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D. M. Smith
J. E. London
G. A. Drake
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 SILASTIC 386 FOAM ELASTOMER

by

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

ABSTRACT

The acute oral LD_{50}^{30} values for Silastic 386 foam elastomer for rats and mice 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 with Silastic 386 foam elastomer demonstrated it to be mildly irritating when administered cutaneously. This compound was a very mild but transitory irritant in rabbit eye application studies. The sensitization study in the guinea pig did not show the compound to be deleterious in this regard.

I. INTRODUCTION

As part of the Mammalian Biology Group's (H-4) applied toxicology program, Silastic 386 foam elastomer was examined as to its toxicity in the following tests: (1) acute oral toxicity; (2) primary skin irritation; (3) skin sensitization; and (4) eye conjunctival instillation. This compound is part of the foam elastomer cushioning agent.

II. EXPERIMENTAL PROCEDURES

A. General

The Silastic 386 foam elastomer (Dow-Corning Corporation, Midland, Michigan) was supplied in 200-mℓ samples by Group WX-3 of the LASL Design Engineering Division. The material was stored at 25°C in a glass container enclosed in 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 rats, weighing 240 to 300 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 by intragastric intubation as a suspension in corn oil using a ball-tipped needle and syringe. This vehicle was used to suspend the mixture because of its innocuous properties.

After treatment, all animals were observed daily over a period of 30 days for aberrant physiological and behavioral responses. The data are on file in the Mammalian Biology Group at the Los Alamos Scientific Laboratory as Compound H-4-#6.

2. Mice. The procedure for single-dose oral-toxicity determination in mice was the same as for rats. Twenty young adult female CD-1 (62-day-old) mice, weighing 25 to 28 g, were used. All animals were observed daily after treatment for 30 days.

C. Long-Term Oral Toxicity

1. Mice. Thirty young CD-1 mice, weighing 20 to 22 g, were given a single 5-g/kg dose and will be followed until death, with pathophysiological observations to be made including gross and microscopic necropsy examinations.

2. Rats. Thirty young Sprague-Dawley rats, weighing 220 to 275 g, were given a single 5-g/kg dose 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[3] was used to assess primary skin irritation. Six New Zealand white rabbits, weighing 3.2 to 3.8 kg each, were used. The back of each rabbit was clipped free of hair 24 h before application of the compound using Oster electric clippers (Oster Corporation, Racine, Wisconsin) with a #40 blade. 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 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 3.2 kg, were used in this test. Both eyes of the animals were checked for abnormalities before instillation. The compound was instilled into the conjunctival envelope in 0.1-mℓ quantities into 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 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 336 to 492 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% with corn oil. Corn oil controls were tested previously. The compound 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 with electric small-animal clippers. 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, the sites 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 results 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.

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

Three of the 6 rabbits treated with Silastic 386 foam elastomer demonstrated erythema, and only 1 had edema at 24 h. The total primary irritation score was 0.24.

C. Eye Irritation

Table I summarizes eye irritation responses for Silastic 386 foam elastomer. Irritation was observed only in the conjunctivae. Conjunctival responses were observed at all treatments and generally involved mild redness, chemosis, and mucoid exudation. The treated eyes of all rabbits had returned to normal in 48 h. The degree of eye irritation caused by Silastic 386 foam elastomer 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 reactions were within the limits of reactions recorded during the sensitizing period. This study did not demonstrate Silastic 386 foam elastomer to be a sensitizer.

TABLE I

EYE IRRITATION RESPONSE IN RABBITS TREATED WITH SILASTIC 386 FOAM ELASTOMER[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	6	6	4	0	0
Wash at 5 min					
Cornea	0	0	0	0	0
Iris	0	0	0	0	0
Conjunctivae	6	6	4	0	0
No Wash					
Cornea	0	0	0	0	0
Iris	0	0	0	0	0
Conjunctivae	6	6	4	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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