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ANTIULCER AND ANTIOXIDANT POTENTIALS OF *CLEOME GYNANDRA* WHOLE PLANT EXTRACTS

CHITRA DEVI K, SUBHASHINI G, SUNDAR S. K. AND RAJAN S*

PG and Research Department of Microbiology, M. R. Government Arts College, Mannargudi - 614001, Affiliated to Bharathidasan University, Tiruchirappalli – 620 024

***Corresponding Author: Rajan S: E Mail: ksrajan99@gmail.com**

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ABSTRACT

Incidence of Peptic Ulcer Disease is high among Indian population and showed the risk of intestinal cancer. Many medicinal plants possess antiulcer properties. *Cleome gynandra* whole plant is selected to assess its antiulcer activity on experimental modals. Ethanol induced ulcer assay was performed along with antioxidant assay. SOD, GPx, GSH, CAT and MDA were assessed using standard textual methods. CGWPAE and CGWPEE proved to be an excellent antiulcer and antioxidant agent, which is similar to omeprazole effect. These two extracts exhibited good ulcer protection effect and reduced gastric acid secretion and also gastric acidity. Experimental evidences confirmed that plant extracts regained its ulcer cure effect and antioxidant effect as like group I normal animals and confirmed power of this plant as an antioxidant and antiulcer agent, which could be due to its phytochemicals.

Key words: *Cleome gynandra*, antiulcer study, antioxidant assay, whole plant

INTRODUCTION

In India, Peptic ulcer disease (PUD) causes serious morbidity with significant reduction in the life span of an individuals. The most common symptoms are pain in abdomen (69%), gastro intestinal bleeding, perforations and vomiting **[1]**. Although potential antiulcer drugs like H_2 blockers are available, all purified chemical-based drugs

created serious side effects, thereby peoples emphasizing the need of safer alternative drug from the nature. About 80% World populations rely on medicinal preparations for their primary health care needs **[2]**. People from village utilized medicinal plants and its preparation for their all types of health care needs. Many herbal preparations are used in India for the treatment of gastrointestinal diseases like Peptic Ulcer **[3]**. *Cleome gynandra L.* is one among the important medicinal plant commonly called Nalvaelai in Tamil and belongs to the family Capparaceae. This plant is an herb that grows up to 4 feet and showed compound palmitate leaves with five leaflets. This plant showed the presence of white hermaphrodite leaves **[4]**. *C. gynandra* whole plant is used topically for the management of fungal infections **[5, 6]**. It also used for the treatment of migraine headache and epilepsy **[7]**; stomach ache **[8]** and snake bite **[9]**. Tabuti *et al.,* **[4]** reported that this plant parts are useful in ear pain, sepsis, diphtheria, vomiting, promotion of labor. These herbal treatments applied by the rural populations need to be documented scientifically for their safety and efficacy. Therefore, the present study was conducted to determine the antiulcer activity of *Cleome gynandra* aqueous and alcoholic extracts on animal models.

MATERIAL AND METHOD

Experimental animals

Wister Albino rats weighing 200- 220 g were utilized for the study. They were maintained in animal house, which is equipped with polypropylene cages and exposed to both light and dark cycle. The animals were fed with standard pelleted diet and water was allowed ad libitum.

Plant material collection and identification

The fresh whole plant of *Cleome gynandra* were collected from the road sides of Mannargudi, Thiruvarur district, Tamil Nadu, India during the month of October 2019. Taxonomic identification was established by Dr. Rabinat Herbarium, St. Josephs College, Tiruchirappalli and the voucher specimen were deposited in the Department of Microbiology, M. R. Government Arts College, Mannargudi.

Preparation of plant extract

Extract from the dried whole plant of *Cleome gynandra* was prepared using ethanol (CGWPEE) and water (CGWPWE) by cold extraction method. The residue was left to air dry at room temperature for about 72 hours. The dry residue was stored at 4°C in air-tight bottle **[10]**.

