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Alleviating Ulcer Burdens Examining the Potential of Albizia Odoratissima Bark Extract as a Therapeutic Agent in Mice

M. Tarannum Sultana [a], Shakir Basha [a*], Y. Sai Charan Teja [b] and Karthick. S [a]

[a] Department of Pharmaceutical Analysis, Raghavendra Institute of Pharmaceutical, Education and Research, K R Palli Cross, Chiyyedu, Anantapur-515721, Andhra Pradesh, India.
[b] Department of Pharmacology, Raghavendra Institute of Pharmaceutical, Education and Research, K R Palli Cross, Chiyyedu, Anantapur-515721, Andhra Pradesh, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Ulcerative stomach disease continues to be a prevalent gastrointestinal illness associated with high worldwide morbidity and medical costs. While nonsteroidal anti-inflammatory drugs (NSAIDs) and Helicobacter pylori infection are well-known risk factors for the development of peptic ulcers, recent evidence suggests a complex interaction between host factors and the gut microbiota in ulcer etiology. This study provides a comprehensive review of recent research investigating the relationship between the genesis and progression of peptic ulcers and dysbiosis of the gut

**Corresponding author: Email: shakirbasha336@gmail.com;*

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microbiota. The study highlights several natural compounds, such as flavonoids, polyphenols, alkaloids, and polysaccharides, that have demonstrated anti-ulcer activity in experimental models and clinical trials. Mechanistic understanding clarifies the many pathways, including antibacterial, anti-inflammatory, and antioxidant ones, through which these drugs perform their medicinal effects. It is interesting to note that many natural compounds focus on many pathogenic procedures that aid in the development and spread of ulcers, resulting in multifactorial effects. Albizia odoratissima is a member of the Fabaceae family and has been used traditionally in many folk medicines due to its medicinal characteristics. This study used experimental models of stomach ulceration to investigate potential anti-ulcer properties of methanolic bark extract from Albizia odoratissima (MAO). The anti-ulcer qualities of MAO were evaluated in rats using models of stomach ulceration brought on by HCL. Many parameters were assessed when different doses of MAO were administered orally, including the ulcer index, mucosal injury to the stomach, mucin content, and antioxidant enzyme levels. Additionally, a histological analysis was carried out to evaluate the possible protective qualities of MAO against harm to the stomach mucosa.

Keywords: Peptic ulcer; gastrointestinal disorder; anti-ulcer activity; anti-oxidant.

1. INTRODUCTION

1.1 Peptic Ulcer

These days, stomach ulcers and hyperacidity are more common and extremely painful for people]. It is brought on by an imbalance between the mucosa's defense mechanisms and toxic chemicals found in the lumen [2]. The exact mechanism underlying the considerable stomach irritation is caused by persistent anxiety, psychological distress, hemorrhagic postoperative shock, burns, and trauma [3,4]. This particular sort of ulcer was formerly believed to be brought on by stress and spicy foods [5]. However current studies have revealed that they are merely aggravating factors. The cause can be either an H. pylori infection or an adverse reaction to some medications, such as NSAIDs.Free radicals produced by oxygen have also been linked to the etiology of numerous diseases in a wide range of animal species [6,7]. Open sores on the lining of the stomach, upper small intestine, or esophagus are known as peptic ulcers [8,9]. Helicobacter pylori infection or prolonged use of nonsteroidal anti-inflammatory substances (NSAIDs) are the usual causes of them [10]. Antibiotics to remove the H. pylori infection, drugs to decrease stomach acid production, and lifestyle modifications like cutting back on NSAIDs and stress management are frequently used in combination with treatment. Surgical intervention may be necessary in extreme cases if complications such as bleeding or perforation occur. Peptic ulcers can recover and recurrence can be avoided with the right care and lifestyle changes [11]. On the other hand, to avoid complications and guarantee efficient treatment of the illness, early detection and fast medical attention are essential. Any class of chemical, such as proteins, lipids, lipoproteins, nucleic acids, glucose, and macromolecules found in tissue connections, can be harmed by oxygen radicals, either permanently or reversibly. Two types of free radicals that mainly impact substrate oxidation are reactive oxygen species (ROS) and reactive nitrogen species (RNS). These species may also have an effect on gene expression, metabolism, and membrane function in biological systems [12] Organisms with one or more unpaired electrons that are capable of independent living are known as free radicals. These are common outcomes of aerobic metabolism in living things [13]. The two main types of free radicals found in cells are superoxide (O2-) and hydroxyl (OH-) species. Reactive oxygen species (ROS) is the collective term for these molecules. Peroxynitrite (ONOO-) and hydrogen peroxide (H2O2) contribute to the cellular redox state but are not free radicals [14,15].

