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ANTIULCER ACTIVITY OF METHANOLIC EXTRACT OF *SALVADORA INDICA* (W.) LEAVES AND ITS COMPARISON WITH RANITIDINE IN SHAY RAT

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Article History	Abstract
Received: 19-06-2026 Revised: 14-07-2026 Accepted: 13-08-2026	Peptic ulcer is a common gastrointestinal disorder associated with an imbalance between aggressive factors, such as gastric acid and pepsin, and the protective mechanisms of the gastric mucosa. Traditional systems of medicine have long utilized medicinal plants for the management of gastrointestinal disorders, including peptic ulcers. In view of the therapeutic potential of herbal medicines, the present study was undertaken to evaluate the anti-ulcer activity of aqueous and alcoholic extracts of <i>Salvadora indica</i> leaves (AQSI and ALSI) in experimentally induced gastric ulcer models in rats. The anti-ulcer activity of AQSI and ALSI was evaluated at a dose of 250 mg/kg using three experimental ulcer models: alcohol-induced, paracetamol-induced, and forced-immersion stress-induced gastric ulcers. Ranitidine at 50 mg/kg was used as the standard drug. Gastric lesions were assessed by determining the ulcer index, while gastric mucus content was evaluated in the alcohol-induced ulcer model. Pretreatment with both AQSI and ALSI produced a significant reduction in gastric lesion formation and ulcer index in the alcohol-induced ulcer model, along with an increase in gastric mucus content. Both extracts also demonstrated significant protection against paracetamol-induced gastric ulcers and stress-induced ulceration. The observed effects were dose dependent and were comparable with the standard anti-ulcer drug. The findings indicate that aqueous and alcoholic extracts of <i>Salvadora indica</i> leaves possess significant anti-ulcer activity. The protective effect may be attributed to a combination of cytoprotective and antisecretory mechanisms, including enhancement of gastric mucosal defense and reduction of gastric aggressive factors. These results support the traditional use of <i>Salvadora indica</i> in the management of gastrointestinal disorders and suggest its potential as a source of anti-ulcer agents.
Keywords: <i>Salvadora indica</i> , anti-ulcer activity, antisecretory, cytoprotective, gastric ulcer, alcohol-induced ulcer, paracetamol-induced ulcer, stress-induced ulcer.	
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INTRODUCTION

Peptic ulcer disease (PUD) is one of the most common disorders affecting the gastrointestinal tract and represents a significant clinical problem worldwide. It is characterized by the development of a localized break or ulceration in the mucosal lining of the stomach or duodenum as a consequence of an imbalance between aggressive factors and protective mechanisms of the gastrointestinal mucosa. Gastric acid and pepsin are important aggressive factors, whereas mucus, bicarbonate, adequate mucosal blood flow, prostaglandins, and epithelial regeneration contribute to mucosal protection. When these protective mechanisms become inadequate, gastric or duodenal mucosal injury may progress to ulcer formation [1]. Peptic ulcers can occur at different sites of the upper gastrointestinal tract and are broadly classified into gastric and duodenal ulcers. Gastric ulcers generally develop in the stomach, particularly along the lesser curvature, whereas duodenal ulcers commonly occur in the first part of the duodenum. Although peptic ulcer disease can affect individuals of different age groups, its occurrence is influenced by several factors, including *Helicobacter pylori* infection, prolonged use of non-steroidal anti-inflammatory drugs (NSAIDs), smoking, alcohol consumption, physiological stress, and other environmental and genetic factors. Among these, *H. pylori*

infection and NSAID-associated mucosal injury are considered major causes of peptic ulceration.