Antiulcer study

Gastric lesions were induced according to the method described by Mahmood *et al*. **[11]**. Animals were randomly divided into five groups of each 6 rats. Group I rat served as the normal control; received saline only, Group II rats were served as the disease control, Group III animals received CGWPAE at a dose of 500mg/kg + ethanol orally, Group IV animals received CGWPEE at a dose of 500mg/kg + ethanol orally. Group V animals received oral admonition of 20mg/kg omeprazole as a standard drug + ethanol orally. Following 21 days of *Cleome gynandra* extract and standard drug omeprazole pre-treatment, gastric ulcer was induced in 12 h fasted rats by oral administration of 1ml of absolute ethanol (96%) from groups II to V. After 1 h of ethanol administration, the animals were sacrificed by an overdose of diethyl ether anaesthetization. The gastric content was collected for determination of gastric juice volume, pH, free and total acidity and acid output and mucus level **[12]**. The stomachs were then dissected and analysed for ulcer score. 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 were opened properly along the greater curvature and rinsed properly with water and assessed for its ulcer formation by making use of magnifier lens. The number of ulcers was counted and then scored by using the Kulkarni method **[13]**.

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

Ulcer index (UI) = UN + US+ UP × 10^{-1};

where U_N = average number of ulcers per animal, U_S = average of severity score, and U_P = percentage of animals with ulcers.

Mean ulcer score for each animal is expressed as ulcer index

% Protection= (C-T/C) X 100

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

Determination of Gastric Juice volume and pH.

The volume and pH of centrifuged gastric juice were measured by pipette and digital pH meter. The volume was expressed as ml **[14]**.

Determination of total and free acidity

The total and free acidity were determined by titrating with 0.01N NaOH using phenolphthalein and Topfer's reagent or methyl orange **[15]**. Pipette 1ml of filtered

gastric contents into a small beaker, add 2 to 3 drops of Topfer's reagent or methyl orange and titrate with 0.01 N NaOH until all trace of the red colour disappears and the colour is yellowish orange. Note the volume of alkali added that indicate free acidity. Then add 2 or 3 drops of phenolphthalein and continue titrating until a definite red tinge reappears. Note the total volume of alkali added that indicate total acidity. The results expressed as MEq/l

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

Antioxidant enzyme assay

Malondialdehyde was estimated by the thiobarbituric acid assay method **[16]**. Similarly, Superoxide dismutase activity was assayed by the procedure of Kakkar *et al.,* **[17]**. The activity of catalase was determined by the method of Beers and Sizer **[18]**. Reduced glutathione was determined by method of Moron *et al.,* **[19]**. The activity of glutathione peroxidase was estimated by the method of Rotruck *et al.,* **[20]**.

Statistical analysis

In vivo values were expressed as Mean ± SD for 6 rats. Statistical analysis of one-way ANOVA, post-hoc followed by DMRT test using SPSS ver. 24. Mean values are within the row followed by different letters, superscript (homogeneous subsets) are mentioned as statistically significant ($P<0.05$) while same letter was statistically non-significant ($P>0.05$) from each other groups.

RESULTS

Ethanol induced stomach ulcer was performed to assess antiulcer potential of *Cleome gynandra* aqueous and ethanol extracts. Average weight of the animals used in this study ranges from 209.85±5.53 to 217.61±3.75g. Ulcer score was significantly reduced in omeprazole treated groups (0.62±0.2) with 83.9% ulcer protection (**Table 1**). Group III and IV animals also showed lower number of ulcer score with improved percentage of ulcer protection with 79.1 and 79.6% protection respectively. Ulcer protection effect of the CGWPAE and CGWPEE was evidenced by the level of pH, gastric volume, total acidity and free acidity (**Table 2**). Disease control animals (Group II) showed increased volume of gastric juice with higher pH and acidity (**Table 2**). On the other hand, CGWPAE, CGWPEE and omeprazole treated animals showed regained nature of pH, gastric volume and acidity. Among the extracts, CGWPEE showed 3.07±0.53ml gastric volume, 3.82±0.48 pH, 27.09±2.53 M Eqa/L free acidity and 53.34±4.15 M Eqa/ L total acidity which indicated efficiency of ethanol extract as an antiulcer agent. Extracts and omeprazole

treated animals showed similar pattern of results which is comparatively very close to the normal animals (**Figure 1**).

