

Antidiarrheal and antiulcer activity of *Stachytarpheta urticifolia* Salisb (sims) in Wistar rats

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Abstract

Introduction: Millions of people were dying in each year from third world countries due to diarrhea and peptic ulcers in non-industrial countries. *Stachytarpheta urticifolia* is endangering plants available in Eastern Ghats of India. It is used as a traditional medicine for curing of diseases. **Materials and Methods:** The material is collected from Araku Valley, Visakhapatnam, Andhra Pradesh, India. Antidiarrheal and antiulcer activity was conducted on Wistar rats as per the OECD 425 guidelines. No lethality was found in any of the groups after treatment up to 2000 mg/kg in acute toxicity test. Experiments were assessed based on histological studies. **Results and Discussion:** The results have shown that methanolic leaf extract of *S. urticifolia* (MESU) possess a significant antidiarrheal activity by inhibiting frequency of defecation and reduced greatly the weight of fecal excretions. Aspirin-induced gastric ulcers in animals showed extensive lesions that were restricted to glandular portions of the stomach as compared to control rats ($P < 0.05$), whereas oral administration of MESU lowered the ulcer index in Group III and Group IV of experimental animals. **Conclusion:** Methanolic extract of *S. urticifolia* was found to understand that it is rich in potent active principles which are able to inhibit the diarrheal and gastric ulcer effectively in experimental rats.

Key words: Anti-peptic ulcer, antidiarrheal, methanolic leaf extract, *Stachytarpheta urticifolia* Salisb (sims)

INTRODUCTION

“Diarrhea” is an alteration in the normal bowel movement and is characterized by an increase in the water content, volume, or frequency of stools.^[1] Diarrheal diseases are a major problem in third world countries and are responsible for the deaths of millions of people each year.^[2] Plants have long been a very important source of new drugs and many plant species have been screened to see if they contain substances with therapeutic activity. Medicinal plants are a promising source of antidiarrheal drugs.^[3,4] International organizations such as the WHO have encouraged studies for the treatment and prevention of diarrheal diseases using traditional medicinal practices.^[5] A medicinal plant widely claimed to be effective in the management of diarrhea and ulcer in Araku Valley Visakhapatnam is *Stachytarpheta urticifolia* Salisb (sims).

Peptic ulcer disease is one of the most common gastrointestinal disorders, which causes a high rate of morbidity particularly in the population

of non-industrialized countries.^[6] Peptic ulcer occurs due to an imbalance between the aggressive (acid, pepsin, and *Helicobacter pylori*) and the defensive (gastric mucus and bicarbonate secretion, prostaglandins, and innate resistance of the mucosal cells) factors.^[7] Number of drugs including proton pump inhibitors, prostaglandins analogs, histamine receptor antagonists, and cytoprotective agents are available for the treatment of peptic ulcer. However, most of these drugs produce several adverse reactions including toxicities and even may alter biochemical mechanisms of the body on chronic usage.^[8] Hence, herbal medicines are generally used in such cases when

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drugs are to be used for chronic periods. Several natural drugs have been reported to possess antiulcerogenic activity by virtue of their predominant effect on mucosal defensive factors.^[9,10] Peptic ulcers are illnesses that affect a considerable number of people in the world. Some of the causes of these disorders are stress, smoking, nutritional deficiencies, and ingestion of nonsteroidal anti-inflammatory drugs.^[11,12] The pathogenesis of gastroduodenal ulcers is influenced by various aggressive and defensive factors, such as acid-pepsin secretion, mucosal barrier, mucus secretion, blood flow, cellular regeneration, and endogenous protective agents (Prostaglandins and epidermal growth factor).^[13]

The *S. urticifolia* is found near the non-cultivated areas in the subtropical areas of Eastern Ghats of India. *S. urticifolia* is an upright, multi-stemmed herb which is woody at the base and grows up to 0.5–1.5 m tall. The *Stachytarpheta* word is derived from Greek, in which “stachys” means spike and “tarpys” means thick that refers to the thickened flower spike. The stems of *S. urticifolia* are 4-angled and are softly pubescent. The leaves are simple and opposite. The *S. urticifolia* is used as ethnomedicine by some traditional healers in Araku Valley of Eastern Ghats to treat sore skin wounds through the topical application, macerated leaves, and roots are used for treating inflammation as well as other diseases. Although *S. urticifolia* plant is used by the traditional healers in treating several diseases, no scientific reports are available to evaluate on phytochemical constituents and their efficacy. Hence, the present study was designed to determine antidiarrheal and antiulcer activity *S. urticifolia*.

