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GASTRO PROTECTIVE ACTIVITY OF AQUEOUS ROOT EXTRACT OF TRAGIA INVOLUCRATA BY PYLORIC LIGATION METHOD

Divya C. V.*

Reserch Scholar, JJTU, Jhunjunu, Rajasthan.

***Corresponding Author: Divya C. V.**
Reserch Scholar, JJTU, Jhunjunu, Rajasthan.

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ABSTRACT
In folk medicine, Tragia involucrata L (Euphorbiaceae) is used to treat stomach problems such as gastric ulcers and acidity. Gastric ulcer is one of the diseases that affect a huge population all over the world. Stress, smoking, dietary deficits, infections, and indiscriminate use of nonsteroidal anti-inflammatory medications are all etiological factors for this condition. The Tragia involucrta has been reported for the constituents including flavonoids, alkaloids, carbohydrates, 2-methylnanone, rutin, protein, vinyl hexylether, shellsol, tannins, sterols, saponins, 2,4-dimethyl hexane, and 2,6-dimethyl heptane ,stigmasterol, and quercetin. The goal of this study aimed for whether the aqueous extract of Tragia involucrata roots had any gastroprotective properties. The roots of tragia involucrata L. was made available from the rural market of Malabar, Kerala. The roots were dried, powdered and extracted with water to get aqueous extract of Tragia involucrata. Here induction of Gastric ulcer was experimentally produced by ligation of pylorus, and the aqueous extract of Tragia involucrata (AETI) roots was evaluated at doses of 200 and 400 mg/kg body weight orally. Gastric output volume, ulcer index , free acidity, total acidity, mucus content, pH and were used to evaluate anti-ulcer efficacy. The AETI was considerably reduced gastric ulceration at doses of 200 and 400 mg/kg.

KEYWORDS: Tragia involucrata, Gastroprotective, anti-ulcer, Pyloric ligation.

INTRODUCTION
Vegetable consumption can reduce the incidence and death rates of a variety of illnesses, including cancer, cardiovascular disease, and cerebrovascular disease.[1] This might be due to the antioxidants found in vegetables.[2] Due to the appearance of many undesirable effects from the usage of traditional medications for a range of diseases, medicinal plants are also regarded as a vast reservoir of potentially new treatments. In many plants, phenolic chemicals make up a large percentage of the antioxidant activity.[3] Gastric ulcer is one of the diseases that affect a huge population all over the world. Stress, smoking, dietary deficits, infections, and indiscriminate use of nonsteroidal anti-inflammatory medications are all etiological factors for this condition (NSAID's)[4-5] Peptic ulcer illness has been a leading risk factor for morbidity and mortality for more than a century. The main techniques for treating peptic ulcer disease have been to reduce stomach acid production and to enhance gastric mucosal development. Lipid peroxidation and Reactive oxygen species accounts for the pathophysiology of gastric ulcers induced by ethanol, according to certain studies, and they destroy numerous biological molecules such as prostaglandins7-9. As a result, antioxidants and free radical scavengers may be useful in the treatment of stomach ulcers.[6-7]

Tragia involucrta L. belongs to family euphorbiaceae and they are useful in pruritic skin eruptions, giddiness, haemorrhoids, gastropathy, septicaemia, dipsia, vomiting, guinea worms and venereal diseases.[10] Different parts of the tragia have been used in Indian conventional therapy for treating pain, bronchitis and high fever. It reduces the elevated body temperature to normal by its diaphoretic action.[10] Pharmacological researches identifies that the roots of tragia have hepato-protective as well as antioxidant activity too.[11-12] The tragia involucrta has been reported for the constituents including flavonoids, alkaloids, carbohydrates, 2-methylnanone, rutin, protein, vinyl hexylether, shellsol, tannins, sterols, saponins, 2,4-dimethyl hexane, , and 2,6-dimethyl heptane ,stigmasterol, and quercetin.[13-15]

The goal of this investigation was to see if the aqueous extract of tragia roots had any gastroprotective properties using experimental gastric ulcer model of pylorus ligation-induced gastric lesion.