1.2 Types of Ulcers

Depending on location, peptic ulcers are classified as

1. Oesophageal ulcers
2. Gastric ulcers
3. Duodenal ulcers

- Oesophageal ulcers:

which are described as open lesions in the esophageal lining—present a challenging clinical issue [16]. Numerous underlying illnesses, such as the bacterium Helicobacter pylori. infections, chronic usage of nonsteroidal anti-inflammatory

drugs (NSAIDs), or conditions like GERD, can cause these ulcers [17] Esophageal ulcer symptoms can include heartburn, trouble swallowing, chest pain, and in extreme cases, bleeding [18]. A comprehensive medical history, physical examination, endoscopic techniques for direct visualization, and if necessary, a biopsy, are usually part of the diagnosis process. Acid-suppressing drugs, lifestyle changes, antibiotic therapy for H. pylori infection, and in some cases, surgical intervention are examples of treatment options that concentrate on treating the underlying cause [19]. Early identification and suitable intervention are essential for esophageal ulcer patients to avoid complications and have better patient outcomes [20].

- Gastric ulcers:

Lesions that develop in the lining of the stomach are known as gastric ulcers. sometimes referred to as stomach ulcers [21]. Numerous causes, such as Chronic usage of anti-inflammatory drugs (NSAIDs) and an infestation of Helicobacter pylori, excessive alcohol intake, smoking, and stress, can cause these ulcers [22]. Abdominal pain, especially after eating, nausea, vomiting, bloating, and inadvertent weight loss are all possible signs of gastric ulcers [23]. A patient's medical history, physical examination, and diagnostic procedures like upper endoscopy and imaging studies are often used in conjunction with one another to provide a diagnosis [24]. Inhibitors of proton pumps and hydrogen receptor antagonists, among other medications, are commonly used in combination for the treatment of stomach acid production [25]. Antibiotics are also sometimes used to treat H. pylori infections that may be present, lifestyle changes are sometimes made, and surgery is occasionally necessary [26]. Timely diagnosis and suitable treatment are crucial. to avoid consequences including bleeding, stomach wall perforation, or obstruction of the gastric outlet [27].

- Duodenal ulcers:

Open sores termed duodenal ulcers develop in the lining of the duodenum, the small intestine's first segment [28]. The major causes of these ulcers are prolonged use of nonsteroidal anti-inflammatory medications (NSAIDs) or Helicobacter pylori infection [29]. Smoking, binge drinking, stress, and certain medical problems are additional risk factors. Abdominal pain, especially at night or when the stomach is empty, bloating, nausea, vomiting, and inadvertent weight loss are all possible signs of duodenal ulcers [30]. A patient's medical history, physical examination, and diagnostic procedures like upper endoscopy and imaging studies are often used in conjunction with one another to provide a diagnosis [31]. Antibiotics to treat H. pylori infection (if present), drugs to decrease stomach acid production (such as proton pump inhibitors and H2 receptor antagonists), and if any, as well as alterations to the way of life [32,33].

Depending on the severity, peptic ulcers are also classified as:

- Acute ulcers

Acute ulcers affect tissues down to the submucosa. They can manifest themselves as a single or many lesions [34]. They can be found in a variety of places throughout the stomach, as well as the first few centimeters of the duodenum. Ulcers classified as acute usually appear quite fast and last for a brief period. The stomach, duodenum, and esophagus are among the body areas where these ulcers can develop [35]. Intense pain and discomfort are frequently the hallmarks of acute ulcers, which can also present with symptoms including bleeding, nausea, vomiting, and bloating in the abdomen [36]. Chronic use of non-steroidal anti-inflammatory medications (NSAIDs), an infestation of Helicobacter pylori, and excessive alcohol consumption, smoking, and stress are common causes of acute ulcers [37]. Antibiotics if a bacterial infection is present, lifestyle changes, and drugs to lower stomach acid production are typically used in the treatment of acute ulcers [38]. Timely identification and treatment are essential to prevent complications and promote the healing of acute ulcers.

- Chronic ulcers

Chronic ulcers are open sores that endure a long time—usually more than six weeks—and frequently come back even after therapy [39]. These ulcers can develop in the epidermis, stomach, duodenum, or esophagus, among other places. Numerous underlying conditions, including poor circulation, diabetes, autoimmune illnesses, prolonged skin pressure (as in the case of pressure ulcers), or infection caused by the bacteria Helicobacter pylori (as in the case of duodenal or stomach ulcers),can cause chronic ulcers [40]. Furthermore, diseases that hinder the body's ability to heal, such as neuropathy,

venous insufficiency, and arterial insufficiency, can be linked to chronic ulcers [41]. Treating the underlying cause of persistent ulcers in addition to using wound care techniques such as cleansing, debridement, dressings, and in certain cases instances, surgical procedures [42]. It may be required to use multidisciplinary techniques involving medical specialists like nutritionists, vascular surgeons, and wound care specialists to effectively manage and prevent persistent ulcer problems [43]

Both have identical pathology characteristics that are highly diagnostic

1.3 Causes of Blisters

1.3.1 Gastritis triggered by Helicobacter Pylori bacteria

The bacterium Helicobacter was found by two Australian researchers and concluded that infections with curved Gram-negative bacteria were the cause of gastritis and ulcerations of the stomach or duodenum [44].