The stomach possesses several physiological mechanisms that protect its mucosa from gastric acid and digestive enzymes. Gastric mucus forms a protective barrier over the epithelial surface, while bicarbonate helps neutralize acid near the mucosal cells. Prostaglandins contribute to mucosal defense by stimulating mucus and bicarbonate secretion and maintaining adequate gastric blood flow. Continuous replacement of damaged epithelial cells also supports mucosal integrity. Disturbance of any of these mechanisms can increase susceptibility to gastric injury. Excessive exposure to gastric acid, pepsin, alcohol, or ulcerogenic drugs may further aggravate mucosal damage [2-4].

Gastric acid secretion is regulated through complex neural, hormonal, and paracrine mechanisms. The major stimulatory mediators are acetylcholine, gastrin, and histamine. Acetylcholine is released from vagal and enteric neurons, gastrin is secreted by G cells of the gastric antrum, and histamine is released from enterochromaffin-like cells. These mediators stimulate parietal cells to secrete hydrochloric acid through the hydrogen-potassium ATPase proton pump. Somatostatin acts as an important inhibitory regulator of gastric acid secretion. An imbalance between these regulatory

mechanisms may contribute to excessive acid production and mucosal injury.

The development of peptic ulcers is also strongly associated with *H. pylori*, a bacterium capable of colonizing the gastric mucosa. Infection can produce chronic inflammation and weaken the mucosal defense system, thereby increasing susceptibility to acid-mediated injury. Another important cause is prolonged or excessive use of NSAIDs such as aspirin and ibuprofen. These drugs inhibit cyclooxygenase-mediated prostaglandin synthesis, resulting in reduced mucus and bicarbonate secretion, impaired mucosal blood flow, and increased vulnerability of the gastric lining. Lifestyle factors such as smoking and excessive alcohol consumption may further delay ulcer healing and increase the risk of complications [5-].

The clinical manifestations of peptic ulcer disease vary according to the site and severity of the lesion. The most common symptom is burning or gnawing epigastric pain. Patients may also experience nausea, vomiting, indigestion, bloating, loss of appetite, and changes in body weight. Some ulcers may remain asymptomatic until a serious complication develops. The major complications include gastrointestinal bleeding, perforation, penetration, and gastric outlet obstruction. Bleeding may present as vomiting of blood or coffee-ground material and passage of black, tarry stools. Perforation can cause sudden and severe abdominal pain and represents a medical emergency.

Several experimental animal models are used to investigate the pathogenesis of gastric ulcers and to evaluate potential anti-ulcer agents. Common experimental models include pylorus ligation, ethanol-induced gastric ulceration, stress-induced ulceration, indomethacin-induced ulceration, paracetamol-induced ulceration, and other chemically or physically induced models. These models provide useful information regarding the antisecretory, cytoprotective, antioxidant, and mucosal protective properties of test substances. Parameters such as ulcer index, gastric volume, gastric pH, free and total acidity, and gastric mucus content are commonly evaluated to determine anti-ulcer activity [6-7].

Conventional treatment of peptic ulcer disease generally involves reduction of gastric acidity, protection of the gastric mucosa, and eradication of *H. pylori* when infection is present. Proton-pump inhibitors, H₂-receptor antagonists, antacids, mucosal protective agents, and appropriate antibiotic combinations are commonly used depending on the underlying cause. Although these therapies are effective, prolonged treatment may be associated with adverse effects, drug interactions, recurrence, or treatment failure in some patients. Consequently, there is increasing interest in identifying safer and potentially effective natural products for the prevention and management of gastric ulceration.

Medicinal plants have historically played an important role in traditional systems of medicine for the treatment of gastrointestinal disorders. Plant-derived compounds such as flavonoids, tannins, alkaloids, saponins, terpenoids, and phenolic constituents have been investigated for their potential gastroprotective properties. These compounds may act through several mechanisms, including reduction of gastric acid secretion, enhancement of mucus production,

improvement of mucosal blood flow, antioxidant activity, inhibition of inflammatory processes, and strengthening of the gastric mucosal barrier [8-9].

