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Subacute Oral Toxicity Study of *Luffa cylindrica* Fruits in Wistar Rats

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Sanjaya Kumar Y.R*, Lakshmi O.S, Thamizh Selvam N, Saketh Ram T, Divya A, Radhakrishnan P.

National Ayurveda Research Institute for Panchakarma, Cheruthuruthy, Thrissur, Kerala

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ABSTRACT

In the present study, *Luffa cylindrica* fruit decoction was evaluated for safety in experimental animals. The test drug was evaluated for acute toxicity (single exposure) at dose 2000 mg /kg body weight and sub-acute toxicity (consecutive exposure for 14 days) at dose 1000 mg /kg body weight in Wistar rats. Mortality, Signs of toxicity, body weight and feed consumption were recorded at weekly intervals during subacute toxicity study. No significant variations were observed between the animals in control and the test group with respect to body weight gain and feed consumption. Haematological and biochemical investigations carried out at the termination of the experiment did not reveal significant differences between test group and control group except for the reduction in cholesterol and triglyceride levels in the test group. In conclusion, the test drug was found to be safe as evidenced by the absence of morbidity and mortality at the tested dose levels during acute and subacute toxicity studies in Wistar rats.

INTRODUCTION

Luffa cylindrica Roem a ground-dwelling vine belongs to family Cucurbitaceae and grows in tropical and subtropical climate (Fig.1). Phytochemical screening revealed the presence of glycosides, carbohydrates, flavonoids, and saponins in Luffa cylindrica fruit extracts (1).

Fig 1. Luffa cylindrica fruits and flowers

Luffa cylindrica is used in traditional medicine; fruits are used in the traditional Chinese medicine as an anthelmintic, stomachic, antioxidant and antipyretic (2). Luffa cylindrica is known as Dhamargava in Ayurveda. The fruit of dhamargava is used in the Ayurveda Panchakarma practice for Vamana karma (induced emesis). This procedure is carried out mainly to treat the ailments of the respiratory tract.Luffa cylindrica fruits also used to induce emesis in cases of poisoning and skin diseases (3). The aim of the present study was to evaluate the safety profile of Luffa cylindrica in Wistar rats.

MATERIALS AND METHODS

Animals

Wistar Rats of either sex were procured from Veterinary College, Mannuthy, Thrissur, Kerala was used in the trial. After the quarantine period, animals were caged individually as per

Committee for the purpose of Control and supervision of experiments on animals (CPCSEA) guidelines.

Test drug

Luffa cylindrica fruits were procured from the banks of river bharatapuzha in the locality of Shoranur, Thrissur. They were dried, powdered and decoction as per standard protocols.

Ethical clearance

The present trial was conducted with the approval of Institutional Animal Ethics Committee (IAEC) meeting held at National Ayurveda Research Institute for Panchakarma, Cheruthuruthy, Thrissur, Kerala.

Experimental design

Acute Toxicity study

Acute study at the dose rate of 2000 mg/ kg bodyweight was carried out in female Wistar rats as per OECD guideline 423 (4). A total of 6 rats were used in the study. The test drug was administered to 3 animals once orally and the animals were observed for a period of 14 for mortality and signs of toxicity. The test was repeated at the same dose levels with another set of 3 female rats.

Subacute toxicity study

The rats were divided into two groups namely Vehicle Control (VC) group, test dose (TD) group each comprising of 12 animals (6 Male and 6 Female). While the VC group received distilled water, the test drug was administered orally at dose 1000 mg/ kg body weight for 14 consecutive days. Animals were observed for signs of mortality and clinical signs of toxicity during the study period. Behavioural and physiological responses were monitored daily and weekly feed consumption and body weight gain were recorded as per OECD guideline 407 (5)

After the dosage period of 14 days, animals fasted and blood samples were collected by retro-orbital plexus puncture under ether anesthesia for hematology and serum biochemistry.

