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Evaluation of anti-ulcer activity of Stachytrapheta jamaicensis leaf extract

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ABSTRACT

Many herbal remedies have been employed in various medical systems for treatment and management of different diseases. The plant *Stachytrapheta jamaicensis*. has been used in different system of traditional medication for the treatment of diseases and ailments of human beings. The review reveals that wide ranges of phytochemical constituents have been isolated from the plant like flavanoids, tannins, phytosterols, phenol, glycosides, fatty acids, galacto-glycerolipid and volatile oil. The leaves contain flavonoids. It is rich source of essential fatty acids like palmitic acid, oleic, linoleic, linolenic and stearic acids. It has been reported that the plant contains anti-inflammatory, anxiolytic, anticonvulsant, antifungal, antinociceptive, anticancer, antidiabetic, hepatoprotective, hypolipedemic, abortificient, antimicrobial and wound healing properties.

INTRODUCTION

Herbal cure for gastrointestinal diseases involves use of herbal supplements for relief of gastrointestinal symptoms and to improve physiologic function of the gastrointestinal tract (GIT).The gastrointestinal disorders include a wide spectrum of disorders that range in importance from simple discomfort to life-threatening disease and include peptic ulcer disease (PUD), dyspepsia, gastro esophageal reflux disease (GERD), constipation, diarrhoea, upper gastrointestinal bleeding, etc. It is noted that most of the upper GI disorders are acid related diseases in which gastric acid play an important role in their development, progression and treatment. The relationship between anxiety and peptic ulcer disease (PUD) has received significant consideration in clinical and research settings over the past few decades. Earlier data from clinical and community-based study have shown that PUDoccurs more frequently than would be expected among persons with anxiety and depressive disorders and have provided evidence of a relationship between anxiety and increased rates of lower gastrointestinal problems though the mechanism of these relations remains unknown .The present study is initiated to evaluate anti-ulcer activity studies of in experimental animals [1-5].

Stachytrapheta jamaicensis is an erect and branched half-woody plant, with stem slightly angled. The leaves are elliptic to oblong-ovate and 2 to 10cm long. The leaf tips are pointed with toothed margins. The leaf base is decurrent on the petiole [6-10].

The spikes are terminal, rather slender, 10-30cm long, 3-4mm thick, green and continuous. The calyx is small, oblique and 4-toothed. The corolla is deep-blue or blue-purple, 1cm long. The fruit is enclosed in the calyx and oppressed to and somewhat sunk in the rachis which is smooth, oblong and about 4mm long [11-15].

Plant anatomy has been found to be very essential in plant taxonomy. The purpose is to develop a system of classifying plants in a way that all the differences and similarities are set out in ordered manner [16-20].

The decision to choice epidermal characters to carryout studies in plants was informed by earlier declaration that these characters represented genetic variations and have been used to solve taxonomic problems in certain plant groups by Taxonomists

The leaf epidermal features observed in all the fourteen species of Cucurbitaceae were enough taxonomic characters which could be implored to support hitherto external morphological characters used to classify plants in this family. In addition, based on epidermal features, some members of the family Cucurbitaceae can readily be distinguished from one another. Leaf epidermis and the leaf cross-sectional anatomy provide extensive taxonomic data and the literature on this subject is now vast.

Collection of Plant & Preparation of the extract

The plant *stachytrapheta jamaicensis* was collected from Coimbatore, Tamilnadu. The plant was identified and authenticated by Botanical Survey of India, Tamilnadu Agricultural University Campus (TNAU), and Coimbatore, India. The voucher specimen (BSI/SRC/5/23/2019/Tech-7) has been deposited in the herbarium of TNAU for future reference. After due authentication, the total aerial parts were collected from mature plants at the same place and cleaned thoroughly to remove adherent materials under running tap water. The cleaned materials were subsequently dried under shade. The shade dried aerial parts were powdered in an electrical grinder and get coarse powder for further study.