1.3.2 Mucus secretions

Reports state that around 50% of patients with stomach ulcers have pepsin and acid hyper secretors As the first line of defense in the mucosal layer, it keeps germs from colonizing and restricts their ability to penetrate the layer [45]. Acid-pepsin secretion, which shields the stomach mucosa against gastric lesions, depends critically on mucus secretion [46]. Additionally, it is acknowledged as a crucial defence mechanism within the stomach mucus barrier. The cause of stomach ulcers has been determined to be decreased manufacturing of sulfated mucus glycoprotein [47].

1.3.3 Gastritis

Some of the instances are transmission, alcohol, specific medications, and some immunological and allergy disorders. The inflammation (irritation) of the stomach lining is known as gastritis [48]. There could be several reasons for this. Gastritis can be classified as chronic (with symptoms lasting longer than a day) or acute (with violent episodes lasting a few of days) (with persistent nausea or loss of appetite) [49]. Gastritis often goes undiagnosed (asymptomatic). One such condition that has been connected to a higher risk of stomach cancer is chronic atrophic gastritis [50]. Two therapy options are to avoid to avoid well-known triggers and to take medicine to lessen the quantity of gastrointestinal secretions [51].

1.3.4 Internal mediators

As they disrupt the delicate balance between variables that promote mucosal injury and preventive mechanisms, endogenous mediators are important players in the pathophysiology of ulcers. Prostaglandins, which are derived from arachidonic acid, have a protective impact on the gastrointestinal system by promoting the secretion of mucus and bicarbonate while suppressing the secretion of stomach acid [52]. Nonsteroidal anti-inflammatory medications (NSAIDs) have the potential to suppress prostaglandin synthesis, which can compromise mucosal protection and heighten the risk of ulcer development. Another important mediator, histamine, increases the release of stomach acid, which can harm mucosa if it is secreted in excess or if defenses are weak. Furthermore, cytokines that play important roles in inflammation and tissue damage, such as TNF-alpha (TNF-alpha), interleukin-6 (IL-6), and interleukin-1 (IL-1), exacerbate the formation of ulcers. Additionally, reactive oxygen species (ROS) and nitric oxide (NO) contribute to ulcer etiology, altering the control of blood flow and resulting in oxidative harm to the stomach mucosa. Comprehending the complex interaction between these endogenous mediators offers important information about possible therapeutic approaches meant to maintain mucosal integrity and avoid ulcer development [53].

1.3.5 Platelet-Activating Factor

Factor that activates platelets Among the strongest ulcerogens is PAF. The sequestration of neutrophil aggregates in the stomach, vasoconstriction, production of free radicals, and release of lysosomal enzymes are the factors that lead to PAF-induced ulceration [54].

1.3.6 Histamine

Humans and other mammals have considerable amounts of histamine (around 40 micrograms per wet weight) in their oxyntic mucosa. Histamine, a potent gastric secretion stimulant, has been discovered to be present in the stomach wall [53]. On the other hand, excessive histamine release—either through histamine release itself or by injecting an aqueous solution of

histamine—causes duodenal and stomach ulcers. Since inhibiting histamine receptors stops stomach ulcers brought on by steroids, NSAIDs, and reserpine in both humans and lab animals, histamine is also involved in another type of ulceration [55]. It has been suggested that histamine blockers, such as ranitidine, can prevent stomach ulcers brought on by psychological stress [56].

1.3.7 Radicals without chains

Free radicals are chemical entities with unpaired electrons in their outer orbit that are incredibly reactive. In reaction to nonradicals, free radicals must produce more free radicals. Whether phagocytosis is occurring or there is a pathogenic state, cells always show this outcome [57]. Transition metals (Fe2+, Cu+) and oxygen, together with its radical equivalents O-2 and OH, H2O2, are the main reactants in free radical biochemistry in aerobic cells.

- Superoxide radicals are formed when oxygen is reduced by a single electron transfer.

$O2 + e – \rightarrow O2 –$

- Superoxide radicals can react with nitric oxide to generate peroxynitrite.

$O2 – + NO–\rightarrow ONOO –$

In biological systems, superoxide dismutase the following oxygen's two-electron reduction to form H2O2. All biological types of components, including proteins, lipids, lipoproteins, free amino acids, nucleic acids, carbohydrates, and macromolecules found in tissue connections, can be irreversibly or partially damaged by hydroxyl radicals [58]. These species may have an impact on gene expression, metabolism, and membrane function in cells.