In this context, *Salvadora indica* is considered a promising medicinal plant for investigation of anti-ulcer activity. Traditional medicinal plants containing bioactive phytoconstituents may provide multiple protective effects on the gastrointestinal mucosa. Therefore, systematic evaluation of aqueous and alcoholic extracts of *Salvadora indica* leaves using experimentally induced gastric ulcer models may help establish their gastroprotective potential. Assessment of ulcer index, gastric mucus content, and other relevant parameters can provide evidence regarding possible cytoprotective and antisecretory mechanisms.

Thus, the present study is undertaken to evaluate the anti-ulcer activity of aqueous and alcoholic extracts of *Salvadora indica* leaves against experimentally induced gastric ulcers. The study may contribute to understanding the pharmacological potential of this medicinal plant and provide a scientific basis for its traditional use in gastrointestinal disorders [10].

EXPERIMENTAL SECTION

The present study aims to scientifically investigate the anti-ulcer and gastroprotective potential of *Salvadora indica* leaves and to identify the major phytochemical constituents that may contribute to its pharmacological activity. The study is focused on developing a natural therapeutic approach that may provide effective ulcer protection with comparatively fewer adverse effects, good affordability, and better accessibility than conventional synthetic drugs. The major objectives of the study are to collect, botanically authenticate, and prepare aqueous and alcoholic extracts of *Salvadora indica* leaves; to perform preliminary phytochemical screening of the prepared extracts; to evaluate their acute oral toxicity; to investigate their anti-ulcer activity using suitable experimental animal models; to assess gastroprotective effects against stress-, alcohol-, paracetamol-, and pylorus-ligation-induced gastric ulceration; to compare the activity of the extracts with a suitable standard anti-ulcer drug; and to obtain preliminary evidence regarding possible cytoprotective, antisecretory, antioxidant, and mucosal defensive mechanisms responsible for the observed activity. Peptic ulcer disease is an important gastrointestinal disorder resulting primarily from an imbalance between aggressive factors, such as gastric acid, pepsin, alcohol, certain drugs, physiological stress, and other irritants, and the protective mechanisms of the gastric mucosa. Damage to the gastric mucosal barrier may result in inflammation, erosion, hemorrhage, and ulcer formation, while persistent or recurrent ulceration may lead to serious complications such as gastrointestinal bleeding, perforation, obstruction, and impaired quality of life. Although conventional therapeutic agents such as proton-pump inhibitors, H₂-receptor antagonists, antacids, and mucosal protective drugs are widely used for the management of peptic ulcers, limitations associated with prolonged treatment, recurrence, adverse effects, drug interactions, and treatment failure emphasize the need for safer and more effective alternatives. Medicinal plants are an important source of biologically active compounds, including flavonoids, tannins, phenolic compounds, alkaloids,

