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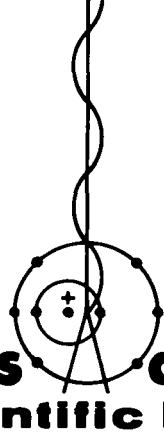
D. M. Smith
G. A. Drake
J. E. London
R. G. Thomas



los alamos
scientific laboratory
of the University of California
LOS ALAMOS, NEW MEXICO 87545

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A PRELIMINARY TOXICOLOGICAL STUDY OF SYLGARD 184 ENCAPSULATING RESIN:CURING AGENT

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 (100 parts encapsulating resin plus 10 parts curing agent) were greater than 5 g/kg in rats and mice. According to classical guidelines, the mixture would be considered slightly toxic or practically nontoxic in both species. Skin application studies in the rabbit demonstrated the mixture to be mildly irritating. Eye irritation tests, also in the rabbit, showed the Sylgard 184 mixture to be a mild but transitory irritant. The sensitization study in the guinea pig demonstrated the mixture to be a very mild sensitizer in two of six animals.

I. INTRODUCTION

As part of the Mammalian Biology Group's (H-4) applied toxicology program, Sylgard 184 (100 parts encapsulating resin and 10 parts curing agent) 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 is composed of silicone with silica reinforcement.

II. EXPERIMENTAL PROCEDURE

A. General

The test materials of Sylgard 184, curing agent and encapsulating resin (Dow-Corning Corporation, Midland, Michigan), were supplied in 200-mℓ samples by Group WX-3 of the LASL Design Engineering Division. While in the possession of Group H-4, these materials were stored at 25°C in glass containers sealed inside plastic bags. Immediately before administration, the materials were mixed by combining 100 parts encapsulating resin and 10 parts curing agent, as suggested by instructions accompanying the products. 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 Toxicity (LD_{50}^{30} Days)

1. Rats. Fifteen young adult (104-day-old) Sprague-Dawley male rats, weighing 320 to 400 g, were used in the 5-g/kg test group to determine the range of toxicity.[1,2] The mixture was administered to ether-sedated, fasted rats as a suspension in corn oil. This vehicle was used to suspend the mixture in an innocuous medium. 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. These data are on file in the Mammalian Biology Group at the Los Alamos Scientific Laboratory as Compound H-4-#7.

2. Mice. The procedure for single-dose oral-toxicity determination in mice was the same as for rats. Twenty young adult female (61-day-old) CFW (Swiss-Webster) mice, weighing 28 to 30 g, were used in the 5-g/kg dose group. As in the rat study, all animals were observed for 30 days for abnormal physiological and behavioral responses.

C. Long-Term Oral Toxicity

1. Mice. Thirty young female CD-1 mice, weighing 24 to 26 g, were given by intragastric intubation a single 5-g/kg dose of the Sylgard 184 mixture and will be followed until death, when pathophysiological observations will be made

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including gross and microscopic necropsy examinations.

2. Rats. Thirty young male Sprague-Dawley rats, weighing 260 to 300 g, were administered a single 5-g/kg dose of the Sylgard 184 mixture, as in the mouse test above.

D. Multiple Oral Doses

Thirty young CD-1 female mice, weighing 28 to 34 g, were administered 1-g/kg doses of the Sylgard 184 mixture daily on 5 consecutive days. These animals will be followed until death, when pathophysiological results including gross and microscopic necropsy examinations will be made.

E. Primary Skin Irritation

The Draize test[3] was used to assess primary skin irritation. Six New Zealand white rabbits, weighing 2.8 to 3.8 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 24 h before application of the compound. Two sites were 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 at 24 h, 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 2.7 to 3.5 kg, were used. Both eyes of the rabbits were checked for abnormalities before instillation. The mixture (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 postapplication. 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 679 to 741 g, were used. The animals were housed individually and fed laboratory stock diets ad libitum supplemented daily by lettuce and cabbage. The test compound was diluted to a concentration of 0.1% by weight with corn oil. Corn oil controls were tested previously. The compound was administered intradermally in a series of 10 "sensitizing" injections into the lower back and flanks of the guinea pigs. 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 remaining 9 were each 0.1 mℓ. At 24 h after each injection, the reaction was scored for erythema (redness), height, and diameter. Redness and height of the lesions were scored as described by Landsteiner and Jacobs;[4] 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 each guinea pig 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. In general, 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.

2. Mice. All mouse behavioral and physiological responses after administration appeared normal. The LD_{50}^{30} was greater than 5 g/kg for Sylgard 184.

B. Primary Skin Irritation

The rabbits treated with 100 parts Sylgard 184 encapsulating resin plus 10 parts curing agent all developed erythema and edema at the 24-h reading, and only 2 showed erythema at the 72-h reading. The total primary irritation score was 0.39. The primary skin irritation study showed this mixture to be mildly irritating to the skin.

TABLE I

EYE IRRITATION RESPONSES IN RABBITS TREATED WITH SYLGARD 184 ENCAPSULATING RESIN:CURING AGENT

	Average Irritation (hours)		Average Irritation (days)		
Tissue Graded[a]	1	4	1	2	3
Wash at 30 s					
Cornea	0	0	0	0	0
Iris	0	0	0	0	0
Conjunctivae	7	5	5	2	2
Wash at 5 min					
Cornea	0	0	0	0	0
Iris	0	0	0	0	0
Conjunctivae	5	5	4	3	0
No Wash					
Cornea	0	0	0	0	0
Iris	0	0	0	0	0
Conjunctivae	5	4	4	2	2

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

C. Eye Irritation

Table I summarizes the eye irritation response for the Sylgard 184 mixture (100 parts encapsulating resin plus 10 parts curing agent). Irritation was observed only in the conjunctivae. Conjunctival responses were observed at all treatment levels and generally involved redness, chemosis, and mucoid exudation. The treated eyes of both rabbits in the 5-min wash and 1 rabbit in the 30-s wash were judged normal at day 4. The treated eye of 1 rabbit in the 30-s wash and of both rabbits in the no wash group was judged abnormal in response until day 7. The degree of eye irritation caused by the Sylgard 184 mixture overall was mild but transitory.

D. Skin Sensitization

Careful review of the data collected from each guinea pig indicated that only 2 challenge injections showed a reaction slightly greater than those during the sensitization period. This study demonstrated the Sylgard 184 mixture to be a very mild sensitizer.

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