Another idea holds that mucosal injury results from the breakdown of hyaluronic acid, which is the primary component of the epithelial basement membrane, by free radicals, especially OH [59]. The body contains defenses against and ways to prevent damage from free radicals. Endogenous antioxidant enzymes include catalase, glucose oxidase, superoxide dismutase and glutathione peroxidase They are in favor of maintaining the equilibrium between the production of reactive oxygen species and their elimination [60]

1.4 Current Treatment of Ulcer

1. Diminished secretion of stomach acid [61]

- H2 Antihistamines: Cimetidine, Ranitidine, Famotidine
- PPIs: Omeprazole, Rabeprazole, Lansoprazole, Pantoprazole
- Anticholinergics: Oxyphenoium, Propantheline, and Pirenzepine
- Analogs of prostaglandins: Misoprostol, Enprostiol, and Rioprostol

2. Antacids Non-systemic (local):

- magnesium hydroxide, magnesium trisilicate, aluminum hydroxide gel, calcium carbonate;
- Systemic: sodium bicarbonate, sodium citrate

3. Sucralfate and CBS (colloidal bismuth subnitrate) are agents that prevent ulcers.
4. Carbenoxolone sodium is an ulcer-healing medication
5. Anti-H. Pyloric medications: Tetracycline, Metronidazole, Tinidazole, Clarithromycin, and Amoxicillin

1.5 Plant Profile

Albizia Odoratissima:
Synonyms: Albizia orissensis K.C Sahni and Bennet
Family: Mimosaceae

1.6 Taxonomical classification

Kingdom: Plantae
Phylum: Angiosperms
Class: Eudicots
Order: Fabales
Family: Fabaceae (Leguminosae)
Subfamily: Mimosoideae
Genus: Albizia
Species: Albizia odoratissima

1.7 Vernacular Names

Assamese: koroi
Bengali: kakur siris
English: black siris, Ceylon rose wood, fragrant Albizia, tea shade tree
Telugu: cinduha
Gujarati: karo shirish
Hindi: Kala siris
Kannada: kaadu barge, Bilvaara

Tamil: Cilai.

2. METHODOLOGY

Plant Material Collection: Albizia odoratissima bark was collected from the forest region of Tirupati, India. The herbarium was created and authenticated by Dr. Madhava Chetty of Sri Venkateshwara University.

Preparation of Methanolic Extract: The collected bark was dried, powdered, and subjected to extraction using a Soxhlet extractor with 90% methanol as the solvent. The extract was filtered and dried to obtain the methanolic bark extract.

Phytochemical Screening: The extract underwent phytochemical screening to determine the presence of various compounds like flavonoids, alkaloids, tannins, steroids, and carbohydrates using standard chemical tests.

Quantification of Flavonoids and Phenolic Content: Total flavonoid content (TFC) and total phenolic content (TPC) were quantified using colorimetric assays with quercetin and gallic acid as standards, respectively.

In Silico Docking Studies: Molecular docking studies were conducted using Schrodinger Glide software to predict the interaction of the extract compounds with the stomach proton pump (PDB code: 6JXH) compared to standard compounds like ferulic acid, quercetin, and gallic acid.

In Vitro Studies: Acid neutralizing capacity (ANC) was determined by titration method, comparing the extract's ANC with standard antacids.

In Vivo Studies: The anti-ulcer activity of the extract was evaluated using an ethanol/HCl-induced ulcer model in mice. Various doses of the extract were administered orally, and parameters like ulcer index and ulcer inhibition rate were measured and compared with a standard drug, ranitidine.

2.1 Materials and Procedures

2.1.1 Gathering plant material

Albizia Odoratissima plant bark was obtained in Tirupati, India's forest region. Dr. Madhava Chetty of Sri Venkateshwara University in Tirupati created and authenticated the herbarium. The specimen number for the authenticity voucher is 0807.

2.1.2 Methanolic extract preparation

A. Odoratissima bark was collected, dried, and powdered. A Soxhlet extractor was used to extract 100g of powdered medication for 72 hours using 90% methanol as the solvent. In a China plate, the extract was filtered and dried.

Table 1. Representing phytochemical tests

S no	Chemical tests	
1	Flavonoids	Lead acetate test NaOH test FeCl3 test Shinoda test
2	The alkaloids	Test of Dragendroff Hager examination Wagner's examination Mayer's examination
3	Tannins	Gelatine test Vanillin test Matchstick test
4	Steroids	Salkowski’s test
5	Carbohydrates	Molisch test Benedict’s test

Picture 1. bark extract prepared by using Soxhlet extractor

Picture 2. extract was filtered and dried in china dishes

2.2 Phytochemical Tests

To detect the presence of flavonoids, alkaloids, tannins, steroids, and carbohydrates, phytochemical screening was carried out.