terpenoids, and saponins, which may enhance gastric mucosal defense, reduce oxidative damage, suppress excessive gastric secretion, inhibit inflammatory processes, and promote tissue repair. Therefore, investigation of medicinal plants may provide useful leads for the development of novel gastroprotective agents [11-12]. *Salvadora indica* has traditional medicinal relevance and belongs to a plant group with reported biological activities, providing a scientific rationale for evaluating its possible anti-ulcer effects. The present study is consequently undertaken to scientifically assess the gastroprotective potential of aqueous and alcoholic leaf extracts of *Salvadora indica* and to provide a basis for further investigation and development of plant-derived anti-ulcer agents. The experimental work was planned in a systematic sequence involving selection and authentication of the plant, collection and processing of plant material, extraction, phytochemical screening, toxicity assessment, pharmacological evaluation, histopathological examination, and statistical analysis. Initially, *Salvadora indica* was selected based on its traditional medicinal importance and potential pharmacological properties. The plant material was collected from an appropriate botanical source and authenticated by a qualified botanist or taxonomic authority to ensure correct identification. The leaves were cleaned, shade-dried, pulverized into a suitable coarse powder, and stored in clean, dry, airtight containers under appropriate conditions until extraction. Aqueous and alcoholic extracts were prepared using suitable standardized extraction procedures. For the aqueous extract, a measured quantity of powdered leaves was extracted with distilled water under controlled heating conditions, followed by filtration and concentration of the filtrate to obtain a concentrated extract. Similarly, the alcoholic extract was prepared by extracting the powdered leaves with an appropriate alcoholic solvent, followed by filtration and concentration under controlled conditions to minimize degradation of active constituents. The prepared extracts were appropriately labelled and stored until further phytochemical and pharmacological evaluation. Preliminary qualitative phytochemical screening was performed to determine the presence or absence of major classes of secondary metabolites, including alkaloids, carbohydrates, saponins, steroids, phenolic compounds, tannins, and flavonoids. Standard qualitative chemical tests were employed, and characteristic colour changes, precipitate formation, ring formation, or persistent froth were considered indicative of the respective phytochemical constituents. The results obtained from phytochemical screening were recorded systematically and used to establish the preliminary chemical profile of the aqueous and alcoholic extracts. The acute oral toxicity of the prepared extracts was evaluated in experimental animals according to the applicable OECD guideline. Healthy experimental animals were appropriately acclimatized before the study, and the extracts were administered orally at the selected toxicity dose according to the approved experimental protocol. Animals were observed carefully for mortality, changes in general behaviour, locomotor activity, respiration, feeding pattern, neurological manifestations, and other visible signs of toxicity during the specified observation period. The findings of the

toxicity study were used to establish a safe and scientifically justified dose range for subsequent pharmacological investigations. Healthy Wistar rats of suitable body weight were used for the experimental studies. The animals were maintained under standardized laboratory conditions with controlled temperature, relative humidity, and a regular light-dark cycle. Standard laboratory pellet diet and water were provided *ad libitum*. Animals were acclimatized to the laboratory environment before initiation of the experimental procedures. All animal experiments were conducted according to applicable institutional ethical requirements and following approval from the appropriate Institutional Animal Ethics Committee, with appropriate measures taken to minimize unnecessary discomfort and distress. The anti-ulcer activity of the aqueous and alcoholic extracts of *Salvadora indica* leaves was evaluated using established experimental models of gastric ulceration. Appropriate normal-control, ulcer-control, standard-drug, and extract-treated groups were included to allow meaningful comparison of the treatment effects. The extracts were administered at predetermined doses, while the standard group received a suitable reference anti-ulcer drug. Depending on the experimental model, gastric injury was induced by stress, alcohol, paracetamol, or pylorus ligation. At the end of the experimental period, the animals were sacrificed according to the approved protocol, and the stomachs were carefully removed and examined for macroscopic gastric lesions. The ulcer index was determined based on the number and severity of gastric lesions, and the percentage ulcer protection was calculated to evaluate the gastroprotective efficacy of the extracts. In the stress-induced ulcer model, appropriately fasted animals were divided into control, ulcer-control, standard-treatment, and extract-treatment groups. Gastric ulceration was induced using a standardized stress procedure following administration of the respective treatments. At the end of the experimental period, the stomachs were removed and opened along the greater curvature. The gastric mucosa was carefully examined for edema, hyperemia, hemorrhage, erosions, and ulcerative lesions, and the severity of mucosal damage was determined by calculating the ulcer index. A reduction in ulcer index compared with the ulcer-control group was considered indicative of gastroprotective activity [13-14]. The alcohol-induced ulcer model was used to investigate the cytoprotective potential of the extracts against chemically induced gastric mucosal damage. Animals were divided into appropriate experimental groups and treated with the respective extract or standard drug according to the experimental schedule. Gastric injury was subsequently induced using an appropriate dose of ethanol. Following the predetermined exposure period, the animals were sacrificed and the stomachs were removed for macroscopic examination. The gastric mucosa was evaluated for linear hemorrhagic lesions, erosions, and other visible abnormalities. The total lesion score was used to determine the ulcer index, and percentage ulcer protection was calculated by comparison with the ulcer-control group. Where applicable, gastric tissues were preserved for histopathological evaluation to provide microscopic confirmation of the observed gastroprotective effects. The paracetamol-induced ulcer model was employed to investigate the protective effects of the

