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Acute and Sub-acute Toxicity Studies of Omavanni Chenduram

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Abstract

Toxicity study is the study of adverse effects of chemical and physical agents and the degree to which a substance can harm human or animals. The present study reveals the acute and sub-acute toxicity studies of Omavanni Chenduram in swiss albino mice and wister rats respectively. In this study different concentration of drug had been administered to the test animals. But there is no mortality of animals in this study. This shows that the Omavanni Chenduram has no toxic effect on animals.

Keywords: Acute toxicity, Sub- acute toxicity, Omavanni Chenduram, Swiss Albino Mice, Wister albino Rats..

Introduction

Siddha system of medicine is the most primitive medical system. Agathiyar is considered as the first Siddhar and the guru of all Siddhars. If the medicine is given in excess dosage it is sure to cause severe & agonizing pathological disturbances, metabolic disturbance & degeneration in the body. Toxicity study is conducted to determine the degree to which substance can damage a living or non-living organisms. It is considered as a part of a preclinical development. Toxicity study is very important for the development of new drug & for the extension of therapeutic potential of existing molecules.

Toxicity study is paramount in the screening of newly developed. Siddha drugs before it can be used on human. Toxicity testing is the determination of potential hazards a test substance, May likely produced & the characterization of its action, most of the toxicity study is carried out on experimental animals. Eventhough the Siddha system in this world certain basic studies like pharmacological, toxicological studies are necessary for the way to standardization of Siddha drugs.

Oma Vanni Chenduram is a traditional Siddha sastric formulation used in the managements of all types of fever. Fever is most of the developing calories are facing major incidences & there is a need to find out a safe & effective. The present study focuses the acute and sub acute toxicity effects of oma vanni chenduram in animals.

Materials and Methods

"OMAVANNI CHENDURAM" is selected for the toxicity study from the text book, Anuboga Vaidhya Navaneetham part - 4, Pg. No. 62, Year of Edition – 1995, Hakkim – Pa.Mu- Abdulla Sayubu.

Collection of Raw drugs:

The raw drugs are purchased from Gopalasan Raw drugs store, Nagercoil Town.]

Ingredients:

Lingam *(Mercuric Sulphide)*
Maruthondri leaf *(Lawsomia inermis, Linn.)*
Omam *(Trachyspermum ammi)*

Purification of Raw drugs:

Lingam Purification:

Lingam is purified by soaking with lime juice for 2 hours.

Purification of Omam:

Omam is soaked in limestone water for 3 hours followed by fried at light flame

Preparation of Medicine:

Ingredients:

Lingam	-	1 Palam (35grams)
Maruthondri leaf	-	5 Palam (175grams)
Omam	-	10 Palam (350grams)

Method of preparation:

The lingam is beavered by the grinded Maruthondri leaves paste and dry it.

Separate the omam into 2 parts. One part of the Omam is placed into the pot, place the lingam in it and put the another part of the omam over the lingam.

Then the pot is closed with pan and sealed by mud cloth for 3 time. It is dried and cupellated with 100 palam varati. Then it go to the cooler area.

Then the cover is removed and take the lingam then it make the powdered and save in the container.

Route of Administration:

Oral

Dose of the Drug:

1 – 1½ Kundri (130-195 mg)

Adjuvant:

Honey, Ghee, Palm Jaggery

Acute oral toxicity OECD423 guidelines:

Animals:

A total of 15 Swiss Albino Mice with an approximate age of 8-12 weeks old and purchased from Nandha College of Pharmacy, Erode. On their arrival a sample of animals was chosen at random and weighed to ensure compliance with the age requested. The mean weights of Swiss Albino Mice were 100-150 g respectively. The animals were housed in metabolic cages (55 x 32.7 x 19 cm), with saw dust litter, in such a way that each cage contained a maximum of 3 animals of the same sex.

All animals underwent a period of 20 days of observation and acclimatization between the date of arrival and the start of treatment. During the course of this period, the animals were inspected by a veterinary surgeon to ensure that they fulfilled the health requirements necessary for initiation of the Study. All experimental procedures described were reviewed and approved by the Institutional Animal ethical Committee of Nandha College of Pharmacy, Erode and the IIEC approval Number: NCB/IAEC/2016-17-12.