2.2.1 Calculating the total amount of flavonoids

- The TFC of crude bark extracts was evaluated using the aluminum chloride colorimetric test. The standard used to create the calibration curve was quercetin (20–100 lg/mL).
- 2.8 mL of double-distilled water, 1 mL of crude extract, and 0.1 mL of potassium acetate solution (1 mg/mL) were mixed.
- The absorbance at 415 nm was measured using a UV-visible spectrophotometer following the addition of 0.1 mL of 10% aluminum chloride to the solution and a 30-minute standing period.
- A calibration curve was used to calculate the TFC and the results are expressed in milligrams (mg/g) of quercetin equivalents per gram of bark (dry weight).

2.3.2 Calculation of the total phenolic content (TPC)

The Folin–Ciocalteu (FC) method was employed. The calibration curve was made using gallic acid (20–500 lg/mL) as a standard.

- After carefully mixing 1 mL of FC reagent (which had been diluted 6-fold with distilled water) with 1 mL of crude extract, 2 mL of 20 percent (w/v) sodium carbonate was added. The mixture was then diluted up to 3 mL with distilled water.
- After letting the mixture remain in the dark for half an hour, the absorbance at 765 nm was measured using a UV-visible spectrophotometer. The results are expressed in milligrams of gallic acid equivalents per gram of bark (mg/g) (dry weight), which was determined by utilizing a calibration curve.

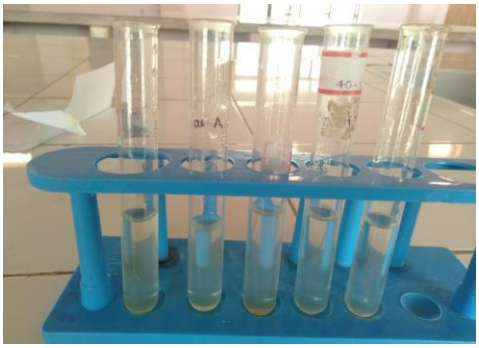
3. INSILICO STUDIES

3.1 Docking Studies

Prior to production, Schrodinger Glide (version 12.8a) was used for in silico molecular docking studies on the library to identify the most appropriate molecule with the greatest docking scores and interactions. To determine antiulcer action, all the proposed compounds were docked with the protein, stomach proton pump (PDB code: 6JXH), as well as standard ferulic acid, quercetin, and gallic acid.

3.2 Ligand Preparation

• The maestro Schrodinger software's 2D Sketcher (Version 12.8) was used to import structures into the workspace using compound SMILES notations. All ligands were subjected to energy minimization via Glide Ligprep while maintaining the essential limitations, such as ionization (Neutralize), chirality, computation, and so on.



Picture 3. Determination of flavonoid and phenolic content

3.3 Protein Preparation

The Glide Protein preparation wizard was used to create an energy-minimized protein appropriate for virtual screening using a well-known approach. The proteins were imported into the workspace using the PDB code 6JXH, which was obtained directly from the protein data bank. The protein is first pre-processed with Epic, which assigns bond ordering, adds hydrogens, creates disulfide bonds, and generates het states. The selected protein was first optimized and then minimized in the refine tab.

3.4 Receptor Grid Generation

• Receptor grid creation is utilized in the maestro task to create a grid at the active binding site of the proteins by selecting any one atom of the co-crystal ligand molecule on the workspace.

3.5 Ligand Docking

After choosing to dock ligand docking (virtual screening), the glide grid and ligand manage zip files were loaded from the working directory.

Next, the write SP descriptor information is chosen to dock according to the settings.