extracts against drug-associated gastric mucosal injury. Experimental animals were divided into normal-control, ulcer-control, standard-treatment, and extract-treatment groups. The respective treatments were administered according to the predetermined experimental schedule, followed by administration of the ulcerogenic agent. At the end of the experimental period, gastric contents were collected and evaluated for relevant gastric parameters, while the stomachs were removed and examined for mucosal lesions. The ulcer index and percentage ulcer protection were calculated and compared with the standard drug to determine the efficacy of the aqueous and alcoholic extracts. The pylorus-ligation-induced ulcer model was employed to evaluate the possible antisecretory and gastroprotective effects of the extracts. In this model, accumulation of gastric secretions following pyloric ligation promotes mucosal injury and allows assessment of the influence of treatment on gastric secretion and mucosal protection. Following completion of the experimental procedure, gastric contents were collected and analyzed for volume, pH, free acidity, and total acidity using standard analytical procedures. The stomach was subsequently opened and examined for ulcerative lesions, and the ulcer index was calculated. A reduction in gastric volume or acidity together with a decrease in ulcer index compared with the ulcer-control group would provide evidence of possible antisecretory and gastroprotective activity. Histopathological evaluation was performed to provide microscopic confirmation of the protective effects of the plant extracts. Representative gastric tissue samples from the experimental groups were collected and preserved in an appropriate fixative. The tissues were processed using standard histological techniques, embedded in paraffin, sectioned, and stained for microscopic examination. Gastric tissues were evaluated for epithelial disruption, mucosal erosion, hemorrhage, edema, inflammatory-cell infiltration, and other pathological alterations. The histological characteristics of extract-treated groups were compared with normal-control, ulcer-control, and standard-drug groups. Improvement in gastric epithelial integrity and reduction in inflammatory and degenerative changes were considered supportive evidence of gastroprotective activity. The overall gastroprotective efficacy of the extracts was assessed primarily through determination of ulcer index and percentage ulcer protection. Percentage ulcer protection was calculated using the formula: **% Ulcer Protection = [(Ulcer Index of Control – Ulcer Index of Test) / Ulcer Index of Control] × 100**. A significant reduction in ulcer index accompanied by improvement in gastric mucosal architecture, reduction in gastric acidity where applicable, and favorable histopathological changes would indicate potential anti-ulcer activity. The experimental results were expressed as mean ± SEM for the respective groups. Statistical analysis was performed using an appropriate statistical method according to the experimental design, with one-way analysis of variance followed by a suitable post-hoc multiple-comparison test where applicable. The extract-treated groups were compared with the ulcer-control and standard-drug groups, and statistical significance was determined at predetermined probability levels such as **P < 0.05, P < 0.01, and P < 0.001**. The final interpretation of the study was based on the

combined findings of phytochemical screening, toxicity assessment, ulcer index, percentage ulcer protection, gastric secretion parameters, biochemical observations, and histopathological changes. Overall, the study is intended to provide systematic scientific evidence regarding the anti-ulcer and gastroprotective potential of *Salvadora indica* leaves and to determine whether its aqueous and alcoholic extracts possess sufficient pharmacological activity to justify further investigation as potential plant-derived gastroprotective agents. **Important:** Your draft uses both *Salvadora indica* and *Salvadora persica*. Before submitting the thesis, please verify the exact species authenticated and used in your experiment and use one scientifically correct species name consistently throughout the entire dissertation [15-16].

