



Scholars Research Library

Der Pharmacia Lettre, 2014, 6 (3):20-26
(<http://scholarsresearchlibrary.com/archive.html>)



ISSN 0975-5071
USA CODEN: DPLEB4

Treatment of peptic ulcer in animal model by *Sirucinni Uppu* (Herbal salt of *Acalypha fruticosa* Forssk.)

^{1*}Mudiganti Ram Krishna Rao, ²A. Ganesan, ³G. Renga Sundari, ¹M. Sathish Kumar and ¹Neema Kumari Jha

¹Department of Industrial Biotechnology, Bharath University, Chennai, India

²Government Primary Health Centre, Jamin Endathur, Kanceepuram Dt., Tamil Nadu, India

³Vellu Maillu Sidha Medical College, Sriperumbudur, Kancheepuram, District, Tamil Nadu, India

ABSTRACT

In Sidha system of medicine use of salts prepared by herbal plants for treatment of diseases is common. *Sirucinni uppu*, herbal salt of *Acalypha fruticosa* (Forssk) is used for the treatment of Gunmam, peptic ulcers. In the present study the efficacy of *Sirucinni uppu* was evaluated in rat model. Five groups of albino rats (150–200 gm), each group consisting of six animals were used. The first group served as a normal control group, which were given 5 ml normal saline/kg for normal comparison, the second group served as negative control, which were also given 5ml saline/kg. The third group animals were given Ranitidine 20 mg/kg body weight and served as positive control group. Fourth and fifth groups served as test groups. The fourth and fifth groups were treated respectively with 'Sirucinni uppu' (HSAF) in the dose of 200mg and 400 mg orally for 15 days. After 15 days of treatment, animals were fasted for 24 hours. Ulcer was produced by administration of aqueous suspension of aspirin (a dose of 200 mg/kg orally) on the day of sacrifice except normal control group animals. After four hours the animals were sacrificed and the stomach was excised along the greater curvature, washed carefully with 5.0 ml of 0.9 % saline and ulcers were scored by a person unaware of the experimental protocol in the glandular portion of the stomach and ulcer index is tabulated. The use of *Sirucinni uppu* has given better results compared to ranitidine treatment as anti ulcer agent and it is suggested that the use of this drug should be more common as compared to the chemical, ranitidine.

Key words: *Sirucinni Uppu* (Herbal Salt of *Acalypha fruticosa*), Peptic Ulcer, Antiulcerogenic, Ranitidine, Aspirin, Sidha, Ayurveda

INTRODUCTION

Siddha system is one of the oldest medical systems of India. It considers food as preventive medicine. Proper diet and eating habits are considered to be the source of both physical and mental health. Food is commonly classified by taste and quality. Herbs are also considered in terms of their taste, potency, the digestive effect and their unique impact.

Siddha system proposes that among the six tastes that it describes, the bitter tasting herbal food is said to have the property of decreasing swelling and fluid retention. The bitter taste kills parasites, neutralizes poisons, purifies

blood, cure-burning and itching, and controls nausea and vomiting. In the Siddha pharmacopeia, herbals of having bitter taste are recommended for the treatment of the disease 'Gunmam' (Peptic Ulcers).

Herbal medicines are being used by about 80% of the world population primarily in the developing countries for primary health care. These medicines have stood the test of time for their safety, efficacy, cultural acceptability and lesser side effects. Indian medicinal plants and their derivatives have been an invaluable source of therapeutic agents to treat various disorders including peptic ulcer disease[1] An indigenous drug possessing fewer side effects is the major trust area of the present day research, aiming for a better and safer approach for the management of peptic ulcer disease.

