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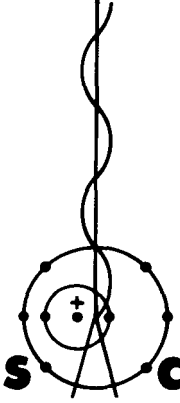

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A PRELIMINARY TOXICOLOGICAL STUDY OF SYLGARD 184 ENCAPSULATING RESIN

by

D. M. Smith, G. A. Drake, J. E. London, and R. G. Thomas

ABSTRACT

The acute oral LD_{50}^{30} values for Sylgard 184 encapsulating resin in mice and rats were greater than 5 g/kg. According to classical guidelines, the compound would be considered slightly toxic or practically nontoxic in both species. Skin application studies in the rabbit demonstrated this material to be mildly irritating. Eye irritation studies, also in the rabbit, showed that Sylgard 184 encapsulating resin was a mild but transitory irritant. The sensitization study in guinea pigs did not show the resin to be deleterious in this regard.

I. INTRODUCTION

As part of the Mammalian Biology Group's (H-4) applied toxicology program, Sylgard 184 encapsulating resin was examined to define its toxic properties with the following tests: (1) acute oral toxicity; (2) primary skin irritation; (3) skin sensitization; and (4) eye conjunctival instillation. Sylgard 184 encapsulating resin is composed largely of silicone with silica reinforcement.

II. EXPERIMENTAL PROCEDURE

A. General

The test material Sylgard 184 encapsulating resin (Dow-Corning Corporation, Midland, Michigan) was supplied in 200-mℓ samples by Group WX-3 of the LASL Design Engineering Division. While in the possession of Group H-4, the material was stored at 25°C in a glass container sealed inside a plastic bag. A maximum dose of 5 g/kg was used for testing. Any compound showing no mortality at this level in 30 days was reported as having an LD_{50}^{30} of greater than 5 g/kg and was considered to be less than slightly toxic or practically nontoxic.

B. Single-Dose Acute Oral Toxicity (LD_{50}^{30} Days)

1. Rats. Fourteen young adult (114-day-old) Sprague-Dawley male rats, weighing 380 to 390 g, were used in the 5-g/kg test group to determine the range of toxicity.[1,2] The compound was administered to ether-sedated, fasted rats as a suspension in corn oil; corn oil controls were tested previously with no deleterious effects. The dose was given intragastrically with a ball-tipped needle and syringe. After treatment, all animals were observed daily for 30 days for aberrant physiological and behavioral responses. All data are on file in the Mammalian Biology Group at the Los Alamos Scientific Laboratory as Compound H-4-#3.

2. Mice. The procedure for single-dose oral-toxicity determination in mice was the same as for rats. Twenty young female adult (55-day-old) CFW (Swiss-Webster) mice, weighing 21 to 29 g, were used in this group. Corn oil controls were tested and reported previously.[3] As with rats, all animals were observed for 30 days for abnormal physiological and behavioral responses.

C. Long-Term Oral Toxicity

1. Mice. Thirty young CFW (Swiss-Webster) female mice, weighing 22 to 26 g, were given a single intragastric dose of 5 g/kg and will be followed until death, with pathophysiological observations to be made including gross and microscopic necropsy examinations.

2. Rats. Thirty young male Sprague-Dawley rats, weighing 220 to 300 g, were given a single dose of 5 g/kg as in the mouse test above.

D. Multiple Oral Doses

Thirty young CD-1 mice, weighing 26 to 32 g, were given 1-g/kg doses daily on 5 consecutive days. These animals will be followed until death, with pathophysiological results observed as above.

E. Primary Skin Irritation

The Draize test[4] was used to assess primary skin irritation. Six New Zealand white rabbits, weighing 2.5 to 3.5 kg each, were used in this test group. The back of each rabbit was clipped free of hair using Oster electric clippers (Oster Corporation, Racine, Wisconsin) with a #40 blade at 24 h before application of the compound. Two sites were superficially abraded and two left unabraded. The compound was applied using 0.5 mℓ on each location. The test sites were covered with a gauze pad, and the entire back was covered with an adhesive plastic surgical drape and overwrapped with a linen cloth. The wraps were removed 24 h later, and each test site was scored visually for erythema and edema. Readings were recorded at 24, 48, and 72 h. A final irritation score was calculated for the 24- and 72-h readings.