Preparation of extract

The aqueous extract of leaf .The powdered materials were defatted using *stachytrapheta jamaicensis* petroleum ether as solvent. The defatted powdered plant material (1000 g) was refluxed with 2000 ml of distilled water for 48h followed by filtration and the filtrate was concentrated under vacuum. A dark brown sticky residue was obtained

Animals

Male albino rats, (150-200 g) and albino mice (20-25 g) were used in the present study. All the rats were kept at room temperature (24 °C ± 2) in the animal house. All the animals were housed and treated as per the internationally accepted ethical guidelines for the care of laboratory animals. Prior to the experiments, rats were fed with standard food and were acclimatized to laboratory conditions. All the experimental procedures were performed on animals after approval from the ethics committee and in accordance with the recommendations for the proper care and use of laboratory animals

EXPERIMENTAL PROCEDURE

Ethanol-induced ulcer

The over-night fasted rats were divided into four groups of six rats each are used for the study. All the groups of rats were given treatments as follows by oral route: group 1 received 1ml/kg of 1% CMC (control group), group 2 received 100 mg/kg sucralfate, group 3 received 250mg/kg, and group 4 received500 mg/kg of *S.JAMAICENSIS*. Thirty minutes after, ulcers were induced by administering 1 ml 99% ethanol to each rat. One hour later all the rats were anaesthetized. The stomach were excised, cut along the greater curvature and smoothly rinsed under tap water the stomachs were stretched on a corkboard and magnifying glass (X10 magnification) used to spot and count the ulcers. Mean ulcer score for each animal will be expressed as ulcer index, Percentage inhibition of ulceration was calculated as below:

$$UI = \frac{\text{mean ulcer index(control group)} - \text{mean ulcer index(test group)}}{\text{mean ulcer index(control group)}} \times 100$$

Pyloric ligation induced ulcers

In this procedure, animals are grouped in to four containing six each. The group 1 was considered as normal control (vehicle) and were treated with 1% Carboxy methyl cellulose (% 1CMC, 1ml/kg), p. o., and group 2 is treated with Omeprazole (10mg/kg, p.o), where as groups 3 and 4 animals are treated with plant extract. at the dose of 250 mg/kg, p.o.

respectively daily for 3 days. Animals were fasted overnight earlier to start of the experiment and water .Pyloric ligation was applied by ligating the pyloric end of the stomach of each animal on 3rd day under phenobarbital anesthesia a dose of 35 mg/kg b.w. After 30 min of plant extract .Omeprazole treatment. Animals were allowed to recover and stabilize in separate cage and were deprived of water during postoperative method.

After 4 h of surgery, rats were sacrificed and the stomach was isolated, then gastric juice was collected for evaluating gastric secretion study and scoring of ulcer. The gastric juice that was collected and centrifuged. The volume and pH was noted and subjected to bio-chemical estimations like free acidity and total acidity total proteins total hexoses fucose activity of the gastric juice were calculated.

The stomachs were opened along the greater curvature, rinsed with saline to eliminate gastric contents and blood clots and examined by a 10X magnifier lens to measure the formation of ulcers. The numbers of ulcers were counted. The following table indicate Ulcer Score and Descriptive Observation.

0	Normal coloured stomach
0.5	Red colouration
1	Spot ulceration
1.5	Haemorrhagic streak
2	Ulcers≥3 but ≤5mm.
3	Ulcers>5mm

Mean ulcer score for each animal will be expressed as ulcer index. The percentage of ulcer protection was determined as follows:
Ulcer index (UI) was measured by using following formula (Gerhard Vogel H., 2002);

$$\mathbf{U_I = U_N + U_S + U_P \times 10^{-1}}$$

Where,

U_I= Ulcer Index; U_N = Average number of ulcers per animal; U_S = Average number of severity score; U_P = Percentage of animals with ulcers

Percentage inhibition of ulceration was calculated as below (Hojage M.G *et al.*, 2010)

$$\text{UI} = \frac{\text{mean ulcer index(control group)} - \text{mean ulcer index(test group)}}{\text{mean ulcer index(control group)}} \times 100$$

BIO-CHEMICAL ESTIMATIONS

Gastric Volume

The gastric juice was collected and poured into the measuring cylinder.