Extraction of herbal salt from certain herbs and its inorganic values are being used in Siddha system of medicine. 'SIRUCINNI UPPU' - Herbal Salt of '*Acalypha fruticosa* (HSAF)' a bitter tasting herb, was selected to evaluate its therapeutic action in treating 'GUNMAM'

Peptic Ulcer

Peptic ulcer disease (PUD) or *Gunmam* is ulceration of gastric mucosal lining leading to severe gastritis and related symptoms. This is caused either due to irregular food habits or even due to infections. Recent treatment strategies encompass the use of medicines which are antacids, proton pump inhibitors, histamine receptor blockers and the use of prostaglandin analogs.[2] The use of these drugs have many side effects. The use of native medicines from ayurveda and sidha can solve this problem in the form of less side effects and have the advantage of cheap availability. The present study is to find out the antiulcerogenic efficacy of herbal salt of '*Acalypha fruticosa*' (HSAF) on rat model.

Acalypha fruticosa Forssk. belongs to Family: *Euphorbiaceae*. (Figure 1)

The plant, *Acalypha* is found in tropical Africa and parts of Indian subcontinent. It is commonly available as a weed in gardens and fields. This is an aromatic shrub up to 4 m tall said to be Attenuant, Alternative, Stomachic and Alexipharmic [3] Decoction of leaves prepared in water is taken internally to treat dysentery. Root and leaf paste is prepared in water and applied externally to treat skin diseases. An infusion of the leaves regarded as a stomachic and alterative. The leaves are used as medicine for many. [4,5,6] This plant extract is reported to be anticancer antioxidant and anti inflammatory [8, 9] Infusion of leaves is used to wash pustules and the root is used for treatment of Gonorrhea.

MATERIALS AND METHODS

2. A. Plant material *Acalypha fruticosa* Forssk. Aerial parts, such as tender stem, leaves, inflorescence and flowers were used for preparation and study. (Figure 1)

Figure 1: *Acalypha fruticosa*.Forssk



A.i. Preparation of “*Sirucinni uppu*” (The Salt of *Acalypha fruticosa*: HSAF))

This procedure for preparation of this salt was collected from ‘*Anuboga Vaidya Navaneetham*’ Part-1. Page 4, written by Hakkem B. Mohamad Abdullah. The plant material was collected from Vandavasi hills, near Kanchipuram, Tamil Nadu, India, in May, 2009 and was authenticated by Dr.Sasikala Ethirajulu, Dept of Botany, CRI, Chennai-106. The plant was shade dried at room temperature, burned to ash and dissolved in distilled water. The solution was distilled at low temperature and the salt was collected in powder form.

2. B. EXPERIMENTAL ANIMALS

Adult albino rats of either sex weighing around 150-180gms were used as experimental animals. The animals were acclimatized to laboratory conditions before experimental procedures were at normal room temperature $\pm 5^{\circ}\text{C}$ and at humidity 55. All the animals were fed with pellet diet from Poultry Research Station, Nandanam, and Chennai-35 and potable water *ad libitum* throughout the experimental period. All the animals were weighed and numbered. The experimental protocol for the ‘*Shirucinniuppu*’ (AJ/IAEC/10/12) was approved by the CPCSEA/IAEC of Mohamed Sathak A.J College of Pharmacy, Sholinganallur, Chennai.

B.i. Haematological studies

The following hematological parameters such as total R.B.C. count, total W.B.C. Count, Hemoglobin (Hb) content and Total Bilirubin content were performed by standard procedures. Serum analysis was done for the following parameters like, Serum Alkaline Phosphate, urea, uric acid, Creatinine, the SGOT and SGPT [10, 11, 12, 13, 14]

B. ii. Toxicological Study-Herbal Salt of ‘*Acalypha fruticosa*’ (HSAF)**ii. a. ACUTE ORAL TOXICITY STUDY (LD₅₀ Determination)**

For carrying out oral toxicity study OECD guidelines 423 was followed. The method uses defined doses (5, 50, 300, 2000mg/kg body weight) and the results allow a substance to be ranked and classified according to the globally harmonized system. The starting dose of 2000 mg/kg body weight p.o. was given, the dose was administered to the rats which were fasted overnight with water *ad libitum* and observed for signs of toxicity.