RESULTS

Preliminary Phytochemical Screening

The freshly prepared aqueous and alcoholic extracts of *Salvadora indica* leaves were subjected to preliminary phytochemical screening to identify the major classes of biologically active constituents. The aqueous extract showed the presence of carbohydrates, tannins, flavonoids, saponins, phenols, steroids, alkaloids, and glycosides. Similarly, the alcoholic extract showed the presence of carbohydrates, tannins, flavonoids, saponins, phenols, steroids, alkaloids, and glycosides. The intensity of the reactions varied between the two extracts. Tannins and saponins were moderately present in the aqueous extract, whereas phenols, steroids, and alkaloids showed comparatively stronger reactions in the alcoholic extract. The presence of these phytoconstituents may contribute to the pharmacological activity of *Salvadora indica*, particularly its potential gastroprotective and anti-ulcer effects. The results of the preliminary phytochemical screening are presented in **Table 01**.

Table 01. Preliminary phytochemical screening of aqueous and alcoholic extracts of *Salvadora indica* leaves

S. No.	Phytochemical constituent	Aqueous Extract	Alcoholic Extract
1	Carbohydrates	+	+
2	Tannins	++	+
3	Flavonoids	+	+
4	Saponins	++	++
5	Phenols	+	++
6	Steroids	+	++
7	Alkaloids	+	++
8	Glycosides	+	+

Note: (+) = Present; (++) = Moderately present; (+++) = Highly present; (–) = Absent.

Acute Oral Toxicity Study

The acute oral toxicity study was performed to evaluate the safety profile of the aqueous and alcoholic extracts of *Salvadora indica* leaves. Following oral administration, the animals were observed for mortality and any visible signs of toxicity, including changes in general behaviour, locomotor activity, feeding pattern, neurological responses, and other abnormal clinical signs. No mortality or treatment-related toxic manifestations were observed during the observation period. The extracts were found to be well tolerated by the

experimental animals. Based on the acute toxicity findings, the median lethal dose (LD₅₀) was considered to be greater than **2000 mg/kg body weight**, as no mortality was observed at the highest tested dose. Therefore, the selected experimental dose of **250 mg/kg body weight** was considered suitable for subsequent pharmacological evaluation. Effect of *Salvadora indica* on Alcohol-Induced Gastric Ulcers

Administration of ethanol produced prominent hemorrhagic lesions in the glandular portion of the stomach of ulcer-control animals, indicating successful induction of gastric mucosal injury. Pretreatment with the aqueous extract of *Salvadora indica* (AQSI) and alcoholic extract of *Salvadora indica* (ALSI) at a dose of 250 mg/kg produced a reduction in gastric lesion formation compared with the ulcer-control group. The alcoholic extract produced a comparatively greater reduction in lesion index than the aqueous extract. The standard drug, ranitidine (75 mg/kg), also produced considerable protection against ethanol-induced gastric injury. The ulcer-protective effect was further supported by changes in gastric mucus content, suggesting that enhancement of the mucosal defensive barrier may contribute to the gastroprotective action of the extracts. The results are presented in **Table 02**.

Table 02: Effect of *Salvadora indica* extracts on alcohol-induced gastric ulcers in rats

Treatment (n=6)	Dose (mg/kg, p.o.)	Lesion Index	% Inhibition of Ulcer*	Mucus Content (µg Alcian blue/g wet tissue)
1% CMC	—	30.10 ± 0.16	—	0.55 ± 0.31
Ulcer Control	—	36.21 ± 1.51	—	0.69 ± 1.42
Ranitidine	75	28.10 ± 2.30	22.40	0.72 ± 1.10
AQSI	250	34.63 ± 0.10	4.36	0.40 ± 2.12
ALSI	250	17.16 ± 1.14	52.61	0.80 ± 1.12

Values are expressed as mean ± SEM; n = 6 animals per group.

*Percentage inhibition was calculated using the ulcer-control group as the reference: % ulcer inhibition = [(Ulcer Index of ulcer control – Ulcer Index of treated group) / Ulcer Index of ulcer control] × 100.

