Knowledge Centre For Innovation Integrity and Implementation

ACUTE TOXICITY STUDY OF CLEVIRA SYRUP IN WISTAR RATS

By

Ki3

For

Apex Laboratories Private Limited.

No 5 Jayalakshmi Street, Radha Nagar, Chromepet Chennai - 600044
www.ki3services.com

MAHATMA GANDHI MEDICAL COLLEGE & RESEARCH INSTITUTE,
SRI BALAJIVIDYAPEETHDEEMED UNIVERSITY
PILLAIYARKUPPAM, CUDDALORE ROAD,
PUDUCHERRY-607403

DEPARTMENT OF PHARMACOLOGY

Title :ACUTE TOXICITY STUDY OF CLEVIRA SYRUP IN WISTAR RATS

Principal Investigator: Dr Mirunalini R,
Assistant Professor, Dept. of Pharmacology.

Study Director: Dr.M.Sakthi Balan.
Principal Investigator, Ki3.

Study Site: Central Animal House,MGMC&RI,Pondicherry (CPCSEA approved)

CRO: Ki3, Chrompet, Chennai.

Sponsor: Apex Laboratories Private Limited, Guindy, Chennai.

Product: Syrup Clevira

Protocol No: CLEVIRA PRECLINICAL/015/18

Species : Female Wistar rats

Assay: Acute Toxicity Study

Date of report: 16-10-2018

TABLE OF CONTENTS

1.0 INTRODUCTION:

Clevira is a herbal preparation from Apex Laboratories Private Limited, Chennai. Clevira is available in syrup and tablet form. Clevira preparations are indicated for the treatment of viral infections as it is claimed for its antiviral property. The in-vitro cytotoxic studies and antiviral activity assays in cell culture has proven its activity. (1)

In this study as an initial step of preclinical study we have assessed the acute toxicity status of the drug which will be followed by repeated dose toxicity study. This study was done in accordance with the OECD guidelines for toxicity studies and after approval from the Institutional Animal Ethics committee (**03/IAEC/MGMC/06/2018-1**).

CLEVIRA SYRUP COMPOSITION

Each 10 ml contain (Aushadh Ghana) extracts derived from medicinal plants of

S. No.	Botanical Name	Common Name (Sanskrit Name)	Plant Parts Used	Label Claim (mg)
1.	Carica papaya	Erandakarkati	Leaves	1000.00
2.	Melia azedarach	Mahanimba	Leaves	1000.00
3.	Andrographis paniculata	Kalmegh	Herb	250.00
4.	Vetiveria zizanioides	Usira	Root	250.00
5.	Trichosanthes dioica	Patola	Whole Plant	250.00
6.	Cyperus rotundus	Musta	Rhizome	250.00
7.	Zingiber officinale	Sunthi	Rhizome	250.00
8.	Piper nigrum	Maricha	Fruit	250.00
9.	Mollugo cerviana	Grismachatraka	Whole Plant	250.00
10.	Tinospora cordifolia	Guduchi	Stem	250.00

2.0 OBJECTIVES:

- To assess the acute toxicity of Clevira syrup in wistar rats.
-To assess the Maximum tolerated dose (MTD) from acute toxicity study followed by repeated dose toxicity study.
-To observe for signs of toxicity throughout the study period (14 days)
- To check for gross pathological changes at the end of study after necropsy(on 14th day)

3.0 OUTCOME PARAMETERS:

- Change in weight of the animals from baseline, day 7 and day 14
- Signs of toxicity
- Gross &Histo- pathological changes at the end of the study

4.0 METHODOLOGY:

Acute Toxicity Study:

Twenty one healthy female Wistar rats weighing 180±20g and 10 to 12 weeks of age were used in this study. The animals were kept in polypropylene cages, with dry paddy husk bedding and covered with stainless steel mesh lid. The environment of the room was maintained on a 12-hour light/dark cycle at a constant room temperature of 26±2°C and relative humidity of 45-55%. The rats had free access to standard rat chow diet and water ad libitum. The rats were acclimatized to the surroundings for 2 weeks prior to the experiment. The animals were randomly selected, marked to permit individual identification. Animals were divided into 3 groups of 7rats in each for testing Acute oral toxicity. Group 1 , 2 and 3 received dose of 300mg/kg, 1000mg/kg and 2000mg/kg respectively.Following the period of fasting, the animals were weighed and the test substance were administered.

