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Research

Evaluation Of Anti-Ulcer Activity Of *Clerodendrum serratum* Leaf Extract In Experimental Animal Models

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Abstract

One of India's oldest medical systems, siddha is thought to have been the primary treatment used by the ancient Tamils and Dravidians in South India. In addition to being the oldest, this system has many specialties that are superior to those utilized in Ayurvedic treatment. A significant medicinal plant, Clerodendrum serratum (L.) Moon. (Verbenaceae) grows in tropical and warm temperate locations such as Africa, Southern Asia, Malaysia, and the forests of India and Sri Lanka. For a long time, it has been used in India to cure fever, malarial fever, respiratory conditions, rheumatism, inflammation, and discomfort. Based on the current findings and reports, it can be said that Clerodendrum serratum's anti-ulcer activity may be partially caused by acid inhibition and primarily by the modulation of defensive factors through an improvement in gastric cytoprotection. The research findings indicated that C. serratum shows potential as a natural treatment for asthma, suggesting the need for additional investigation into its bioactive elements and underlying molecular processes. Furthermore, phytochemical studies have revealed the existence of alkaloids, flavonoids, and saponins.

Keywords: Clerodendrum serratum, Anti-ulcer activity, Gastric mucosal protection, NSAID-induced ulcers, Alcohol-induced gastric injury, Flavonoids.

INTRODUCTION

Nutrient absorption and digestion are handled by the gastrointestinal (GI) system, which is essential for preserving general health. To help with food digestion, the stomach, a key part of the GI system, secretes hydrochloric acid (HCl). The stomach's extremely acidic pH level, which is normally between 1.5 and 3.5, creates the ideal conditions for the activation of digesting enzymes. However, this acidity also increases the risk

of gastric ulcers, which happen when the mucosal barrier is weakened and the stomach lining is exposed to dangerous substances.

Peptic Ulcer Pathophysiology

An imbalance between the GI tract's protective and destructive forces is the main cause of peptic ulcers, which are painful lesions in the stomach or duodenum's lining. The overproduction of gastric acid, Helicobacter pylori infection, and the use of nonsteroidal anti-inflammatory medicines (NSAIDs), which prevent the production of protective prostaglandins, are important factors that lead to the development of ulcers. By controlling blood flow and encouraging the release of mucus and bicarbonate, prostaglandins are essential for preserving the integrity of the stomach mucosa. Oxidative stress, which arises from an imbalance between reactive oxygen species (ROS) and the body's antioxidant defenses, is another factor in the pathophysiology of peptic ulcers. Overproduction of ROS can harm the stomach lining and increase the risk of ulcer development. Although the body possesses defense mechanisms such buffering systems and mucosal regeneration, persistent diseases can overcome these and cause ulcers.

Limitations of Conventional Therapies

Nowadays, antacids, proton pump inhibitors (PPIs), H2 receptor antagonists, and antibiotics for H. pylori infections are commonly used to treat peptic ulcers. These treatments frequently have drawbacks, such as long-term adverse effects and the development of antibiotic resistance, even though they are successful in lowering stomach acid and accelerating recovery. Furthermore, NSAID-induced mucosal injury and oxidative stress are two underlying causes that PPIs and H2 antagonists might not adequately treat. Because they may provide extra advantages without the disadvantages of traditional treatments, complementary therapies—including natural remedies—are becoming more and more popular.

The Role of Natural Products

For millennia, gastrointestinal disorders have been treated using natural remedies, especially those made from plants. There is a growing emphasis on investigating plant-based chemicals for their potential as therapeutics due to the emergence of antimicrobial resistance and worries about the adverse effects of synthetic medications. These natural treatments frequently have a variety of qualities, such as antibacterial, anti-inflammatory, and antioxidant effects, which may aid in healing and reestablishing the equilibrium of the stomach environment.

Focus on Parthenium hysterophorus

Parthenium hysterophorus, popularly referred to as "Congress grass," is unique among the plants being studied for its potential medical uses because of its intricate pharmacological profile. Research has shown that Parthenium hysterophorus may be used to treat gastrointestinal issues, despite its well-known toxicity, which can result in allergic reactions and harm to livestock when consumed. Flavonoids, alkaloids, and terpenoids are among the plant's many bioactive substances that have antibacterial, anti-inflammatory, and antioxidant properties. Preliminary research indicates that Parthenium hysterophorus may offer protection against stomach ulcers despite its toxicity. This has led to more research into its pharmacological processes, which include gut microbiota modification, inflammation reduction, and oxidative stress inhibition. The plant's medicinal usage, however, needs to be carefully considered in light of its known negative effects, with an emphasis on determining safe dosages and application techniques.

