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## Effect of *Andrographis echinoides* (L) Nees Whole Plant Extracts as an Antiulcer and Antioxidant Agent

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### ABSTRACT

Peptic Ulcer Disease is a major complication among 10% of the human population. Management of this disease is a global issue and can be achieved by multiple therapies. Though this disease is treated with antibiotics, proton pump inhibitors, h2 blockers, antacids, and cytoprotective agents, which creates lots of side effects and microorganisms developed drug resistance. *Andrographis echinoides* is an herb traditionally and still in villages used for the treatment of various ailments. Antiulcer activity of this plant's whole part was done by making use of ethanol-induced experimental animals. SOD, GPx, GSH, CAT, and MDA were assessed using standard textual methods. Aqueous and ethanolic extracts of whole parts of this plant revealed 69.1 – 83% ulcer protection and restored the levels of gastric volume, gastric acidity, and gastric pH. Levels of antioxidant enzymes were also restored in control animals and omeprazole-treated animal groups. Phytochemicals like flavonoids, tannins, and phenolic compounds are essential in controlling ulceration and the free radical scavenging power of the plant materials and are confirmed as antioxidant and antiulcer agents.

**Key words:** *Andrographis echinoides*, Antiulcer study, Antioxidant assay, Whole plant, AEWPAE, AEWPEE

Peptic ulcers are among the most important complications affecting about 10% of the population. It is caused by an imbalance between the aggressive and the defensive factors, free radicals, and environmental factors [1]. The overuse of drugs like aspirin and corticosteroids can also be a probable cause. *Helicobacter pylori* can cause peptic ulcer, which is acquired from an unhygienic environment [2]. Metabolic disturbances and activities of *Helicobacter pylori* are the major factors, which cause peptic ulcers and may also lead to cancer. Eradication of *Helicobacter pylori* and treatment of peptic ulcers has become a global challenge. Multiple therapeutic agents like proton pump inhibitors, H<sub>2</sub> blockers, antacids, cytoprotective agents, and antibiotics like clarithromycin, tetracycline, amoxicillin, Levofloxacin, and metronidazole are used for the management of peptic ulcer [3-5]. Though these drugs can manage up to 90% of the cases of peptic ulcers, they cause various side effects like headache, abdominal discomfort, and inhibition of gastrin release affecting the uptake of certain vitamins, especially vitamin B<sub>12</sub>. Suppression of acid secretion may lead to overgrowth of gastroenteritis causing pathogens. Hence people from the

villages rely on the phytomedicine from the medicinal plants. Medicinal plants act as anti-inflammatory, antioxidant, antiproliferative, and antimicrobial agents [6-9]. *Andrographis echinoides* is an herb widely available in semi-dry places of India and Srilanka [9-10]. The whole plant is used for the treatment of microbial infections, to control hair fall to control hair color change, to heal wounds [10-11], used in goiter and liver problems [11], fertility problems [12-13], acts as an anti-inflammatory [13], antioxidant [9] and anti-ulcer agent [13]. The prime aim of this study is to assess this plant whole parts as an anti-ulcer agent.

### MATERIALS AND METHODS

#### Experimental animals

Wister Albino rats weighing 200-220 g were utilized for the study. They were maintained in the animal house, which is equipped with polypropylene cages that are exposed to both light and dark cycles. The diet consisted of standard pellets with water being provided when needed. Permission and approval for animal studies were obtained from the Srimad Andavan Arts and Science College, Trichy with code SAC/045/20/US/10.

#### Plant material collection and identification

The fresh whole plant of *Andrographis echinoides* was collected in October 2019 from the campus of M. R. Government Arts College, Mannargudi, Thiruvavur district, Tamil Nadu, India. Taxonomic identification was established

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by Dr. Rabinat Herbarium, St. Joseph's College, Tiruchirappalli, and the voucher specimen was deposited in the Department of Microbiology, M. R. Government Arts College, Mannargudi.

#### Preparation of plant extract

Extract from the dried whole plant of *Andrographis echinoides* was prepared using ethanol (AEWPPE) and water (AEWPWE) by cold extraction method. A break of 72 hours was allowed for the air drying of the residue. An air-tight container maintained at was used to store the dry residue [14].