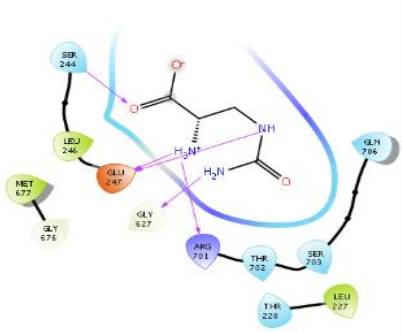


Image. 1. Albizzin A

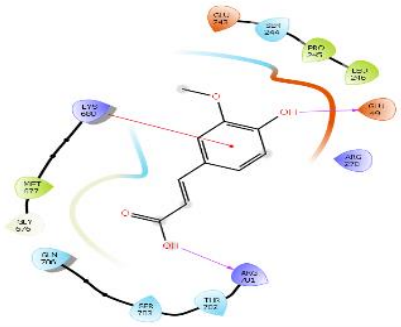


Image. 2. Gallic acid

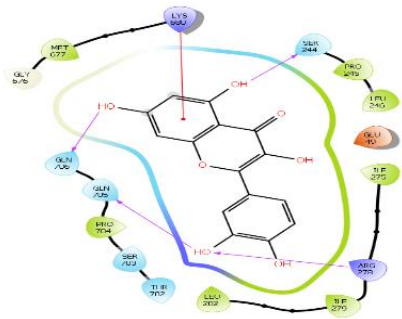


Image 3. Quercetin

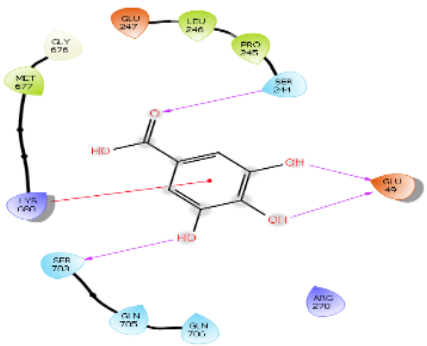


Image 4. Ferulic acid

4. *In vitro* STUDIES

4.1 Acid Neutralizing Capacity

The ANC value achieved for the methanolic extract (500, 1000, and 1500 mg/5 ml) was compared to the standard antacids' mixture (containing magnesium hydroxide and aluminum hydroxide gel in 1:1 proportion, 250 mg each/5 ml). To make 70 ml total, 5 ml of this mixture was mixed with water, and the mixture was then agitated for a minute.

- After that, the standard and test preparations (aqueous extracts 500, 1000, and 1500 mg/5 ml) were combined with 30 ml of 1.0 N HCl and left to mix for 15 minutes. The surplus HCl was quickly titrated with 0.5 N sodium hydroxide solution (for 10 to 15 sec) to reach a constant pH of 3.5.
- During the experiment, the combination's temperature was maintained at 37 experiment at 0.5 °C. The formula was then used to determine how many milliequivalents of acid were consumed.
- Where N HCl and N NaOH are the normalcy of HCl and NaOH, respectively, and NaOH is the volume of NaOH used for titration, the total mEq of acid consumed is (30 × N HCl) – (V NaOH × N NaOH).
- Both the test preparation and the ANC values are expressed as mEq of acid absorbed by 5 ml of standard.

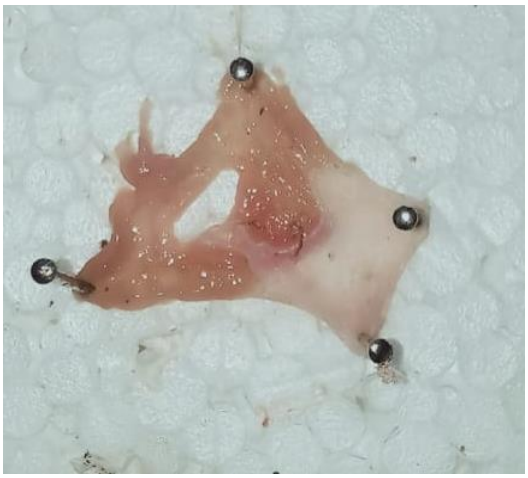
5. *In vivo* STUDIES

5.1 Animals and the Methods used in Experiments

- We collected 15 mature male mice weighing between 21 and 39 grams. The experimental setup is displayed below. Five groups of the aforementioned mice were randomly assigned for seven days.
- Control group
- HCL/ethanol group
- HCL/ethanol + Methanolic extract of Albizia odoratissima (M.E.A.O) (250mg/kg)
- HCL/ethanol + M.E.A.O(500mg/kg)
- 50 mg/kg of ranitidine + HCL/ethanol.

5.2 Development of a Model of HCl/Ethanol-Induced Gastric Ulcer

To create a mouse model of an acute gastric ulcer, the mice in the other groups—aside from the CON group—were gavaged with 150 mmol HCl and 0.1 ml HCl/ethanol per 10 g BW.



Picture 4. ethanol/HCl-induced ulcers

6. RESULTS

6.1 Phytochemical Screening

6.1.1 Total phenolic content

The absorbance of the methanolic extract was 0.223. The total phenolic content in terms of gallic acid was determined to be 28.96µg based on the calibration curve of gallic acid. This was computed using the gallic acid standard curve regression equation, ($y=0.0077x$, $R^2=0.9981$).

6.1.2 Total flavonoid content

The absorbance of the methanolic extract was 0.417. The total flavonoid content in terms of quercetin was determined to be 58.73µg based on the quercetin calibration curve. This was computed using the quercetin standard curve regression equation ($y=0.0071x$, $R2=0.9965$).

6.2 Docking Results

6.2.1 Invitro antiulcer activity

Invivo antiulcer activity: Each value is given as mean ± SEM (n = 6). NC denotes a control group that is typical. ulcers caused by ethanol and HCl were treated with 250 mg/kg of Albizia Odarotissima methanolic extract. A 500 mg/kg dose was administered to a different group. The other group received the usual dosage of 50 mg/kg of ranitidine. These are contrasted, in turn, with the ethanol/chlorocarbon group.