PLANT PROFILE

Identification

Fig 1: Clerodendrum serratum plant showing leaves, flowers, and roots

2. Scientific Classification
Kingdom: Plantae
Subkingdom: Tracheophytes
Superdivision: Angiosperms
Division: Eudicots
Class: Asterids
Order: Lamiales
Family: Lamiaceae
Genus: Clerodendrum
Species: C. serratum

3. Synonyms
English: Blue Glory, Blue Fountain Bush
Sanskrit: Bharangi, Sirisha
Hindi: Bharangi
Tamil: Siruthekku
Telugu: Bhandira
Malayalam: Cheruthekku
Kannada: Bharangi
Bengali: Bharangi

4. Dispersal
India, Sri Lanka, and Southeast Asia are among the tropical and subtropical regions of Asia where Clerodendrum serratum is indigenous. The plant thrives in damp, well-drained soils and grows naturally in hillsides, grasslands, and woodlands. It is frequently found in Assam, the Western Ghats, and portions of the Himalayas in India.

5. Conditions of Cultivation
Warm areas with temperatures between 20 and 30°C and moderate rainfall are ideal for Clerodendrum serratum growth. It favours fertile, well-drained soils with a pH of 6.0 to 7.5, which is slightly acidic to neutral. The plant grows best in full sun to medium shade and is easily propagated by stem cuttings and seeds. Frequent pruning promotes flowering and helps keep it in form.

6. Description of Botany
Clerodendrum serratum is a perennial shrub with a maximum height of two to three meters. Its simple, opposite leaves have serrated edges, and its stems are woody. The flowers are tubular, bluish-purple, and grouped in axillary or terminal clusters. The monsoon season is when the plant blooms. When they ripen, the tiny, drupe-like fruits turn black. In traditional medicine, the fibrous, thick roots are highly prized.

7. Phytochemistry
Clerodendrum serratum contains a wide range of bioactive compounds, including:

- Alkaloids: Clerodendrine
- Flavonoids: Quercetin, kaempferol
- Terpenoids: Serratagenic acid
- Steroids: Stigmasterol, β-sitosterol
- Other Compounds: Phenolic acids, saponins, and glycosides
  These compounds exhibit anti-inflammatory, antimicrobial, antioxidant, and expectorant activities.

8. Traditional Uses
Clerodendrum serratum has been extensively used in traditional medicine systems, including Ayurveda, Siddha, and Unani.

- Ayurveda: Prescribed for respiratory disorders, including asthma, bronchitis, and cough. It is also used for fever, inflammation, and skin diseases.
- Siddha Medicine: Recommended as an expectorant, diuretic, and for managing arthritis.
- Unani Medicine: Used for treating spleen enlargement, liver disorders, and joint pain.
- Folk Medicine: Roots are used to prepare decoctions for treating snake bites, fever, and gastrointestinal issues. Leaves are applied as poultices for wounds and skin ailments.

Aim and objective

Aim and objective of the purposed research work

1. Collection, authentication, processing and drying leaf extract of *Clerodendrum serratum*
2. Cleaning, drying and grinding leaf extract of *Clerodendrum serratum*
3. Preparation of hydro alcoholic leaf extract by using cold percolation method.
4. Preliminary qualitative Phytochemical analysis to identify chemical compound.
5. Investigation of Evaluation of Anti-Ulcer Activity of *Clerodendrum Serrratum* Leaf Extract In Experimental Animal Models
6. From the studies Anti-Ulcer Activity and phytochemical analysis performed under

It is possible that the anti-ulcer effect of Clerodendrum serratum is partially related to acid inhibition and mostly to the modulation of defensive factors through an improvement in stomach cytoprotection, based on the current findings and relevant reports.