MATERIALS AND METHODS

Crude drug

Plant material the roots of tragia involucrata L. was made available from the rural market of Malabar, Kerala and identified by Dr. **S.Rajan,** field botanist, Survey of medicinal plant and collection unit, Central council for research in homeopathy, Department of AYUSH, Ministry of Health & Family Welfare, Government of India,Emerald, The Nilgiris,643209 who had identified, and authenticated the plant Tragia Involucrata family euphorbiacea.

Preparation of the aqueous extract

The dust free roots were allowed to dry under shade. The root powder is then sieved through a No.10 sieve to separate the coarse powder; which was selected for extraction, take this substance for extracting with double distilled water after charging in the Soxhlet extractor. filter and reduce the volume of extract under low pressure to get Tragia involucrata root Aqueous extract (AETI). Extracts obtained by this process are preserved in refrigerator for the further studies**.**

Animals

Wistar Albino rats of both sexes, averaging 150-200 g, are obtained from the animal house. They are brought from animal house facility of Cape Bio Lab & Research Centre, CSI Complex, Marthandam – 629 165, and are maintained in poly propylene cages meeting the standard animal house conditions and controlled environment. Food and water were provided *ad labitum*, except when the experimental protocols warrants abstinence from it. The entire study was verified and approved by Institutional Animal Ethical Committee of Cape Bio Lab & Research Centre, CSI Complex, Marthandam – 629165 constituted as per CPCSEA guidelines.

Every test was carefully planned to avoid coprophagy before it began. In each design, the animals are separated into three groups of six animals. Group I was the control group (vehicle treatment), Group II was the standard group (Ranitidine -150 mg/kg), and Group III was the test group (AETI 200 and 400 mg/kg).

Experimental procedure

The technique of pyloric ligation caused gastric ulceration was used, as described by Shay et al. One hour after therapy, the pylorus was ligated. The animals were killed four hours only after ligature, and their stomachs were excised. The juices of the stomach were recovered, centrifuged for 30 minutes at 3000 rpm, and the supernatant was quantified. The volume of the stomach, pH, free acidity, and total acidity were all calculated. The ulcer index and gastrointestinal mucus levels were calculated. A pH metre was used to titrate one millilitre of entire centrifuged stomach contents from each pylorus ligated rat against a 0.01 Normal solution of NaOH to determine hydrogen ion concentration.

The ulcer inhibition percentage was determined as follows

$$\% \text{ inhibition of ulcer} = \frac{(\text{Mean ulcer index of control} - \text{Mean ulcer index of test}) \times 100}{\text{Mean ulcer index of control}}$$

ANOVA was used for statistical analysis, followed by Dunnet's post hoc test, with significance of difference between treatments accepted at $P < 0.01$, $P < 0.05$ Data are expressed as Mean± SEM.

RESULTS

Gastric ulceration induced by Pylorus ligation

Table 1 shows the effects of gastric ulcers caused by pylorus ligation. At doses of 200 and 400 mg/kg, the AETI caused substantial dose-dependent reductions in stomach volume, with maximal percentages of inhibition of 24.22 and 60.45 percent, respectively. At doses of 200 and 400 mg/kg, the AETI increases the pH and mucus content of the stomach mucosa while decreasing free acidity, total acidity, and ulcer index in a dose-dependent manner.

Table 1: Effect of treatments on various parameters of pylorus ligated rat model.

