

Study Title

Approximate Lethal Dose (ALD) of H-21953 in Rats

Laboratory Project ID

Haskell Laboratory Report No. 795-96

Author

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Performing Laboratory

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[REDACTED]

GENERAL INFORMATION

Substance Tested:

Synonyms/Codes:

• H-21953

Physical Form:

Opaque tan to white liquid

Composition:

Contaminants:

Purity:

Submitter's Notebook No.:

CAS Registry No.:

Sponsor:

Study Initiated - Completed:

DuPont Specialty Chemicals
E. I. du Pont de Nemours and Company
Wilmington, Delaware

6/21/96 - 9/3/96

In Life Phase

Initiated - Completed:

6/22/96 - 7/8/96

All raw data and the final report will be stored in the archives of Haskell Laboratory for Toxicology and Industrial Medicine, E. I. du Pont de Nemours and Company, Newark, Delaware or at Iron Mountain (formerly DuPont Records Management Center, Wilmington, Delaware).

SUMMARY

H-21953 was administered as a single oral dose by intragastric intubation to male rats. No deaths occurred during the study. Clinical signs of toxicity were observed in non-lethally dosed animals. Under the conditions of this test, the ALD was greater than 11,000 mg/kg of body weight. This substance is considered to be very low in toxicity (ALD greater than 5000 mg/kg) when administered as a single oral dose to male rats.

SIGNATURE PAGE

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INTRODUCTION

The purpose of this test was to determine an approximate lethal dose of H-21953 when administered as a single oral dose to male rats. The ALD was defined as the lowest dose administered which caused death either on the day of dosing or within 14 days post exposure.

MATERIALS AND METHODS

A. Animal Husbandry

Male CrI:CD[®](SD)BR rats, approximately 7 weeks old, were received from Charles River Laboratories, Raleigh, North Carolina. Rats were housed singly in suspended, stainless steel, wire-mesh cages. Each rat was assigned a unique identification number which was recorded on a card affixed to the cage. The rats were tail-marked, using a water-insoluble marker, with the last 3 digits of the animal number. Purina[®] Certified Rodent Chow[®] #5002 and water were available *ad libitum*.

Haskell Laboratory has an animal health monitoring program. This program is monitored and administered by the Laboratory Veterinarian. Water samples are periodically analyzed for total bacterial counts and for the presence of coliforms, lead, and other contaminants. Additionally, samples from freshly washed cages and cage racks are periodically analyzed to assure adequate sanitation by the cagewashers. Data from this program are maintained separately from study records. Animal feed is certified by the manufacturer to meet specified nutritional requirements and to be free of a list of specified contaminants. On the basis of these analyses, there is no evidence suggesting that contaminants were present in the feed or water in amounts which may have interfered with the results of this study.

Rats were quarantined, weighed, and observed for general health for approximately one week, prior to testing. Animal rooms were maintained on a timer-controlled, 12-hour light/12-hour dark cycle. Environmental conditions of the rooms were targeted for a temperature of $23^{\circ}\text{C} \pm 1^{\circ}\text{C}$ and relative humidity of $50\% \pm 10\%$. Excursions outside these ranges were of small magnitude and/or brief duration and did not adversely affect the validity of the study.

B. Protocol

The test substance was administered neat to 1 rat per dose rate by intragastric intubation. The density of the test substance was 1.03 g/mL. In the absence of visible evidence to the contrary, the test substance was assumed to be stable under the conditions of administration. Dose rates administered ranged from 2300 to 11,000

mg/kg of body weight in increments of approximately 50%. Additionally, 1 rat was dosed at 670 mg/kg. The dosing day was test day 1; postexposure day 14 was test day 15. Following administration of the test substance, rats were observed for clinical signs of toxicity. The rats were weighed and observed daily until signs of toxicity subsided and then at least 3 times a week throughout the 14-day observation period. Observations for mortality and signs of illness, injury, or abnormal behavior were made daily throughout the study. Pathological examinations of test animals were not performed.

RESULTS

A. Dosage and Mortality Data

The dosage regimen and the mortality resulting over the 15-day test period are detailed below. No deaths occurred during this study.

<u>Dosage</u> (mg/kg)	<u>Dose Volume</u> (mL)	<u>Density</u> (mg/mL)	<u>Initial Body</u> <u>Weight (g)</u>	<u>Mortality</u>
670	0.18	1030	280	No
2300	0.61	1030	275	No
3400	0.83	1030	250	No
5000	1.1	1030	236	No
7500	1.7	1030	234	No
11,000	2.5	1030	238	No

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B. Clinical Signs

Nonlethal Doses

No clinical signs of toxicity or weight losses were observed in the rats treated at 670 or 2300 mg/kg. The rats treated at 3400 and 5000 mg/kg exhibited lung noise 1 day after dosing; the 3400 mg/kg rat also exhibited lung noise 2 days after dosing. Weight losses of approximately 2 - 12% of initial body weight were observed in rats treated from 3400 - 11,000 mg/kg 1 day after dosing.

CONCLUSION

Under the conditions of this study, the ALD for H-21953 was greater than 11,000 mg/kg of body weight. This substance is considered to be very low in toxicity (ALD greater than 5000 mg/kg) when administered as a single oral dose to male rats.

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