ejpmr, 2022,9(10), 347-351

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

ACUTE TOXICITY STUDY OF KARISALAI KARPAM IN ANIMAL MODEL

Dr. G. Bharathkumar*[1] and Dr. M. Pitchiah Kumar[2]

[1]Asst. Professor, The Tamilnadu Dr. M.G.R. Medical University, Chennai.
[2]State Drug Licensing Authority (IM), Chennai.

***Corresponding Author: Dr. G. Bharathkumar**

Asst. Professor, The Tamilnadu Dr. M.G.R. Medical University, Chennai.

Article Received on 25/07/2022 **Article Revised on 15/08/2022** **Article Accepted on 05/09/2022**

ABSTRACT

Karisalai Karpam (KK) is considered as a valuable herbal medicine of Siddha system of medicine. A *Karpam* medicine is believed to protect all organs against diseases. The composition of *Karisali Karpam* as per the Siddha traditional preparation are Eclipta alba (*Vellai Karisalai Samoolam*), Wedelia chinensis (*Manjal Karisalai samoolam*), Indigofera tinctoria *(Neeli Samoolam*), Sphaeranthus indicus (*Kottaikarandhai Samoolam*), Centella asiatica (*Vallarai Samoolam*), Acalypha indica (*Kuppeimeni*) and Coldenia procumbens (*Siruserupadai*). KK has various medicinal properties. The toxicity profile of *Karisalai Karpam* has not been addressed, hence it was taken for acute toxicity study. It was carried out as per OECD guidelines. Animals were divided into two groups of 6 animals each. The dose utilized for evaluation of acute toxicity study is about 2000 mg/kg higher than that of the therapeutic dose. Occurrence of toxicity in animals were observed continuously for the first 4 h and observed periodically for the next 14 days. Results obtained from this study concluded that the oral dose up to 2000mg/kg of *Karisalai Karpam* did not cause any mortality.

KEYWORDS: *Karisalai Karpam, Siddha, Herbal medicine, Toxicity study, Animal study.*

1. INTRODUCTION

Over a millennium and against many odds, Siddha system of medicine has retained much of its originality and value, owing primarily to the practical benefits the common man experiences from the system. The very vast Siddha literature, having thousands of formulations belonging to the three kingdom of herbal, mineral and animal origins are providing enough literature evidence medicine which, if researched properly can give humanity with the much needed solutions it is seeking for. *Karisalai Karpam* (KK) is considered as a valuable herbal medicine of Siddha system of medicine. A *Karpam* medicine is believed to protect all organs against diseases.

Karisalai Karpam is a hepato protective herb in its combination. In Bogar 7000 the Siddha literature this drug has been mentioned. The composition of *Karisali Karpam* as per the Siddha traditional preparation are Eclipta alba (*Vellai Karisalai Samoolam*), Wedelia chinensis (*Manjal Karisalai samoolam*), Indigofera tinctoria *(Neeli Samoolam*), Sphaeranthus indicus (*Kottaikarandhai Samoolam*), Centella asiatica (*Vallarai Samoolam*), Acalypha indica (*Kuppeimeni*) and Coldenia procumbens (*Siruserupadai*). KK has various medicinal properties.

World Health organization recommends investigating the medicinal herb and its product for better understanding of its medicinal properties, effectiveness and safety.[1] Since ancient times, mankind has made use of plants in the treatment of various ailments because their toxicity factors appear to have lower side effects. Many of the currently available drugs were derived either directly or indirectly from medicinal plants. The toxicity profile of *Karisalai Karpam* has not been addressed, hence it was taken for acute toxicity study. It was carried out as per OECD guidelines. (Guideline - 423).

2. MATERIALS AND METHODS

2.1 Selection of Animals

Healthy adult Wistar albino rat weighing between 200-220 g were used for the study. The animals were housed in poly propylene cages and were kept in well ventilated with 100% fresh air by air conditioning. A 12 light / dark cycle were maintained .Room temperature was maintained between 22 $\pm$ 2^0 Cand relative humidity 50–65%. They were provided with food (Sai feeds, Bangalore, India) and water *adlibitum*. All the animals were acclimatized to the laboratory for 7 days prior to the start of the study. The experimental protocol was approved by The Institutional Animal Ethics Committee of Sathyabama University, Chennai, Tamil Nadu, India. Approval reference number-SU/CLATR/IAEC/IV/013/2016.