MATERIALS AND METHODS

The designing of methodology involves a series of steps taken in a systematic way in order to achieve the set goal(s) under the prescribed guidelines and recommendations. It includes in it all the steps from field trip to the observation including selection and collection of the medicinal plant, selection of dose value, standardization of protocol, usage of instruments, preparation of reagents, selection of specific solvents for extraction, formation of protocols and final execution of the standardized protocol. All this requires good build of mind and a good and soft technical hand to handle the materials and procedure in a true scientific manner.

Drugs and Chemicals

Drugs and Chemicals used in this study were of analytical grade and of highest purity procured from standard commercial sources in India.

Test animals

Wistar rats weighing 150–200 g were purchased from The animals were kept in suitable cages with consistent hygienic conditions, fed a standard pellet food (Amrul Laboratory Animal food), and given unlimited access to water. All of the animals were kept under conventional settings, which included a 12:12 h light-dark cycle, ambient temperature of 26 ± 1°C, and relative humidity between 45 and 55%. Throughout the duration of the trial, the animals were kept in roomy, clean cages. IAEC approved animal experiments.

Plant extracts preparation

Making the Aqueous Extract

Clerodendrum serratum fresh leaves were gathered and cleaned with tap water. Twenty grammes of finely chopped leaves were added to a 250 ml beaker with 200 ml of water to create the leaf extract that was employed. After thoroughly mixing the ingredients, the mixture was cooked for four to five hours at 800-1000 degrees Celsius. Whatmann filter paper was used to further filter the extract. The concentrated residue was generated by boiling the filtrate. The concentrated product was utilised for additional experiments to verify the activities after being sealed in sample covers and kept at room temperature.

Preparation of Alcoholic Extract

Fresh Clerodendrum serratum leaves were gathered and cleaned with tap water. To make the leaves extract, 20 grammes of finely chopped leaves were added to a 250 ml beaker with 200 ml of alcohol. The mixture was then thoroughly mixed and boiled for four to five hours at 50 to 600 degrees Celsius. The resulting filtrate was then filtered through Whatmann filter paper, and the concentrated product was sealed in sample covers, kept at room temperature, and used for additional experiments to verify the activities.

Dosage selection for animal research

The human dose of Clerodendrum serratum (3-5 g/kg) was converted to determine the dose used in the rat experiment. For rats, the human dose conversion factor (per 200 g body weight) is 0.018 (Ghosh 1984). Therefore, 200 mg/kg is the estimated dose for the rats (taking into account human doses 3 and 5 g/kg). A dosage of 2000 mg/kg body weight was used to test for acute toxicity.

Pharmacological assessment

Extract preparation

Clerodendrum serratum aqueous and alcoholic extracts were suspended in water with a 3% v/v Tween-80 solution present. For the purposes of the trial, all of the medications were taken orally. When necessary,

extract preparations were made each time. Each animal received the medications at a consistent volume of 10 millilitres per kilogramme.

RESULTS AND DISCUSSIONS

Acute Toxicity Study

Administration of the Clerodendrum serratum extracts *in* rats at doses of 250 mg/kg by oral gavage did not reveal any adverse effects or signs of toxicity.

Observations twice daily for fourteen days also did not reveal any drug related observable changes or mortality. Accordingly, the acuteoral LD50 of the extractives was concluded to exceed 2000 mg/kg bodyweight, the highest dose tested in the study.

Effect on alcohol induced gastric ulcers

Oral administration of 80% alcohol produced hemorrhagic gastric lesions in glandular portion of stomach. Pretreatment with AQCS and ALCSat the dose of 250 mg/kg and omeprazole (10 mg/kg) significantly ($p<0.001$) protected the gastricmucosa as shown by reduced values of lesion index (35.26 ± 0.89 and 17.4± 0.55respectively) against alcohol challenge as compared to solvent control (29.23± 0.12).

Table 1: Effect of Clerodendrum serratum**at various doses on alcohol induced gastric ulcer in rats.**

Treatment (n=6)	Dose mg/kg(p.o.)	Lesion index	% In hibitionof ulcer	Mucus content (μg Alcian blue/g wet tissue)
1% CMC	-	29.23 ± 0.12	-	0.49 ± 0.01
Ulcer control	-	40.81±0.72	-	0.53±0.02
Omeprazole	10	30.44± 0.34	26.28	0.75 ± 0.01
AQCS	250	35.26 ± 0.89	8.50	0.52 ± 0.02
ALCS	250	17.4± 0.55	50.08	0.83 ± 0.01

Values are mean ± S.E.M. n=number of animals in each group.Significant differences with respect to solvent control group were evaluated byStudent's *t* – test. ($p<0.05$, $p<0.01$ and $p<0.001$).

