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Gastric Antiulcer Activity of *Achyranthes aspera* L. Roots in Pylorus Ligated Rats

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Abstract: In the present work gastric antiulcer activity and *in-vitro* acid neutralizing capacity of methanol extract of *Achyranthes aspera* L (MEAA) root was studied. The study was done on female albino rats. Gastric ulcers were induced by Pyloric ligation. Ranitidine (10 mg/kg) was used as the standard drug for comparison. Treatment with MEAA extract in different doses significantly protected the ulceration induced by pyloric ligation models. MEAA at dose of 300 mg/kg showed 91.89% ulcer protection. Anti-secretoary studies in pyloric ligated rats revealed that MEAA extract (in three different doses) significantly reduced total acidity, but has no effect on gastric output Which indicates that MEAA possesses significant antiulcer activity due to its cytoprotective action. Chemical constituents of *Achyranthes aspera* L. like oleanolic acid and quercetin may be responsible for activity.

Key words: *Achyranthes Aspera* L. · Antiulcer Activity · Pyloric Ligation

INTRODUCTION

Gastritis and gastric ulcers are pathological conditions caused by an imbalance between aggressive factors, such as gastric acid, pepsin, stimulation of the vagus nerves, secretion of gastrin and increase in the number of parietal cells and protective factors, such as bicarbonate ion, mucus productivity, mucus secretion and prostaglandins [1]. To regain the balance, drugs of plant origin are investigated to inhibit the gastric acid secretion or to activate the mucosal defense mechanism by increasing mucus production [2].

A number of products have been used for the treatment of gastric ulcers such as antacids, proton pump inhibitors or antihistaminics, but most of these drugs produce several adverse reactions [3].

Achyranthes aspera Linn. (Family Amaranthaceae), commonly known Rough chaff tree in English, is an annual herb that grows throughout India [4]. In indigenous system of medicine, whole plant exploited for the treatment of renal dropsy, bronchial affections and leprosy [5]. Some pharmacological properties as diuretic, anti- inflammatory, antifungal, larvicidal, hypoglycemic, antifertility and anticancer were reported [6-11].Various chemical constituents oleanolic acid, quercetin and ecdysteron were isolated and structure elucidated by spectral studies [12, 13].

Literature survey revealed that chemical constituents like flavonoids and triterpenoids, are responsible for antiulcer activity[14-17] and these chemical constituents were reported in the methanolic extract of aerial parts of *Achyranthes aspera* L. [18, 19]. Based on this hypothesis, the aim of this study is to explore *Achyranthea aspera* L for antiulcer activity.

MATERIAL AND METHODS

Collection of Plant Material: Plant material was collected in the month of August from Makhamalabad region of Nashik district, Maharashtra, India. The plant material was taxonomically identified by the Botanical Survey of India, Pune and a voucher specimen VND-1 was retained in herbarium of BSI, Pune for future reference.

Preparation of Extract: Roots and leaves were separated and dried in shade and powdered. Dried powder of leaves and roots were extracted exhaustively with methanol in Soxhlet apparatus and extract was obtained and preserved in tightly closed container.

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Chemicals and Reagents: Diethyl ether, Chloroform, NaOH were purchased from Merck specialties Pvt.Ltd. Mumbai. Ranitidine (Zydus Healthcare, East Sikkim) was used as a standard in the study.

Animals: The experiments were performed on female Wistar albino rats (150–200 g). The animals were housed under standard environmental conditions (22±1°C and 85% relative humidity) on a 12-h light–12-h dark cycle and were given food and water *ad libitum* Before the experiments, they were deprived of food but allowed free access to water. Animal experimental studies were conducted according to the guidelines of institutional animal ethical committee and approval was obtained for the protocol designed.

Statistical Analysis: All data were analyzed by one ANOVA followed by Dunnett's test using primer software.