6.3 Advanced Research Regarding Anti-ulcer Activity

Probiotics: Research suggests that probiotics, particularly strains of lactobacilli and bifidobacteria, may play a role in preventing and treating gastric ulcers by modulating the gut microbiota and enhancing mucosal defense mechanisms.

Novel Drug Delivery Systems: Scientists are developing innovative drug delivery systems to improve the bioavailability and efficacy of anti-ulcer drugs. These include nanoparticles, liposomes, and mucoadhesive formulations that can target specific sites in the gastrointestinal tract and prolong drug release.

Peptide Therapeutics: Peptides derived from natural sources or designed synthetically have shown promise as anti-ulcer agents. Peptides like ghrelin and gastrin-releasing peptide (GRP) analogs have been investigated for their ability to stimulate gastric mucosal repair and reduce ulcer formation.

Herbal Formulations: Traditional herbal remedies continue to be explored for their potential in ulcer management. Formulations containing herbs like licorice (Glycyrrhiza glabra), aloe vera, and chamomile have been studied for their anti-ulcer effects in both preclinical and clinical trials.

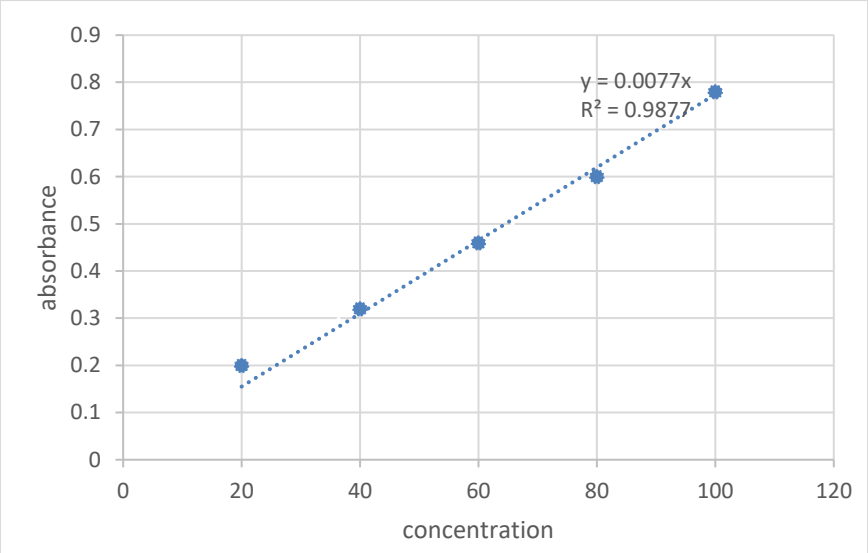
Biological Agents: Biologic drugs targeting specific molecular pathways involved in ulcer formation, such as tumor necrosis factor-alpha (TNF-α) inhibitors and growth factors like epidermal growth factor (EGF), are being investigated as potential therapies for severe or refractory ulcers.

Stem Cell Therapy: Emerging research suggests that stem cell therapy may promote ulcer healing by enhancing tissue regeneration and modulating inflammatory responses in the gastric mucosa. Mesenchymal stem cells (MSCs) derived from various sources have shown promise in preclinical studies.

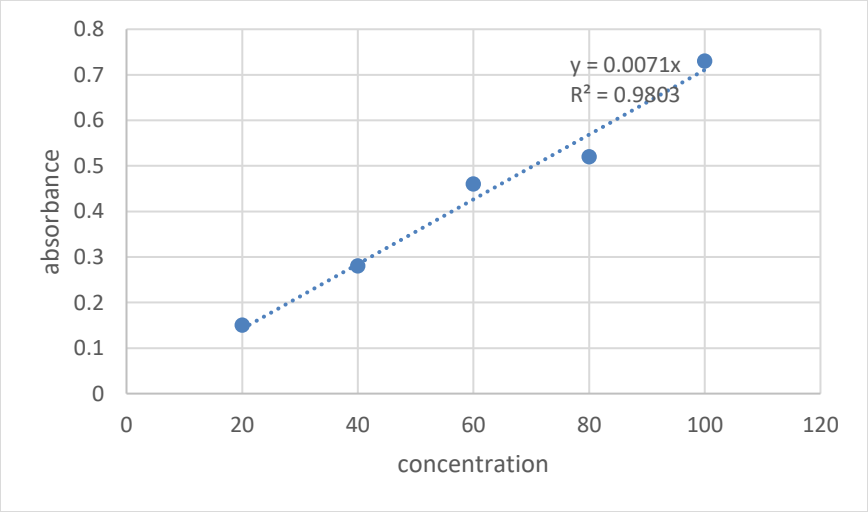
MicroRNA (miRNA) Therapeutics: Dysregulation of microRNAs, small non-coding RNAs that regulate gene expression, has been implicated in the pathogenesis of gastric ulcers. Targeting specific miRNAs involved in inflammation, angiogenesis, and mucosal integrity represents a novel approach for developing anti-ulcer therapies.