Total Leucocyte Count (TLC), Polymorph Percentage, Lymphocyte percentage, Packed Cell Volume , Hemoglobin (HB)levels, Total red Cells Count (TRC) and platelets Count, Serum Glucose, Serum glutamic oxaloacetic transaminase (SGOT), Serum glutamic pyruvic transaminase (SGPT), Creatinine, Total Protein (TP) and Prothrombin Time (PT) were analysed at Biochemistry division of the Institute.

Animals were sacrificed by cervical dislocation under ether anesthesia and the detailed post-mortem examination was carried out. Vital organs were individually weighed and tissue samples of the same were stored in 10% formalin for histopathology studies.

Statistical analysis

The statistical difference between the control and test groups were calculated by means of analysis of variance followed by Dunnet's test with the minimal level of significance set at $P \leq 0.05$. The results were expressed as the Mean ± standard error of the mean.

RESULTS AND DISCUSSION

Acute toxicity study

No mortality and signs of toxicity were recorded in female Wistar rats upon single exposure to the drug at a dose of 2000 mg/kg body weight.

Subacute Toxicity study

Wistar Rats of either sex did not show any signs of toxicity during the period of 14 days and no mortalities were observed too. Animals in the test groups did not show any significant variation in body weight gain (Table 1) and feed consumption (Table 2) as compared to those in control groups. Significant (P<0-05) reduction in serum cholesterol and triglyceride levels were observed in the group which received the test drug, The results were in accordance with the findings of a clinical study wherein induced emesis with *Luffa cylindrica* has shown to reduce the lipid levels in patients suffering from dyslipidemia (6). Other Hematology and serum biochemical values were found to be in normal range in both control group and test group (Tables 3 and 4)

The test drug did not affect the normal development of internal organs and significant differences were not observed with respect to the relative organ weights (Table 5).

Histopathology studies did not reveal any pathological changes in the internal organs of animals at any of the dose levels (Fig. 2 – 5)

Table 1. Effect of *Luffa cylindrica* on Weekly % body weight gain as compared to day 1 in Wistar rats (Mean ±SEM)

Weeks	VC		TD	
	Male	Female	Male	Female
0-1	35.23 ± 3.2	19.08 ± 2.33	33.66 ± 4.76	19.35 ± 0.89
0-2	39.48 ± 2.58	24.75 ± 1.43	37.27 ± 2.87	26.13 ± 0.87

(Average of 6 Values)

Table 2.Effect *of Luffa cylindrica* fruit on Weekly % feed intake in Wistar rats (Mean ±SEM).

Weeks	VC		TD	
	Male	Female	Male	Female
I week	154.58±14.8	109.99±18.79	184.3±25.2	143.23±25.54
II week	78.76±7.09	57.869±6.906	67.69±8.38	60.235±12.039

(Average of 6 Values)

Table 3. Effect of *Luffa cylindrica* fruit on hematological parameters in Wistar rats (Mean ±SEM).

	VC		TD	
	Male	Female	Male	Female
TLC (x10^3)	9.43 ± 0.81	7.4 ± 0.89	8.33 ± 0.63	6.86 ± 1.29
POLY (%)	35.33 ± 3.76	37.45 ± 2.16	32.1 ± 3.13	30.73 ± 4.6
LYM (%)	60.82 ± 4.11	59 ± 2.22	64.48 ± 3.27	86.17 ± 4.83
MON (%)	3.95 ± 0.42	3.55 ± 0.29	3.42 ± 0.18	3.1 ± 0.33
PCV (%)	37.25 ± 0.71	36.4 ± 0.84	35.13 ± 0.75	35.3 ± 0.62
HB (g %)	13.73 ± 0.27	13.76 ± 0.17	13.35 ± 0.26	13.17 ± 0.24
TRC (x 10^3)	6.86 ± 0.17	6.61 ± 0.11	6.52 ± 0.18	6.33 ± 0.14
Platelets(x 10^6)	1.025±107	0.956±39	1.180±92	1.025±82

(Average of 6 Values)

Table 4. Effect of *Luffa cylindrica* on serum Biochemical parameters in Wistar rats (Mean ±SEM).