Acute toxicity study will be carried out in accordance with OECD guideline 423.[2] The animals were fasted

overnight with free access to water. The study was conducted with single oral dose administration of *Karisalai Karpam* (KK).

2.2 Animal Grouping

Animals were divided into two groups of 6 animals each. The dose utilized for evaluation of acute toxicity study is about 2000 mg/kg higher than that of the therapeutic dose. Group I: Animals received normal saline 5 ml/kg b.w (p.o) Group II: Animals received Test drug 2000 mg/kg (p.o)

The animals were fasted overnight (12- 16 hrs) with free access to water. The study was conducted with single oral administration of study drug *Karisalai Karpam*. The animals are grouped in two groups of 6 animals each. First group was administered with normal saline 5 ml/kg b.w (p.o). Second group received 2000 mg/kg of study drug *Karisalai Karpam* (p.o). The animals were observed continuously for first 72 h and then 14 days for any sign of behavioral changes, body weight changes and for mortality.

Occurrence of toxicity in animals were observed continuously for the first 4 h and observed periodically for the next 14 days. Observation includes the change in skin, fur, eyes and mucus membrane. Appearance of C.N.S,C.V.S and A.N.S related toxicity such as tremors, convulsions, sedation, steric behavior, respiratory distress, cardiovascular collapse, response to sensory stimuli, salivation, diarrhea, lethargy, sleep, coma and mortality were observed with special attention. Body weight was recorded for all the animals in both the groups each day till 14 days. At the end of the experiment all animals were subjected for gross necropsy and observed for pathological changes.

2.3 Histopathological evaluation

Organs included of heart, brain, lungs, spleen, kidneys, liver, stomach. Histological slides of organs were made and observed under the microscope. The pathological observations of cross section of these organs were performed on gross and microscopic bases. Histological examinations were performed on the preserved tissues with particular emphasis on those which showed gross pathological changes.

2.4 Statistical analysis

The statistical analysis was carried by one way ANOVA (GRAPH PAD PRISM 5 computer program). Results were expressed as mean ± standard error. A statistical comparison was carried out using the Dunnet's test for the control and treatment group. P-values less than 0.05 were set as the level of significance.

3. RESULTS

3.1 Effect of *Karisalai Karpam* on clinical signs of female rats in acute toxicity study

The maximum dose used for acute toxicity was 2000 mg/kg .There is no significant change observed in control and treatment group animals with respect to mortality or any clinical signs of acute toxicity observed for a short period (24-48 h) and a long period (14 days). Results were tabulated in Table 1.

Table 1: Assessment of clinical signs in rats treated with *Karisalai Karpam* on Acute toxicity study

Clinical Signs Parameters for the duration of 14 days	Group I Control	Group II *KarisalaiKarpam* (KK) 2000mg/ Kg
Number of animals observed	6 Female	6 Female
Lacrimation	Absence	Absence
Salivation	Absence	Absence
Animal appearance	Normal	Normal
Tonic Movement	Absence	Absence
Clonic Movement	Absence	Absence
Laxative action	Absence	Mild
Touch Response	Normal	Normal
Mobility	Normal	Normal
Respiratory Distress	Nil	Nil
Skin Color	Normal	Normal
Stereotype behavior	Absence	Absence
Piloerection	Absence	Absence
Limb Paralysis	Absence	Absence
Posture	Normal	Normal
Open field behavior	Normal	Normal
Muscular coordination	Normal	Normal
Muscle grip	Normal	Normal
Sedation	Absence	Absence
Social Behavior	Normal	Normal
Urine Analysis	No Abnormality	No Abnormality
Fecal Pellet consistency	Normal	fluffy
Mortality	Nil	Nil

3.2 Effect of *Karisalai Karpam* on body weight of rats in acute toxicity study

No significant change was observed in body weight of animals treated with 2000 mg/kg of test drug *Karisalai Karpam* when compare to control group animal. Results were tabulated in Table 2.

Table 2: Quantitative data on the body weight of rats treated with *Karisalai Karpam* in Acute toxicity study.

Treatment	Mean body weight in gms	
	Pre-Treatment	Post-Treatment
Group I	199 ± 0.8	211 ± 0.96
Group II	202.5 ± 1.89	215 ± 1.50

Values are mean ± S.D (n = 6 per group). Control and treatment group were compared statistically using one way ANOVA followed by Dunnett's test.