Determination of pH

The pH of the gastric juice was collected and measured using the pH meter.

Determination of Free Acidity and Total Acidity

1ml of gastric juice was pipetted into a 100 ml conical flask, added 2-3 drops of Topfer's reagent (dimethyl amino-azo-benzene 1% in absolute ethanol) and titrated with 0.01 N NaOH until all traces of the red colour disappears and the colour of solution was yellowish orange. The volume of alkali added was noted. The volume corresponds to free acidity. Then 2-3 drops of phenolphthalein solution were added to it and titration was sustained until a definite red tinge reappears. The total volume of alkali added was again noted. The volume corresponds to total acidity (Hawk *et al*.1947). Acidity was calculated by using the formula (Raju. D *et al.*, 2009);

$$Acidity = \frac{\text{Volume of NaOH} \times \text{Actual normality} \times 100}{0.1} \times \mu\text{eq /L/100 g}$$

NSAID induced ulcers

Four groups of Wistar Albino rats (n=6) were selected and divided them to four groups of six each. In this model, Group 1 served as Normal control (vehicle) received 1% CMC, p. o., and Group 2 Ranitidine (10mg/kg, p.o), whereas Groups 3 and 4 animals received aqueous extract of aerial parts of *Passifloraedulis*Sims.(250 and 500 mg/kg, p.o. respectively) daily for 3 days. Animal were fasted overnight prior to start of the experiment, and water .On day 3, after 30 min of extract or Omeprazole treatment, rats were immobilized in a stress cage and were placed at 4–6^0C in an environmental cage. The animals were sacrificed 2 h later and ulcer index was calculated following the method as described earlier

Ethanol-induced ulcer

The over-night fasted rats were divided into four groups of six rats each are used for the study. All the groups of rats were given treatments as follows by oral route: group 1 received 1ml/kg of 1% CMC (control group), group 2 received 100 mg/kg sucralfate, group 3 received 250mg/kg, and group 4 received 500 mg/kg of *S.JAMAICENSIS*. Thirty minutes after, ulcers were induced by administering 1 ml 99% ethanol to each rat. One hour later all the rats were anaesthetized. The stomach were excised, cut along the greater curvature and smoothly rinsed under tap water (Ukwe *et al*., 2010). The stomachs were stretched on a corkboard and magnifying glass (X10 magnification) used to spot and count the ulcers. Mean ulcer score for each animal will be expressed as ulcer index, Percentage inhibition of ulceration was calculated as below:

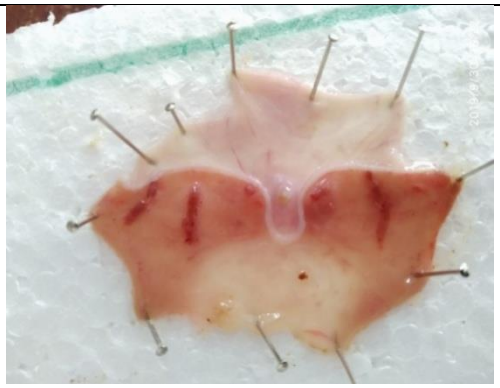
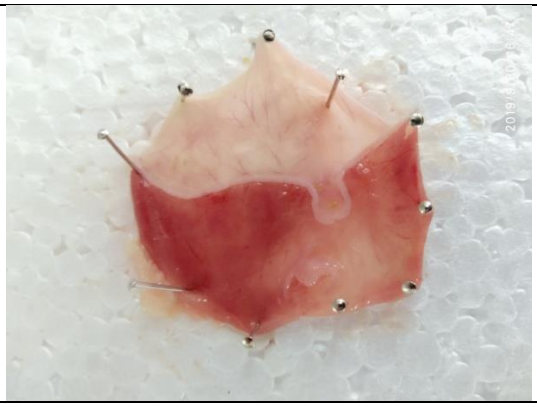
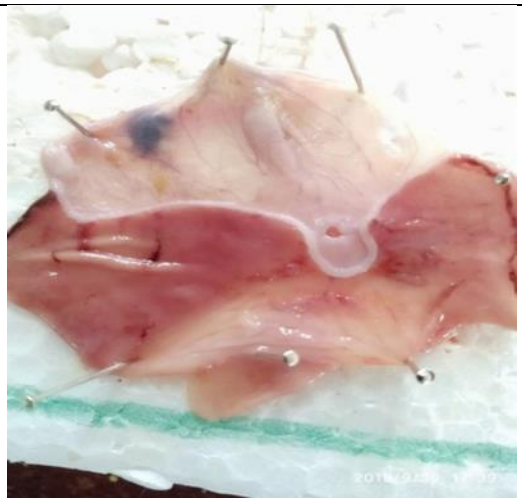
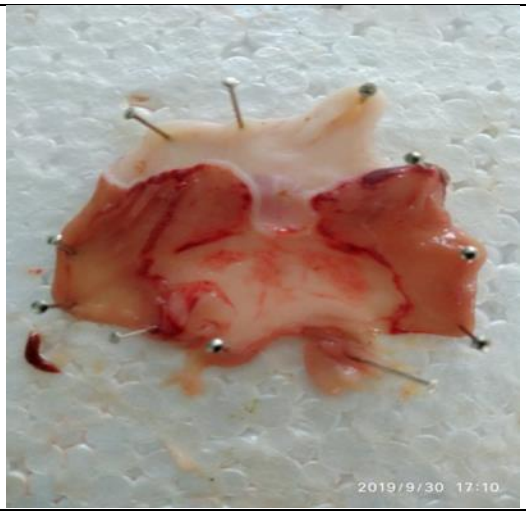
$$UI = \frac{\text{mean ulcer index(control group)} - \text{mean ulcer index(test group)}}{\text{mean ulcer index(control group)}} \times 100$$

Effect of *stachytrapheta jamancinsis*.on Ethanol Induced Ulcer Model Indicating Ulcer index & Percentage Ulcer Protection

S.No.	Treatment	Ulcer index	% ulcer protection
1	Solvent control (1% CMC-1ml/kg)	22.34±0.57	_
2	Sucralfate (100mg/kg)	4.21±0.40**	81.15
3	*s.jamancinsi* extract1 (250 mg/kg)	11.12±0.32**	50.22
4	*s.jamancinsi* extract2 (500 mg/kg)	6.69±0.41**	70.85

(Results are mean± S.E.M; (n = 5) Statistical comparison was performed by using ANOVA followed by Dunnet't' test. * P < 0.05, **P < 0.01, ***P < 0.001 were consider statistically significant when compared to control group.)

Photographs showing the effect of *stachytrapheta jamancinsis* on the enaphetol induced Ulcer Model

Ethanol induced-control (1% CMC 1ml/kg)	**Ethanol induced-standard (sucralfate100mg/kg)**
	
Ethanol induced S.JAMAICENSIS, (250mg/kg)	**Ethanol induced S.JAMAICENSIS, (500mg/kg)**
	

Pylorus ligation model

Plate No.1. Photographs showing the effect of aqueous extract of aerial parts of on the Ulcer induction by ethanol 90% Rat Model.