No mortality was recorded. As per OECD guidelines 423 the effective dose was fixed at 200 mg per kg. The same dose was once again tried with another three rats and were observed for 72 hours and found normal for symptoms like change in skin colour, salivation, diarrhea, sleep, tremors, convulsions and also respiratory, autonomic and CNS effects.

ii. b SUBACUTE TOXICITY STUDY

The duration of the study was 45 days. Three dose levels of the ‘*Shirucinni uppu*’ were used (100, 200 & 400mg/kg). Each group consists of six animals (three animals /sex /group). The drug was administered orally once daily for 45days. On 46th day the animal was anaesthetized and blood was collected by retro orbital puncture. Hematological parameters were evaluated. Serum was separated and biochemical parameters were estimated. Animal was sacrificed and organs like liver, kidney, lungs and spleen were removed and weighed. The organs were kept in 10% formalin and used for histopathological analysis. For toxicity study the various parameters were observed in animals like, water consumption, food consumption, body weight, kidney function test, liver function test and hematological profiles.

B.iii. Aspirin-induced gastric ulcer

In the aspirin-induced ulcer experiments, five groups of albino rats (150–200 gm), each group consisting of six animals were used. The first group served as a normal control group, which were given 5 ml normal saline/kg for normal comparison, the second group served as negative control, which were also given 5ml saline/kg. The third group animals were given Ranitidine 20 mg/kg body weight and served as positive control group. Fourth and fifth groups served as test groups. The fourth and fifth groups were treated respectively with ‘*Sirucinni uppu*’ (HSAF) in the dose of 200mg and 400 mg orally for 15 days. After 15 days of treatment, animals were fasted for 24 hours. Ulcer was produced by administration of aqueous suspension of aspirin (a dose of 200 mg/kg orally) on the day of sacrifice except normal control group animals. After four hours the animals were sacrificed and the stomach was excised along the greater curvature, washed carefully with 5.0 ml of 0.9 % saline and ulcers were scored by a person unaware of the experimental protocol in the glandular portion of the stomach. A score for the ulcer was made as: 0- Normal, 0.5- Red colour, 1- Spot ulcers, 1.5- Hemorrhage, 2- Ulcer, 3- Perforation. Mean ulcer score for each animal was expressed as ulcer index.

The percentage of ulcer protection was determined as follows:

$$\% \text{ Protective} = \frac{\text{Control mean ulcer index}}{\text{Control mean ulcer index} - \text{test mean ulcer index}} \times 100$$

3. Animal studies

3 A. Observation of Dissected stomach of animals

Stomach sections of control and experimental animals which was pinned on a board is used compare with other animal group's section on the aspect of physiology and pathology. Animal's section of stomach belongs to the negative control group shows red colour, spot -ulcers, hemorrhage, ulcers. Animals of positive control show red colour in stomach field. Animals belong to low dose group shows red colour, spot -ulcers, Animals belong to high dose group of test drug '*Sirucinni uppu*' show red colour. (Figure 2, 3, 4, 5 and Figure 5) (Table 1)



Figure 1.NEGATIVE CONTROL (SIIRUCINNI UPPU)

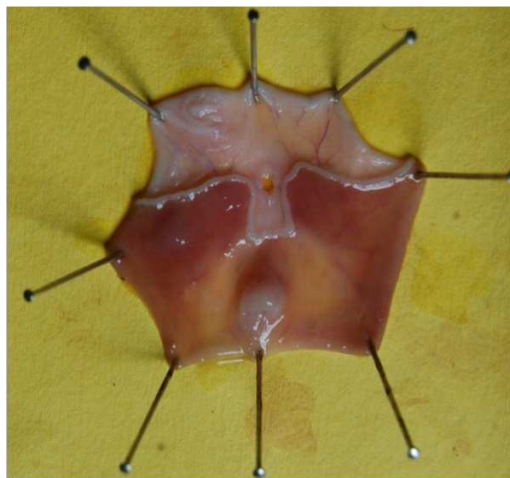


Figure 2 POSITIVE CONTROL (SIIRUCINNI UPPU)

