SHORT COMMUNICATION

Study on Acute Toxicity of Anti–Flatulent Siddha Formulation *Kattu Maantha Kudineer* in Swiss Albino Rats

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ABSTRACT

Background: The Siddha system of Medicine deals with various branches, one among the branch was *Kuzhanthai Maruthuvam* which deals with numerous pediatric diseases. Functional dyspepsia is a major health problem in all over the world among childrens. **Objective:** To study the acute toxicity of Siddha formulation *kattumaanthakudineer* in swiss albino rats. **Methods:** The *kattumaanthakudineer* is prepared and administrated at the dosage of 2000 mg/kg. Healthy swiss albino rats (3 females) of 200-240 g of body weight were selected and allowed for an acclimation period of 7 days. The animals were fasted before the treatment. All animals were treated with 2000 mg/kg signs of toxicity were observed for every one hour for first 24 hours and every day for about 14 days from the beginning of the study. The test substance was administered orally. **Results:** Single dose oral administration of *kattumaanthakudineer* at 2000mg/kg caused no adverse toxic effects. The animals did not show any changes in body respiration, urination, defecation, locomotion, salivation, body weight. **Conclusion:** The acute oral LD50 of test substance in swiss albino rats was observed to be greater than 2000mg/kg. This indicates the safety of *kattumaanthakudineer* through oral administration.

KEY WORDS: *Kattumaanthakudineer*, Oral administration, Swiss albino rats, Acute toxicity.

1. INTRODUCTION

The Siddha formulation *Kattumaanthakudineer* toxicity study wasconducted in C.L. Baid Mehta College of Pharmacy, Thoraippakkam, Chennai. *Kattumaanthakudineer* is very effective in treating *kattumaantham* (functional dyspepsia). Functional dyspepsia (Indigestion) is a collective term for any symptoms thought to originate from the upper gastro intestinal tract. It encompasses many different symptoms and disorders including some arise outside the digestive system. This can be described as non-ulcer dyspepsia, pseudo-ulcer syndrome, pyloro-duodenal irritability, nervous dyspepsia, or gastritis. Functional dyspepsia is characterized by impairment of the power of function of digestion, usually applied to epigastric discomfort following meals. Dyspepsia is a condition of farinaceous malnutrition found in badly nourished infants who are fed with solution of polished grains [1].

The frequency of functional dyspepsia in childhood reached a percentage 70%. The most common complaint in children aged late childhood and adolescent. It is a condition of farinaceous malnutrition found in badly nourished infants, who are fed mostly on solution of polished rice powder[2].

Nearly 25% of population has abdominal discomfort at least 6 times yearly, but only 10 – 20% consults Physician. Functional Dyspepsia accounts for 60% of Pediatric cases[3].

The clinical features of functional dyspepsia correlate with the symptoms of *kattumaantham* like abdominal pain, excessive sweating, diarrhoea, weight Loss, feeling of gastric fullness**,** constipation, pellet-like stools,fever, lethargy, head ache described in Siddha text. In Siddha literature *kattumaantham*is one of the twenty-one types of *maantham* that occurs in children. The medicine was chosen for treatment and management of the *kattumaantham* was *kattumaanthakudineer*[4] dosage 15 – 30 ml, twice a day, before meals for seven days.

The acute toxic class method is a stepwise procedure with the use of 3 animals of a single sex per step. Depending on the mortality and/or the moribund status of the animals, on average 2-4 steps may be necessary to allow judgment on the acute toxicity of the test substance. Morbid animals or animals obviously in pain or showing signs of severe and enduring distress shall be humanely killed, and are considered in the interpretation of the test results in the same way as animals that died on test. The method allows for the determination of an LD50 value only when at least two doses result in mortality higher than 0% and lower than 100%.

2. MATERIALS AND METHODS

2.1 Preparation of kattumaanthakudineer

Kattumaanthakudineer[4] is a herbal Siddha formulation comprising of ten different types of herbs like Poduthalaierkku *(Phyla nodiflora)* Maaelaierkku *(Mangifera indica),* Puliyamerkku *(Tamarindus indica), V*embuerkku *(Azadirachta indica),* Nunaerkku *(Morinda tinctoria)*, Veliparuthierkku (*Pergularia daemia),* Nochierkku *(Vitex negundo), Poondu (Allium sativum),* Tippili (*Piper longum), Omam* (*Carum copticum).* The raw drugs were identified and authenticated by the Botany department in Arumbakkam, Chennai. The purified raw drugs are made into course powder and stored in clean dry air tight container.

2.2 Acute oral toxicity- OECD guidelines 423

Acute toxicity study was carried out as per OECD guideline[5-10] (Organization for Economic Co - operation and Development, Guideline-423). The Project was completed on March 24th2015, after the animal ethical clearance from C.L. Baid Mehta college of pharmacy, Thoraipakkam, Chennai-97. The approval number IAEC NO:IAEC/XLIV/09/CLBMCP/2014.

2.3 Preparation of the test Substance

The test substance was dissolved in distilled water and administered as such at the dose of 2000 mg/kg body weight [11].

3. Test animal

Healthy Swiss albino female rat weighing 220–240 gm. Study was carried out in three female rats under fasting condition; signs of toxicity were observed for every one hour for first 24 hours and every day for about 14 days from the beginning of the study.

4. METHODOLOGY

3.1 Selection of animal species

The preferred rodent species is rat, although other rodent species may be used. Healthy young adult animals of commonly used laboratory strain Swiss albino is used. Females should be nulliparous and non-pregnant. Each animal at the commencement of its dosing should between 8 and 12 weeks old and its weight should fall in an interval within±20 % of the mean weight of the animals[12].