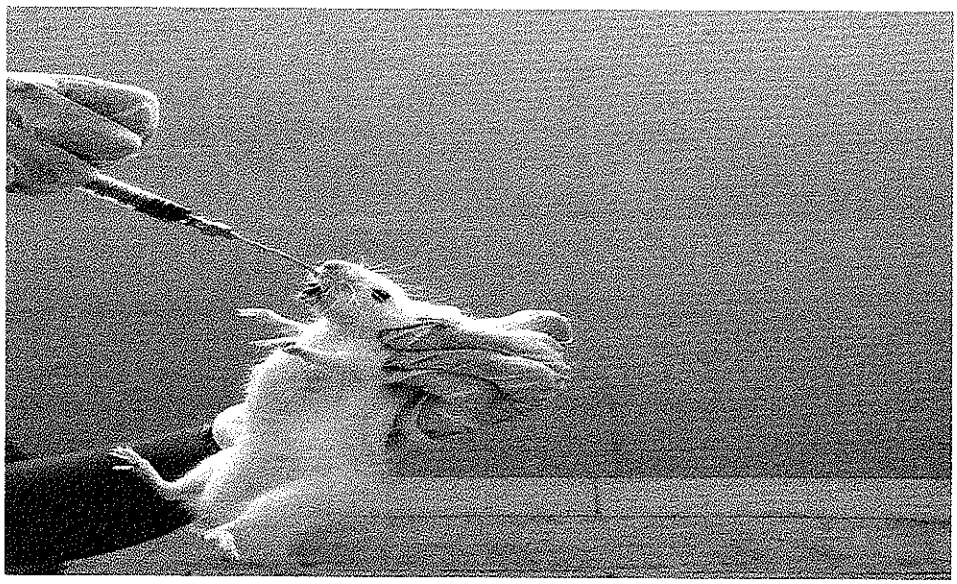

Figure 1: Oral Administration of test Drug- Syrup Clevira

After the substance had been administered, food was withheld for a further 3-4 hours. Animals were observed individually after dosing, during the first 30 minutes, then periodically during the first 24 hours, with special attention given during the first 4 hours, and daily thereafter, for a total of 14 days. All observations were systematically recorded with individual records being maintained for each animal.

Individual weights of animals were determined before the test substance was administered and then weekly thereafter. The weight changes were recorded. At the end of the study, the test animals were weighed and humanely killed.