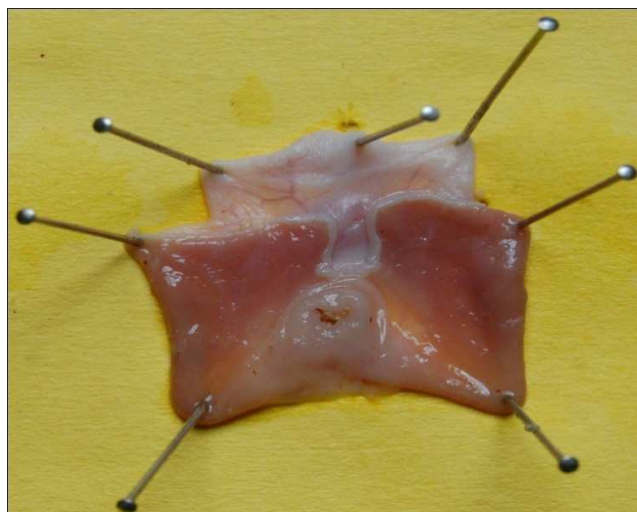


Figure 3. NORMAL CONTROL (SIIRUCINNI UPPU)



Figure 4 LOW DOSE (SIRUCINNI UPPU)



Figure 5 HIGH DOSE (SIRUCINNI UPPU)

Figure 1 to 5. Depicting the representative photographs of stomach sections in control and treated rats with Sirucinni Uppu

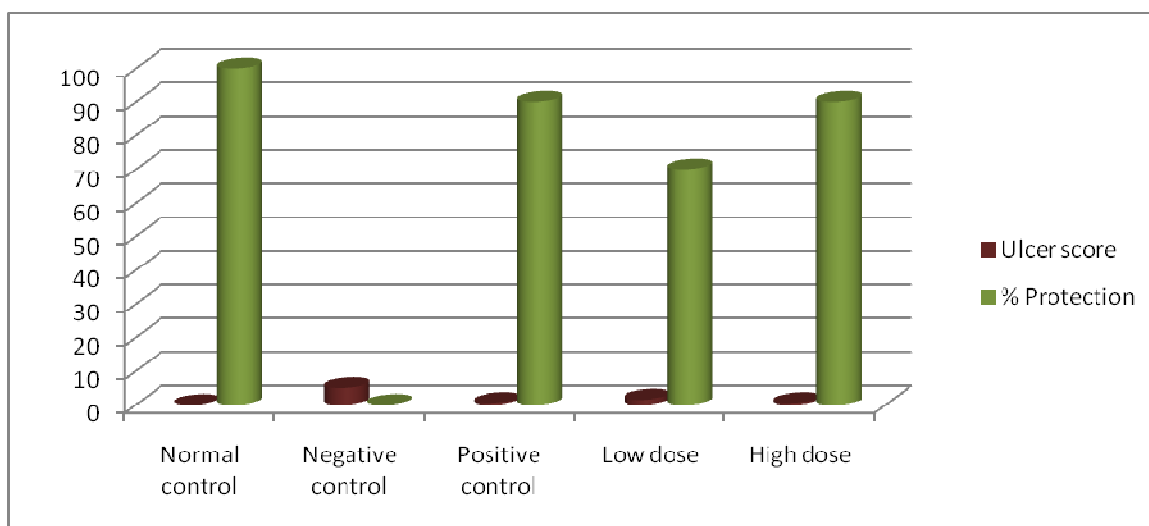


Figure 6 Bar diagram for ulcer score and ulcer protection

Table 1 Ulcer Score

Group	Drug/Dose	Score	% protection	Pathological findings
Normal control	5 ml saline/kg of rat, p.o.	0	-----	No ulcers, No haemorrhage
Negative control	5 ml saline/kg of rat, p.o.	0.5+1+1.5+2= 5	-----	Red colour, spot -ulcers, Haemorrhage, Ulcers.
Positive control	Ranitidine 20mg/kg. p.o	0.5	90	Red colour
Low dose	'SIRUCHNNI UPPU' 200 mg /kg with honey. p.o.	0.5+1=1.5	70	Red colour, Spot -ulcers,
High dose	'SIRUCINNI UPPU' 400 mg /kg with honey. p.o	0.5	90	Red colour.

