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STUDY ON ACUTE TOXICITY OF SIDDHA FORMULATION "UPPU CHENDURAM - II" IN WISTAR RATS

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ABSTRACT

OBJECTIVE : To study the acute toxicity of siddha formulation *Uppu Chenduram – II* in wistar rats.

METHODS : The *Uppu Chenduram*(test substance) dissolved in distilled water, to be administered at the dosage of 2000 mg/kg/bw. Healthy Wistar rats (5 females) were selected and allowed for an acclimation period of 7 days. The animals were fasted overnight prior to treatment. Feed was made available *ad libitum* immediately after the treatment. Before commencing the experiment, the body weights of rats were recorded. All the animals were treated with 2000 mg/kg/bw of *Uppu Chenduram*. The test substance was administered by oral gavage.

RESULTS : Single dose oral administration of *Uppu Chenduram* @ 2000 mg/kg/bw caused no adverse toxic effects on the body weight / body weight changes, feed and the gross anatomy of treated female Wistar rats. The animals did not show any changes in respiration, circulation, autonomic and central nervous system, behavioral pattern.

CONCLUSION: The acute oral LD_{50} of test substance (247) in Wistar rats was observed to be greater than **2000 mg/kg b.w.** This indicates the safety of *Uppu Chenduram-II* through oral administration.

KEY WORDS: *Uppu Chenduram - II*, Wistar rats, Acute -Toxicity, Dose

INTRODUCTION

The siddha formulation, *Uppu Chenduram - II* is very effective in treating *Erigunmam* (Peptic ulcer disease). There is an emerging increase in the consumption of herbal formulations by the public, because of the strong belief that these products are natural; hence, they are safe for the treatment of ailments [1]. However, herbal preparations assumed to be safe may contain contaminants such as heavy metals [3], aflatoxins and pathogenic microbes due to the manner in which they are prepared or as a result of acquisition of metals (e.g. cadmium) from the soil[4,5]. Determination of acute oral toxicity is usually the initial screening step in the assessment and evaluation of the toxic characteristics of all compounds. Acute toxicity is involved in estimation of LD50 (the dose which has proved to be lethal (causing death) to 50% of the tested group of animals)[6].The *Uppu Chenduram – II* was analysed for their acute toxicity profile with reference to behavioural aspects in Wistar rats. The limit test dose of 2000mg/kg body weight was used following OECD guidelines. [7]

MATERIAL AND METHODS

The Siddha formulation, *Uppu Chenduram* was taken from the text book of *Siddha Vaithiya thirattu.*

Ingredients of *Uppu Chenduram-II*

Sottruppu (Common salt)

Juice of *Agayathamarai (Pistia stratiotes)*

Preparation of *Uppu Chenduram-II*

The *Sottruppu* was purified using rain water and grind with *agayathamarai* leaf juice, made it into disc shaped pellets. Then it was allowed to *pudam* (calcination process)for 6times ranging from 10 to 20 *varatties(*cow dung cakes). Then made into fine powder and kept in dried air tight container. [8]

Acute Toxicity Study

The present study work was conducted in Central Animal Facility, SASTRA DEEMED UNIVERSITY,Thanjavur-613401.

The siddha preparation *Uppu Chenduram – II* administered orally for acute oral toxicity of is carried out as per the Organization of Economic Co-operation and Development (OECD) -423 guidelines after the animal ethical clearance from Institutional Animal Ethics

Committee. The experiment was approved by the Institutional Animal Ethics Committee (IAEC) under CPCSEA (approval no: 485/SASTRA/IAEC/RPP).

Preparation of Test Substance

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

Treatment

Healthy Wistar rats (5 females, females rats are preferable for acute toxicity studies as per OECD - 425) were selected and allowed for an acclimation period of 7 days. The animals were fasted overnight prior to treatment. Feed was made available *ad libitum* immediately after the treatment. Before commencing the experiment, the body weights of rats were recorded. All the animals were treated with 2000 mg/kg of test substance (247). The test substance was administered by oral gavage using an appropriately sized syringe and stainless steel ball- tipped intubation needle. The animals were returned to their cages immediately after the drug treatment.

OBSERVATIONS

Observation Period: 14 days

Mortality

All animals were observed twice every day for mortality for 14 days.

Body Weight

Body weight of each animal was recorded just prior to the test substance treatment (Day 0), Day 7 and 14 using electronic Animal weighing balance (Sartorius AG, Germany).

Feed Intake

Feed intake for individual animals was recorded daily for the entire study period.

Toxicity Signs

All the animals were observed individually after the treatment of the test substance during the entire observation period for the presence of any signs of toxicity including alopecia, catalepsy, chromodacryorrhea, clonic, coma, convulsion, diarrhea, dullness, excessive grooming, change in gait, hyperactivity, lacrimation, nasal discharge, nasal irritation, piloerection, polyuria, prostration, repetitive circling, respiratory distress, salivation, scaling, tonic, tremor and uro-genital staining.