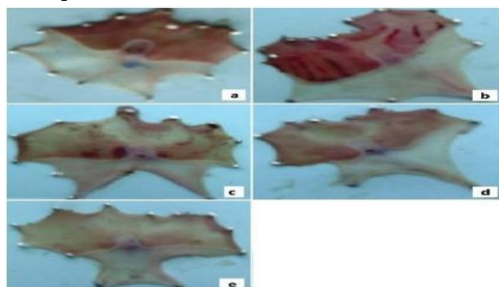


Figure 01. Effect of *Salvadora indica* extracts on alcohol-induced gastric ulcers in rats: (A) Normal control, (B) Ulcer control, (C) AQSI-treated group (250 mg/kg), (D) ALSI-treated group (250 mg/kg), and (E) Ranitidine-treated group (75 mg/kg).

Effect of *Salvadora indica* on Paracetamol-Induced Gastric Ulcers

Administration of the ulcerogenic agent produced an increase in the ulcer index in the ulcer-control group, confirming the development of gastric mucosal injury. Pretreatment with the aqueous and alcoholic extracts of *Salvadora indica* at a dose of 250 mg/kg significantly reduced the ulcer index compared with the ulcer-control group. The alcoholic extract showed a greater reduction in ulcer index than the aqueous extract. Ranitidine (75 mg/kg) produced marked gastroprotection and served as the standard reference drug. Based on the values presented in Table 03, the percentage inhibition of ulcer formation was approximately **37.50% for AQSI, 52.50% for ALSI, and 63.75% for ranitidine**. These findings indicate that both extracts possess protective activity against chemically induced gastric mucosal injury, with the alcoholic extract demonstrating comparatively stronger activity. The results are summarized in **Table 03**.

Table 03: Effect of *Salvadora indica* extracts on paracetamol-induced gastric ulcers in rats

Treatment (n=6)	Dose (mg/kg, p.o.)	Ulcer Index	% Inhibition of Ulcer*
1% CMC	—	0.65 ± 0.12	—
Ulcer Control	—	0.80 ± 0.31	—
Ranitidine	75	0.29 ± 0.10	63.75
AQSI	250	0.50 ± 0.09	37.50
ALSI	250	0.38 ± 0.05	52.50

Values are expressed as mean ± SEM; n = 6 animals per group.

*Percentage inhibition was calculated using the ulcer-control group as the reference. Statistical significance was assessed by comparison with the ulcer-control group, with **P < 0.001** considered highly significant where applicable.

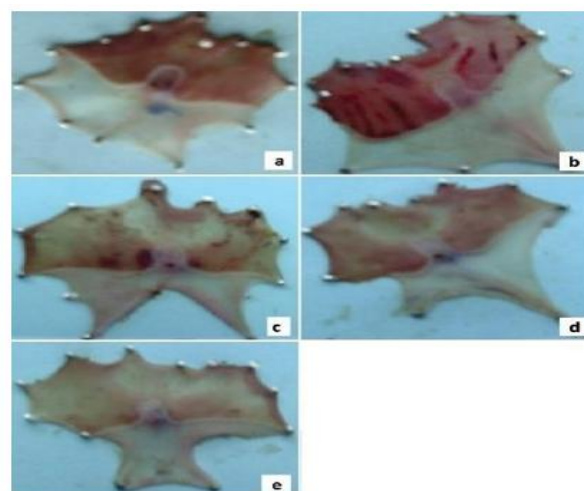


Figure 02: Effect of *Salvadora indica* extracts on paracetamol-induced gastric ulcers in rats: (A) Normal control, (B) Ulcer control, (C) AQSI-treated group (250 mg/kg), (D) ALSI-treated group (250 mg/kg), and (E) Ranitidine-treated group (75 mg/kg).