3. B Toxicological studies

Toxicological studies indicated that there was not much variation in the water consumption among control and experimental animals (Table-2). There was a remarkable increase in body weight resulting directly due to more food intake (Table-3). No significant change was noted in the kidney function test and liver function tests (Table-4, Table-5). The hematological tests also did not show much variation among test and control animals (Table -6).

Table 2 Water consumption

Groups	Average water consumption for 24hr per animal (ml)		
	1 day	14 th day	28 th day
1- control	14.5	16.1	15.9
2- Low dose <i>Sirucinni uppu</i> 100 mg/kg	14.3	17.2	15.5
3- Medium dose <i>Sirucinni uppu</i> 200 mg/ kg	14.3	17.2	15.5
4- High dose of <i>Sirucinni uppu</i> 400 mg/kg	17.1	16.4	15.8

Table 3 Body weight

Groups	Body weight in grams / animal		
	1 st day	14 th day	28 th day
I- control	135.2	142.3	151.7
I- low dose <i>Sirucinni uppu</i> -100 mg/kg	136.4	143.2	158.7
II- high dose of <i>Sirucinni uppu</i> -200 mg/kg	134.3	147.9	158.9
III- high dose of <i>Sirucinni uppu</i> -400 mg/kg	135.6	149.5	156.3

Table 4 KIDNEY FUNCTION TEST

Groups	Kidney function tests (mg/dl)		
	Urea	Uric acid	Creatinine
I- control	25	3.8	0.3
I- low dose <i>Sirucinni uppu</i> -100 mg/kg	26	3.9	0.4
II-Medium dose <i>Sirucinni uppu</i> -200 mg/kg	26	3.8	0.3
III- high dose <i>Sirucinni uppu</i> -400 mg/kg	26	3.7	0.4

Table 5 Liver function test

Groups	SGOT	SGPT	Alkaline Phosphatase	Total Bilirubin mg/dl
I-Control	81	33	23	0.6
II-Low Dose of <i>Sirucinni Uppu</i> 100mg/Kg B.W.	80	34	23	0.6
III-Medium Dose of <i>Sirucinni Uppu</i> 200 mg/Kg B.W.	81	34	23	0.6
III-High Dose of <i>Sirucinni Uppu</i> 400 mg/Kg B.W.	84	35	23	0.7

Table 6 Hematological Studies

Groups	RBC count (million cells/c.mm)	WBC count (cells/c.mm)	Hb (G%)
I- control	4	6900	12.2
II- low dose <i>Sirucinni uppu</i> -100 mg/kg	4.2	7400	12.6
II-Medium dose of <i>Sirucinni uppu</i> -200 mg/kg	4.4	7600	12.2
III- high dose of <i>Sirucinni uppu</i> -400 mg/kg	4.6	7800	12.8

3. C PHARMACOLOGICAL RESULT

Pharmacological studies of '*Sirucinni uppu*' shows effective ulcer protective property as seen in high dose test animals (with 400 mg/kg) where the hemorrhage has come down almost as compared with the group tested with ranitidine.

DISCUSSION

Although Sidha medicine system has documented the use of *Acalypha fruticosa* for its various medicinal values, scanty research reports are available on its various properties. Thus this work assumes significance. The antioxidant potential, anthelmintic, cytotoxicity and DNA cleavage protective properties of methanolic and ethanolic extract of this plant was reviewed by Raj Kumar *et al.* (Raj Kumar *et al.*, 2012).^[15] The antibacterial and larvicidal activities of this plant was recorded (Senthil Kumar and Dandapani, 2009, Samuel *et al.*, 2012 and Ileri *et al.*, 2010).^[16, 17, 18]

Acute and sub acute toxicological studies reveal that the drug '*Sirucinni uppu*' does not have any toxic effect and safety of the drug is recorded through the histopathological results of animal model. The hematological study results

confirmed the safety of the drug. The liver function test and renal function test of animal model in toxicological studies reveal the normal function of the vital organs and also registered the efficacy and safety of the drug.