#### Antiulcer study

Gastric lesions were induced according to the method described by Mahmood *et al.* [15]. Animals were randomly divided into five groups of 6 rats each. Group I rats served as the normal control; received saline only, Group II rats were served as the disease control, Group III animals received AEWPPE at a dose of 500mg/kg + ethanol orally, Group IV animals received AEWPPE at a dose of 500mg/kg + ethanol orally. Group V animals received oral omeprazole (20mg/kg) as a standard drug + ethanol orally. Following 21 days of *Andrographis echinoides* extract and standard drug omeprazole pre-treatment, the rats in groups II to V were starved for 12 hours through the oral administration of 1ml of 96% ethanol the gastric ulcer was introduced into their system. An hour later, using the anastatic overdose of diethyl ether the rats were sacrificed. For the analysis of the gastric juice volume, acid output, mucus level, free and total acidity, and pH the gastric content was collected. [16]. For ulcer score analysis the stomachs were dissected and evaluated. The glandular portion of the stomach was immersed in sodium carbonate buffer (pH 10) for biochemical analysis.

#### Macroscopic evaluation of stomach

The stomach of rats was opened properly along the greater curvature and rinsed properly with water and assessed for ulcer formation by making use of a magnifier lens. The number of ulcers was counted and then scored by using the Kulkarni method [17].

Ulcer Scoring - Normal colored stomach (0), Red coloration (0.5), Spot ulcer (1), Hemorrhagic streak (1.5), Deep ulcers (2), and Perforation (3).

Ulcer index (UI) =  $\frac{UN + US + UP}{N} \times 10^{-1}$ ; where  $U_N$  = average ulcer number animal,  $U_S$  = average severity score, and  $U_P$  = animal percentage with ulcers. An ulcer index was given for each animal based on the mean scores:

$$\text{Percent protection} = \frac{C - T}{C} \times 100$$

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

#### Determination of Gastric Juice volume and pH

A pipette and digital pH meter were utilized in the determination of the volume in ml as well as the pH [18].

#### Determination of total and free acidity

Either phenolphthalein and Topfer's reagent or methyl orange were employed as indicators in the titration reaction with 0.01N NaOH to determine the total and free acidity [19]. Pipette 1ml of filtered gastric contents into a small beaker, add 2 to 3 drops of Topfer's reagent or methyl orange and perform the titration with 0.01 N NaOH up to when the solution turns yellowish-orange from the initial red color. The free acidity is indicated by the volume of alkali added. Continue with the titration procedure after adding 2 or 3 drops of phenolphthalein

until the red tinge is regained. The total acidity is indicated by the volume of alkali added. The results expressed as mEq/l:

$$\text{Calculation} = \frac{\text{Titration endpoint}}{\text{Normality of acid}} \times \text{Normality of alkali}$$

#### Antioxidant enzyme assay

Malondialdehyde was estimated by the thiobarbituric acid assay method [20]. Similarly, Superoxide dismutase activity was assayed by the procedure of Kakkar *et al.* [21]. The activity of catalase was determined by the method of Beers and Sizer [22]. Reduced glutathione was determined by the method of Moron *et al.* [23]. The activity of glutathione peroxidase was estimated by the method of Rotruck *et al.* [24].

#### Statistical analysis

All the results were expressed as Mean  $\pm$  SD. Statistical analysis is done using SPSS ver. 24. Mean values are within the row followed by different letters, superscripts (homogeneous subsets) are mentioned as statistically significant ( $p < 0.05$ ) while the same letter was statistically non-significant ( $p > 0.05$ ) from each other groups.

## RESULTS AND DISCUSSION

The whole plant of *Andrographis echinoides* aqueous and ethanol extracts (AEWPPE and AEWPPEE) were used to assay for its efficiency against ethanol-induced stomach ulcers. On average of 210 – 225-gram weight of animals were subjected to antiulcer study, after completion of treatment standard drug, plant extracts, and disease control animals reduced average weight, which ranges from 208.78 $\pm$ 4.65 to 215.37 $\pm$ 4.92g (Table 1). The weight reduction could be due to oral consumption of drugs.

Table 1 Average weight of animals after treatment

Group	Weight of animals
Group I (Normal)	215.37 $\pm$ 4.92 <sup>a</sup>
Group II (Disease control)	210.92 $\pm$ 5.07 <sup>a</sup>
Group III (AEWPPE)	209.58 $\pm$ 5.74 <sup>a</sup>
Group IV (AEWPPEE)	208.78 $\pm$ 4.65 <sup>a</sup>
Group V (Std. drug)	211.49 $\pm$ 4.73 <sup>a</sup>