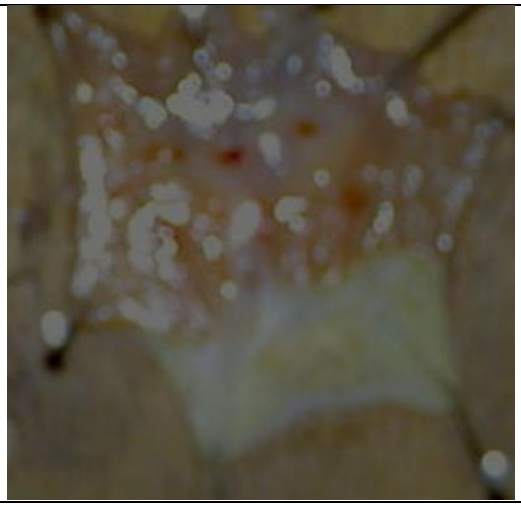
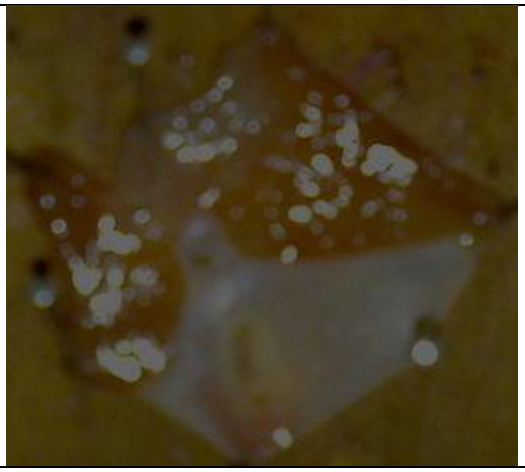
Pylorus ligation:-Control (1%CMC 1 ml/kg)	**Pylorus ligation:-sucralfate10mg/kg)**
	
Pylorus ligation:- S.Jamancensis.(250mg/kg)	**Pylorusligation:- S.jamancinsi .(500mg/kg)**
	

Table.1 Effect of *Stachytarpheta jamaicensis*.onPylorus Ligated (Shay) Rat Model Indicating Ulcer index & Percentage Ulcer Protection.

S.No.	Treatment	Ulcer index	% ulcer protection
1	Solvent control (1% CMC 1ml/kg)	16.78±0.75	_
2	Omeprazole(10mg/kg)	1.68±0.14**	89.99
3	Extract of S. JAMAICENSIS. (250mg/kg)	4.56±0.13**	72.91
4	Extract of S. JAMAICENSIS. (500mg/kg)	3.43±0.09**	79.56

(Results are mean± S.E.M; (n = 5) Statistical comparison was performed by using ANOVA followed by Dunnet't' test. * P < 0.05, **P < 0.01, ***P < 0.001 were consider statistically significant when compared to control group.)

The antiulcer activity of *Stachytarpheta jamaicensis*. was carried out by pylorus ligation induced ulcer model (Table 1). *Stachytarpheta jamaicensis*. showed a significant dose dependent antiulcer effect at the dose of 250 mg/kg and 500

mg/kg (p.o) with an ulcer index of (4.56± 0.13),(3.43±0.09) and % ulcer protection (72.91),(79.56) respectively. This shows the decrease in ulcer index and increase in % of ulcer protection. It was compared with the standard drug Omeprazole.

Effect of *Stachytarpheta jamaicensis*.on Pylorus ligation Rat model indicating biochemical parameters

Sl.No.	Treatment	Gastric volume(ml)	pH	Free acidity (µeq/ml/100g)	Total Acidity (µeq/ml/100g)
1	Solvent control (1% CMC 1ml/kg)	6.55±0.51	2.63 ±0.19	42.80 ±3.01	73.47 ±2.42
2	Omeprazole (10mg/kg)	2.35 ±0.24**	4.65 ±0.29*	18.27± 1.71**	21.88± 1.41**
3	*S. JAMAICENSIS* (250mg/kg)	3.47 ±0.19**	3.50 ±0.19**	26.43± 1.10**	53.51 ±1.57**
4	*S. JAMAICENSIS* (500mg/kg)	2.65 ±0.24**	4.15 ±0.22**	23.18 ±1.49**	31.38± 2.72**

(Results are mean± S.E.M; (n = 5) Statistical comparison was performed by using ANOVA followed by Dunnet't' test. * P < 0.05, **P < 0.01, ***P < 0.001 were consider statistically significant when compared to control group)

The result of gastric volume determination of .treated groups indic *s.jamancinsi* ates that there is a significant dose dependent decrease in the volume of the gastric juice. The activity was compared with standard drug Omeprazole (p< 0.01).