Gross Pathology

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

RESULTS

Mortality

No mortality was observed in treated group of rats throughout the observation period (**Table 1**).

Table 1:Mortality Data

Details of the Group	Total no. of rats	Dose (mg/kgb.w.)	Percent mortality
Test substance (247) treated	5 Female	2000	0

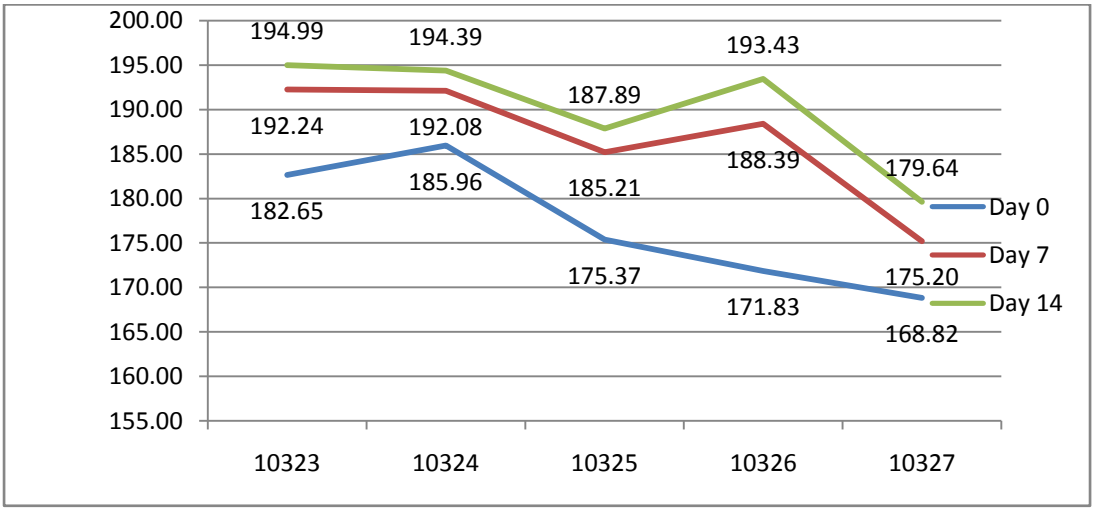
b.w. - Body Weight.

Body Weight

The animals treated with test substance (247) did not show a significant change in body weight gain on day 7 and 14 when compared with Day 0 (**Table 2**).

Table 2: Weekly Mean Body Weight Changes in Rats

Animal ID	Sex	Body Weight (g)		
		Day 0	Day 7	Day 14
10323	Female	182.65	192.24	194.99
10324	Female	185.96	192.08	194.39
10325	Female	175.37	185.21	187.89
10326	Female	171.83	188.39	193.43
10327	Female	168.82	175.2	179.64
Mean		**176.93**	**186.62**	**190.07**
SD		**7.22**	**7.02**	**6.47**