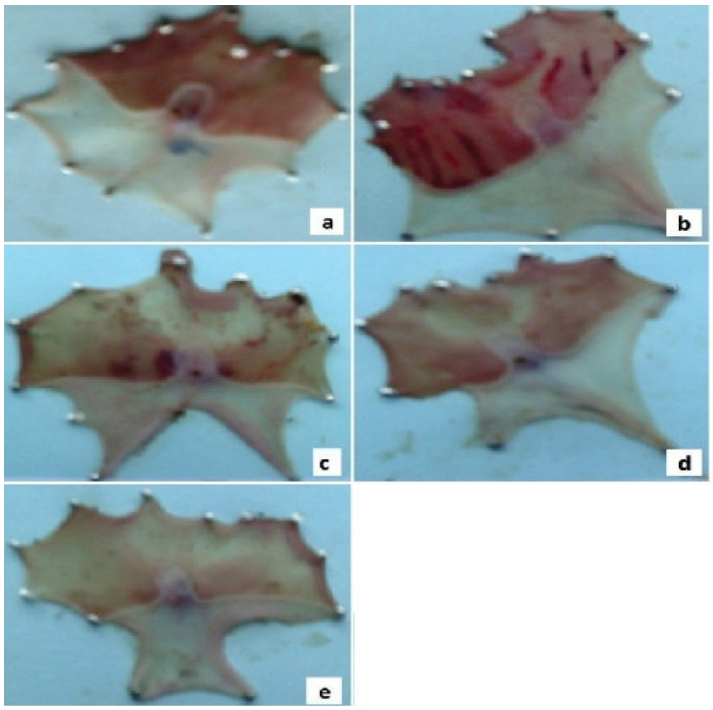

Fig 2: Effect of Clerodendrum serratum**on alcohol induced ulcers in the rats in the study (a) Normal Control (b) Ulcer Control (c) *AQCS*(250 mg/kg) treated (d) *ALCS* (250 mg/kg) treated (e) Omeprazole (10 mg/kg treated)**

Effect on Paracetamol induced gastric ulcers

In Clerodendrum serratumtreated groups (250 mg/kg), the ulcer index values (0.56 ± 0.02 and 0.38 ± 0.02 respectively) weresignificantly reduced ($p<0.001$) when comparedto solvent control (0.75 ± 0.02), while the ulcer index for ranitidine treated group was 0.35 ± 0.02 ($p<0.001$). The %inhibition of ulcer showed by AQCS and ALCS (250mg/kg) and ranitidine was 49.2%, 36.2% and 55.2% respectively. (Refer Table 2, fig 3)

Table 2: Effect of Clerodendrum serratum**at various dose levels on paracetamol induced gastric ulcer in rats.**

Treatment(n=6)	Dosemg/kg (p.o.)	Ulcer index	% Inhibition of ulcer
1% CMC	-	0.75 ± 0.02	-
Ulcer control	-	0.86±0.01	--
Ranitidine	50	0.35 ± 0.02	49.2
AQCS	250	0.56 ± 0.02	36.2
ALCS	250	0.38 ± 0.02	55.2

Values are mean ± S.E.M. n=number of animals in eachgroup; Significant differences with respect to solvent controlgroup were evaluated by Student's *t* - test. ($p<0.001$).

