Acute Oral Toxicity Screen

with T-3065CoC

in Albino Rats

Experiment No.: 0981AR0145

Conducted At: Safety Evaluation Laboratory
Riker Laboratories, Inc.
St. Paul, Minnesota

Dates Conducted: April 2, 1981 to April 16, 1981

Conducted By: KDO'Malley 5/8/81

K. D. O'Malley, BS Date
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Reviewed By: 5/15/81

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Summary

An acute oral toxicity screen with T-3065CoC was conducted from April 2, 1981 to April 16, 1981 using male and female albino rats ranging in body weight from 209-293 grams. The test material was administered by gastric intubation at a dosage level of 5,000 mg/kg body weight with mortalities of 3/10 noted from day 1 to day 5 post dose administration. Diarrhea, lethargy and hypoactivity were the untoward reactions which were noted from 120 minutes to day four and body weight gains were noted in all animals which survived the 14 day observation period. Necropsy of the animals performed upon termination of the study revealed no visible lesions while hemorrhage of the gastrointestinal tract and lungs were noted in the animals which died acutely. The LD50 of T-3065CoC appears to be greater than 5,000 mg/kg in fasted male and female rats.

Introduction

The objective of this study was to approximate the acute oral LD50 of T-3065CoC in fasted albino rats. This study is not regulated by the Food and Drug Administration's Good Laboratory Practice Regulation of 1978, although the standard operating procedures of this laboratory adhere to the general principals of this regulation. The raw data generated by the Study Director and the final report are stored in the conducting laboratory's archives.

Method and Results

Young albino rats[a] were used in this test. All animals were held under quarantine for several days prior to testing with only animals which appeared to be in good health and suitable as test animals at the initiation of the study used. The rats were housed in suspended, wire-mesh cages in temperature and humidity controlled rooms and permitted a standard laboratory diet[b] plus water ad libitum except during the 16 - 20 hour period immediately prior to gastric intubation when food was withheld.

Five male and five female rats were administered the test material at a preselected dosage level. All doses were administered at a constant volume of 10 ml/kg directly into the stomachs of the rats using a hypodermic syringe equipped with a ball-tipped intubating needle[c].

After gastric administration of the test article, the rats were returned to their cages and observed for the following 14 days. Initial and final body weights, mortalities (Table 1) and adverse reactions (Table 2) were recorded. A necropsy was conducted on all animals that died during the study as well as those euthanatized at the end of the 14 day observation period (Table 1). The protocol, principal personnel involved in the study, composition characteristics, and Quality Assurance statement are contained in Appendices I - IV.

[a] Charles River Breeding Laboratories, Inc., Wilmington, MA
[b] Ralston Purina Laboratory Chow, Ralston Purina, St. Louis, Missouri
[c] Popper and Sons, Inc., New Hyde Park, New York

TABLE 1

ACUTE ORAL TOXICITY SCREEN - ALBINO RATS

with T-3065CoC

Mortality, Necropsy and Body Weight Data

Dose [a] (mg/kg)	Sex	Animal Number	Individual Body Weights (g) Test Day Number: 0	14	Number Dead / Number Tested	Percent Dead
5,000	M	1R2607	274	(5 Days)	3/5	60
		1R2608	293	377		
		1R2609	289	(1 Day)		
		1R2610	279	373		
		1R2611	287	(2 Days)		
5,000	F	1R2590	235	274	0/5	0
		1R2591	241	281		
		1R2592	231	275		
		1R2593	233	275		
		1R2594	209	251		

[a] The test article was administered as a suspension in cottonseed oil.

The approximate oral LD50 appears to be greater than 5,000 mg/kg in fasted male and femal albino rats.

Necropsy

Necropsies performed upon termination of the study revealed no visible lesions, however, necropsy of the animals which died acutely revealed hemorrhagic gastrointestinal tracts and hemorrhagic lungs (one incidence).