	VC		TD	
	Male	**Female**	**Male**	**Female**
Glucose(mg / dl))	86.33 ± 4.9	89.17 ± 6.9	102.5 ± 7.3	98.67 ± 6.9
Cholesterol (mg/ dl))	83.17 ± 4.13	102.67 ± 11.9	66.66 ± 4.58*	72 ± 6.9*
Triglycerides(mg/ dl)	77 ± 6.79	66.8 ± 5.79	59.17 ± 2.4*	48.83 ± 5.53*
Total Protein (mg / dl)	6.42 ± 0.17	6.86 ± 0.10	6.4 ± 0.17	6.56 ± 0.17
Urea (mg / dl)	31.5 ± 2.86	33 ± 2.74	27.5 ± 1.43	31 ± 3.59
Creatinine (mg / dl)	0.43 ± 0.02	0.46 ± 0.03	0.44 ± 0.03	0.42 ± 0.02
SGOT (U/L)	111.33 ± 4.94	111.66 ± 16.45	95.16 ± 8.49	108.5 ± 4.36
SGPT (U/L)	53.16 ± 4.24	91.67 ± 2.75	56.16 ± 6.65	57.33 ± 3.81
Alkaline phosphatase (U/L)	123.33± 13.52	72.67 ± 13.21	123.67 ± 17.58	77.32 ± 25.47
Tot. Bilirubin(mg / dl)	0.29 ± 0.03	0.28 ± 0.17	0.27 ± 0.03	0.24 ± 0.01
Sodium (mmol/L	142.83 ± 0.31	141.5 ± 0.80	142.16 ± 0.98	136.3 ± 4.55
Potassium (mmol/L)	4.85 ± 0.16	4.73 ± 0.12	5.15 ± 0.11	5.23 ± 0.24
Chloride (mmol/L)	100.67 ± 0.49	101.67 ± 1.78	99.67 ± 1.02	100.33 ± 0.99
Calcium (mg / dl)	9.23 ± 0.34	9.5 ± 0.23	9.73 ± 0.24	9.6 ± 0.27

***** P<0.05 (Average of 6 Values)

Table 5. Effect of *Luffa cylindrica* on relative organ weights (in % body weight) in Wistar rats (Mean ±SEM)

	VC		TD	
	Male	**Female**	**Male**	**Female**
Heart	0.32 ± 0.01	0.30 ± 0.03	0.32 ± 0.01	0.35 ± 0.01
Lungs	0.92 ± 0.08	0.76 ± 0.07	0.76 ± 0.08	1.02 ± 0.10
Liver	3.08 ± 0.10	2.26 ± 0.22	2.95 ± 0.11	2.83 ± 0.17
Spleen	0.21 ± 0.02	0.20 ± 0.01	0.22 ± 0.02	0.25 ± 0.03
Kidneys	0.67 ± 0.04	0.55 ± 0.07	0.63 ± 0.05	0.72 ± 0.04
Stomach	0.71 ± 0.03	0.61 ± 0.03	0.58 ± 0.04	0.68 ± 0.03
Testis	0.92±0.03	-	0.84±0.17	-
Ovaries	-	0.032 ± 0.01	-	0.04 ± 0.06
Brain	0.61 ± 0.01	0.64 ± 0.05	0.62 ± 0.03	0.79 ± 0.06

(Average of 6 Values)

