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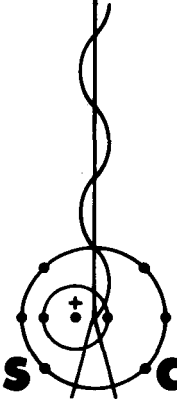

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A PRELIMINARY TOXICOLOGICAL STUDY OF SYLGARD 184 CURING AGENT

by

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

ABSTRACT

The acute oral LD_{50}^{30} values for mice and rats receiving Sylgard 184 curing agent 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 the compound to be mildly irritating. Eye irritation studies, also in the rabbit, showed that Sylgard 184 curing agent was a mild but transitory irritant. The sensitization study in guinea pigs did not show the resin to be deleterious.

I. INTRODUCTION

As part of the Mammalian Biology Group's (H-4) applied toxicology program, Sylgard 184 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.

II. EXPERIMENTAL PROCEDURE

A. General

The test material Sylgard 184 curing agent (Dow-Corning, 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. Twenty young adult (104-day-old) Sprague-Dawley male rats, weighing 325 to 405 g, were used in the 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. 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-#4.

2. Mice. The procedure for single-dose oral-toxicity determination in mice was the same as for rats. Twenty-five young female adult (55-day-old) CFW (Swiss-Webster) mice, weighing 22 to 28 g, were used in this 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 CFW (Swiss-Webster) mice, weighing 26 to 30 g, were given an intragastric intubation dose of 5 g/kg and will be followed until death, with pathophysiological observations made including gross and microscopic necropsy examinations.

2. Rats. Thirty young Sprague-Dawley male rats, weighing 300 to 400 g, were given a single 5-g/kg dose as in the mouse test above.

D. Multiple Oral Doses

Thirty young female 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 changes observed as above.

E. Primary Skin Irritation

The Draize test[3] was used to assess primary skin irritation. Six New Zealand white rabbits, weighing 2.5 to 3.5 kg, 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 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. Both eyes of the animals 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 of the 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 examined 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 350 to 560 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 with corn oil and was administered 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. Intradermal 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, reactions were scored for erythema (redness), height, and diameter. Redness and height 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} for rats was greater than 5 g/kg for Sylgard 184 curing agent.

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

B. Primary Skin Irritation

All 6 rabbits treated with Sylgard 184 curing agent showed erythema at 24 h, with 3 animals showing edema. No animals showed erythema or edema at the 72-h reading. The total primary irritation score for Sylgard 184 curing agent was 0.46.

C. Eye Irritation

Table I summarizes eye irritation responses for Sylgard 184 curing agent. Irritation was observed only in the conjunctivae. Conjunctival responses were observed at all treatments and generally involved mild redness and mucoid exudation. The treated eyes of all rabbits had returned to normal within 24 h. The degree of eye irritation caused by Sylgard 184 curing agent 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. The guinea pig skin sensitization study did not demonstrate Sylgard 184 curing agent to be a sensitizer.

TABLE I

EYE IRRITATION RESPONSE IN RABBITS TREATED WITH SYLGARD 184 CURING AGENT[a]

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

[a] Two rabbits per wash condition.

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

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