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ACUTE TOXICITY STUDIES ON LEAF EXTRACTS OF *Chloroxylon switenia. DC*

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ABSTRACT

The aim of performing acute toxicity studies is for establishing the Therapeutic Index (TI) of a particular drug and to ensure the safety *in vivo*. Acute Toxicity study is generally carried out for the determination of LD_{50} value in experimental animals. Thus the author aimed to perform acute toxicity studies to investigate the toxicity profile of the selected plant following the up-dated OECD guidelines-425. The crude methanolic extract, hexane and ethyl acetate fractions showed neither visible signs of toxicity nor mortality. The results clearly indicated non-toxicity of the extracts at a dose of 2000 mg/kg body weight. This infers that the LD_{50} of test extracts may be greater than 2000 mg/kg body weight and hence all the extracts tested are considered safe and non-toxic.

Key Words: *Chloroxylon swietenia,* Acute Toxic Category Method

INTRODUCTION

Organization for economic co-operation and development (OECD) regulate guidelines for acute oral toxicity study. OECD Guidelines for the Testing of Chemicals are periodically reviewed in the light of scientific progress or changing assessment practices. It includes three guidelines 420, 423 and 425. The guideline-425 was adopted on 3rd October 2008 as the alternative to the conventional acute toxicity test [1-4]. The acute toxic class method set out in this Guideline is a stepwise procedure with the use a maximum of 5 animals of a single sex preferably females. Depending on the mortality and/or moribund status of the animals, on average 2-4 steps may be necessary to allow judgments on the acute toxicity of the test substance. This procedure is reproducible, uses very few animals and is able to rank substances in a similar manner to the other acute toxicity testing method (Test Guidelines-420 and 425).

The acute toxic class method is based on biometric evaluations with fixed doses, adequately separated to enable a substance to be ranked for classification purposes and hazard assessment. The method as adopted in 2008 was extensively validated *in vivo* against LD_{50} data obtained from the literature, both nationally and internationally Guidance on the selection of the most appropriate test method for a given purpose can be found in the Guidance Document on Acute Oral Toxicity Testing. This Guidance Document also contains additional information on the conduct and interpretation of Test Guideline 425.

MATERIAL AND METHODS

PRINCIPLE OF LIMIT TEST

The limit test is a sequential test that uses a maximum of 5 animals. A test dose of 2000 mg/kg or exceptionally 5000 mg/kg may be used. The procedures for testing at 2000 and 5000 mg/kg are slightly different. The selection of a sequential test plan increases the statistical power and also has been made to intentionally bias the procedure towards rejection of the limit test for compounds with LD_{50S} near the limit dose; *i.e.,* to error on the side of safety. As with any limit test protocol, the probability of correctly classifying a compound will decrease as the actual LD_{50} more nearly resembles the limit dose.

Acute Toxic Category Method is a method for assessing acute oral toxicity that involves the identification of a dose level that causes mortality. This test involves the administration of a single bolus dose of test substances to fasten healthy young adult rodents by oral gavage, Observation for up to 14 days after dosing and recording of body weight and the necropsy of all the animals. In this method pre-specified fixed doses of the test substances were used *i.e.,* 2000 mg/kg body weight (prepared in 1 % sodium CMC) and the no. of mortalities due to these changes were observed.

EXPERIMENTAL DESIGN REQUIREMENTS

Animal species and number	5 Swiss female Albino mice (20-25gm) / each group.
Drugs	Crude Methanolic extract, hexane and ethyl acetate fractions of Chloroxylon switenia
Suspending agent	Sodium CMC
Vehicle	Distilled water
Feeder	Oral gastric feeding needle for mice.

PROCEDURE

As a general rule, the acute toxicological studies on *Chloroxylon switenia* were performed as per OECD-guidelines 425 in female mice. The fixed test dose *i.e.,* 2000 mg/kg body weight was selected based on the Guideline-425.

The experimental protocol has been approved by the Institutional Animal Ethics Committee and by the Animal Regulatory Body of the Government. (Regd. No. 516/01/A/CPCSEA).

ACCLIMATISATION

Healthy and adult female albino swiss mice weighing between 20-25 g were used in this investigation. The albino mice of fair sex, weighing between 20 to 25 gram were selected and divided in to 5 groups each consisting of 5 animals. They were maintained under standard conditions (room temperature at 22±3˚C, 12 h light/dark period) and allowed free access to water along with standard pellet diet for one week before the experiment.

ADMINISTRATION OF THE FIXED DOSE

Animals were fasted overnight for 24 h and divided into groups of five animals each. The test extracts of *Chloroxylon switenia* suspended in Sodium Carboxy Methyl Cellulose (Sodium CMC) solution (1%), were administered *per oral* (orally) at a dose of 2000 mg per kg body weight. The control group of animals received only the vehicle (1 % sodium CMC).

OBSERVATION PERIOD

The animals were subjected for acute toxicity study by administering each extract per oral (orally) at a dose of 2000 mg/kg body weight in 4 groups and observed at regular intervals of 1, 2, 4, 8, 12 and 24 hours for skin changes, morbidity, aggressiveness, increase oral secretion, sensitivity to the sound and pain as well as respiratory movements and mortality. As a rule, the animals were observed for the subsequent 14 days from the time of administration of test extract to record the mortality. All the extracts used in the present study and employed in the later described pharmacological screening have been found to be free from toxicity as well as toxic symptoms at a fixed dose of 2000 mg/kg body weight and hence they were considered safe.

Table 1: LD_{50} Values of different extracts of *Chloroxylon swietenia*

Sl. No.	Group No.	Name of extract/fraction	No. of Animals/Group	Dose in mg/kg body weight	No. of deaths/group
1.	I	*Chloroxylon swietenia* methanolic extract	5	2000	0
2.	II	*Chloroxylon swietenia* hexane fraction	5	2000	0
3.	III	*Chloroxylon swietenia* ethyl acetate fraction	5	2000	0

RESULTS and DISCUSSION

The crude methanolic extract, hexane and ethyl acetate fractions showed neither visible signs of toxicity nor mortality. The results clearly indicated non-toxicity of the extracts at a dose of 2000 mg/kg body weight. This infers that the LD_{50} of test extracts may be greater than 2000 mg/kg body weight and hence all the extracts tested are considered safe and non-toxic.

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