3.3 Effect of *Karisalai Karpam* on absolute organ weight of rats in acute toxicity study

No significant change was observed in the vital organs weight of treatment group when compare to that of the control group animals. Further no significant abnormalities was observed in gross and macroscopic examination of the organs belongs to treatment group when compare to that of the control group animals. Results were tabulated in Table 3.

Table 3: Quantitative data on absolute organ weight of rats treated with *Karisalai Karpam* in Acute toxicity study.

Treatment	Heart (gms)	Liver (gms)	Kidneys (gms)	Spleen (gms)	Brain (gms)	Lung (gms)
Group I	0.8 ± 0.05	5.53 ± 0.53	1.17 ± 0.07	0.36 ± 0.05	1.83 ± 0.24	1.01 ± 0.12
Group II	0.72 ±0.08	5.5 ±0.66	1.16 ±0.06	0.39 ±0.07	1.93 ±0.18	1.02 ±0.11

Values are mean ± S.D (n = 6 per group). Control and treatment groups were compared statistically using one way ANOVA followed by Dunnett's test.

3.4 Effect of *Karisalai Karpam* on Histopathological changes of female rats inacute toxicity study

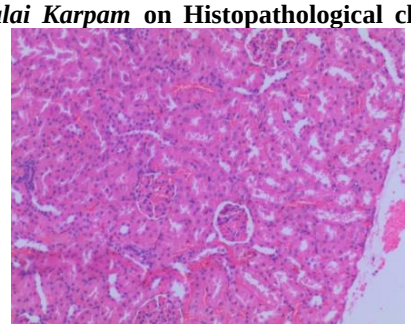

Fig1.1 GROUP I

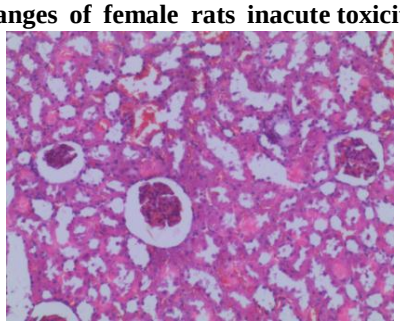

Fig 1.2 GROUP II

Fig 1: Histopathology of Kidney – High Power Magnification 40X.

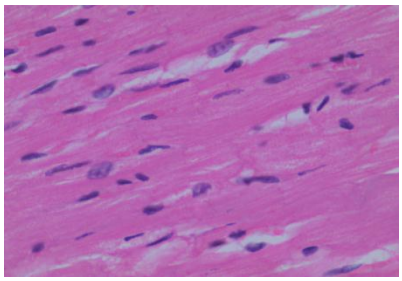

Fig2.1 GROUP I

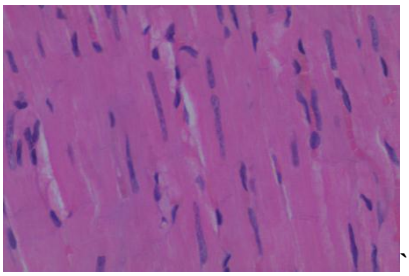

Fig2.2 GROUP II

Fig 2: Histopathology of Heart - High Power Magnification 40X.

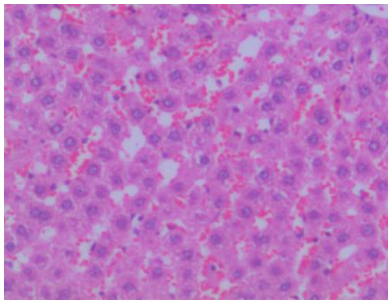

Fig. 3.1: GROUP I

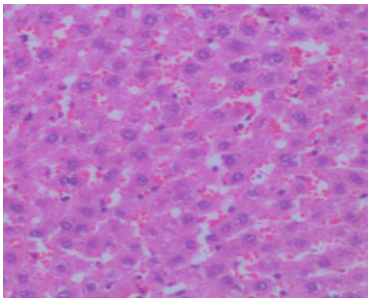

Fig. 3.2: GROUP II

Fig. 3: Histopathology of Liver – High Power Magnification 40X.