Doses

The doses for the study were selected based on literature search and range finding study. Following the period of fasting, the animals were weighed and then drug was administered orally as single dose using a needle fitted onto a disposable syringe of approximate size at the following different doses.

Table-1 Doses

GROUP	DOSE
Group-I	**Control (Distilled Water 1ml/kg)**
Group-II	**5 mg/kg**
Group-III	**50 mg/kg**
Group-IV	**300 mg/kg**
Group-V	**2000 mg/kg**

The test item was administered as single dose. After single dose administration period, all animals were observed for 14 days.

Dose Preparation

OMAVANNI CHENDHURAM was added in distilled water and completely dissolved form for oral administration. The dose was prepared of a required concentration before dosing by dissolving, in distilled water. It was mixed well. The preparation for different doses was vary in concentrations to allow a constant dosage volume.

Administration

The test item was administered orally to each Female Swiss Albino Mice as single dose using a needle fitted onto a disposable syringe of appropriate size at the following different doses. The concentration was adjusted according to its body weight. The volume was not exceeding 10 ml/kg bodyweight. Variability in test volume was minimized by adjusting the concentration to ensure a constant volume at all dose levels.

Observation period

All animals were observed for any abnormal clinical signs and behavioral changes. The appearance, change and disappearance of these clinical signs, if any, were recorded for approximately 1.0, 3.0 and 4.0 hours post-dose on day of dosing and once daily thereafter for14 days. Animals in pain or showing severe signs of distress were humanely killed. The cageside observation was included changes in skin, fur, eyes and mucous membranes, occurrence of secretions and excretions. Autonomic activity like lacrimation, piloerection, pupil size and unusual respiratory pattern, changes in gait, posture, response to handling, presence of clonic or tonic movements, stereotypes like excessive grooming and repetitive circling or bizarre behavior like self-mutilation, walking backwards etc were observed. At the 14th day, sensory reactivity to stimuli of different types (e.g. auditory, visual and proprioceptive stimuli) was conducted. Auditory stimuli responses were measured by clicker sound from approximately 30 cm to the mice; visual stimuli response were measured with the help of shining pen light in the eye of mice and placing a blunt object near to the eye of rats. Response to proprioceptive stimuli was measured by placing anterior/dorsal surface of animals paw to the table edge. The responses of reactions for these three exercises were normal in animals belonging to both the controls as well as drug treatment dose groups.

Sub-acute toxicity study in wister rats to evaluate toxicity profile of *OMAVANNI CHENDHURAM*

Objective

The objective of this '**Sub-Acute Toxicity Study of *OMAVANNI CHENDHURAM* ON Wister Rats**' was to assess the toxicological profile of the test item when treated as a single dose daily. Animals should be observed for 28 days after the drug administration. This study provides information on the possible health hazards likely to arise from exposure over a relatively limited period of time.

Test Guideline Followed

OECD 407 Method - Sub-Acute Toxic Class Method (Repeated Dose 28-Day Oral Toxicity Study in Rodents)

Doses

The doses for the study were selected based on literature search and range finding study. Following the period of fasting, the animals were weighed and then extract was administered orally for 28 days using a needle fitted on to a disposable syringe of approximate size at the following different doses.

Table-2 Dose level

Test Group	Dose To Animals (mg/kg body-weight/day)	Number Of animals
Group-1	**1. Control**	6 (3 MALE and 3 FEMALE)
Group-II	**2. Low Dose Of *OMAVANNI CHENDHURAM* 200mg/kg**	6 (3 MALE and 3 FEMALE)
Group-III	**3. High Dose Of *OMAVANNI CHENDHURAM* 400mg/kg**	6 (3 MALE and 3 FEMALE)

Dose Preparation

OMAVANNI CHENDHURAM was added in distilled water and completely dissolved form for oral administration. The dose was prepared of a required concentration before dosing by dissolving

OMAVANNI CHENDHURAM in distilled water. It was mixed well. The preparation for different doses was vary in concentrations to allow a constant dosage volume.