Treatment	Gastric acid content (ml)	pH	Acidity (mEq/lt		Pepsin activity (Per ml/h)	Ulcer index	% Inhibition
Control	11.20 ± 0.55	3.92 ± 0.13	123.10 ± 1.51	98.10 ± 0.93	3.92 ± 0.12	4.85 ± 0.30	
AETI 200mg/kg	6.12 ± 0.43*	5.82 ± 0.23*	56.15 ± 1.88*	47.25 ± 0.45*	3.10 ± 0.26*	2.71 ± 0.16 *	47.70*
AETI 400 mg/kg	7.48 ± 0.27**	6.10 ± 0.12**	47.70 ± 0.83**	43.34 ± 0.52**	2.86 ± 0.33**	2.08 ± 0.63 **	65.10**
Ranitidine 150 mg/kg	8.60 ± 0.52**	6.45 ± 0.35**	39.50 ± 0.7**	39.20 ± 0.75**	2.60 ± 0.60**	1.95 ± 0.48 **	78.82**

Values are expressed as Mean ± SEM, n= 6, *p < 0.05 and ** p < 0.01 when compared with vehicle control group. (Statistically analysed by one-way ANOVA followed by Dunnet's t-test).

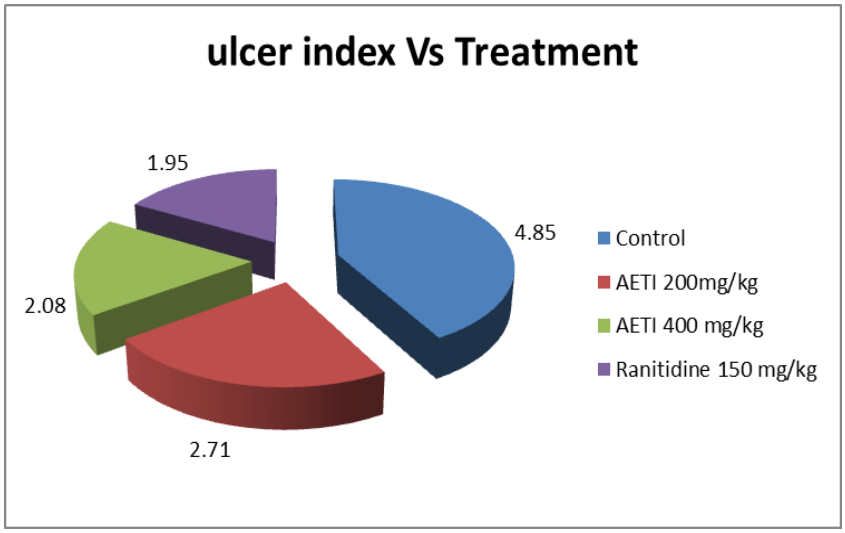

Fig. 1: Ulcer index Vs Treatment.

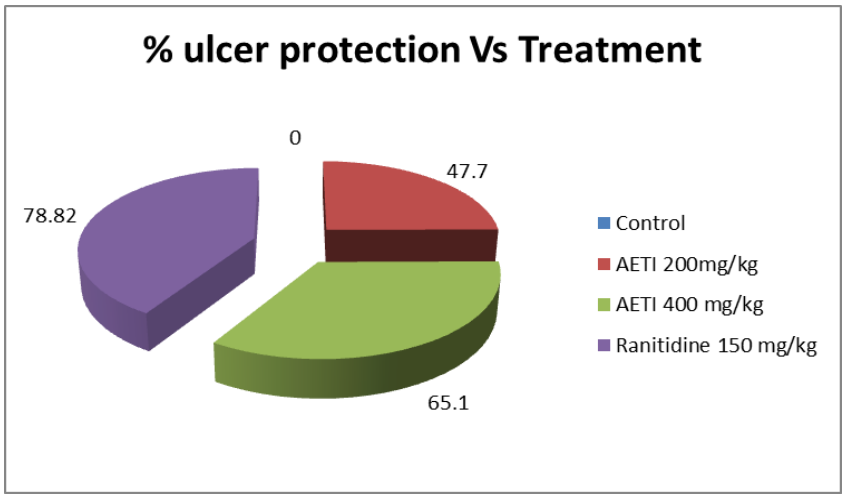

Fig. 2: % ulcer Protection Vs Treatment.