Experimental

***In vitro* Acid-Neutralizing Capacity USP:** The Acid-Neutralizing capacity was carried out as per USP29. In short, all tests were conducted at temperature 37±3°C. A pH meter was standardized using the 0.05M potassium biphthalate and 0.05M potassium tetraoxalate standardized buffers. Magnetic stirrer was used to produce stirring rate 300± 30rpm. 0.5 gm of methanol extract of *Achyranthes aspera* L roots and leaves were transferred to 250 ml beaker and 70 ml distilled water was added. It was mixed with magnetic stirrer for 1 min. Then 30 ml 1.0N HCl was added to the test solutions with continuous stirring for 15 min. Excess HCl was titrated with 0.5 N NaOH to attain a stable pH of 3.5. The number of mEq of acid consumed was calculated by formula:

$$\text{Total mEq (ANC)} = [30 \times N_{HCL}] - [V\text{NaOH} \times N_{NaOH}]$$

$N_{HCL=}$ Normality of HCL
$V_{naOH=}$ Normality of NaOH
$N_{naOH=}$ Normality of NaOH

The results were expressed as total mEq per gm of substance (USP).

Gastric Antiulcer Activity: Adult female Wistar albino rats weighing 150-250 g. were divided into five groups consisting of five animals each. Rats were fasted for 24 hrs. They were placed on wire mesh to avoid caprophagy [20]. One hr before pyloric ligation under light ether anesthesia, test or standard was administered orally. After 4 hrs of pyloric ligation all animals were sacrificed by over dose of chloroform. Stomach was removed and contents were centrifuged. The gastric contents were analyzed for hydrogen ion concentration by titration against 0.01N NaOH. Ulcer formed in gastric mucosa was measured and scored as described by Shey *et al*. [1].

Group I: Normal saline solution treated 10 ml/kg orally.
Group II: Ranitidine 10 mg/kg b. wt.
Group III: MEAA 100 mg/kg b.wt./ p.o.
Group IV: MEAA 200 mg/kg b.wt./ p.o.
Group V: MEAA 300 mg/kg b.wt./p.o.

RESULTS

The effect of methanol extract of *Achyranthes aspera* L. on pylorus ligated rats is presented in Tables 1 and 2. In-vitro acid neutralizing capacity showed that methanol extract of leaves does not possess antacid property but root extract showed antacid property with ANC of 1 mEq/gm. MEAA showed significant ($P<0.01$) antiulcer activity at all selected doses as compared to standard. MEAA showed 91.89% ulcer protection at dose of 300 mg/kg.

As shown in Figure 1, control animals had ulcers and haemorrhagic streaks, whereas in animals administered with the MEAA there was significant reduction in ulcer index ($P < 0.01$). Ulcer index was 0.6 for maximum dose i.e. 300 mg/kg at same dose MEAA significantly reduced total acidity but has no effect of gastric acid secretion.

DISCUSSION

Many products are available in the market for the treatment of gastric ulcers, including antacids, proton pump inhibitors, anticholinergics and histamine H_2-antagonists, most of these drugs produce several adverse reactions, such as gynecomastia, hematopoietic changes, acute interstitial nephritis [21], thrombocytopenia [22], anaphylaxis reactions [23], nephrotoxicity and hepatotoxicity [24]. Medicinal plants are amongst the most attractive sources of new drugs and shows promising results in treatment of gastric and duodenal ulcers [25].

The pylorus ligation induced ulcer model was used to study the effect of drugs on gastric secretion. The ligation of the pyloric end of the stomach causes accumulation of gastric acid in the stomach that produces ulcers. Agents that reduce secretion of gastric aggressive factors such as acid and pepsin (antisecretory) and/or increase secretion mucin (cytoprotective) are effective in reducing development of gastric ulcers in this model [1].