MATERIALS AND METHODS

Plant Material and Preparation of Extract

The leaves of *S. urticifolia* were collected from the Damuku rai village of Araku Valley near Ananthagiri Mandal in Visakhapatnam District, Andhra Pradesh state, India. The plant was taxonomically identified and authenticated by Dr. P. Venkaiah, Professor of the Department of Botany, Andhra University, Visakhapatnam, Andhra Pradesh, India. The *S. urticifolia* plant samples were deposited in the herbarium, Department of Botany, Andhra University. The plant reference number assigned to *S. urticifolia* is 28083 is obtained from the department. The leaves were air-dried and then powdered. Lipids were removed through petroleum ether extraction by maceration method. It was then filtered and the filtrate discarded. The residue was successively extracted with methanol (99%) using a Soxhlet apparatus. The solvent was completely evaporated under reduced pressure and the dry extract dissolved in normal saline before further study.

Drugs and Chemicals

Castor oil (Qualikems Fine Chemicals Pvt. Ltd. New Delhi), loperamide were used for antidiarrheal activity test, aspirin,

ranitidine were purchased from Sigma-Aldrich Chemicals Co., (India) were used for antiulcer activity test.

Experimental Animals

All experiments were conducted using adult Wistar rats of both sexes and weighing about 180–200 g weight, at about 6–8 weeks of age. All animals were procured from Sainath enterprises, Hyderabad, India. The animals used in the current study were maintained at the animal facility center of GITAM deemed University, Visakhapatnam. The animals were housed in polyacrylic cages (38 cm × 23 cm × 10 cm) with not more than six animals per cage. The animals were maintained under standard conditions of humidity (60–65%), temperature (25 ± 2°C), and 12:12 light:dark cycles. The animals were then fed with the standard diet and were left to a free access to water. The animals were acclimatized for 7 days. The care and maintenance of the animals were carried out as per the standard guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), New Delhi. The study protocols were approved by the GITAM deemed University, Institutional Animal and Ethical Committee (IAEC). The IAEC approval number is GU/GIS/IAEC/2013/Protocol No.15/2013.

Acute Toxicity Study

Acute toxicity assay was performed in rats according to the OECD 425 guidelines and no lethality was found in any of the groups after treatment up to 2000 mg/kg.

Antidiarrheal Activity

Castor oil-induced diarrhea

The antidiarrheal activity was studied using animal models with the method employed by Adeyemi and Akinde and AOAC.^[14] The castor oil was employed in the study to induce diarrhea in Wistar rats as per the methodology mentioned.^[15] The study animals fasted for 18 h were brought to test room. Then, the rats were divided into four groups containing five animals in each group; diarrhea was induced by administering 1 mL of castor oil orally to each rat. Then, Group I rats received distilled water (1 mL/kg, p.o.) served as control. Group II received the standard drug, loperamide (3 mg/kg, p.o.). Then, Group III and Group IV have received the methanolic leaf extract of *Stachytarpheta urticifolia* (MESU) dose range of 100 and 200 mg/kg p.o., respectively. 1 h after, all the animals received castor oil (0.5 ml/kg p.o.).

Drug treatment schedule

Group I: Served as a control group (1 ml/kg p.o. distilled water)

Group II: Received standard drug, loperamide (3 mg/kg p.o.)

Group III: Treated with 100 mg/kg p.o. (MESU)

Group IV: Treated with 200 mg/kg p.o. (MESU)

Then, each animal was placed in an individual transparent cage and the floor of the cage was lined by blotting paper. The diarrheal is defined as an unformed and watery stool. Later, the floor lining was changed every hour. The consistency of the released fecal matter and both the wet and the dry diarrheal droppings were counted every hour for a period of 4 h to obtain the total number of excreted feces. Mean of the wet and dry stools excreted by the treated groups was compared with those of the control groups.

$$\% \text{ Inhibition of diarrhoea} = \frac{C - T}{C} \times 100$$

Where C= Mean weight of stool from control animals;
T= Mean weight of stool from drug or extract treated animals

Effect on castor oil-induced enteropooling

Intestinal fluid accumulation was determined by the method described by Yasmeen *et al.*^[16] The test animals (rats) were fasted for 12 h and divided into four groups of five animals each. The Group I received 10 ml/kg p.o. distilled water served as a negative control. Group II received loperamide (3 mg/kg p.o.) orally served as positive control. Groups III and IV received MESU of 100 and 200 mg/kg p.o. orally, respectively. 1 h after, all the rats received 1 ml of castor oil, and the animals sacrificed 1 h after administration of castor oil. The small intestine was separated and tied on both sides with thread and taken weight. The intestinal contents were milked into a graduated tube and their volumes were measured. The intestine was reweighed and the difference between full and empty intestines was calculated.

Drug treatment schedule

- Group I: Served as a control group (01 ml/kg p.o. distilled water)
- Group II: received standard drug, loperamide (3mg/kg p.o.)
- Group III: Treated with 100 mg/kg p.o. (MESU)
- Group IV: Treated with 200 mg/kg p.o. (MESU).