Observations

These observations were also performed on week-ends. The observations included but were not limited to changes in skin and fur, in the eyes and mucous membranes, in the respiratory, circulatory, central nervous and autonomous systems, somatomotor activity and behavior.

Clinical signs of toxicity

All the rats were observed at least twice daily with the purpose of recording any symptoms of ill- health or behavioral changes. Clinical signs of toxicity daily for 28 days.

Food intake

Prior to the beginning of treatment, and daily, the food intake of each cage was recorded for period of 28 days and the mean weekly intake per rats was calculated.

Water intake

Water intake was checked by visual observation during the Study. In addition, the water consumption in each cage was measured daily for a period of 28 days.

Bodyweight:

The body weight of each rat was recorded one week before the start of treatment, and during the course of the treatment on the day of initial, 1st, 7th, 14th, 21st and 28th days (day of sacrifice). The mean weights for the different groups and sexes were calculated from the individual weights.

Blood Collection

Blood was collected through retro-orbital sinus from all the animals of different groups on 28th day. The blood was collected in tubes containing Heparin/EDTA as an anticoagulant. Animals were fasted over night prior to the blood collection.

Laboratory Studies

During the 4th week of treatment, samples of blood were withdrawn from the orbital sinus from each group, under light ether anesthesia after fasting for 16 hours. The blood samples are used to evaluate Hematological parameters like RBC, WBC, and PLATELETS etc….. The collected blood samples also centrifuged 10000 rpm in 10 minutes to separate the serum.

Results

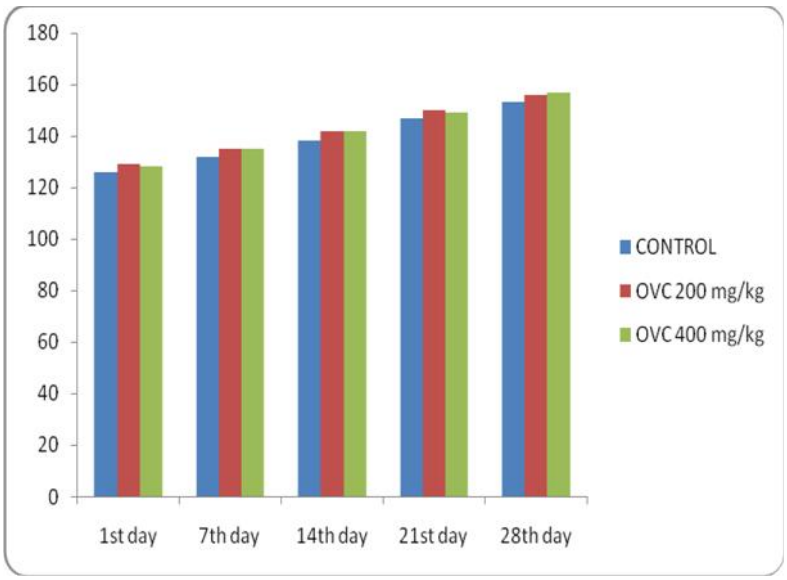
Acute toxicity Study:

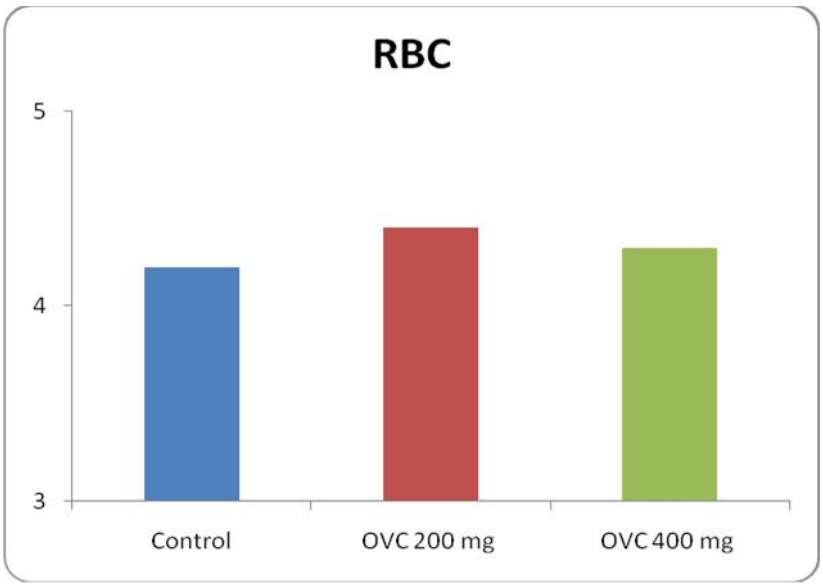
The trial drug Omavanni Chenduram was administered to Swiss albino mice at the dose of 2000 mg/kg. Treated with Omavanni Chenduram upto 2000 mg/kg has produced no mortality in animals. Based on OECD423 guidelines the drug is considered to be non toxic upto the dose of 2000mg/kg of body weight.

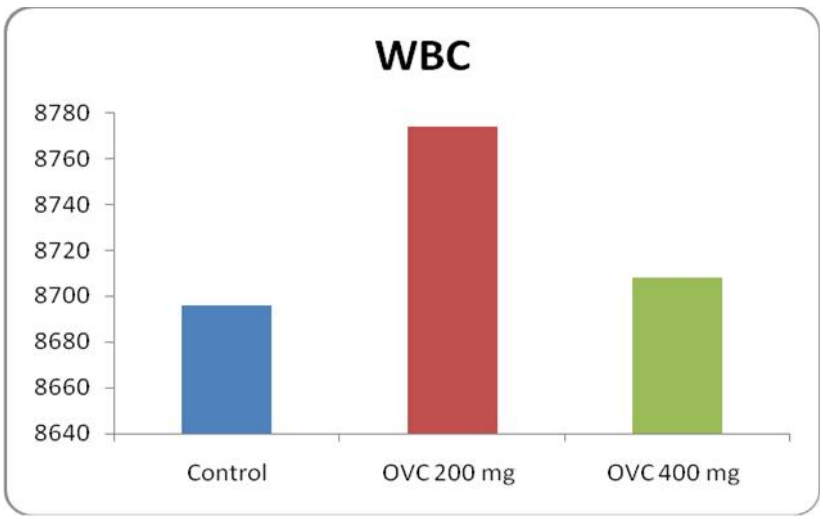
Observation	Control	**5 mg/kg**	**50mg/kg**	**300mg / kg**	**2000mg / kg**
I. Stimulation:					
Hyperactivity	-	-	-	-	-
Pyloerection	-	-	-	-	-
Twitching	-	-	-	-	-
Rigidity	-	-	-	-	-
Irritability	-	-	-	-	-
Jumping	-	-	-	-	-
Clonic convulsions	-	-	-	-	-
Tonic convulsions	-	-	-	-	-
II.Depression:					
Ptosis	-	-	-	-	-
Sedation	-	-	-	-	-
Sleep	-	-	-	-	-
Loss of Traction	-	-	-	-	-
Loss of pinna reflex	-	-	-	-	-
Ataxia	-	-	-	-	-
Loss of Musle tone	-	-	-	-	-
Analgesia	-	-	-	-	-
III.Autonomic effect:					
Straub tail	-	-	-	-	-
Laboured respiration	-	-	-	-	-
Cyanosis	-	-	-	-	-
Reddening	-	-	-	-	-
Abnormal secretions	-	-	-	-	-
IV. Mortality:					
After 24 hours	-	-	-	-	-