The result of gastric pH determination of .treated groups indi *s.jamancinsi* cates that there is significant dose dependent increase in the pH of the gastric juice. The activity was compared with standard drug Omeprazole (p<0.01).

The result free acidity and total acidity estimation of gastric juice of treated groups indicate that *s.jamancinsi* there is a significance and dose dependent decrease in both free acidity and the total acidity. It was compared with standard drug omeprazole (p<0.01).

Effect of *Stachytarpheta jamaicensis*.on Pylorus ligation Rat model indicating biochemical parameters

Sl.No.	Treatment	Gastric volume(ml)	pH	Free acidity (µeq/ml/100g)	Total Acidity (µeq/ml/100g)
1	Solvent control (1% CMC 1ml/kg)	6.55±0.51	2.63 ±0.19	42.80 ±3.01	73.47 ±2.42
2	Omeprazole (10mg/kg)	2.35 ±0.24**	4.65 ±0.29*	18.27± 1.71**	21.88± 1.41**
3	*S. JAMAICENSIS* (250mg/kg)	3.47 ±0.19**	3.50 ±0.19**	26.43± 1.10**	53.51 ±1.57**
4	*S. JAMAICENSIS* (500mg/kg)	2.65 ±0.24**	4.15 ±0.22**	23.18 ±1.49**	31.38± 2.72**

(Results are mean± S.E.M; (n = 5) Statistical comparison was performed by using ANOVA followed by Dunnet't' test. * P < 0.05, **P < 0.01, ***P < 0.001 were consider statistically significant when compared to control group)

The result of gastric volume determination of .treated groups indic *s.jamancinsi* ates that there is a significant dose dependent decrease in the volume of the gastric juice. The activity was compared with standard drug Omeprazole (p< 0.01).

The result of gastric pH determination of .treated groups indi *s.jamancinsi* cates that there is significant dose dependent increase in the pH of the gastric juice. The activity was compared with standard drug Omeprazole (p<0.01).

The result free acidity and total acidity estimation of gastric juice of treated groups indicate that *s.jamancinsi* there is a significance and dose dependent decrease in both free acidity and the total acidity. It was compared with standard drug omeprazole (p<0.01).

NSAID induced model

Plate No.2 .Photographs showing the effect of *S. jamancinsis* .on the cold restraint induced Ulcer Model

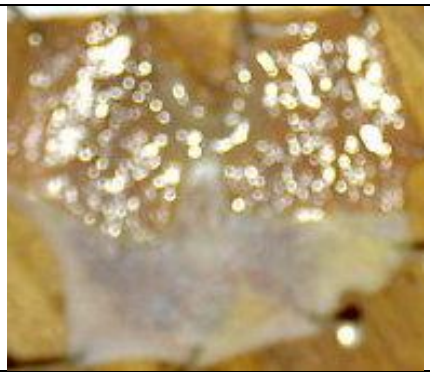
NSAID-control (1%CMC 1ml/kg)	NSAID-RANIDIDINE(10mg/kg)
	
NSAID model-s.jamancinsis(250mg/kg)	**NSAIDmodel- s.jamancinsis(500mg/kg)**
	

Table 5. Effect of *S. jamancinsis*.on Cold restraint Induced Ulcer Model Indicating Ulcer index & Percentage Ulcer Protection