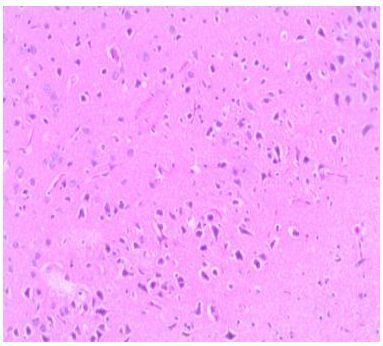

Fig. 4.1 GROUP I

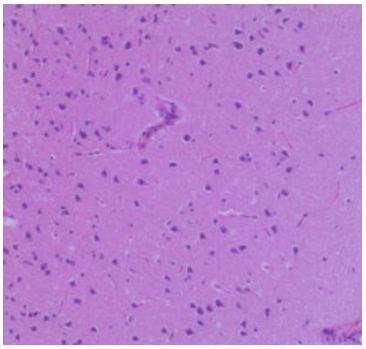

Fig. 4.2 GROUP II

Fig. 4: Histopathology of Brain - High Power Magnification 40X.

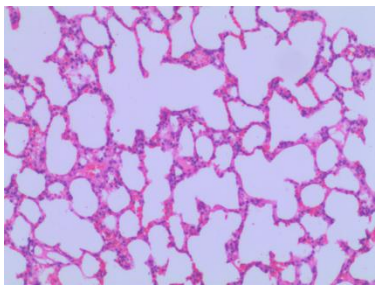

Fig. 5.1: GROUP I

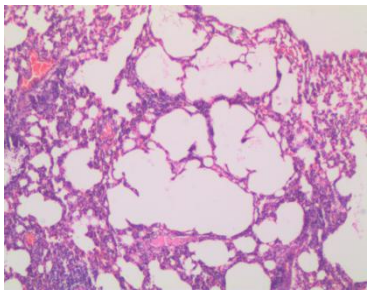

Fig. 5.2: GROUP II

Fig 5: Histopathology of Lung - High Power Magnification 40X.

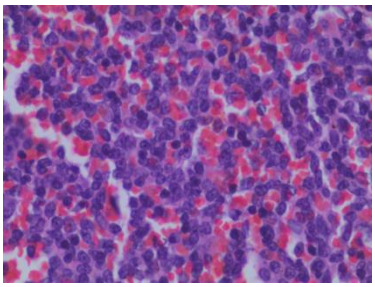

Fig. 6.1 GROUP I

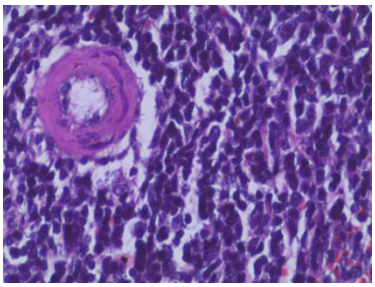

Fig. 6.2 GROUP II

Fig 6: Histopathology of Spleen - High Power Magnification 40X.

4. DISCUSSION

For centuries Siddha preparation including herbal and herbomineral formulations have been the basis for the treatment of various ailments. The results on the acute toxicity study has proven that *Karisalai Karpam* was well tolerated in rats up to oral dose of 2000 mg/Kg.

Appearance of glomeruli and convoluted tubules of kidney was normal in both the groups (I and II), no signs of tubular degeneration. Light microscopic observation of heart reveals the presence of normal cardiomyocytes with well striated cardiac muscle fibers. No signs of infarction or degeneration was observed in both the samples belongs to group I and II.

The neuronal architecture appears normal with sufficient numbers. Neuronal cells revealed well present nucleus in both the samples belongs to group I and II. The appearance of hepatocytes, sinusoids and hepatic cord was normal in both the samples. Portal triad appears normal with clear projection of central vein in both the samples. Perivascular region of the lung appears normal. Alveolar septa and the wall appeared widen and normal. No signs of lymphocyte cuffing in both the samples belong to group I and II. Appearance of LF- lymphoid follicle; PALS- Periarterial lymphoid sheath in the spleen was normal with no significant signs of enlargement in both the groups (I and II).

5. CONCLUSION

Results obtained from this study provides valuable preliminary data on the toxicity profile of study drug *Karisalai Karpam*. Hence it is concluded that the oral dose up to 2000mg/kg of *Karisalai Karpam* did not cause any mortality. The drug KK appears to be relatively safe, non-toxic, causes no apparent organ damage.

6. ACKNOWLEDGEMENT

Authors are grateful to Centre for Laboratory Animal Technology and Research, Sathyabama University, Chennai for their support in animal studies to complete this research work successfully.

7. REFERENCE

1. Johnson, B A, Market report, Herbal Gram, 1997; 40: 49- 50.
2. OECD Guideline for testing of Chemicals Guideline 423: Acute Oral Toxicity-Acute Toxic Class Method, 2001.