Aspirin-induced gastric ulcer

The Wistar rats of either sex weighing about 180–200 g were divided into four Groups (I, II, III, and IV) of six each. They were housed in standard conditions and maintained in 12 h light and dark cycle. They were fed with standard pellet diet and water was provided *ad libitum*. The Group I animals received distilled water (5 ml/kg p.o.) served as control and Group II animals received the standard drug, ranitidine (20 mg/kg p.o.) served as positive control group. Groups III and IV have received MESU 100 mg/kg p.o. and 200 mg/kg p.o. orally. Gastric ulcers were induced in rats by administration of aqueous suspension of aspirin (100 mg/kg p.o.) orally. The rats were fasted for 24 h with free access to water, the standard and test drugs were administered orally 30 min before the aspirin dose.

Drug treatment schedule

- Group I: Treated with distilled water + aspirin (100 mg/kg)
- Group II: Treated with ranitidine (20 mg/kg) (Std. drug) + aspirin (100 mg/kg)
- Group III: Treated with 100 mg/kg (MESU) + aspirin (100 mg/kg)
- Group IV: Treated with 200 mg/kg (MESU) + aspirin (100 mg/kg).

The animals were then sacrificed after 5 h of administration of aspirin and the stomachs of the rats were removed, and the gastric juice was collected into centrifuge tubes. The contents were subjected to centrifugation at 1000 rpm for 10 min, and the volume was noted. The supernatant is used for the determination of biochemical parameters. The pH of the gastric contents was measured by pH meter and considered as one of the parameters for antiulcer activity. Then, the gastric juice is subjected for analysis of total acidity by titrating with 0.01N NaOH, using phenolphthalein as an indicator and it was expressed as mEq/5 h.^[17]

The stomachs were opened along greater curvature then washed with normal saline, and the inner surface of the stomach is observed for ulceration as described,^[18] to determine and to calculate the ulcer index (U.I). Each stomach was examined for gastric erosions under a dissecting microscope with ×10 magnification. The ulcers were scored as shown in Table 1. Mean score in each test group was calculated and used for the determination of U.I.^[19,20]

Ulcer index = 10/x, where “x” is total mucosal area/total ulcerated area.

$$\% \text{ Inhibition} = \frac{C - T}{C} \times 100$$

Where C= ulcer index in control group, T= ulcer index in treated group

Statistical Analysis

All experiments in the study were repeated thrice and the results were expressed as mean ± standard error of the mean. The statistical analysis of the obtained data was done

Table 1: Rating scale for ulcer diameter^[21]

Observations on opened stomach diameter)	Ulcer score
Normal colored stomach	0
Red coloration	0.5
Spot ulcers	1.0
Hemorrhagic streaks ≤ 1 mm	1.5
Ulcers ≥ 3 ≤ 5 mm	2.0
Ulcers > 5 mm	3.0

using one-way analysis of variance with a level of statistical significance considered as $P < 0.05$.

RESULTS

Castor Oil-induced Diarrhea (Antidiarrheal Activity)

After administration of castor oil, all the rats in the control groups produced copious diarrhea. The MESU on oral administration at doses of 100 and 200 mg/kg to rat reduced in a dose-dependent manner the frequency of feces as well as the wet weight of fecal droppings when compared with untreated control significantly ($P < 0.05$). The observed experimental results are presented in Table 2.

Diarrhea is considered as altered motility and accumulation of fluid within the intestinal tract. The antidiarrheal agents reduce the gastrointestinal motility or reduce the secretions. The acute toxicity study results have illustrated that the MESU administration to rats is found to be safe up to 2000 mg/kg as per the OECD guidelines 425. As no significant clinical sign like changes in the skin, eyes, mucous membranes, fur were observed in experimental (Wistar) rat. The reason might be due to the nontoxic nature of *S. urticifolia* leaf extract as rat have fully tolerated and has neither the water nor the food intake was reduced during the study period. Further, it was observed that no mortality has occurred in any of the groups with all the dosages.

Based on the observed results at doses of 100 and 200 mg/kg, the extract of *S. urticifolia* has significantly reduced ($P < 0.05$) the number of total feces produced on the castor oil administration. The standard drug loperamide (3 mg/kg p.o.) and the 100 and 200 mg/kg doses of the extract produced a reduction frequency of fecal droppings and wet weight of feces [Table 2]. However, the standard drug produced a better result. This could be due to the crude nature of the plant extract as further fractionation may produce a better effect. The results showed that 100 mg/kg p.o. dose of MESU extract produced 35.26% inhibition of diarrhea, whereas, 200 mg/kg, p.o. dose produced 67.63% inhibition in diarrhea. Hence, the methanolic extract of *S. urticifolia* at 200 mg/kg dose level has significantly ($P < 0.05$) reduced the extent of diarrhea when compared to the control.