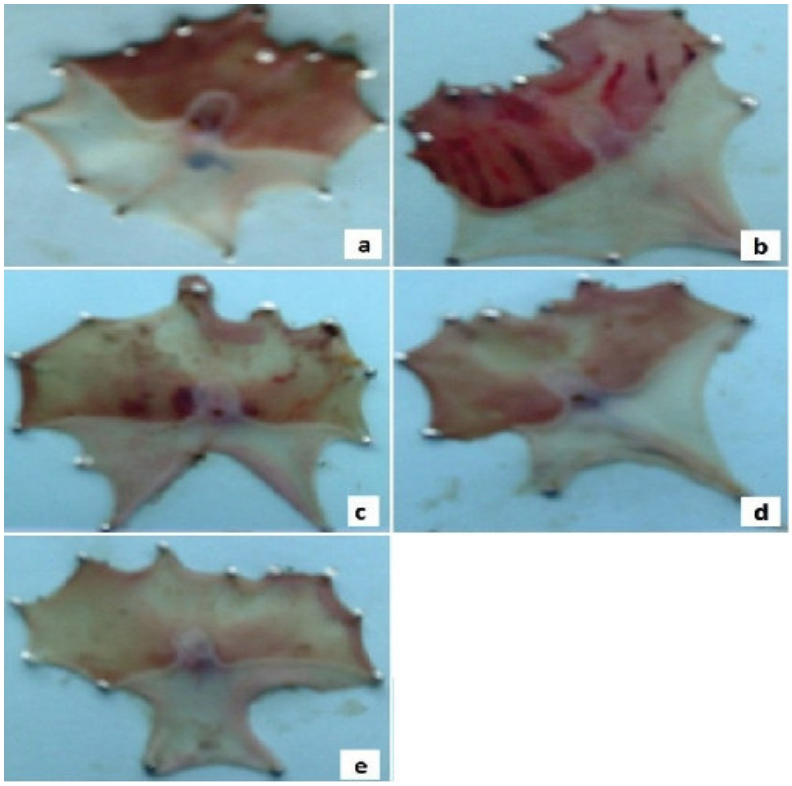

Fig 3: Effect of Clerodendrum serratum**on paracetamol induced ulcers in the rats in the study (a) Normal Control (b) Ulcer Control (c) *AQCS*(250 mg/kg) treated (d) *ALCS*(250 mg/kg) treated (e) Ranitidine (50 mg/kg treated)**

Stress-induced ulcers

In water immersion stress induced ulcers, the mean score value of ulcer inhibition was found to be significant ($P<0.001$) for 250 mg/kg of the extract. The percentage ulcer inhibition was 81.37 and 74.82 for 250 mg/kg for both aqueous and alcoholic extracts, and that of the standard was found to be 92.67. [Table 3 Fig 4].

Table 3. Effect of Clerodendrum serratum**at various dose levels on Stress induced gastric ulcer in rats.:**

Group	Ulcer index	Percentage inhibition
Normal Control	00.00±0.00	-----
Ulcer control	22.73±4.31	------
Standard	2.86±0.13	92.67
AQCD	6.90±3.02	81.37
ALCD	4.34±2.87	74.82

Values are mean ± S.E.M. n=number of animals in eachgroup; Significant differences with respect to solvent controlgroup were evaluated by Student's *t* - test. ($p<0.001$).

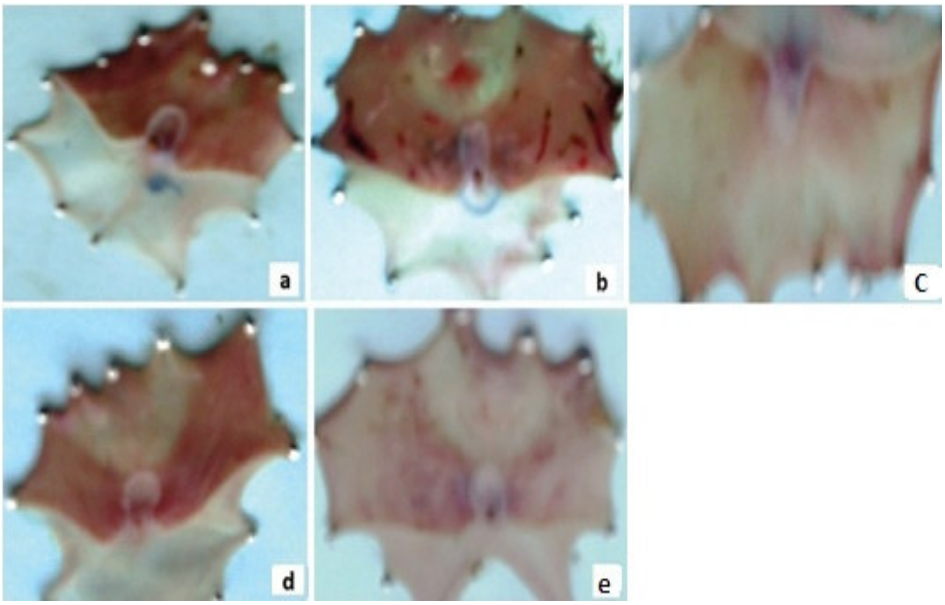

Fig 4: Effect of Clerodendrum serratum**on stress induced ulcers in the rats in the study (a) Normal Control (b) Ulcer Control (c) *AQCS* (250 mg/kg) treated (d) *ALCS* (250 mg/kg) treated (e) Omeprazole (10 mg/kg treated)**

PHYTOCHEMICAL STUDIES

Qualitative Analysis

Detection of Carbohydrates and glycosides

Small amount of extract was treated with few drops of dilute hydrochloric acid and filtered. The filtrate was collected and subjected for following tests.