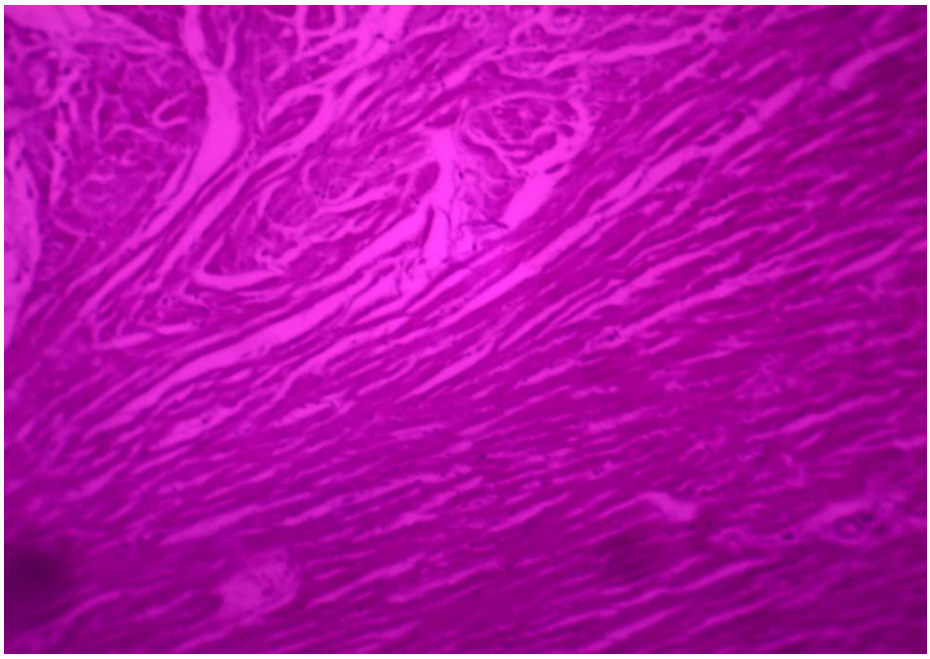

Fig 2. Histopathology of section of heart of a female rat showing normal endocardium, myocardium, and pericardium

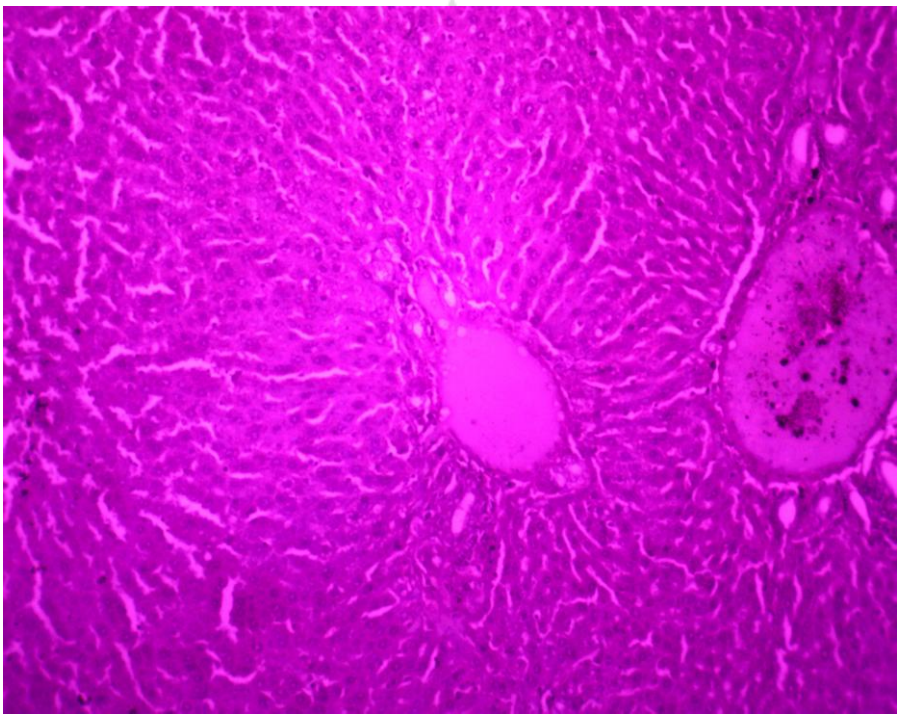

Fig 3. Histopathology Section of Liver of a male rat showing normal hepatocytes, portal triads, and sinusoidal spaces