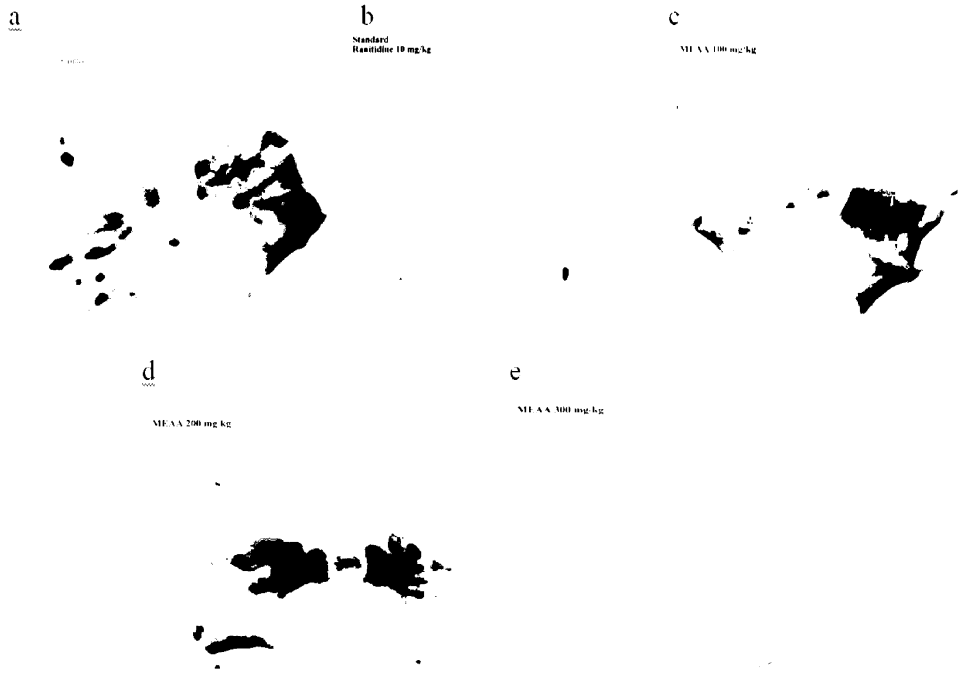

Fig. 1(a-e): Photographs of stomach showing ulcer
a: Control, b: Ranitidine 10mg/kg, c: MEAA 100mg/kg, d: MEAA 200mg/kg e: MEAA 300mg/kg

Table 1. Antiulcer activity of Methanol extract of *Achyranthes aspera* L.

Sr No	Group	Dose mg/kg p.o.	Volume of stomach content	ml of NaOH Required	Acidity *mEq/l*/100kg	Ulcer index	%Ulcer protection
1	Control	10 ml/kg p.o.	4.38±0.49	10.98±1.11	164.7±16.69	7.4±0.82	000
2	Standard	10	2.22*±0.25	4.24*±0.52	66*±9.09	2*±0.77	72.97
3	MEAA 100	100	4.22±0.37	10.98±0.54	164.7±8.11	2.1*±0.18	71.62
4	MEAA 200	200	4.34±0.44	5.26*±0.36	78.9*±5.48	4.3*±0.24	41.89
5	MEAA 300	300	4.14±0.20	6.28*±1.00	94.2 *±15.09	0.6*±0.24	91.89

All values are expressed as mean±SEM of 5 animals in each group. *P<0.01 compared with control group.

Table 2: *In vitro* acid neutralizing capacity

Sr no	Sample	ANC/gm
1	ME of Roots	1
2	Distilled water	0

In the present study, antiulcer activity of methanol extract of *Achyranthes aspera* L. was studied by using pyloric ligation model of ulcer in rats. Results showed that MEAA at dose of 300 mg/kg shows maximum ulcer protection as compared to control group as shown in fig 1. At lower dose MEAA do not show significant decrease in gastric acidity but at higher doses it showed decrease in gastric acidity as shown in Table 1. MEAA do not have any effect on gastric acid secretion as compared to control group. This findings suggests that MEAA may have cytoprotective action and not antisecretory action. *In vitro* studies:

Quercetin and oleanolic acid are reported to have antiulcer activity and both these compounds are present in I *Achyranthes aspera* L. so these compounds may be responsible for antiulcer activity of MEAA.

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