Ethanolic and aqueous extracts treatment in animals significantly regained its GSH, SOD, Catalase, GPx and MDA levels significantly. Higher level of MDA (7.26±1.34) followed by lower levels of GSH, SOD, Catalase and GPX were noted with diseased animals in Group II (1.59±1.29, 2.59±1.74, 4.37±1.5 and 4.71±1.16 respectively). Group III, IV and V animals revealed improved version of antioxidant enzymes, which is due to therapeutic nature of extracts as well as omeprazole. Though antioxidant power of omeprazole treated animal is greater than plant extract treated animals, omeprazole is chemical hydrogen blocker and induce chemical mediated side effects (**Figure 2**). Among the extract tested, ethanol extract has potential antiulcer activity was noticed from the morphological observation. **Plate I** revealed the efficiency of CGWPAE and CGWPEE as a antiulcer agent. There are no injuries noted in normal Group I animals' gastric mucosa. Severe injuries and red bands were noted in animals administered only with ethanol (Group II). Mild stomach mucosal disturbances with lower ulcer score were noted with Group III (Aqueous extract treated animal), Group IV (Ethanol extract treated animals) and Group V (Omeprazole treated animal).

Table 1: Ulcer Protective effect of *Cleome gynandra* extracts

S. No	Group	Ulcer score	Percentage Protection
1	I	Nil	100
2	II	3.87 ± 0.54^{b}	-
3	III	0.81 ± 0.17^{a}	79.1
4	IV	0.79 ± 0.18^{a}	79.6
5	V	0.62 ± 0.21^{a}	83.9

Table 2: Effect of *Cleome gynandra* extract and omeprazole in gastric volume, ulcer score, pH, free and total acidity in ethanol-induced ulcerated rats

Parameters	Experimental groups				
	Group I	Group II	Group III	Group IV	Group V
Weight of animals (g)	212.74 ± 4.38^{a}	217.61 ± 3.75^{a}	210.42 ± 5.19^{a}	209.85 ± 5.53^{a}	215.58 ± 4.07^{a}
Gastric volume (ml)	1.15 ± 0.17^{a}	6.75 ± 1.22^{c}	3.11 ± 0.49^{b}	3.07 ± 0.53^{b}	2.94 ± 0.49^{b}
pH	4.06 ± 0.54^{a}	2.72 ± 0.29^{b}	3.79 ± 0.41^{a}	3.82 ± 0.48^{a}	3.97 ± 0.45^{a}
Free acidity (Meq/l)	25.43 ± 2.96^{a}	42.76 ± 3.29^{b}	28.19 ± 3.18^{a}	27.09 ± 2.53^{a}	26.57 ± 2.71^{a}
Total acidity (Meq/l)	49.74 ± 4.21^{a}	81.65 ± 3.96^{b}	54.29 ± 5.04^{a}	53.34 ± 4.15^{a}	52.13 ± 4.29^{a}

Values are expressed as Mean ± SD for 6 rats. Statistical analysis of one-way ANOVA, post-hoc followed by DMRT test using SPSS ver. 24. Mean values are within the row followed by different letters, superscript (homogeneous subsets) are mentioned as statistically significant (P<0.05) while same letter was statistically non-significant (P>0.05) from each other groups