F. Eye Irritation

Six New Zealand white rabbits, weighing 2.5 to 3.5 kg, were used in this test. Both eyes were checked for abnormalities before instillation. The compound (0.1 mℓ) was instilled into the conjunctival envelope of the left eye of each rabbit; the right eye served as a control. Two rabbits had the compound washed from the eye with 0.15 M NaCl 30 s after instillation, 2 at 5 min after instillation, and 2 did not have the compound washed from the eye. Each eye was graded for ocular lesions at 1 and 4 h on the day of application and again at 24, 48, and 72 h. Of particular interest was whether the cornea, iris, and conjunctivae became inflamed. The procedure and grading system were taken from the Draize test.

G. Skin Sensitization

Six female guinea pigs, weighing 380 to 642 g, were used. The animals were housed individually and fed commercial laboratory stock diets ad libitum supplemented daily by lettuce and cabbage. The test compound was diluted to a concentration of 0.1% by weight in corn oil and was administered intradermally in a series of 10 "sensitizing" injections in the lower back and flanks of the animals. Before each injection, the test sites were clipped free of hair. The injections were made randomly over the test area on Sunday, Tuesday, and Thursday with a 1-mℓ tuberculin syringe fitted with a 25-gauge needle. The volume of the first injection was 0.05 mℓ, and the other 9 were 0.1 mℓ each. The sites were scored for erythema (redness), height, and diameter 24 h after each injection. Redness and height were scored as described by Landsteiner and Jacobs;[5] the diameters of the reactions were measured in millimeters using a micrometer caliper. At 2 wk after administration of the tenth sensitizing injection, the lower back and flanks of the guinea pigs were clipped free of hair, and a challenge injection of 0.05 mℓ was administered. The reaction of each animal was graded 24 h later and compared with those from the sensitizing injections.

III. RESULTS AND DISCUSSION

A. Single-Dose Acute Oral Toxicity (LD_{50}^{30} Days)

1. Rats. All rat behavioral and physiological responses after administration appeared normal for 30 days. The LD_{50}^{30} was greater than 5 g/kg for Sylgard 184 encapsulating resin.

2. Mice. All mouse behavioral and physiological responses after administration appeared normal. The LD_{50}^{30} was greater than 5 g/kg.

B. Primary Skin Irritation

Four of the 6 rabbits treated with Sylgard 184 encapsulating resin developed erythema at 24 h, with 3 rabbits also having edema. All animals were judged normal at 72 h. The total primary irritation score was 0.25.

C. Eye Irritation

Table I summarizes the eye irritation responses for Sylgard 184 encapsulating resin. Irritation was observed only in conjunctival tissue. Conjunctival responses were observed at all treatments and generally were composed of mild redness and mucoid exudation. The eyes of the 5-min wash group cleared at 48 h, and the others were judged normal at 72 h. The degree of eye irritation caused by Sylgard 184 encapsulating resin overall was mild but transitory.

D. Skin Sensitization

Review of the data collected for each guinea pig in the treatment group indicates that all challenge injection reactions were within the limits of reactions recorded during the sensitizing period.

TABLE I

EYE IRRITATION RESPONSE IN RABBITS TREATED WITH SYLGARD 184 ENCAPSULATING RESIN[a]

	Average Irritation (hours)		Average Irritation (days)		
Tissue Graded[b]	1	4	1	2	3
Wash at 30 s					
Cornea	0	0	0	0	0
Iris	0	0	0	0	0
Conjunctivae	4	3	3	2	0
Wash at 5 min					
Cornea	0	0	0	0	0
Iris	0	0	0	0	0
Conjunctivae	3	4	3	0	0
No Wash					
Cornea	0	0	0	0	0
Iris	0	0	0	0	0
Conjunctivae	4	2	2	2	0

[a]Two rabbits per wash condition.

[b]Maximum cornea response = 80; maximum iris response = 10; and maximum conjunctivae response = 20.

This study did not show Sylgard 184 encapsulating resin to be a sensitizer.

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