A) **Molisch's test**
1 ml of filtrate was mixed with 2 drops of molisch's reagent and 1 ml of concentrated sulphuric acid was added along the sides of the test tube.(Brown to violet ring indicates the presence of carbohydrates) (Surekha, 1991, Kokate, C.K., et al., 2006).

B) **Legal's test**
Filtrate was hydrolysed with hydrochloric acid on water bath. 1 ml of pyridine and few drops of sodium nitro prusside were added and then made alkaline with sodium hydroxide solution. (Pink to red colour indicates the presence of glycosides)

C) **Borntrager's test**
Filtrate was hydrolysed with hydrochloric acid on water bath and then treated with chloroform. Chloroform layer was separated and dil. Ammonia solution was added to it. (If ammonia layer acquire pink or red or violet colour, indicates the presence of glycosides).

Detection of Alkaloids

Small quantity of extract was treated with few drops of dil. HCl and filtered. The filtrate was collected and subjected for following tests.

A) **Dragendroff's test**
Methanol extract of the plant (2 ml) and dilute hydrochloric acid (0.2 ml) were taken in a test tube. After adding 1 ml of Dragendroff's reagent. If reddish brown precipitate with filtrate, alkaloids are present

B) **Mayer's test**
2 ml of concentrated HCl was added to 2 ml of the respective plant extract samples followed by an addition of few drops of Mayer's reagent. If cream precipitate with filtrate, alkaloids are present.

C) **Wagner's test**
Two drops of Wagner reagent was added to 2 ml of extract and mixed well. If reddish brown precipitate with filtrate, alkaloids are present.

D) **Hager's test**
The extract was treated with few drops of Hager's reagent. A yellow precipitate was formed, indicating the presence of alkaloids. (Surekha, 1991).

Detection of Steroids
Small quantity of extract was treated with 5 ml of chloroform and subjected to the following tests.

A) Salkowsky test
To 1 ml of chloroform solution, 2ml of Conc. Sulphuric acid was added. If chloroform layer appears red color, and acid layer shows greenish yellow fluorescence indicates the presence of steroids.

B) Liebermann-Burchard test
To 2 ml of root extract add 1-2 ml of acetic anhydride was added and2 drops of Conc. Sulphuric acid was added along the sides of the test tube. First red, then blue and finally green color appearance indicates the presence of steroids.

Detection of Proteins and Amino acids:
Small quantity of extract was treated with in few ml of water and subjected to the following tests

A) Biuret Test:
Filtrate was treated with 4% NaOH and few drops of CuSO4 solution. Violet or pink color indicates the presence of proteins.

B) Millon's Test:
Filtrate was treated with Millon's reagent. White precipitate turns to brick red indicate the presence of proteins.

C) Ninhydrin Test:
Filtrate was treated with 3 drops of 5% Ninhydrin solution in boiling water bath for10 min. Purplish or bluish color appearance indicates the presence of Aminoacids (Khandelwal, K.R., 2004).

Detection of Flavonoids
Shinoda Test
Alcoholic extract treated with 5 ml of 95 % ethanol, few drops of Conc. HCl and 0.5 g Magnesium turnings. Pink color indicates the presence of flavonoids. (Khandelwal, K. R., 2004). To small quantity of extract, lead acetate solution was added. Formation of yellow colored precipitate indicates the presence of flavonoids. Extract was treated with sodium hydroxide; yellow coloration indicates the presence of flavonoids. (Kumar et al., 2008).