Castor Oil-induced Enter Pooling

Castor oil oral administration (1 ml, p.o.) has produced a marked and significant ($P < 0.05$) increase in the intestinal fluid volume and intestinal content in control group of rats when compared animals treated with normal water only.

Compared with the control group of rats, pre-treated with MESU at the doses of 100 mg/kg, p.o. and 200 mg/kg, p.o. dose-dependently and significantly ($P < 0.05$) inhibited the castor oil induced enteropooling in test rats [Table 3]. The standard drug loperamide (3 mg/kg p.o.) and the 100 and 200 mg/kg doses of the extract produced a reduction in intestinal weight and fluid

Table 2: Effect of *Stachytarpheta urticifolia* methanolic leaf extract on castor oil-induced diarrhea

Groups	Treatment	Dose (mg/kg)	Mean total number of diarrheal feces	Mean wet weight of feces after 4h (g)	Percent Inhibition of diarrhea
I	Control	Water (1ml/kg)	2.9±0.88 ^a	1.73±0.43 ^a	-
II	Loperamide	3	0.6±0.32 ^b	0.39±0.28 ^b	77.46*
III	MESU	100	1.85±0.48 ^c	1.12±0.62 ^c	35.26*
IV	MESU	200	0.96±0.68 ^{ab}	0.56±0.68 ^{ab}	67.63*

Results are expressed as mean±SEM; $n=5$. Data were analyzed by one-way ANOVA followed by Tukey's honest difference analysis.

*Significantly different when compared to control $P < 0.05$. Means within columns followed by the same letter are not significantly different at $P=0.05$ (Tukey's honest significant difference). SEM: Standard error of mean, MESU: Methanolic leaf extract of *Stachytarpheta urticifolia*, ANOVA: Analysis of variance

Table 3: Effect of *Stachytarpheta urticifolia* methanolic leaf extract on castor oil-induced enteropooling in rat (mean±SEM)

Groups	Treatment	(Dose mg/kg)	Volume of fluid (ml)	Weight of intestinal content (g)	% inhibition
I	Control	Water (1 ml/kg)	1.85±0.76 ^{ab}	2.48±0.48 ^a	-
II	Loperamide	3 mg/kg p.o	0.78±0.88 ^a	0.72±0.22 ^{ab}	70.96*
III	MESU	100 mg/kg p.o.	0.98±0.32 ^c	1.26±0.68 ^c	49.19*
IV	MESU	200 mg/kg p.o.	1.68±0.28 ^{ab}	0.82±0.58 ^{ab}	66.94*

Results are expressed as mean±SEM; $n=5$. Data were analyzed by one-way ANOVA followed by Tukey's honest difference analysis.

*Significantly different when compared to control $P < 0.05$. Means within columns followed by the same letter are not significantly different at $P=0.05$ (Tukey's honest significant difference). MESU: Methanolic leaf extract of *Stachytarpheta urticifolia*, ANOVA: Analysis of variance, SEM: Standard error of mean

Table 4: Antiulcer activity of *Stachytarpheta urticifolia* methanolic leaf extract on aspirin-induced ulcer in rat

Groups	Treatment	Dose (mg/kg)	Volume (ml/100 g) of gastric juice	Acid output (mEq/100 g)	pH of gastric juice	Ulcer index	% ulcer inhibition
I	Ulcer control (aspirin)	100	2.22±0.05 ^a	530±5.43 ^a	1.31±0.48 ^c	7.25±1.25 ^a	-
II	Ranitidine (standard)	20	1.32±0.16 ^b	350±4.55 ^b	4.55±0.72 ^a	1.76±0.34 ^c	75.72*
III	MESU	100	1.57±0.22 ^{ab}	392±3.64 ^c	2.83±2.83 ^{ab}	3.63±0.63 ^{ab}	49.93*
IV	MESU	200	1.38±0.36 ^b	355±4.68 ^b	3.68±1.28 ^b	2.84±0.84 ^b	60.83*

Results are expressed as mean±SEM; n=6. Data were analyzed by one-way ANOVA followed by Tukey's honest difference analysis.

*Significantly different when compared to control $P < 0.05$ means within columns followed by the same letter are not significantly different at $P = 0.05$ (Tukey's honest significant difference). MESU: Methanolic leaf extract of *Stachytarpheta urticifolia*, ANOVA: Analysis of variance, SEM: Standard error of mean

volume [Table 3]. However, the standard drug produced a better result. This could be due to the crude nature of the plant extract as further fractionation may produce a better effect. The results showed that 100 mg/kg p.o. dose of MESU extract produced 49.16% inhibition of volume of intestinal content (enteropooling), whereas, 200 mg/kg, p.o. dose produced 66.94% inhibition in intestinal content (enteropooling), respectively. Hence, the methanolic extract of *S. urticifolia* at 200 mg/kg dose level has significantly reduced the extent of the enteropooling with ($P < 0.05$) compared to the control.