Table 2. Results of phytochemical tests

S.NO	Chemical tests		Results
1	Flavonoids	Lead acetate examination	-
		NaOH examination	-
		FeCl3 examination	+
		Shinoda examination	+
2	The Alkaloids	Dragendroff examination	+
		Hager's examination	+
		Wagner's examination	+
		Mayer's examination	+
3	Tannins	Gelatine examination	+
		Vanillin examination	+
		Match stick examination	+
4	Steroids	Salkowiski test	+
5	Carbohydrates	Molish test	-
		Benedict's test	-



Graph 1. Result showing phenolic content



Graph 2. Result showing flavonoid content

Table 3. Representing docking score

Serial n.o	compounds	Docking score
1	quercetin	-9.2999056
2	Gallic acid	-5.0838821
3	Ferulic acid	-4.5185849
4	Albizzin	-4.2609688
5	Gallic acid	-4.1777507
6	Ferulic acid	-4.0136824
7	Albizzin	-3.5777582

Table 4. results of invitro studies

Formulation	The quantity of NaOH ingested(ml)	mEq of acid supplied
M.E.A.O batch 1	19.8	10.2
M.E.A.O batch 2	19.5	10.5
M.E.A.O batch 3	19.1	10.9
Standard (magnesium hydroxide)	23.4	14.8

Table 5. Results of in vivo studies

Formulation	Ulcer Index	Ulcer inhibition rate
NC	0.0±0.00	100±0.00
HCl/Ethanol	3.3±0.49	0.00±0.00
HCl/Ethanol +M.E.A.O [250mg/kg]	1.8±0.30	38.3±13.0
HCl/Ethanol +M.E.A.O [500mg/kg]	1.0±0.36	75.3±8.51
Standard (ranitidine),50mg/kg	0.6±0.33	84.2±8.21

7. DISCUSSION

Millions of people worldwide suffer from gastric hyperactivity, a condition that is often caused by an imbalance between protective and aggressive elements. Proton pump inhibitors, antimuscarinics, and H2 receptor antagonists are the mainstays of contemporary peptic ulcer treatment. Unfortunately, many of these treatments result in side effects including hematological problems, hypersensitivity, arrhythmia, and impotence. As an alternative to conventional medications, a lot of extracts or active components from natural plants have been studied. Herbal remedies have long been utilized in clinical settings and have shown promise in the management of a wide range of illnesses. This study was conducted for the first time to assess Albizia Odarotissima's methanolic extract's gastroprotective properties.

The study's findings are then discussed in detail, starting with the phytochemical analysis which revealed the presence of flavonoids in the methanolic extract. Flavonoids are known for their antioxidant properties, which are crucial for protecting the gastric mucosa from oxidative damage. This observation aligns with previous research indicating the potential of flavonoids in ulcer management.

Moreover, the in silico docking studies provided valuable insights into the molecular interactions between the extract compounds and proton pump inhibitors, further supporting the potential therapeutic efficacy of Albizia odoratissima bark extract in inhibiting gastric acid secretion.

The in vitro experiments, particularly the assessment of antacid neutralizing capacity, demonstrated the extract's ability to counteract acid-induced damage, thereby reinforcing its gastroprotective properties.

Finally, the in vivo studies conducted on mice corroborated the findings from earlier experiments, confirming the extract's protective role against ethanol/HCl-induced ulcers. This protective effect was attributed to the antioxidant properties of flavonoids present in the extract.

8. CONCLUSION

The current investigation found that the bark extract (methanolic) of Albizia Odarotissima showed adequate amounts of flavonoids, which

played a protective role against ulcers. Through In silico studies (Docking with proton pump inhibitors), Invitro antacid neutralizing capacity was observed and In vivo studies show the protective role is due to the antioxidant properties of flavonoids.

In conclusion, the study provides compelling evidence for the gastroprotective properties of Albizia odoratissima bark extract. The presence of flavonoids, validated through phytochemical analysis, in combination with in silico docking studies, in vitro experiments, and in vivo evaluations, collectively support the efficacy of the extract in mitigating gastric hyperactivity and preventing ulcer formation.

The findings of this study offer a promising avenue for the development of natural remedies for peptic ulcers, potentially offering a safer and more effective alternative to conventional medications. Further research, including clinical trials in human subjects, is warranted to validate these findings and explore the full therapeutic potential of Albizia odoratissima bark extract in clinical settings.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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