Detection of Tannins
To 5 ml of extract, 1ml of 10 % aq. Potassium dichromate solution was added. Red precipitate indicates the presence of tannins. To 5 ml of extract, 1 ml of 5 % ferric chloride solution was added, deep blue-black color, tannins. Small quantity of extract was treated with Dil. HNO3, reddish to yellow color (tannins). Extract treated with Dil. Iodine solutions, transient red color (tannins). Extract treated with Dil. KMnO4, decoloration (tannins) (Khandelwal, K.R., 2004).

Detection of Saponins
Foam Test
Dried root extract of plant was shaked with 20 ml distilled water vigorously. Persistent foam indicates the presence of Saponins.

Detection of Terpenoids

A) **Knoller's Test**
The extract was diluted with 2 ml of 0.1 % stannic chloride in pure thionylchloride. Pink to red to green to purple color indicates the presence of terpenoids.

Detection of Phenol

A) Test by Ferric chloride

Three drops of newly produced, 1% ferric chloride and potassium ferro cyanide were added to the aqueous extract solution to spike it. A bluish- green tinge was thought to be appealing. The extract of methanol was diluted with water. A few crystals of ferric sulphate were added to the mixture as well. The presence of phenolic compound is attested to by their deep violet blue.

Table 4: *Bidens pilosa* leaf extract Phytochemical test

S.No	PhytochemicalTest	Ethanolic extract
1.	Alkaloids	_
2.	Flavonoids	+
3.	Tannins	+
4.	Phenols	+
5	Carbohydrates	_
6.	Proteins	_
7.	Steroids	_
8.	Saponins	_

[- absence; + presence]

The anti-ulcer properties of Clerodendrum serratum were assessed using various models of gastric ulcers in rats, specifically those induced by alcohol, paracetamol, acetic acid, and stress. The choice of alcohol and paracetamol models is significant, as they are among the leading causes of gastric ulcers in humans. The study highlights several factors and mechanisms that contribute to ulcer formation and gastric mucosal damage, including increased gastric acid secretion, vascular injury, reduction of gastric wall mucin, mucosal damage from non-steroidal anti-inflammatory drugs, and the generation of free radicals.

Alcohol-induced gastric injury is linked to a substantial generation of oxygen free radicals, which results in heightened lipid peroxidation, ultimately damaging cells and their membranes. Clerodendrum serratum has demonstrated a notable protective effect on the gastric mucosa when exposed to alcohol, as evidenced by lower lesion index values in comparison to the solvent control group, indicating its strong cytoprotective properties. This effect is further supported by an increase in gastric mucus content resulting from the extract of Clerodendrum serratum.

Non-steroidal anti-inflammatory drugs (NSAIDs) such as paracetamol, aspirin, and indomethacin can harm the gastric mucosa by reducing prostaglandin levels due to the inhibition of prostaglandin synthesis. The extract of Clerodendrum serratum demonstrated significant efficacy in safeguarding the gastric mucosa from ulcers induced by paracetamol across all tested dosages. Therefore, Clerodendrum serratum extract provides substantial protection to the gastric mucosa against various damaging factors by enhancing gastric mucus production and lowering both the volume of gastric acid and its free and total acidity in rats.

Stress significantly contributes to the development of ulcers. The underlying mechanisms of stress-related gastric ulcers are intricate. It is likely that these ulcers are facilitated by the release of histamine, which increases acid secretion while decreasing mucus production. Both aqueous and alcoholic extracts of Clerodendrum serratum have proven effective in alleviating stress-induced ulcers.

The outcomes observed in all three models examined were dose-dependent. In summary, we have, to our knowledge, for the first time, shown that the extract of Clerodendrum serratum exhibits gastroprotective effects against ulcers induced experimentally in rats. The gastroprotective mechanism is likely linked to its antisecretory and cytoprotective properties. Nevertheless, additional studies are necessary to clarify and detail the molecular mechanisms underlying its anti-ulcer activity.

CONCLUSION

The study demonstrated that Clerodendrum serratum exhibits significant anti-ulcer activity in rat models of ulcers induced by paracetamol, alcohol, and stress. The protective effects appear to be primarily due to enhanced mucosal defense, reduced acid secretion, and antioxidant properties. Both aqueous and alcoholic extracts showed dose-dependent gastroprotective effects, likely attributed to the presence of flavonoids and other bioactive compounds. These findings support the traditional use of C. serratum and suggest its potential as a natural therapeutic agent for gastric ulcers. Further research is recommended to explore its active constituents and underlying molecular mechanisms.

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