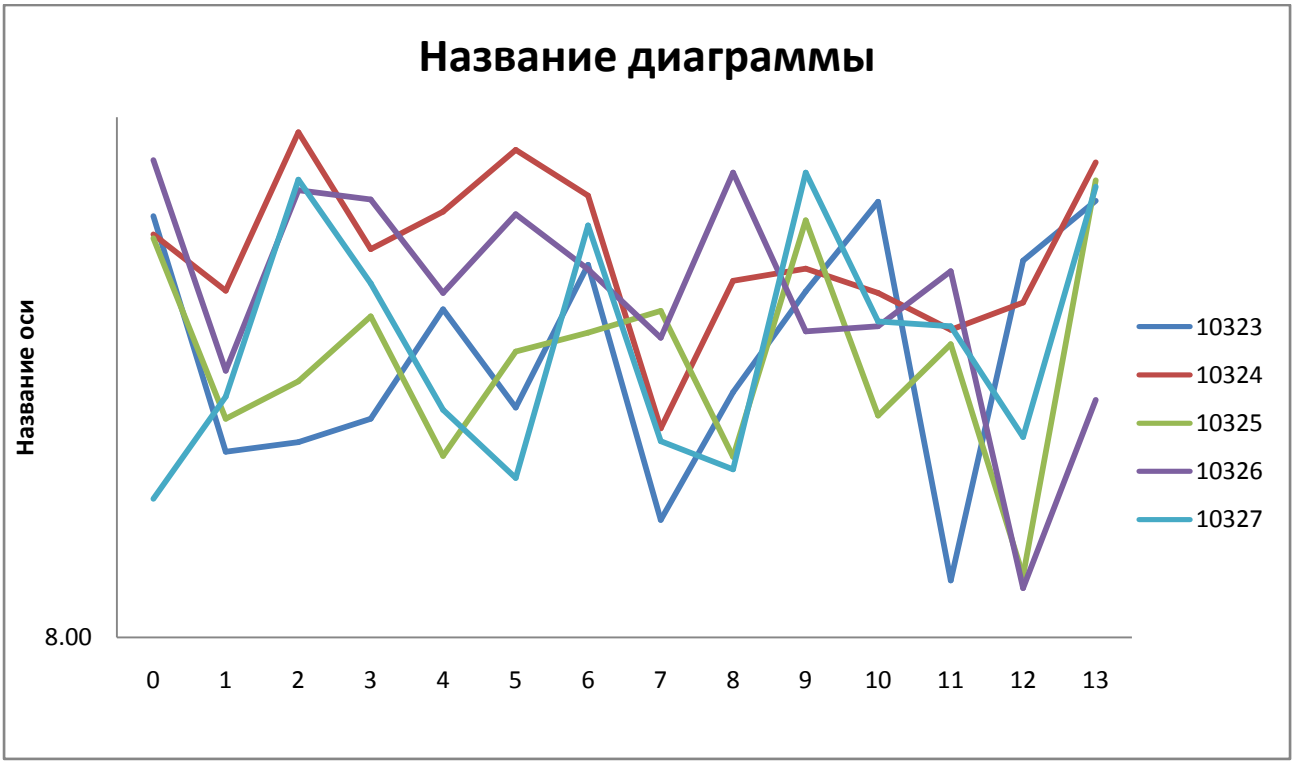
Feed Intake

The daily feed intake of rats remained unaffected throughout the experimental period **(Table 3).**

Table 3: Daily Feed Intake (g) by Rats

Animal ID	Sex	D													
		0	1	2	3	4	5	6	7	8	9	10	11	12	13
10323	**F**	13.31	10.01	10.13	10.42	11.89	10.56	12.55	9.22	10.76	12.15	13.54	8.57	12.61	13.56
10324	**F**	13.02	12.16	14.73	12.79	13.38	14.42	13.64	10.30	12.31	12.49	12.13	11.60	11.99	14.20
10325	**F**	12.96	10.42	10.90	11.79	9.96	11.30	11.56	11.87	9.95	13.24	10.46	11.40	8.62	13.90
10326	**F**	14.24	11.04	13.73	13.58	12.13	13.34	12.48	11.49	14.03	11.58	11.65	12.45	8.49	10.66
10327	**F**	9.46	10.70	13.91	12.27	10.53	9.70	13.16	10.14	9.80	14.03	11.72	11.65	10.19	13.79
Mean		12.60	10.87	12.68	12.17	11.58	11.86	12.68	10.60	11.37	12.70	11.90	11.13	10.38	13.22
SD		1.83	0.82	2.03	1.18	1.36	1.96	0.78	1.07	1.79	0.96	1.11	1.49	1.89	1.45

M - Male; F- Female; SD – Standard deviation;



Toxicity Signs

No visible signs of toxicity such as changes in respiration, circulation, autonomic and central nervous system, behavioral pattern were observed during the entire observation period**(Table 4)**.

Table 4: Toxicity signs observed in Female Rats

Observation*	Day														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Appeared Normal	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5
Found death	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Catalepsy	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Chromodacryorrhea	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Clonic	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Coma	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Convulsion	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Diarrhea	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Dullness	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Excessive grooming	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Change in Gait	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Hyperactivity	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Lacrimation	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Nasal discharge	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Nasal irritation	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Piloerection	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Polyuria	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Prostration	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Repetitive circling	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Respiratory distress	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Salivation	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Tonic	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Tremor	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5
Uro-genital staining	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5

* No. of animals showing the clinical sign / No. of animals per group

Gross Pathology

1. No test compound related findings were observed at necropsy. All gross observations were agonal in nature and bore no relation to treatment with the test substance **(Table 5)**.

Table 5 : Gross Pathology

S.No	Sex	Animal No	Status of the animal at the time of receipt at necropsy	Lesions observed at necropsy
1	F	10323	Live	NAD
2	F	10324	Live	NAD
3	F	10325	Live	NAD
4	F	10326	Live	NAD
5	F	10327	Live	NAD

F–Female; NAD- No Abnormalities Detected

2. All animals survived until the end of study.

CONCLUSION

1. Single dose oral administration of test substance (247) @ 2000 mg/kg caused no adverse toxic effects on the body weight / body weight changes, feed and the gross anatomy of treated female Wistar rats.
2. The acute oral LD_{50} of test substance (247) in Wistar rats was observed to be greater than **2000 mg/kg b.w.**

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