

Deaths occurred on the first and second day after application of the chemical. During this period, three of the rabbits had convulsions. (Convulsions were also observed immediately following the intravenous injection of 0.05 ml. amounts undiluted to rats). At autopsy, gross examination revealed some hemorrhage and congestion of the lungs, pale mottled livers with prominent acini, pale spleens, and pale mottled kidneys. A bloody discharge was present around the nose and mouth of two animals.

Inhalation

Concentrated vapor, generated at a temperature of approximately 22°C. by passing dried air at the rate of 2.5 liters per minute through a fritted glass disc immersed to a depth of at least one inch in 50 ml. of epoxy cyclohexylethyl trimethoxysilane, caused no mortality among six CFE, female albino rats after an eight-hour inhalation period in a 9-liter chamber.

The animals appeared to be normal upon removal from the chamber and five of the six gained weight normally during the subsequent two-week observation period. At sacrifice on the 14th day, 60% lung consolidation was observed in the rat that lost weight. This pathology was probably due to a pre-existing extraneous infection and in no way related to inhalation of the test chemical.

The calculated concentration, based on weight-loss of sample in relation to dilution air, was approximately 5 mg./liter.

24-Hour Irritation Tests

Uncovered application of 0.01 ml. amounts of epoxy cyclohexylethyl trimethoxysilane to the clipped skin of the rabbit belly caused from moderate to marked capillary injection on five animals. Grade 3 in our 10-grade rating system.

Five rabbit eyes were unharmed by the instillation of an excess (0.5 ml) of the undiluted chemical. Grade 1 in our 10-grade rating system.


Jean A. Striegel, B.S.
Junior Fellow

Approved:


Charles P. Carpenter, Ph.D.
Assistant Administrative Fellow

Acknowledgments

Skin Penetration, Irritation Tests

Inhalation Studies

Nacmi I. Condra, B.S.
Junior Fellow
Charles C. Haun, B.S.
Research Associate

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Table 25-217

Epoxy Cyclohexylethyl Trimethoxysilane (25-95)

Single Doses to Male Albino Rats Fed Undiluted by Stomach Tube

<u>Rat Number</u>	<u>1962 Date Dosed</u>	<u>Grams Weight</u>	<u>Weight Change in 14 Days</u>	<u>Dosage; ML. per Kilo</u>	<u>Dose in ML.</u>	<u>Days to Death</u>
54850	5-8	105	-	16.0	1.7	0
54852	5-8	111	-	16.0	1.8	0
54898	5-8	110	-	16.0	1.8	0
54901	5-8	118	-	16.0	1.9	2
54899	5-8	105	+36	16.0	1.7	-
54897	5-8	118	+72	8.0	0.94	-
54902	5-8	109	+19	8.0	0.87	-
54906	5-8	108	+67	8.0	0.86	-
54907	5-8	95	+64	8.0	0.76	-
54908	5-8	120	+81	8.0	0.96	-

LD50 = 12.3 (9.98 to 15.3) ml./kg.

Table 25-218

Epoxy Cyclohexylethyl Trimethoxysilane (25-95)

Single Doses to Male Albino Rabbits by Skin Penetration
Administered Undiluted under Polyethylene Dam for 24 Hours

<u>Rabbit Number</u>	<u>Date Clipped</u> 1962	<u>Date Applied</u>	<u>Grams Weight</u>	<u>Weight Change in 14 Days</u>	<u>Dosage; ML. per Kilo</u>	<u>Dose in ML.</u>	<u>Days to Death</u>
52029	5-7	5-8	2180	-	10.0	21.8	1
52018	5-7	5-8	2348	-	10.0	23.5	1
52032	5-7	5-9	2256	-	10.0	22.6	2
52034	5-7	5-9	2355	-	10.0	23.6	2
49756	5-7	5-9	3240	-	5.0	16.2	1
51973	5-2	5-3	2264	+184	5.0	11.3	-
51958	5-2	5-3	2482	+210	5.0	12.4	-
52004	5-7	5-9	2238	- 14	5.0	11.2	-

LD50 = 6.30 (4.66 to 8.52) ml./kg.

Table 25-219

Epoxy Cyclohexylethyl Trimethoxysilane (25-95)

Single Inhalation by a Group of Female Albino Rats of
Concentrated Vapor Generated at Approximately 22°C.

<u>Rat Number</u>	<u>Date and Duration of Inhalation</u>	<u>Conc. Mg./L.</u>	<u>Initial Weight Grams</u>	<u>Weight Change in 14 Days</u>
54223	5-3-62 8 Hours 9-Liter Chamber	5 Mg./L.	146	+31
54231			146	+47
54233			144	-14
54256			130	+43
54265			156	+44
54268			152	+37