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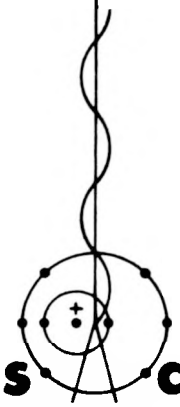

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A PRELIMINARY TOXICOLOGICAL STUDY OF KERIMIDE 601 RESIN

by

D. M. Smith, G. A. Drake, J. E. London, J. S. Wilson,

L. M. Holland, and R. G. Thomas

ABSTRACT

The acute oral LD_{50} values for kerimide 601 resin for mice and rats is greater than 5 g/kg. According to classical guidelines, the mixture would be considered slightly or practically nontoxic in both species. Skin application studies in the rabbit with kerimide 601 resin demonstrated that it was cutaneously nonirritating. This resin was also nonirritating in rabbit eye application studies. The sensitization study in the guinea pig did not show resin to be deleterious in this regard, although delayed necrosis was seen at the injection sites 96 h after administration.

I. INTRODUCTION

Kerimide 601 resin has a variety of applications. At the Los Alamos Scientific Laboratory, it is used as a plastic binding agent in syntactic foam. This report describes its minimal toxic properties according to standard methodologies.

II. EXPERIMENTAL PROCEDURES

A. Source of Material

The test material kerimide 601 resin, lot number 77052 (1 kg), was supplied in powder form from the Bendix Corporation in Kansas City, Missouri. The material was stored at 25°C in a plastic bucket.

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

1. Rats. Twenty young adult (~ 72 days) Sprague-Dawley male rats weighing 260 to 340 g were used in the test group. The compound was administered to ether-sedated, fasted rats as a suspension in corn oil; corn oil controls were made previously. This vehicle was used to solubilize 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.[1,2] We initially conducted range-finding studies at various dose levels to identify the zone of toxicity with 10 animals being used per level. The results of this preliminary work are not presented herein, but the data are on file in the Mammalian Biology Group (H-4) at the Los Alamos Scientific Laboratory as Compound H-4-#2.

2. Mice. The procedure for single-dose oral toxicity in the mouse was identical to that for the rat. Twenty young adult CFW (Swiss-Webster) mice 78 days old weighing 20 to 28 g were used in groups. Corn oil controls were done previously. As in the rat study, all animals were observed daily after treatment for 30 days.

C. Long-Term Oral Toxicity

1. Mice. Thirty young CFW mice weighing 22 to 27 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 325 to 405 g were given a single 5-g/kg dose as in the mouse test above.

D. Multiple Oral Doses

Thirty young CFW mice weighing 25 to 37 g were given 1-g/kg doses daily on 5 consecutive days. These 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 2.5 to 3.0 kg each were used in this test group. The back of each rabbit was electrically clipped free of hair 24 h before application of the compound. Two sites were abraded and 2 left unabraded. The compound was applied as a paste consisting of 500 mg in 0.5 cc corn oil to each location. The test sites were covered with a gauze pad, and the entire back was covered with an adhesive plastic drape and overwrapped with taped linen to hold it in place. At 24 h later, the wraps were removed, and each test site was visually scored for erythema and edema. Readings were recorded for 24, 48, and 72 h. A final irritation score was calculated for the 24-, 48-, and 72-h readings.

F. Eye Irritation

Six white rabbits weighing 2.5 to 3.0 kg were used in this facet of the study. Both eyes were checked for abnormalities before instillation. The compound was instilled into the conjunctival envelope in 100-mg 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 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 were whether the cornea, iris, and conjunctiva became inflammed. The procedure and grading system were taken from the Draize test.

G. Skin Sensitization

Eight male guinea pigs weighing 475 to 700 g were used in each of the vehicle control treatment groups. The animals were housed individually and fed commercial laboratory stock diets ad libitum supplemented by daily lettuce and cabbage because of their need for vitamins.

The test compound was diluted to a concentration of 0.1% with corn oil. The control group received corn oil alone. 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. Injections were made randomly over the test area on Sunday, Tuesday, and Thursday via a 1-cc tuberculin syringe fitted with a 25-gauge needle. The volume of the first injection was 0.05 mℓ, and the other 9 were each 0.1 mℓ. At 24 h after injection, the reaction was 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 micrometer calipers.

Two weeks 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} value was greater than 5 g/kg.

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

B. Primary Skin Irritation

The kerimide 601 resin caused no edema or erythema on the abraded and unabraded treated rabbits; therefore, the primary skin irritation studies demonstrated that the compound was nonirritating.

C. Eye Irritation

The kerimide 601 resin did not result in conjunctival, corneal, or uveal (iris) inflammation in any of the 3 groups of rabbits (no wash, 5-min wash, and 30-s wash).

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 the reactions recorded during the sensitizing period. The guinea pig skin sensitization study did not show kerimide 601 resin to be a sensitizer. However, in some animals (5 of 8), areas of necrosis developed at each injection site 96 to 120 h after intradermal administration of this material.

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