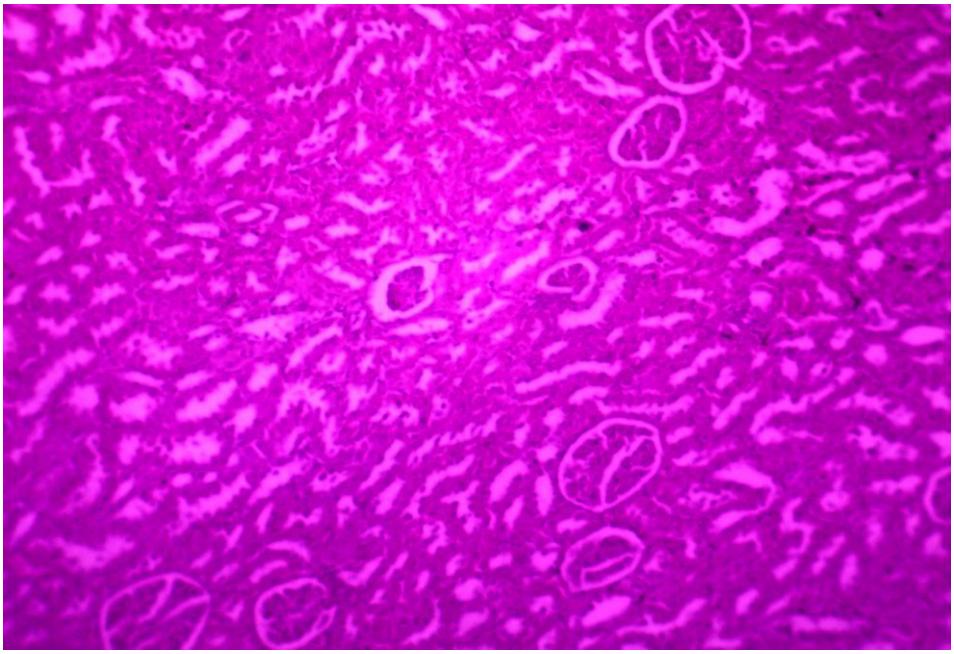

Fig 4. Histopathology of section of Kidney of a male rat showing normal glomeruli and Bowman's capsule

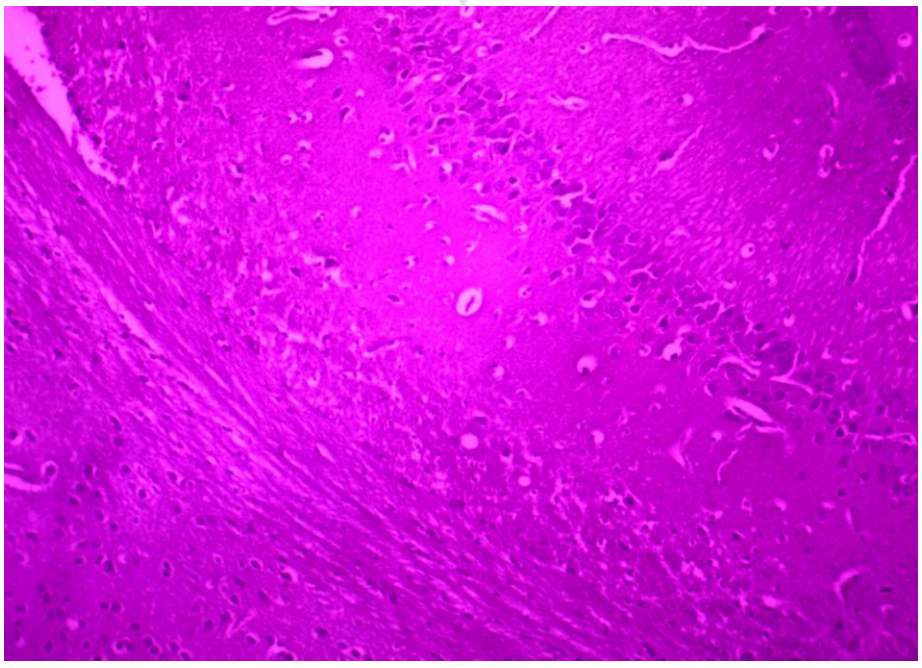

Fig 5. Section of Brain of a female rat showing astrocytes, glialcells andstroma

CONCLUSION

In this study, the single exposure to *Luffa cylindrica* decoction up to the dose of 2000 mg /kg body weight per oral was found to be safe in Wistar rats. During subacute toxicity study, 14

days oral administration of to *Luffa cylindrical* decoction up to the dose of 1000 mg /kg body weight did not cause any adverse effects or lethality to Wistar rat.

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