Antiulcer Activity

Aspirin-induced gastric ulcers in animals showed extensive lesions that were restricted to glandular portions of the stomach as compared to control rats ($P < 0.05$), whereas oral administration of MESU lowered the U.I in Group III and Group IV [Table 4]. MESU also showed antiulcer activity by reducing the volume of gastric juice and acid output significantly ($P < 0.05$).

When compared with the control group of rats, pre-treated with MESU at the doses of 100 mg/kg, p.o. and 200 mg/kg, p.o. dose-dependently and significantly ($P < 0.05$) inhibited the volume of gastric juice, acid output, and U.I [Table 4]. There was also a significant ($P < 0.05$) increase in pH of gastric content in the presence of MESU when compared with the control. The standard drug ranitidine (20 mg/kg, p.o.) and the 100 and 200 mg/kg doses of the extract produced a significant reduction in U.I, volume gastric juice, and acid output [Table 4]. However, the standard drug produced a better result. This could be due to the crude nature of the plant extract as further fractionation may produce a better effect. The results showed that standard drug, ranitidine (20 mg/kg, p.o.) produced 75.72% inhibition and MESU extract at 100 mg/kg p.o. dose produced 49.93% inhibition of ulcer, whereas 200 mg/kg, p.o. dose produced 60.83% inhibition of ulcer, respectively. Hence, the methanolic extract of *S. urticifolia* at 200 mg/kg dose level has significantly reduced ulcer formation when ($P < 0.05$) compared to the control.

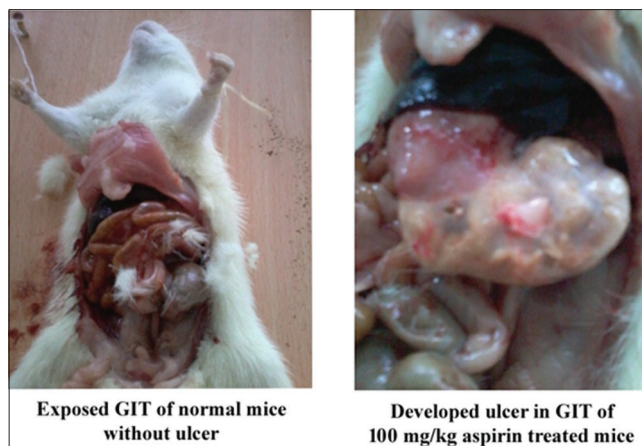


Figure 1: Effect of aspirin on induction of ulcers in Wistar rats

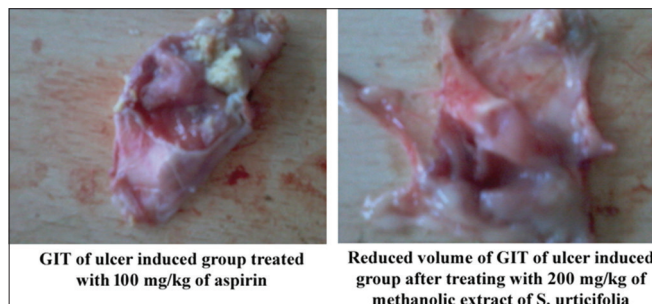


Figure 2: Antiulcer activity of the methanolic leaf extract of *Stachytarpheta urticifolia* on aspirin-induced ulcer rats

The experimental results illustrate that the methanolic extract efficiently reduces the U.I at 200 mg/kg with inhibition of 60.83% compared to the ulcer induced group. The observed result was further confirmed by the physical observation of the gastrointestinal tract (GIT) of the ulcer induced group and the GIT of the rat treated with 200 mg/kg shown in Figure 1. Figure 2 illustrates and confirms that the methanolic extract treatment *S. urticifolia* at a dose of 200 mg/kg has significantly reduced the volume of the GITs. The Group II treated with ranitidine standard drug has significantly inhibited the U.I with 75.72% of inhibition of ulcer. However, the results of standard drug ranitidine of Group II cannot be compared with Group IV as the ranitidine is the most effective and widely used antiulcer drug (Ray and Thokchom, 2006).

DISCUSSION

From the results of the current study, it is clear that the methanolic leaf extracts of *S. urticifolia* (MESU) have significant antidiarrheal and antiulcer activity in animal models. Diarrhea and gastric ulcers have long been identified as the most important problems in developing countries and are responsible for many deaths. Nearly 60–80% of populations in developing countries depend on traditional medicines for their primary health-care requirement.^[22] As there is growing interest among the public about traditional/natural medicines, researches have screened many plants and reported to be useful in treating and preventing diarrhea and gastric ulcers.