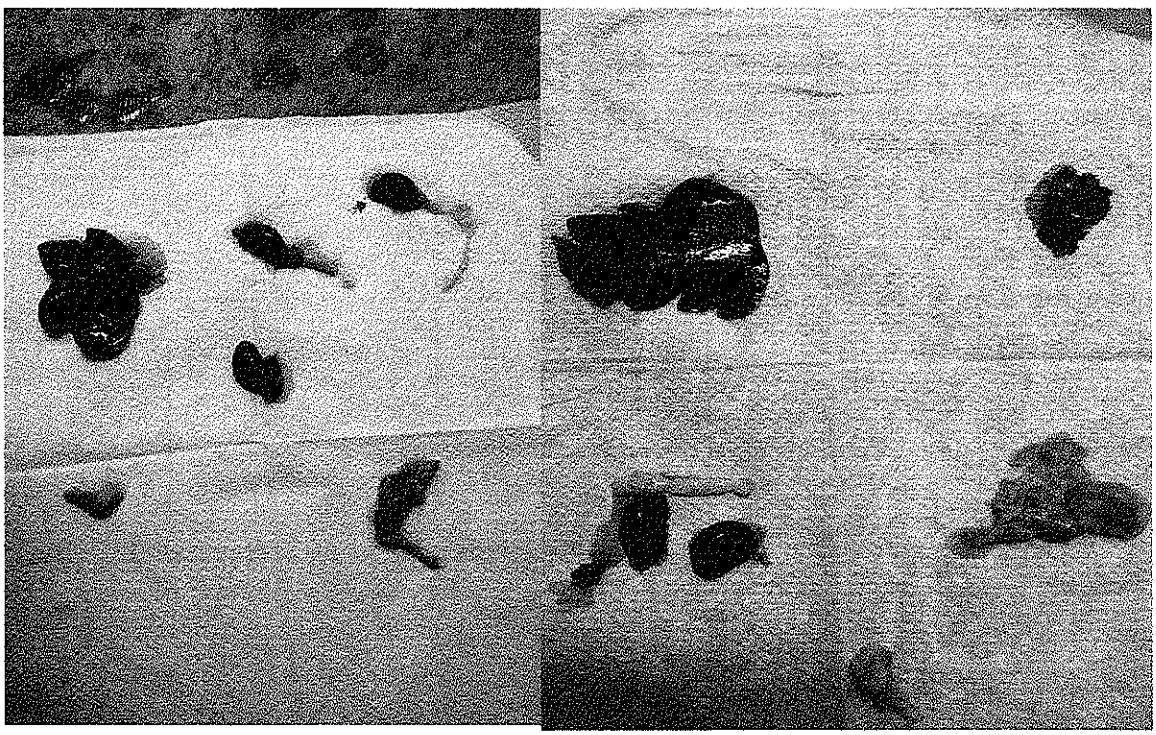

Figure 2: Gross appearance of the vital organs- after necropsy.

All test animals were subjected to gross necropsy looked for gross and histo-pathological changes for each animal.

5.0 RESULTS:

Table 1: Weight changes in wistar rats baseline, day 7 and day 14

Group designation	No. of Rats	Dose of Syp.Clevira	Baseline weight on Day 0 in kg	Weight on Day 7 in kg	Weight on Day 14 in kg
G1	7	300mg/kg	150+169+146+152+ 149+160+156	170+188+165+158+ 154+161+165	167+190+160+165+ 161+167+172
G2	7	1000mg/kg	180+168+150+171+ 161+159+154	209+198+184+179+ 159+164+160	224+210+186+181+ 165+160+169
G3	7	2000mg/kg	170+159+160+154+ 161+155+174	185+189+170+165+ 158+164+170	180+190+172+161+ 155+169+180

Table 2: Observation on signs of toxicity

DAYS / GROUPS	0	7	14
G1	Nil	Nil	Nil
G2	Nil	Nil	Nil
G3	Nil	Nil	Nil

6.0 OBSERVATION:

The animals in each group was observed for their activity and looked for signs of toxicity. All systems were carefully examined and recorded on individual basis. During the study period none of the animals showed signs of toxicity or had a moribund status.

At the end of the study animals were sacrificed and necropsy was done. There were no gross or histo- pathological changes noted in any of the groups.

7.0 CONCLUSION:

Thus, it is evident that Clevirais non-toxic even at a maximal dose of 2000mg/kg. Thus the LD 50 of the test compound can be classified as GHS category 5(LD50>2000mg/kg) as per OECD guideline. Hence, from the data obtained from this acute toxicity study we will be planning for repeated dose toxicity study.

8.0 REFERENCES:

1. In vitro cytotoxic and Antiviral study of Clevira; JSS academy of higher education and research.
2. OECD (2000) Guidance Document on Acute Oral Toxicity. Environmental Health and Safety Monograph Series on Testing and Assessment No 24.
3. OECD. (2006). Report of the Validation of the Updated Test Guideline 407: Repeat Dose 28-day Oral Toxicity Study in Laboratory Rats. Series on Testing and Assessment No 59, ENV/JM/MONO(2006)26
4. Schlede E., Mischke U., Diener W. and Kayser D. (1994). The International Validation Study of the Acute-Toxic-Class Method (Oral). Arch. Toxicol. 69, 659-670.
5. OECD(2008). Guidance for the testing of chemicals.Repeated Dose 28-Day Oral Toxicity Study in Rodents. 407

16/10/2018

SIGN:

Principal Investigator: Dr.R.Mirunalini.

SIGN:

Study Director: Dr.M.Sakthi Balan