TABLE 2

ACUTE ORAL TOXICITY SCREEN - ALBINO RATS

with T-3065CoC

Summary of Reactions

Dose mg/kg	Reactions / Sex	Observation Periods: Number Affected/Number Dosed — Minutes: 1-30	60	120	Days: 1	2	3	4	5	6	7	8	9	10	11	12	13	14
5000	F																	
	Hypoactivity	-	-	-	5/5	5/5	0/5	-	-	-	-	-	-	-	-	-	-	-
	Diarrhea	-	-	-	5/5	0/5	-	-	-	-	-	-	-	-	-	-	-	-
5000	M																	
	Hypoactivity	-	-	-	4/4	3/3	1/3	0/3	-	-	-	-	-	-	-	-	-	-
	Diarrhea	-	-	2/5	4/5	0/3	-	-	-	-	-	-	-	-	-	-	-	-
	Lethargy	-	-	-	1/4	0/3	-	-	-	-	-	-	-	-	-	-	-	-

No significant reaction (-)

APPENDIX I
PROTOCOL

TEST: Acute Oral Toxicity
SPONSOR: 3M Commercial Chemicals Division
CONDUCTED BY: Safety Evaluation Laboratory, Riker Laboratories, Inc., St. Paul, Minnesota
TEST ARTICLE: T-3065CoC
CONTROL ARTICLE: None
PROPOSED STARTING/COMPLETION DATE OF TEST: 3/31 4/14
TEST SYSTEM AND SOURCE: Rat, Charles River Breeding Laboratories, Inc., Willmington, MA

Sex: M,F
Number: 5,5
Weight Range: 200-300 gm.

OBJECTIVE: The objective of this test will be to characterize the acute oral toxicity of the test article in albino rats. Rats were selected as a test system for reproducibility of response, historical use, ease in handling and general availability.

METHOD: The animals will be housed in stainless steel suspended wire mesh cages in temperature and humidity controlled rooms during both the quarantine and test periods, with food[a] and water offered ad libitum[b]. Each animal will be identified by color coding, according to the laboratory's standard operating procedure, which will correspond to a card affixed to the outside of the cage. A single dosage of 5,000 mg/kg will be administered each animal, however, if this dosage level does not adequately characterize the toxicity of the test article, additional animals will be administered the test article at supplemental dosage levels. Any additional dosage levels will be documented and filed with this protocol. The test article will be administered to the animals in the form received from the sponsor. After administration of the test article, the animals will be returned to their cages and observed for any untoward behavioral reactions for the following 14 days. Initial and final body weights will be recorded. A gross necropsy which will include, but not be limited to, heart, lungs, liver, kidneys and general gastrointestinal tract will be conducted on all animals which die during the conduct of the test as well as the animals surviving the test period. Any gross abnormalities which are observed during the conduct of the necropsy will be recorded with specific mention to the organ and/or site observed. The acute median lethal dose (LD50) of the test article will be calculated, if possible, using a probit analysis method at the end of the observation period. All raw data and the final report will be stored in the Riker Laboratories Archives, St. Paul, Minnesota.

[a] Purina Laboratory Chow, Ralston Purina, St. Louis, Missouri

[b] Except during a 16-20 hour period immediately prior to dosing when food will be withheld.

3/24/81 3/31/81

Sponsor Date Study Director Date

APPENDIX II

Principal Participating Personnel Involved in the Study

Name	Function
G. E. Hart	Laboratory Technician Acute Toxicology
K. D. O'Malley, BS	Advanced Toxicologist Study Director
K. L. Ebbens, BS	Supervisor Acute Toxicology
G. C. Pecore	Supervisor Animal Laboratory

APPENDIX III

Composition Characteristics

This study is not regulated by the Good Laboratory Practice Regulation of 1978 and therefore information pertaining to composition characteristics is not applicable for inclusion in this study.

APPENDIX IV

Quality Assurance Statement

This study is not regulated by the Good Laboratory Practice Regulation of 1978 and therefore a statement signed and prepared by the Quality Assurance group is not applicable. This study was, however, audited by the Quality Assurance group.

In addition to the data audit, different significant phases for studies underway in the Toxicology Laboratory are inspected weekly on a recurring cycle, and the facilities are examined by Laboratory Quality Assurance on a three month schedule.