

**SC-19192: ACUTE TOXICITY STUDIES IN THE RAT, MOUSE AND RABBIT**

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## ACUTE TOXICITY STUDIES OF SC-19192

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### INTRODUCTION

The acute toxicity of SC-19192 (diketopiperazine) has been studied in three species of laboratory animals. Rats, mice and rabbits have received this compound - a conversion product of a nutritive sweetening agent (SC-18862) currently under study - for the purpose of determining LD-50 values.

### METHODS

Animals used for studies of the acute toxicity of SC-19192 included mature male albino rats of the Charles River and Sprague-Dawley (Schmidt Ha/ICR) strain and mature male New Zealand White rabbits of the Luenberg strain. All animals were housed under standard laboratory conditions with controlled temperature, humidity and light/dark cycle. Food and water were available ad libitum. Rats and mice were fed Teklad Mouse/Rat Diet. Rabbits received Teklad Rabbit Diet (Teklad, Incorporated, Monmouth, Illinois).

Formulation of SC-19192 varied with the route and magnitude of the dose to be administered. For the highest intragastric doses administered to all species, highly concentrated aqueous suspensions were prepared. A 1% solution of Tween-80 in distilled water was employed as vehicle for these

suspensions. Compound was added slowly with constant stirring (Corning magnetic stirrer plus manual stirring) until high viscosity was evident. The viscous mixture was then sonicated with a Heat Systems-Ultrasonics, Inc. Model W185D Sonifier until a homogeneous suspension of low viscosity had been attained. Additional compound was added and the above procedure repeated until the desired concentration (compound weight/total volume) was reached. Suspensions were of low viscosity at time of administration and homogeneity was maintained by means of a magnetic stirrer throughout the drug administration regimen.

Compound was formulated as an aqueous suspension in distilled water (without suspending agent) for intraperitoneal and lower dose intragastric administration to rats and mice. These suspensions were heated to 56°C, then cooled to room temperature before administration.

All doses were administered on a mg of SC-19192/kg of body weight basis. Animals received a single dose of compound, followed by a period of seven days of observation for mortality. Values for the LD-50 and its standard error were to be calculated on the basis of mortality ratios (number of animals dead within seven days of treatment/number of animals treated) at the various dose levels.

## RESULTS

Results of acute toxicity studies of SC-19192 are summarized in Tables 1 and 2. It is important to note that no mortality resulted within seven days of treatment for any animal receiving SC-19192 at the stated dose levels; in addition, motor and behavioral activities of all animals were generally unremarkable throughout the seven day post-dosage period. As no mortalities were

observed, true LD-50 values could not be calculated. It can be assumed that LD-50 values are in excess of the highest doses administered to each species by the respective routes employed.

#### SUMMARY

The acute toxicity of SC-19192 (diketopiperazine; DKP) has been studied in three species of laboratory animal. Rats, mice and rabbits have received SC-19192 by the intragastric route at doses ranging up to 5,000 mg/kg of body weight with no deaths or unusual behavior patterns observed within seven days after treatment. In addition, rats and mice have received SC-19192 by intraperitoneal injection at doses ranging to 1,562 and 1,577 mg/kg, respectively. Again no deaths or unusual behavior patterns were observed within seven days of treatment.

Table 1

ACUTE TOXICITY STUDIES OF SC-19192:  
MORTALITY RATIOS AFTER THE SEVEN DAY OBSERVATION PERIOD

Species	Route	Drug Conc. (w/v)	Mortality Ratios (No. Deaths/No. Treated)									
			Dose Levels (mg/kg)									
			1,562	1,577	2,000	2,191	2,500	3,200	3,710	4,000	5,000	
Rat	ig (a)	15.0%	—	—	—	—	—	—	—	—	0/6	
Rat	ig	3.5%	—	—	—	0/6	—	—	—	—	—	
Rat	ip (b)	2.0%	0/6	—	—	—	—	—	—	—	—	
Mouse	ig	15.0%	—	—	—	—	—	—	—	—	0/6	
Mouse	ig	3.5%	—	—	—	—	—	—	0/6	—	—	
Mouse	ip	2.0%	—	0/6	—	—	—	—	—	—	—	
Rabbit	ig	17.5%	—	—	0/1	—	0/1	0/1	—	0/3	0/3	

<sup>a</sup> Intragastric (stomach tube) administration

<sup>b</sup> Intraperitoneal injection

Table 2

ACUTE TOXICITY STUDIES OF SC-19192:  
A TABULAR SUMMARY

Species	Strain	Sex	Route	Drug Conc. (w/v)	LD-50 $\pm$ S.E. (mg/kg)
Rat	Charles River	Male	ig <sup>a</sup>	15.0% aq. susp. <sup>c</sup>	>5,000
Rat	Sprague-Dawley	Male	ig	3.5% aq. susp. <sup>d</sup>	>2,191
Rat	Sprague-Dawley	Male	ip <sup>b</sup>	2.0% aq. susp. <sup>d</sup>	>1,562
Mouse	Sprague-Dawley	Male	ig	15.0% aq. susp. <sup>c</sup>	>5,000
Mouse	Sprague-Dawley	Male	ig	3.5% aq. susp. <sup>d</sup>	>3,710
Mouse	Sprague-Dawley	Male	ip	2.0% aq. susp. <sup>d</sup>	>1,577
Rabbit	New Zealand White; Luenberg Strain	Male	ig	17.5% aq. susp. <sup>c</sup>	>5,000

<sup>a</sup> Intragastric (stomach tube) administration

<sup>b</sup> Intraperitoneal injection

<sup>c</sup> Vehicle consisted of 1% Tween-80 in distilled water

<sup>d</sup> Heated to 56°C