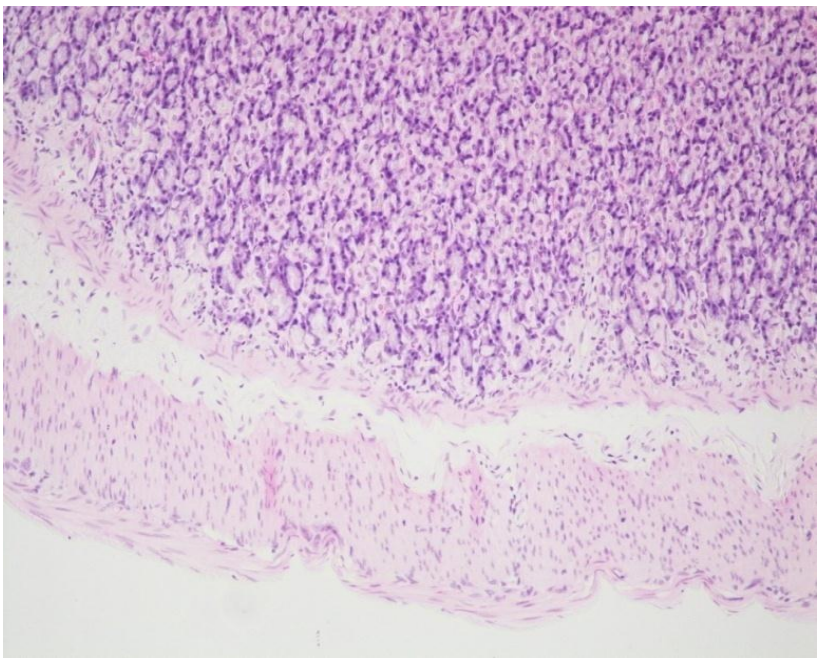

Fig. 3: Histopathology of the gastric mucosa of aqueous extract of Tragia involucrata 400 mg/kg treated group.

With more mucus globules, the surface epithelium is better protected. Few denuded simple columnar epithelial cells could be seen in the mucosa's superficial surface, gastric glands near the mucosa's basement membrane appeared to be normal, and blood vessels in the submucosa were congested in some regions.

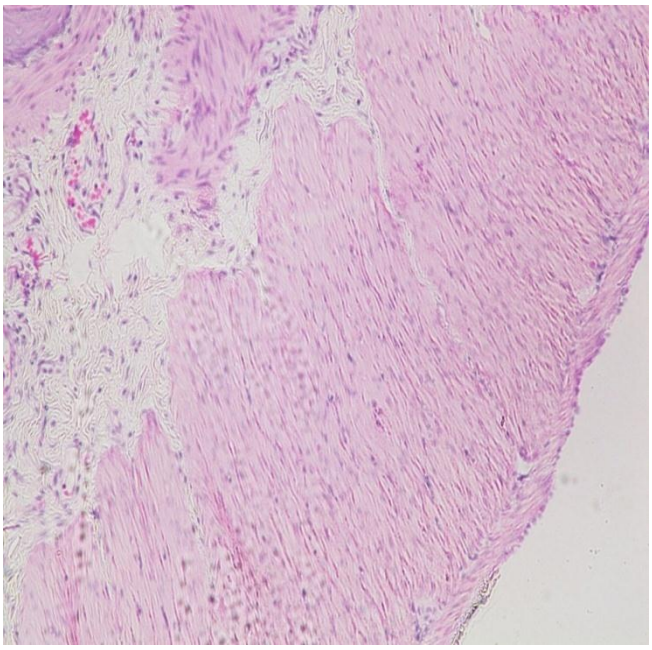

Fig. 4: Histopathology of gastric mucosa with Ranitidine (Standard drug) treated group.