3.2 Housing and feeding conditions

The temperature in the experimental animal room should be 22ºC (+3ºC). Although the relative humidity should be at least 30% and preferably not exceed 70% other than during room cleaning the aim should be 50-60%. Lighting should be artificial, the sequence being 12 hrs light, 12 hrs dark. For feeding, conventional laboratory diets may be used with an unlimited supply of drinking water. Animals may be grouped and tagged by dose, but the number of animals per cage must not interfere with clear observations of each animal.

3.3 Preparation of animals

The animals are randomly selected, marked to permit individual identification, and kept in their cages for at least 7 days prior to dosing to allow for acclimatization to the laboratory conditions.

3.4 Observation done

Observations were made and recorded systematically and continuously observed as per the guideline after substance administration[13]. The animals were monitored for behavioral parameters like

1. Awareness: Alertness, Visual placing, Stereotype, Passivity
2. Mood: Grooming, Restlessness, Irritability, Fearfulness
3. Motor activity: Spontaneous activity, Reactivity, Touch response, Pain response.

Animals were observed for body weight and mortality for 14 days. If animals died during the period of study, the animals were sacrificed. At the end of the 14th day all animals were sacrificed and necropsy was done[14].

3.5 Gross pathology

All animals were subjected to necropsy at the end of 14-day observation period for gross pathological examination.

5. RESULTS AND DISCUSSION

Acute toxicity effect of *kattumaanthakudineer* was estimated by close observation of animals for about 24 hours after single dose administration of the *kattumaanthakudineer* at 2000mg/kg caused no adverse toxic effects. The animals did not show any changes in body respiration, urination, defecation, locomotion, salivation, body weight. In Necropsy, the organs of the animal such as, Liver, Heart, Lungs, Pancreas, Spleen, Stomach, Intestine, Kidney, Urinary bladder, Uterus all appeared normal.

Table1: Toxicity signs observed in rats.

Group	Day
Body weight	Normal
Assessments of posture	Normal
Signs of Convulsion	Absence of sign (-)
Limb paralysis	
Body tone	Normal
Lacrimation	Absence
Salivation	Absence
Change in skin color	No significant colour change
Piloerection	Not Observed
Defecation	Normal
Sensitivity response	Normal
Locomotion	Normal
Muscle grip ness	Normal
Rearing	Mild
Urination	Normal

Dose mg/kg	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
2000	+	-	-	-	-	+	-	-	-	-	-	+	-	-	-	-	-	-	+	-

1. Alertness 2.Aggressiveness 3. Pile erection 4. Grooming 5.Gripping 6.TouchResponse7. Decreased Motor Activity 8.Tremors 9.Convulsions 10. Muscle Spasm11. Catatonia 12.Musclerelaxant 13.Hypnosis 14.Analgesia15.Lacrimation16.Exophthalmos 17.Diarrhoea 18.Writhing 19.Respiration 20.Mortality.No visible signs of toxicity such as respiration, urination, defecation, locomotion, salivation, convulsions, tremors, lacrimation, diarrhoea, mortality were observed during the entire observation period.

6. CONCLUSION

The acute oral LD50 of test substance in Swiss albino rats was observed to be greater than 2000mg/kg. This indicates the safety of kattumaanthakudineer through oral administration.

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REFERENCES

1. Colledge NR, Walker BR, Ralston S, Davidson S. Davison's Principles and Practice of Medicine (18th Ed). 2010; Edinburgh: Churchill Livingstone/Elsevier.
2. Spiroglou K, Paroutoglou G, Nikolaides N, Xinias I, Giouleme O, Aros G, Demertzidou V, Eugenides N. Dyspepsis in Childhood. Clinical manifestation and management. Annals of Gastroenterology 2004;17(2):173-80.
3. Larry Jameson J, Anthony S Fauci, Dennis L Kasper, Stephen L Hauser, Dan L Longo, Joseph Loscalzo. Harrison's Principle of Internal Medicine (20th Ed). 2001; Vol 1: 222.
4. Koshayianuboga Brahma Ragasiyam. Thamarainoolagam: 32.
5. OECD. Guidance Document on Acute Oral Toxicity. Environmental Health and Safety Monograph Series on Testing and Assessment No 24: 2000.
6. Roll R, Höfer-Bosse T, Kayser D. New Perspectives in Acute Toxicity Testing of Chemicals. Toxicol Lett Suppl. 1986;31:86.
7. Roll R, Riebschläger M, Mischke U, Kayser D. Neu Wege zur Bestimmung der akuten Toxizitat von Chemicalein. Bundesgesundheitsblatt 1989;32:336-41.
8. Diener W, Sichh L, Mischke U, Kayser D, Schlede E. The Biometric Evaluation the Acute Toxic Class Method (Oral). Arch Toxicol 1994;68:559-61
9. Diener W, Mischke U, Kayser D, E Schlede. The Biometric Evaluation of OECD Modified Version of the Acute Toxic Class Method (Oral). Arch Toxicol 1995;69:729-34.
10. Diener W, Schelde E. Acute toxic class method: alternatives to LD/LC50 tests. ALTEX 2000; 16:129-34.
11. Deepa, Alwar, MC. Acute toxicity studies and determination of median lethal dose. Current science 2007;93:917.
12. OECD. Guidance Document on the Recognition, Assessment and Use of Clinical Signs as Humane Endpoints for Experimental Animals Used in Safety Evaluation Environmental Health and Safety Monograph Series on Testing and Assessment No 19: 2000.
13. Schlede E, Mischke U, Roll R, Kayser D. A national validation study of the acute-toxic-class method-an alternative to the LD50 test. Arch Toxicol 1992;66(7):455-70.
14. Chan PK, Hayes AW. Acute toxicity and eye irritancy. In Hayes' Principles and Methods of Toxicology, 6th Edition. CRC Press: 2014; 1117-72.