Antidiarrheal and Enteropooling Activities

Diarrhea is highly prevalent in developing and tropical countries, which is a cause of 4–5 million deaths worldwide every year.^[23,24] Diarrhea is the most common disease and highly prevalent in developing and tropical countries, which is a cause of 4–5 million deaths worldwide every year. Along with the modern allopathic treatment, the use of plant-based drugs has become common in the treatment of diarrheal diseases in Asian countries. There are a number of reports on medicinal plants possessing antidiarrheal activity^[25] and they are used in traditional therapeutics. The plants that are used in the treatment of diarrhea are: *Rumex maritimus*^[26] *Cylicodiscus gabaunensis*^[27] *Byrsocarpus coccineus*,^[28] *Calotropis procera*,^[29] *Vinaca major*,^[30] *Rauwolfia serpentina*,^[31] and others. The current study was taken up to substantiate the scientific rationale behind the use of *S. urticifolia* leaf extract in the treatment of diarrhea by the local tribal doctors.

The antidiarrheal activity of the MESU was evaluated by castor oil-induced diarrhea and enteropooling methods. The results of the current study showed that the MESU in castor oil-induced diarrhea and enteropooling at 100 and 200 mg/kg body weight doses significantly lowered several biochemical parameters of diarrhea by producing a statistically significant lowering in the severity and number of diarrhea in rats. Castor oil is known to have active compound ricinoleic acid responsible for induction of diarrhea in animals. *S. urticifolia* leaf methanolic extract at 100 and 200 mg/kg body weight significantly reduced the intestinal content of the rat in the enteropooling study. However, the antidiarrheal potential of the aqueous plant extract was not comparable to the loperamide (standard drug), which is one of the most effectively used antidiarrheal drug. Thus, the significant inhibition of diarrhea induced by castor oil using leaf extract of *S. urticifolia* suggests that the plant extract can be used as a preventive agent for relief from diarrhea.

The results indicated that MESU possesses a significant antidiarrheal activity by inhibiting frequency of defecation and reduced greatly the weight of fecal excretions. These

findings provide scientific evidence for the local utilization of the plant extract in treatment diarrheal diseases.

Antiulcer Activity

Gastric ulcer is a common disorder of modern living that is changed food habits and high amount stress, which leads to an imbalance of factors associated in gastric secretions such as mucosal blood flow, prostaglandins, cell membrane recognition, and hormones are considered as major mechanisms. Along with the allopathic drugs there are also many plants possess antiulcer activity such as *Buchanania lanzan*,^[32] *Ficus religiosa*,^[33] *Careya arborrea*,^[34] *Abutilon indicum*,^[35] *Encholirium spectabile*,^[36] *Biswellia serrate*,^[37] *Cissus quadrangularis*,^[38] and others. Reduction of U.Is similarly, several methanolic plant extracts were experimentally reported to possess potent antiulcer activity in rats.^[39,40]

The results of the current investigation showed that crude MESU is an effective antiulcer agent. The protections might be due to the activation of antioxidant systems and involvement of the nitric oxide synthase pathway and prostaglandins. Aspirin has been known to reduce the pH of gastric juices^[41] aspirin produces severe gastric hemorrhagic lesions. It has not been noticed to increase the gastric acid and pepsin but significantly decreases the gastric acid output. This is due to inhibition of mucosal blood flow, back diffusion of HCl through the broken barrier, acute inflammation.^[41,42] MESU showed significant antiulcer activity by decreasing the ulcer lesions and an increased pH in gastric content.

In the histological study, animals pretreated with MESU found to be effective in preserving the functional architecture of cells and the entire gastric mucosa. It is also showed regeneration of gastric mucosa in the damaged regions. There also many reports published on the traditional use of herbal based drugs in the treatment of gastric ulcers. The present study was to understand and substantiate the scientific rationale behind the traditional use of *S. urticifolia* leaf in the treatment of gastric ulcers.

Although there many reports on the plants possessing antiulcer activity in support of the current study, the mechanism of ulcer prevention by MESU is not clear, phytochemicals such as flavonoids, triterpenoids, glycosides, saponins, tannins, and amino acids present in the extract might play an important role.^[43] From the current study, it is clear that *S. urticifolia* methanolic leaf extracts have significant antidiarrheal and antiulcer activities in animal models.

CONCLUSION

Based on the results of antidiarrhoeal and antiulcer activities of the *S. urticifolia*, it was understood that the MESU is rich in potent active principles which are able to inhibit the diarrhea and gastric ulcer effectively in rats. More work is needed

for an understanding of the hidden mechanism of action for such significant nature of the active principle involved in the management diarrhea and ulcer disorders.