There was modest degradation of superficial epithelium with denuded epithelial cells, mild hemorrhages with in lamina propria, and very few inflammatory cells. Gastric lesions are noticeably decreased, with normal mucosa cells infiltrating the area

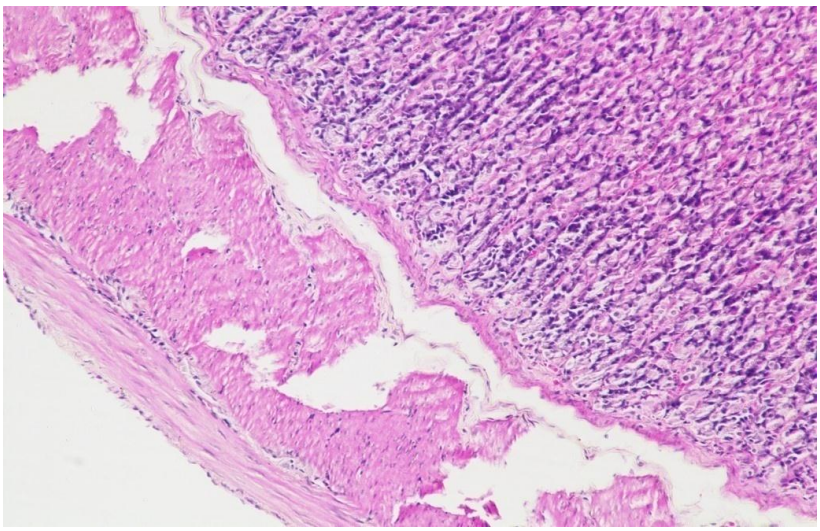

Fig. 5: Histopathology of gastric mucosa of Control group.

Histopathological investigations of gastric mucosa revealed erosion of the superficial epithelium, infiltrating mononuclear cells in the mucosa, bleeding in the lamina propria, degenerative modifications in gastric glands, blood vessel congestion, and gastric lesions.

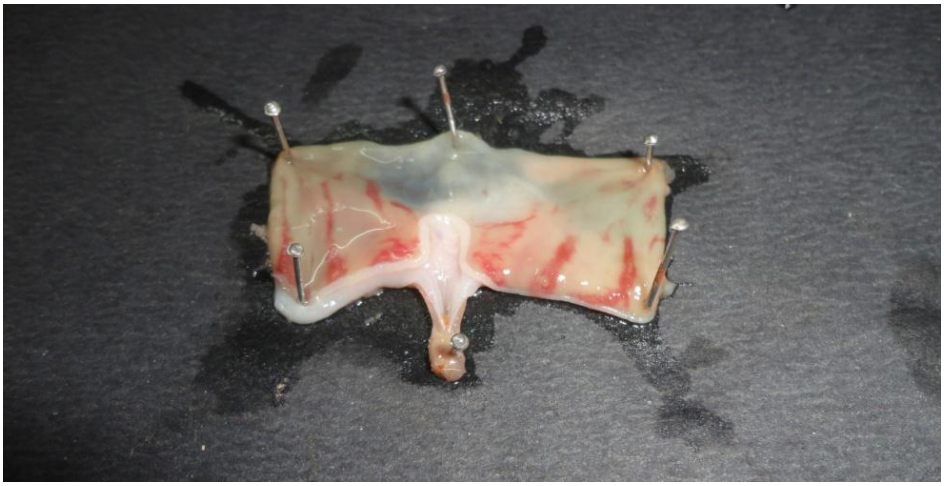

Fig. 6: Dissected stomach of rats after pylorus ligation (control).