SL.No.	Treatment	Ulcer index	% ulcer protection
1	Solvent control(1%CMC-1ml/kg)	20.38±1.04	_
2	ranitidine(10mg/kg)	2.67±0.41**	86.90
3	*S.JAMAICINSIS*.(250mg/kg)	6.46±0.25**	68.30
4	S.JAMAICINSIS.(500mg/kg)	3.80±0.29**	81.35

(Results are mean± S.E.M; (n = 5) Statistical comparison was performed by using ANOVA followed by Dunnet't' test. * P < 0.05, **P < 0.01, ***P < 0.001 were consider statistically significant when compared to control group.)

DISCUSSION

The present study was aimed to evaluate antiulcer, activity studies of ethanol extract of aerial parts of *Stachytrapheta jamaicensis* by using laboratory animals. The plant has been traditionally consumed by some Okinawan elders either as a beverage or used as a medicinal herb by the folks to treat diabetes, dizziness, high blood pressure, and neuralgia. Several studies have been performed on the composition of *Stachytrapheta jamaicensis* Phytochemical analysis was performed and confirmed the presence of carbohydrate, glycosides, sterols, flavonoids and triterpenes. The important constituents isolated in the previous study were apigenin, luteolin, rutin, genistein, hesperidin, astragalin, isoquercitrin, and chrysin Herbal cure for gastrointestinal diseases involves

use of herbal supplements for relief of gastrointestinal symptoms and to improve physiologic function of the gastrointestinal tract (GIT).

The reason of gastric ulceration by pyloric ligation are assumed to be due to stress induced increase in the level gastric hydrochloric acid secretion and/or stasis of acid, and the volume of secretion is also a chief factor in the development of ulcer due to exposure of the unprotected lumen of the stomach to the accumulating acid .It is reported that pylorus ligation induced ulcers are due to auto digestion of the gastric mucosa and breakdown of the gastric mucosal barrier. These factors are related with the progress of upper gastrointestinal damages such as lesions, ulcers and life threatening perforation and haemorrhage. Gastric wall mucus, an essential component of which is hexosamines, is thought key role as a defensive factor against gastrointestinal damage.

Chronic use of NSAIDs including low-dose aspirin is associated with gastrointestinal mucosal injury. However, major adverse events are relatively infrequent. Patients with multiple risk factors such as a previous history of peptic ulcer disease, increasing age, co-prescription of corticosteroids and anticoagulants, and high-dose and long-term use of NSAIDs are at the highest risk of major gastrointestinal toxicity. In patients with multiple risk factors, physicians need to assess these risks before prescribing NSAIDs and adopt risk-minimising strategies.

Simple measures such as using the lowest dose for short periods of time when possible will prevent some of the NSAID-related toxicity. Selective COX-2 inhibitors also will reduce gastrointestinal adverse events when compared to non-selective NSAIDs. Proton pump inhibitor therapy is efficacious and has an acceptable adverse effect profile in comparison with misoprostol.

Before prescribing an NSAID, prophylactic proton pump inhibitor therapy needs to be offered to patients with a past history of peptic ulcer disease and those on dual antiplatelet therapy or anticoagulant therapy.

CONCLUSION

From the above results we can concluded that the aqueous extract of aerial parts of *Stachytarpheta jamaicensis.* possesses significant antiulcer, anxiolytic and antidiarrhoeal activity .

Chemical substances derived from plants have been used to treat human diseases since the dawn of medicine. Roughly 50% of new chemical entities introduced during the past two decades are from natural products. Therefore, efforts should be directed towards isolation and characterization of the active principles and elucidation of the relationship between structure and activity. Furthermore, detailed analysis of the active constituents of natural drugs should be directed towards clinical relevance.

Further research is required to isolate the active phytoconstituents present in the extract and experimentation on the healing action of drug on chronic ulcer as well as on the possible side effects. The investigation on mode of action may pave way for establishment of new anti-ulcer therapy regimen.

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