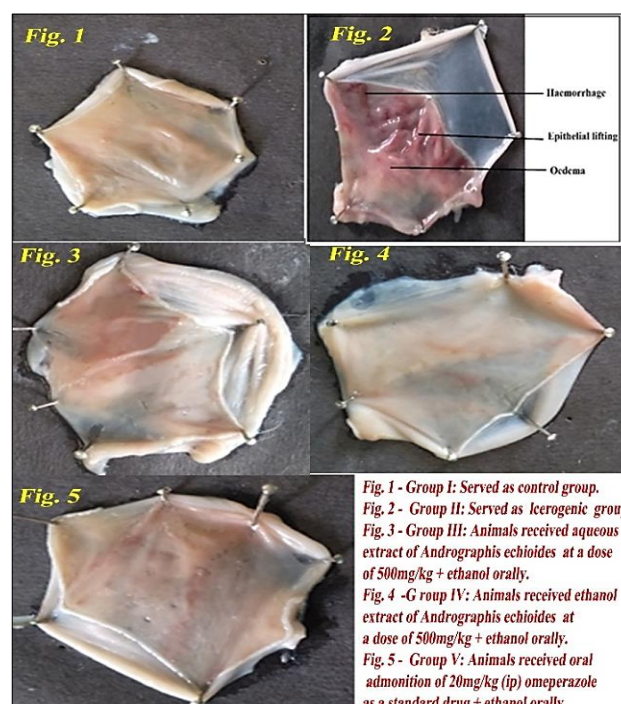


Plate 1 Effect of *Andrographis echinoides* extract on ulcer healing

Animals treated with AEWP AE (Group III) treated animals produced a significant reduction of ulcer scores with 83% ulcer protection. Group IV and V animals also showed lower ulcer scores with an improved percentage of ulcer protection with 69.1 and 83.5% protection respectively. The effects of the protective measures of the extracts were verified in (Table 2, Plate 1) (Fig 1-5). Ethanol-induced gastric damage showed gross mucosal lesion, including long hemorrhage bands and petechial lesions. Animals pretreated with AEWP AE, AEWP EE and standard drug omeprazole showed very mild lesions and no lesions at all (Group III, IV, and V), when compared to the ulcer control group (Group II). There was a decrease in the total and free acidity as well as the volume of

acid secretion whereas the gastric juice pH increased in *Andrographis echinoides* extract-treated animal groups (Table 3). A very high quantity of gastric volume was produced ( $6.68 \pm 1.65$  ml) in disease control animals followed by AEWP AE AEWP EE and standard drug-treated animals.

Table 2 Ulcer score and percentage protection by the extracts of *Andrographis echinoides*

Group	Ulcer score	% Protection
Group II (Disease control)	$3.69 \pm 0.83^b$	0
Group III (AEWP AE)	$0.90 \pm 0.25^a$	83.0
Group IV (AEWP EE)	$3.14 \pm 0.52^b$	69.1
Group V (Std. drug)	$0.61 \pm 0.31^a$	83.5

Table 3 Effect of *Andrographis echinoides* extract and omeprazole in gastric volume, pH, free and total acidity in ethanol-induced ulcerated rats

Groups	Parameters			
	Gastric volume (ml)	pH	Free acidity (mEq/l)	Total acidity (mEq/l)
Group I (Normal)	$1.13 \pm 0.14^a$	$4.12 \pm 0.27^a$	$26.01 \pm 2.19^a$	$48.75 \pm 3.17^a$
Group II (Disease control)	$6.68 \pm 1.65^c$	$2.70 \pm 0.25^b$	$43.29 \pm 2.76^b$	$82.41 \pm 4.21^b$
Group III (AEWP AE)	$3.24 \pm 0.57^b$	$3.85 \pm 0.32^a$	$29.04 \pm 3.47^a$	$53.11 \pm 4.01^a$
Group IV (AEWP EE)	$3.14 \pm 0.52^b$	$3.92 \pm 0.21^a$	$28.92 \pm 2.84^a$	$51.87 \pm 3.98^a$
Group V (Std. drug)	$2.95 \pm 0.49^b$	$3.95 \pm 0.19^a$	$27.94 \pm 2.68^a$	$50.96 \pm 3.21^a$

*Andrographis echinoides* extract-treated animals significantly improved the nature of antioxidant enzymes like GSH, SOD, Catalase, GPx, and MDA. The higher level of LPO in terms of MDA ( $7.13 \pm 1.29$ ) followed by lower levels of GSH, SOD, Catalase, and GPx was noted with diseased animals in

Group II. On the other hand, Group III, IV, and V animals regained their normal levels of antioxidant enzymes. Among the extracts, AEWP AE showed great potential as an antioxidant AGENT (Table 4, Fig 6-7).