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REFERENCES

- Guerrant R, Van Gilder T, Steiner T, Thielman NM, Slutsker L, Tauxe RV. Practice guidelines for the management of infectious diarrhea. *Clin Infect Dis* 2001;32:331-51.
- Shoba FG, Thomas M. Study of antidiarrhoeal activity of four medicinal plants in castor-oil induced diarrhoea. *J Ethnopharmacol* 2001;76:73-6.
- Maikere-Faniyo R, Van Puyvelde L, Mutwewingabo A, Habiaryemye FX. Study of rwandese medicinal plants used in the treatment of diarrhoea I. *J Ethnopharmacol* 1989;26:101-9.
- Ammon HV, Thomas PJ, Phillips SF. Effects of oleic and ricinoleic acids on net jejunal water and electrolyte movement. Perfusion studies in man. *J Clin Invest* 1974;53:374-9.
- Lutterodt GD. Inhibition of gastrointestinal release of acetylcholine by quercetin as a possible mode of action of *Psidium guajava* leaf extracts in the treatment of acute diarrhoeal disease. *J Ethnopharmacol* 1989;25:235-47.
- Falk GW. Disease of the stomach and duodenum. In: Andreoli Cecil Essentials of Medicine. 5th ed. Edinburgh: WB. Saunders Company; 2001. p. 334-43.
- Tripathi KD. Gastrointestinal drugs: Drugs for peptic ulcers. In: Essentials of Medical Pharmacology. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd.; 1999. p. 628-42.
- Ariyphisi I, Toshiharu A, Sugimura F, Abe M, Matsuo Y, Honda T. Recurrence during maintenance therapy with histamineH2 receptors antagonist in cases of gastric ulcers. *Nikon Univ J Med* 1986;28:69-74.
- Sairam K, Rao CV, Goel RK. Effect of *Centella asiatica* Linn on physical and chemical factors induced gastric ulceration and secretion in rats. *Indian J Exp Biol* 2001;39:137-42.
- Sairam K, Rao CV, Goel RK. Effect of *Convolvulus pluricaulis* chois on gastric ulceration and secretion in rats. *Indian J Exp Biol* 2001;39:350-4.
- Nash J, Lambert L, Deakin M. Histamine H2-receptor antagonists in peptic ulcer disease. Evidence for a prophylactic use. *Drugs* 1994;47:862-71.
- Basil MD, Howard MS. Clinical gastroenterology. In: Companion Handbook. 4th ed. USA: McGraw-Hill; 1995.
- Jafri MA, Farah H, Javed K, Singh S. Evaluation of the gastric antiulcerogenic effect of large cardamom (fruits of *Amomum subulatum* Roxb). *J Ethnopharmacol* 2001;75:89-94.
- Adeyemi OO, Akindele AJ. Antidiarrhoeal activity of the ethyl acetate extract of *Baphia nitida* (Papilionaceae). *J Ethnopharmacol* 2008;116:407-12.
- Association of official Analytical Chemists. Official Methods of Analysis. 11th ed. Washington DC: Association of official Analytical Chemists; 1984/1975. p. 236-48.
- Galvez J, Zarzuelo A, Crespo ME, Lorente MD, Ocete MA, Jiménez J, *et al.* Antidiarrhoeic activity of *Euphorbia hirta* extract and isolation of an active flavonoid constituent. *Planta Med* 1993;59:333-6.
- Yasmeen M, Prabhu B, Agashikar NV. Evaluation of the antidiarrhoeal activity of the leaves of *Ixora coccinea* Linn. In rat. *J Clin Diagn Res* 2010;4:3298-303.
- Szabo S, Trier JS, Brown A, Schnoor J, Homan HD, Bradford JC, *et al.* A quantitative method for assessing the extent of experimental gastric erosions and ulcers. *J Pharmacol Methods* 1985;13:59-66.
- Patil PH, Surana SJ. Gastroprotective effect of *Eranthemum roseum* R. Br. Linn root extracts in albino rats. *Int J Pharmacol Biol Sci* 2009;3:81-93.
- Paunikar G, Kadam P, Dongare S, Nakkawar M, Sutar R, Tarte P. *Ficus arnottiana* leaf extract offer anti-ulcer ac-tivity against absolute ethanol induced gastric ulcer in rats. *Int J Pharmacol Biol Sci* 2009;3:161-6.
- Ray DK, Thokchom IS. Antidiarrhoeal, hypoglycaemic and hepatoprotective activities of ethyl acetate extract of *Acacia catechu* wild, in albino rats. *Indian J Pharmacol* 2006;38:408-13.
- Antwi S, Martey ON, Donkor K, Okine, LK. Antidiarrhoeal activity of *Blighia sapida* (Sapindaceae) in rats and mice. *J Pharmacol Toxicol* 2009;4:117-25.
- Snyder JD, Merson MH. The magnitude of the global problem of acute diarrhoeal disease: A review of active surveillance data. *Bull World Health Organ* 1982;60:605-13.
- Abdullahi AL, Agho MO, Amos S, Gamaniel KS, Wambebe C. Antidiarrhoeal activity of the aqueous extract of *Terminalia avicennooides* roots. *Phyther Res* 2001;15:431-4.
- Chopra RN, Nayar SL, Chopra IC. Glossary of Indian Medicinal Plants. New Delhi: Council of Scientific and Industrial Research; 1956. p. 276-8.
- Rouf AS, Islam MS, Rahman MT. Evaluation of antidiarrhoeal activity *Rumex maritimus* root. *J Ethnopharmacol* 2003;84:307-10.
- Kouitcheu ML, Panlap BV, Kouam J, Ngadjui BT, Fomum ZT, Etoa FX. Evaluation of antidiarrheal activity of the stem bark of *Cylicodiscus gabaunensis* (mimosaceae). *Afr J Biotechnol* 2006;5:1062-6.