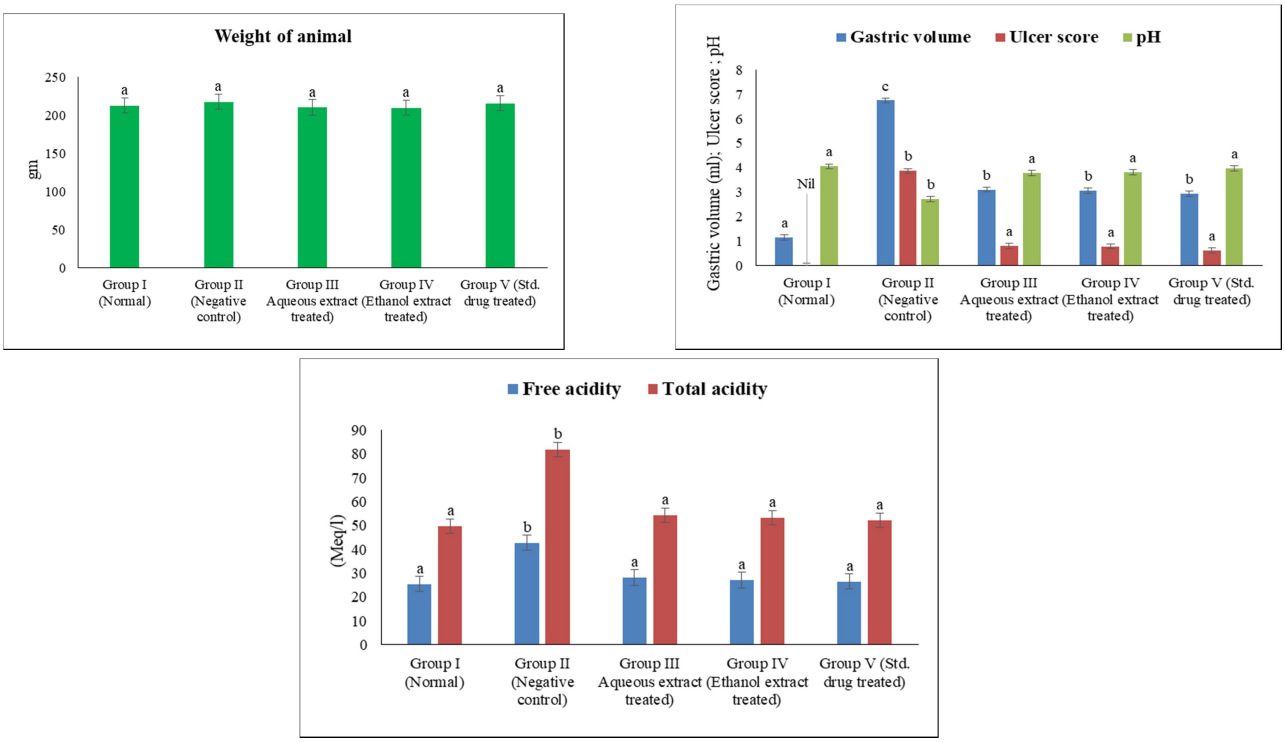


Figure 1: Effect of Cleome gynandra extract and omeprazole in gastric volume, ulcer score, pH, free and total acidity in ethanol-induced ulcerated rats.

Table 3: Effect of *Cleome gynandra* extract and omeprazole in oxidative stress and antioxidant markers in ethanol-induced ulcerated rats

Parameters	Experimental groups				
	Group I	Group II	Group III	Group IV	Group V
MDA (nmole of MDA/ mg protein	4.36±1.07[a]	7.26±1.34[b]	4.93±1.55[a]	4.87±1.26[a]	4.52±1.19[a]
GSH (µg of GSH/mg protein)	4.75±0.85[a]	1.59±1.29[b]	4.18±0.85[a]	4.32±0.92[a]	4.36±0.77[a]
SOD (Unit/mg protein)	6.04±1.32[a]	2.59±1.74[b]	5.75±1.13[a]	5.81±1.08[a]	5.97±1.15[a]
Cat. (µmoles of H_2O_2 consumed/min/mg protein)	11.74±1.85[a]	4.37±1.51[b]	10.90±1.52[a]	11.09±1.73[a]	11.53±1.68[a]
GPx (Unit/mg protein)	8.19±1.03[a]	4.71±1.16[b]	7.18±1.21[a]	7.96±1.37[a]	8.05±1.25[a]

