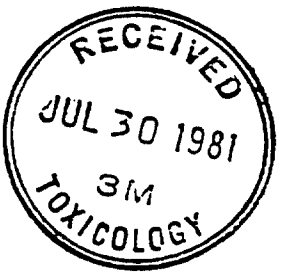
AR226-0238



Acute Oral Toxicity Screen with T-3066CoC in Albino Rats

Experiment No.: 0981AR0146

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

Dates Conducted: April 2, 1981 to May 14, 1981

Conducted By:

K. D. O'Malley, BS — Date 6/8/81
Advanced Toxicologist
Study Director

Reviewed By:

K. L. Ebbens, BS — Date 7/13/81
Supervisor, Acute Toxicology

dc: M. T. Case
K. L. Ebbens
F. D. Griffith
W. C. McCormick

Summary

The acute oral toxicity screen with T-3066CoC was conducted from April 2, 1981 to May 14, 1981 at Riker Laboratories, Inc., St. Paul, Minnesota using male and female albino rats ranging in body weight from 157-289 grams. The test article was administered by gastric intubation at dosage levels of 5,000 and 500 mg/kg body weight with mortalities of 7/10 and 0/10 respectively. Untoward behavioral reactions were noted only in the 5,000 mg/kg dose group animals and consisted of hypoactivity, lethargy, prostration and diarrhea. The onset of the reactions occurred from 120 minutes to 1 day post dose and all reactions subsided by day 4 or death precluded recovery. Body weight gains were noted in all animals which survived the 14 day study period. Necropsies performed at termination of the study revealed no visible lesions among the surviving animals while hemorrhage of the gastrointestinal track or lungs were noted in all animals which died acutely. The approximate LD50 of T-3066CoC is less than 5,000 mg/kg and greater than 500 mg/kg in fasted male and female albino rats.

Introduction

The objective of this study was to approximate the acute oral LD50 of T-3066CoC in fasted male and female 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 principles 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.

Groups of five male and five female rats were administered the test article at preselected dosage levels. The doses were administered at a constant volume of 10ml /kg directly into the stomachs of the rats using a hypodermic syringe equipped with a ball-tipped intubation 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-3066CoC

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
5000	M	1R2612	246	(1 Day)	5/5	100
		1R2613	267	(1 Day)		
		1R2614	289	(4 Days)		
		1R2615	266	(1 Day)		
		1R2616	263	(1 Day)		
5000	F	1R2595	234	(2 Days)	2/5	40
		1R2596	238	(2 Days)		
		1R2597	219	252		
		1R2598	239	290		
		1R2599	232	272		
500	M	1R4113	235	320	0/5	0
		1R4114	227	319		
		1R4115	235	310		
		1R4116	228	332		
		1R4117	213	295		
500	F	1R4051	166	218	0/5	0
		1R4052	167	213		
		1R4053	160	192		
		1R4054	158	191		
		1R4055	157	205		

Note: Figures in parenthesis indicate time of death.

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

The acute oral LD50 is less than 5000 mg/kg and greater than 500 mg/kg in fasted male and female albino rats.

Necropsy

Necropsy of the animals which died acutely revealed hemorrhagic gastrointestinal track lungs while no visible lesions were noted upon necropsy of the animals which survived the 14 day observation period.

Table 2

ACUTE ORAL TOXICITY SCREEN - ALBINO RATS

with T-3066CoC

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	M																	
	Hypoactivity	-	-	-	-	1/1	1/1	*										
	Prostration	-	-	-	1/1	0/1	-	*										
	Diarhhea	-	-	1/5	0/1	-	-	*										
5000	F																	
	Hypoactivity	-	-	-	1/5	0/3	3/3	0/3	-	-	-	-	-	-	-	-	-	-
	Lethargy	-	-	-	4/5	3/3	0/3	-	-	-	-	-	-	-	-	-	-	-
	Prostration	-	-	-	1/5	0/3	-	-	-	-	-	-	-	-	-	-	-	-
500	M																	
	No significant reaction																	
500	F																	
	No significant reaction																	

No significant reactions (-)
*Total death

Riker Experiment Number: [illegible]

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-3066L0C

CONTROL ARTICLE: N/A

PROPOSED STARTING/COMPLETION DATE OF TEST: 4/[illegible] - 7/81

TEST SYSTEM AND SOURCE: Rat, Charles River Breeding Laboratories, Wilmington, [illegible]

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.

William T. McCormick 3/24/81 [illegible] 3/31/81

Sponsor Date Study Director Date

Amendment to Protocol

1. The weight limit is extended to 150 - 310 gms in order to expediate initiation of the study

ICDEmalley 5/4/81
Study Director Date

2. _____

Study Director Date

3. _____

Study Director Date

4. _____

Study Director Date

5. _____

Study Director Date

6. _____

Study Director Date

7. _____

Study Director Date

8. _____

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.