28. Akindede AJ, Adeyemi OO. Evaluation of the antidiarrhoeal activity of *Byrsocarpus coccineus*. *J Ethnopharmacol* 2006;108:20-5.
29. Kumar S, Dewan S, Sangraula H, Kumar VL. Anti-diarrhoeal activity of the latex of *Calotropis procera*. *J Ethnopharmacol* 2001;76:115-8.
30. Rajput MS, Nair V, Chauhan A. Evaluation of antidiarrheal activity of aerial parts of *Vinca major* in experimental animals. *Middle East J Sci Res* 2011;7:784-8.
31. Ezeigbo II, Ezeja MI, Madubuike KG, Ifenkwe DC, Ukwani IA, Udeh NE, *et al.* Antidiarrhoeal activity of leaf methanolic extract of *Rauwolfia serpentina*. *Asian Pac J Trop Biomed* 2012;2:430-2.
32. Devendra K, Surendra P, Kartik CP. Antiulcer activity of ethanolic extract of *Buchanania lanzan* Spreng. *Roots. Ann Biol Res* 2010;1:234-9.
33. Gregory M, Vithalrao KP, Franklin G, Kalaichelavan V. Antiulcer (ulcer-preventive) activity of *Ficus arnottiana* Miq (Moraceae) leaf methanolic extract. *Am J Pharm Toxicol* 2009;4:89-93.
34. Kamal K, Mruthunjaya K, Satish K, Rajendran M. Anti ulcer activity of ethanol extract of the stem bark of *Careya arborea* Roxb. *Int Curr Pharm J* 2013;2:78-82.
35. Dashputre NL, Naikwade NS. Evaluation of anti-ulcer activity of methanolic extract of *Abutilon indicum* Linn. Leaves in experimental rats. *Int J Pharm Sci Drug Res* 2011;3:97-100.
36. de Carvalho KI, Fernandes HB, Machado FD, Oliveira IS, Oliveira FA, Nunes PH, *et al.* Antiulcer activity of ethanolic extract of *Encholirium spectabile* Mart. Ex Schult and Schult f. (Bromeliaceae) in rodents. *Biol Res* 2010;43:459-65.
37. Khaja Z, Lakshmi NM, Abid M, Ibrahim M. Evaluation of antiulcer activity of *Boswellia serrata* bark extracts using aspirin induced ulcer model in albino rats. *J Med Allied Sci* 2011;1:14-20.
38. Jainu M, Vijai Mohan K, Shyamala Devi CS. Gastroprotective effect of *Cissus quadrangularis* extract in rats with experimentally induced ulcer. *Indian J Med Res* 2006;123:799-806.
39. Vinohapoochan G, Sundar K. Anti-ulcer activity of *Mimosa pudica* leaves against gastric ulcer in rats. *Res J Pharm Biol Chem Sci* 2010;1:606-14.
40. Shah JS, Patel JR. Anti-ulcer activity of lucer against experimentally induced gastric ulcers in rats. *Ayu* 2012;33:314-6.
41. Sanyal AK, Mitra PK, Goel RK. A modified method to estimate dissolved mucosubstances in gastric juice. *Indian J Exp Biol* 1983;21:78-80.
42. Akhtar MS, Munir M. Evaluation of the gastric antiulcerogenic effects of *Solanum nigrum*, *Brassica oleracea* and *Ocimum basilicum* in rats. *J Ethnopharmacol* 1989;27:163-76.
43. Bandyopadhyay RM, Charles PA, Shahbaz T, Wagner RM. Infrared photometric variability of GX 13+1 and GX 17+2. *Astrophys J* 2002;570:793.

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