Values are expressed as Mean ± SD for 6 rats. Statistical analysis of one-way ANOVA, post-hoc followed by DMRT test using SPSS ver. 24. Mean values are within the row followed by different letters, superscript (homogeneous subsets) are mentioned as statistically significant (P<0.05) while same letter was statistically non-significant (P>0.05) from each other groups

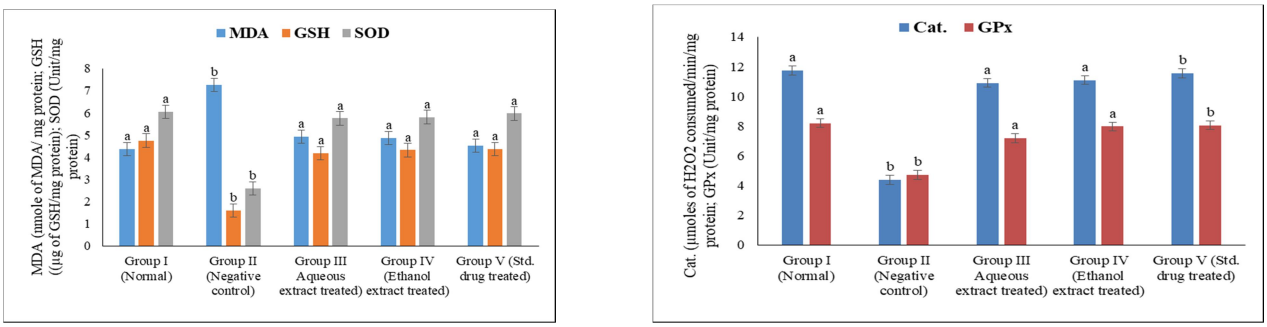
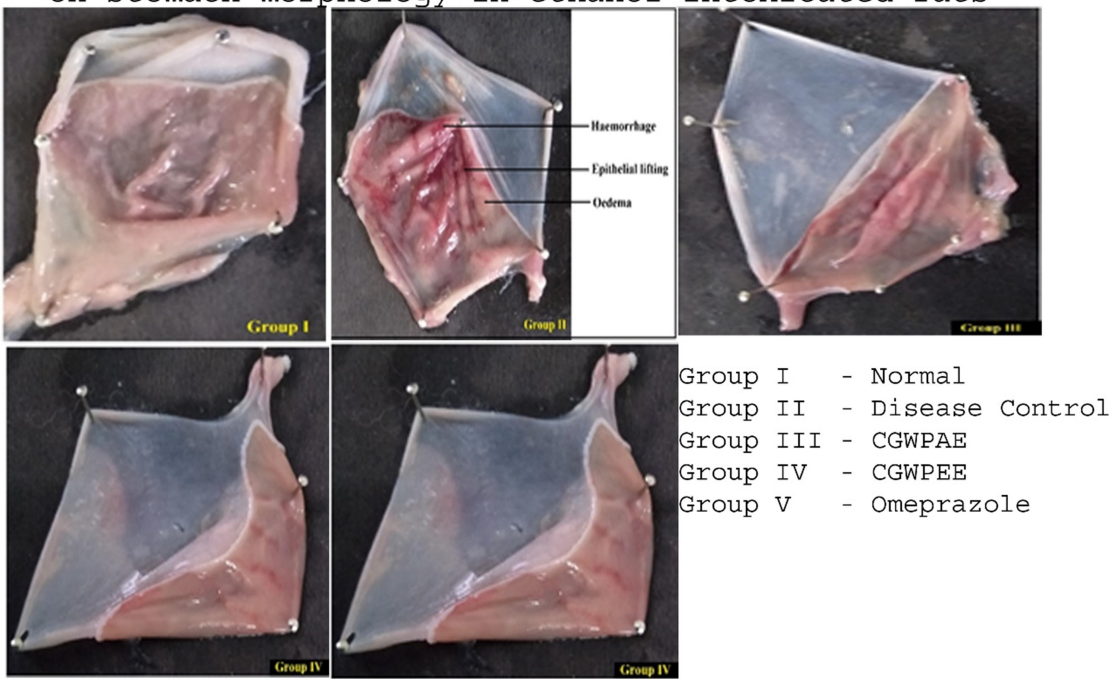