Table 4 Effect of *Andrographis echinoides* extract and omeprazole in oxidative stress and antioxidant markers in ethanol-induced ulcerated rats

Parameters	Experimental groups				
	Group I (Normal)	Group II (Disease control)	Group III (AEWP AE)	Group IV (AEWP EE)	Group V (Std. drug)
LPO (nmole of MDA/ mg protein)	$4.25 \pm 1.52^a$	$7.13 \pm 1.29^b$	$4.62 \pm 1.20^a$	$4.56 \pm 1.43^a$	$4.31 \pm 1.27^a$
GSH (( $\mu$ g of GSH/mg protein)	$4.52 \pm 0.56^a$	$1.29 \pm 0.63^b$	$4.27 \pm 0.39^a$	$4.39 \pm 0.49^a$	$4.48 \pm 0.41^a$
SOD (Unit/mg protein)	$6.34 \pm 1.02^a$	$2.71 \pm 1.36^b$	$5.87 \pm 1.15^a$	$6.01 \pm 1.18^a$	$6.15 \pm 1.07^a$
Cat. ( $\mu$ moles of $H_2O_2$ consumed / min / mg protein)	$11.25 \pm 1.29^a$	$4.52 \pm 1.64^b$	$10.82 \pm 1.21^a$	$10.97 \pm 1.38^a$	$11.05 \pm 1.17^a$
GPx (Unit/mg protein)	$8.15 \pm 1.65^a$	$4.19 \pm 0.74^b$	$7.74 \pm 1.45^a$	$7.82 \pm 1.13^a$	$8.04 \pm 1.38^a$

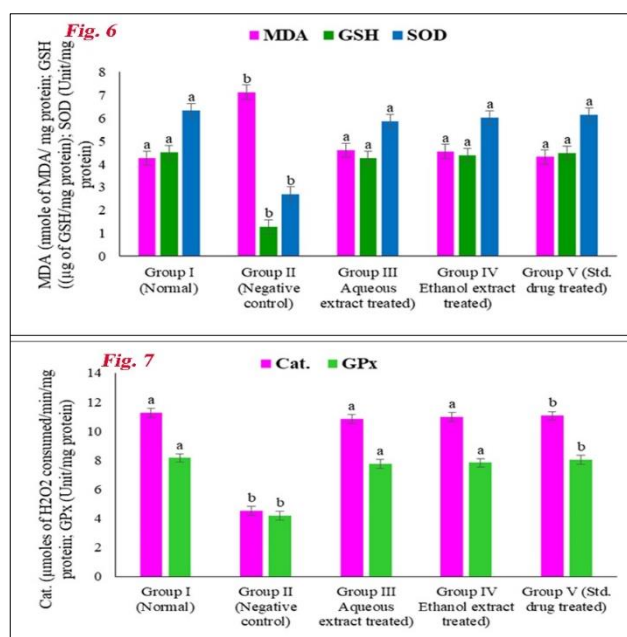


Fig 6-7 Effect of *Andrographis echinoides* extract and omeprazole in oxidative stress and anto-oxidant markers in ethanol induced ulcerated rats

An investigation of the antiulcer activity of the aqueous and ethanol extract of *Andrographis echinoides* whole plant was the aim of the study. *Andrographis echinoides* extracts showed a good antioxidant and antiulcer activity evidenced in experimental animals at 500mg/kg bw. The efficiency of *Andrographis echinoides* extract was comparatively good when compared to positive control omeprazole treatment. AEWP AE produced about 83% ulcer protection, which could be due to phytochemicals found in the extract. The whole plant of *Andrographis echinoides* contains flavonoids, saponins, tannins, phenols, terpenoids, and steroids [12], [25-30], which may exert a gastroprotective effect. The antiulcerogenic efficiency of these phyto compounds was confirmed by various scientists from all over the world [31-36]. These compounds are said to instigate the secretion of certain fluids bicarbonate, prostaglandin, and mucus which are responsible for counteracting the corrosive effects of reactive oxidants in the gastrointestinal lumen. The protein precipitating and vasoconstriction effects of tannins are responsible for the prevention of ulcer development. An impervious layer is formed when the tannins' astringent action results in the precipitate proteins on the microvilli. This in turn blocks gut secretions preventing the irritant and toxin attack to the underlying mucosa [37-38]. Many authors from India also



illustrated the role of phytochemicals as antioxidant and antiulcer agents [39-43]. Some of the positive effects of Polyphenols and tannins include antimicrobial, antiulcer, antioxidant, and wound healing [44]. As revealed by the study of the aqueous extract of *Andrographis echinoides* whole plant they can be viewed as beneficial remedies in gastric lesions treatment. Plant extracts stimulate the synthesis of prostaglandin, which protects the stomach's cellular system [45-46].

## CONCLUSION

On the basis of the observed results, it is concluded that whole plant extracts of *Andrographis echinoides* showed effective antiulcer activity, which is evidenced via lowered acid

secretion, reduced ulcer score and effective antioxidant power. These activities could be due to tannins, phenolic compounds and Flavonoids.

## Conflict of interest

The authors declare there is no conflict of interest.

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## Ethics statement

Studies involving animals have been performed with the approval of an appropriate ethics committee [SAC/045/20/US/10]

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