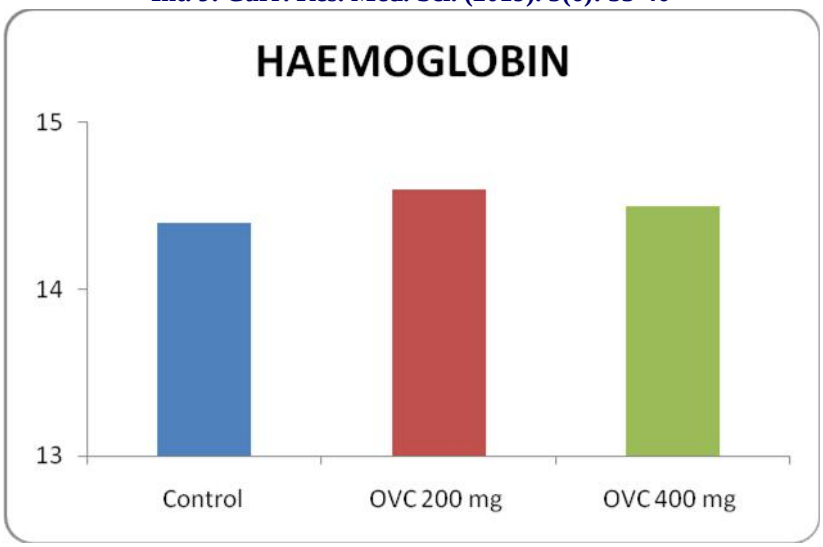
Sub Acute Toxicity study

Body weight









Discussion

The present study with ***OMAVANNI CHENDHURAM*** was conducted with an objective to find out whether this drug has got any side effects or adverse reactions in short and Long term administration

On the basis of acute toxicity Results the study shows that ***OMAVANNI CHENDHURAM*** did not produce any toxic Effect at the dose of 2000mg/kg to rats.

On the basis of subacute toxicity Results, the study reveals that ***OMAVANNI CHENDHURAM*** did not cause either any lethality or adverse changes with general behaviour of rats and also there were no observable detrimental effects in 200 to 400mg/kg body weight over a period of 28 days.

Haematological analysis revealed no abnormalities attributable to the treatment.

These results indicate that ***OMAVANNI CHENDHURAM*** did not produce any adverse effects and changes in the organ upto 200-400mg/kg body weight.

Conclusion

From acute toxicity study it was observed that the administration of ***OMAVANNI CHENDHURAM*** up to the dose of 2000 mg/kg to the mice do not produce drug-related toxicity and mortality. So No-Observed-Adverse-Effect- Level (NOAEL) of ***OMAVANNI CHENDHURAM*** is 2000 mg/kg.

The sub-acute toxicity studies also reveals that the drug "OMAVANNI CHENDHURAM" can be considered safe, as it did not cause either any lethality or adverse effects with general behaviour of rats and also there were not observable determental effects in the doses (200 to 400 mg/kg body weight) over a period of 28 days. It is concluded that the Omavanni chendhuram is relatively safe for long term administration in human upto the dose of 400mg/kg.

Summary

The present study was conducted to know single dose toxicity of ***OMAVANNI CHENDHURAM*** on female swiss albino mice. The study was conducted using 15 female swiss albino mice. The female animals were selected for study of 8- 12 weeks old with weight range of within ± 20 % of mean body weight at the time of randomisation. The groups were numbered as group I, II, III, IV and V and dose with 5mg/kg, 50mg/kg, 300mg/kg and 2000mg/kg of ***OMAVANNI CHENDHURAM***. The drug was administered by oral route single time and observed for 14 days. Daily the animals were observed for clinical signs and mortality. Body weight of all animals was recorded once in a week.

There were no physical and behavioral changes observed in swiss albino mice of 5mg/kg, 50mg/kg , 300mg/kg and 2000mg/kg to mice during 14 days. Body weight of all animals did not reveal any significant change as compared to vehicle control group. Food consumption of all group animals was normal. Mortality was not observed in all treatment groups.

Conclusion

The study shows that ***OMAVANNI CHENDHURAM*** did not cause any toxic effect and mortality at dose of 5mg/kg, 50mg/kg , 300mg/kg and 2000mg/kg to mice. So No-Observed-Adverse-Effect-Level (NOAEL) of ***OMAVANNI CHENDHURAM*** is 2000 mg/kg.

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