Figure 2: Effect of *Cleome gynandra* extract and omeprazole in oxidative stress and antioxidant markers in ethanol-induced ulcerated rats

Plate I: Effect of Cleome gynandra extract and omeprazole on stomach morphology in ethanol intoxicated rats



Group I - Normal
Group II - Disease Control
Group III - CGWPAE
Group IV - CGWPEE
Group V - Omeprazole

DISCUSSION

This study was carried out to evaluate the anti-ulcer effect of CGWPAE and CGWPEE on ethanol-induced gastric ulcer models. The etiology of peptic ulcer could be aspirin NSAIDs and *Helicobacter pylori*. Peptic ulcer is also due to imbalance of aggressive factors and mucosal integrity. Treatment of peptic ulcer is aimed at reducing acidity in stomach and reducing microbial burden. Hydrogen blockers and other acid secretion blockers are able to reduce ulceration. Currently amoxicillin clarithromycin and Vonoprazan were used to clear *Helicobacter pylori*. Peptic ulcer formation was effectively controlled by the extracts of medicinal plants. *C. gynandra* aqueous and ethanol extracts effectively regained all antiulcer parameters as like normal control animals (Group I). herbal treatment reduce acidity by increasing pH. Extracts also increases mucous secretion, which is one of the mucosal defense mechanisms. They also stabilize the surface epithelial cells and interferes prostaglandin synthesis **[21, 22]**.

Irritants like ethanol could disturb gastric mucosa and cause hemorrhage within one hour of exposure. Gastric damage may increase gastric mucous as a defense feature. Prevention and treatment of PUD is directly relying on the prevention of gastric

secretions and the ability of the gastric mucosa to resist injury by endogenous secretions and ingested irritants can be attributed to a mucosal defense. Gastric cytoprotection is directly attributed towards the management of PUD. Ulceration induce prostaglandin levels, glutathione, mucosal blood flow and bicarbonate secretion as well as an increase in lipid peroxidation, oxidative stress, leukotriene production and generation of free radicals leading to cell and membrane damage **[23]**. Increased acid in stomach induces histamine production by mast cells, there by gastric secretion disturbance, mucosal damage, change in permeability and free radical production were noticed in this study, which was also noticed by Sakat and Juvekar **[24]**. Jude and Paul **[25]** reported that gastric disturbances also disturb the release of superoxide anion and hydroperoxyl free radicals which may cause acute and chronic ulceration. Many reports also suggested that ethanol induces gastric lesion formation, creation of hemorrhage and also cause necrotic tissue **[26, 27]**. Extracts of *Cleome gynandra* significantly reduces mean ulcer count and showed up to 86% ulcer protection. It may be due to antisecretory effect of *Cleome gynandra*, which significantly reduces the formation of ulcers. It also increases the pH, reduce the acidity of stomach and also it reduces the protein content in ulcer affected animals. All these antioxidant and antiulcer activity of the plant extracts were due to the presence of flavonoids, phenolic compounds, tannins, alkaloids **[28, 29, 30, 31, 32]**. Flavonoids also exerts ulcer prevention by free radicals scavenging mechanisms. In vivo antioxidant assay (LPO, SOD and GSH) confirms the efficiency of CGPWAE and CGPWEE. Polyphenols and tannins have been reported to possess antioxidant, wound healing, antimicrobial and antiulcer activity **[33, 34]**. The results of the present study suggest that the ethanolic extract of *Cleome gynandra* whole plant may be beneficial in the treatment of gastric lesions. Plant extracts stimulates the prostaglandin synthesis, which protects cellular system in the stomach **[34, 35]**.

CONCLUSION

Aqueous and ethanolic extracts of *Cleome gynandra* whole plant confirmed its efficiency as an antiulcer and antioxidant agent.

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