Tabulated parameters such as water consumption, food consumption, body weight of animals in sub chronic toxicity study of 'Sirucinni uppu' registered the improvement of body weight, food consumption which shows normal physiology of gastro intestinal system of animals which was enhanced by the drug 'Sirucinni uppu'.

Anti ulcer activity of 'Sirucinni uppu' in lower and higher dose level in animal model demonstrate its efficacy as ulcer protective agent. High dose (400 mg/kg) level shows 90% of protective effect as equal to the positive control drug Ranitidine.

REFERENCES

- [1] Kirtikar K R, Basu B D. *Illustrated Indian Medicinal plants III, Revised and enlarged Edition*. **2000**(3): 997-999.
- [2] Mafertheiner P, Chan F K L, McColl K E L. *The Lancet*, **2009**, 374(9699): 1449-1461. Doi:10.1016/SO 140-6736(09)60938-7.
- [3] Duraipandian V, Ayyanar M, Ignacimuthu S. *BMC Complimentary and Alternative Medicine*, **2006**, 6:35.
- [4] Mudaliar M. *Siddha Metria Medica (Medical Plants Division)*. **1988**, Published by The Directorate Of Indian Medicine and Homeopathy, Chennai.
- [5] Muthukumarasamy S, Mohan V R, Kumaresan S, Chelladurai V. *Journal of Economic and Taxonomic Botany* **2003**, 27(3):711-714.
- [6] Ignacimuthu S, Ayyanar M and Sankarasivaraman K. *J Ethnobiol and Ethnomed.*, **2006**, 2:25.
- [7] Mothana R A A, Gruenert R, Lindequist U, Bednarski P J. *Pharmazie*, **2007**, 62, 305-307.
- [8] Thambiraj J, Paulsamy S, Seukuperumal R. *Asian Pac J Trop Biomedicine*, **2012**; 2(1): S127-30.
- [9] Gupta M, Mazumdar U K, Sivakumar T, Kuarki S, Sambathkumar R, Manikandan L. *Nigerian Journal of Natural Products and Medicine*, **2003**, 7:27-29.
- [10] Balasubramanian M P, Dhandayuthapani S, Nellaiappan K, Ramalingam K. *Helminthologia*, **1983**, 20: 111-120.
- [11] Natelson S, Scott M L, Beffa C. *Am. J. Clin. Pathol.*, **1951**, 21: 275-281.
- [12] Caraway WT 1963. Uric acid. In: *Standard Methods of Clinic Chem.*, Seligson, D. (Ed.) Academic Press, New York, **1963**, Vol- IV: 239-247.
- [13] Owen J A, Bely Iggo, Scandrett F J, Stewart C P. *Biochem. J.* **1954**, 58: 426-437.
- [14] King J. *The phosphatases*. In H.J. Princeton (eds.) *Practical clinical embryology*. D Van Nostrand company Ltd, London: **1965b**, pp-191-208.
- [15] Raj Kumar, Elumalai A and Eswaraiah M C. Review on anthelmintic medicinal plants. *J Pharmaceu. Sci. Innovation*, **2012**, 1:32-34.
- [16] Senthil Kumar S and Dhandapani, R. *Advaved Biotech*. **2009**, 9(6): 34-37.
- [17] Samuel M, Ng'ang'a Zipporah, Rosebella M, Zipporah O, Peter N, Philip Nand Tonui Willy. *American International Journal of Contemporary Research*, **2012**, Vol. 2 (8):194.
- [18] Ileri L N, Kongoro J, Ngure P, Mutai C, Langat B, Tonui W, Kimutai A, Mucheru O. *J of Vector Borne Diseases* **2010**, 47(3):168-174.