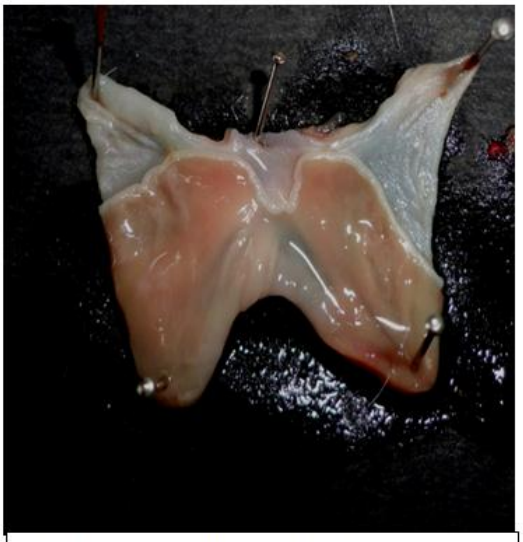

Fig. 7: Dissected stomach of rat treated with test drug AETI400mg/kg

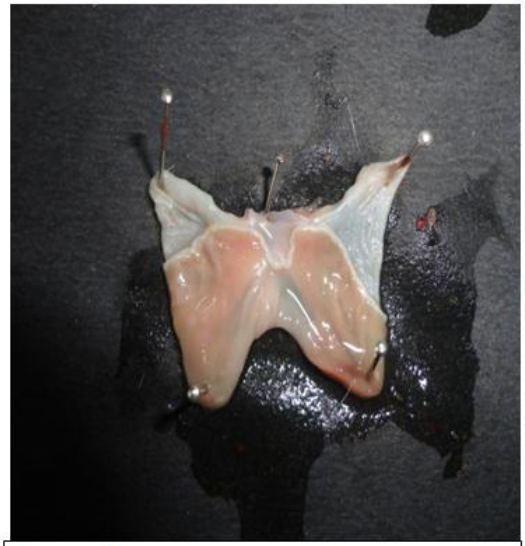

Fig. 8: Dissected stomach of rat treated with Standard drug ranitidine 150mg/kg

DISCUSSION

Stress, prolonged use of anti-inflammatory medications, and persistent alcohol use are all factors that can cause ulcers in humans. Although the cause of ulcers is unknown in the majority of instances, it is widely believed that they are caused by a conflict between aggressive forces and the endogenous defence mechanism's ability to maintain mucosal integrity.[17] Histamine H2-antagonists, proton pump inhibitors, anticholinergics, and antacids are among the various medications available to treat stomach ulcers. Gynecomastia, haematological abnormalities, acute interstitial nephritis, thrombocytopenia, anaphylactic responses, nephrotoxicity, and hepatotoxicity are all common side effects of this medications.[18-22] In 1980, the World Health Organization suggested that the efficacy of plants be evaluated in situations when there are no safe synthetic drugs.[23] As a result, most effective, minimal toxic, and less costly antiulcer agents are required. Medicinal herbs have been found to offer promising effects in treatment of stomach ulcers, making them one of the most appealing sources of novel therapeutic molecules.

The molecule for a successful peptic ulcer medication should primarily work by enhancing mucosal resistance or lowering aggressive factors on the gastrointestinal mucosa.[33] Pylorus ligation was used to inhibit secretory activity. Stress-induced increases in gastric hydrochloric acid output and/or acid stasis are thought to be the causes of stomach injury following pyloric ligation. The buildup of gastric acid and pepsin causes the stomach mucosa to self-digest.[5]

Many plants that contain flavonoids have been shown to have anti-ulcerogenic properties. Increased mucosal PG content, decreased histamine release from mast cells, suppression of acid secretion, and prevention of H. pylori development have all been postulated as mechanisms to explain their biological effects. Furthermore, flavonoids

are free radical scavengers that have been linked to ulcerative and erosive gastrointestinal tract lesions. Flavonoids have been found to have anti-ulcerogenic effects in a variety of plants. Increased mucosal PG content, reduced mast cell histamine release, acid secretion reduction, and H. pylori avoidance have all been proposed as methods to explain their biological benefits. Flavonoids are also free radical scavengers, which have been related to ulcerative and erosive gastrointestinal ulcers. As a result, the existence of antioxidants, flavonoids, and other bioactive substances in Tragia involucrta may be linked to the gastro protective action. Tragia involucrata contains antioxidants that may protect the stomach mucosa from free radical damage and may also have antiulcer properties.

CONCLUSION

Finally, the current study's findings revealed that Tragia involucrta roots extract possesses antiulcer and gastro protective properties. This backs up the traditional usage of Tragia involucrta roots for stomach ulcer therapy. Tragia involucrata roots might be a promising new treatment option for patients with stomach ulcers. However, elucidating the precise mechanism of action is difficult. As a result, more research is needed to understand the Tragia involucrta's anti-ulcer action.

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Conflict of interest

Nil.

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