Effect of *Salvadora indica* on Stress-Induced Gastric Ulcers

Water-immersion stress produced marked gastric mucosal lesions in the ulcer-control group, with a mean ulcer index of 24.21 ± 2.32 . Pretreatment with the aqueous and alcoholic extracts of *Salvadora indica* at a dose of 250 mg/kg significantly reduced the severity of gastric lesions compared with the ulcer-control group. The aqueous extract produced an ulcer index of 7.74 ± 0.20 , corresponding to **68.04% inhibition**, whereas the alcoholic extract produced an ulcer index of 5.11 ± 2.49 , corresponding to **78.89% inhibition**. Ranitidine at 75 mg/kg produced the greatest protection, with an ulcer index of 3.50 ± 0.22 and approximately **85.54% inhibition** based on the values provided. These findings indicate that both extracts possess significant gastroprotective activity against stress-induced gastric mucosal injury, with the alcoholic extract showing greater protective potential than the aqueous extract. The results are presented in **Table 04**.

Table 04: Effect of *Salvadora indica* extracts on stress-induced gastric ulcers in rats

Treatment Group	Dose (mg/kg, p.o.)	Ulcer Index	% Inhibition of Ulcer*
Normal Control	—	0.00 $\pm$ 0.00	—
Ulcer Control	—	24.21 $\pm$ 2.32	—
Ranitidine (Standard)	75	3.50 $\pm$ 0.22	85.54
AQSI	250	7.74 $\pm$ 0.20	68.04
ALSI	250	5.11 $\pm$ 2.49	78.89

Values are expressed as mean $\pm$ SEM; n = 6 animals per group.

*Percentage inhibition was calculated using the ulcer-control group as the reference: % ulcer inhibition = [(Ulcer Index of ulcer control – Ulcer Index of treated group) / Ulcer Index of ulcer control] $\times$ 100. Statistical significance was reported as **P < 0.001** where applicable.

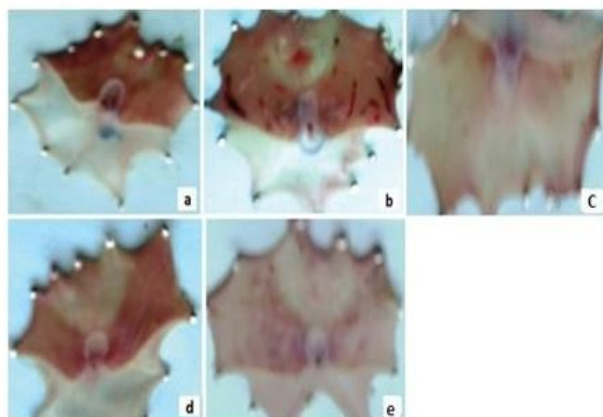


Figure 03: Effect of *Salvadora indica* extracts on stress-induced gastric ulcers in rats: (A) Normal control, (B) Ulcer control, (C) AQSI-treated group (250 mg/kg), (D) ALSI-treated group (250 mg/kg), and (E) Ranitidine-treated group (75 mg/kg).

DISCUSSION

The present study was undertaken to evaluate the gastroprotective and anti-ulcer potential of *Salvadora indica* leaf extracts using different experimentally induced gastric ulcer models in rats. Aqueous and alcoholic extracts were evaluated against alcohol-, paracetamol-, stress-, and acetic acid-induced gastric mucosal injury. The use of different ulcer models was intended to investigate the protective activity of the extracts against diverse ulcerogenic mechanisms, including oxidative stress, mucosal barrier disruption, excessive gastric secretion, reduced mucus protection, and tissue injury. Preliminary phytochemical screening revealed the presence of several biologically active constituents, including alkaloids, flavonoids, tannins, saponins, phenolic compounds, steroids, carbohydrates, and glycosides. These phytoconstituents may contribute individually or synergistically to the observed gastroprotective activity of *Salvadora indica* [17].

The acute oral toxicity study demonstrated that the aqueous and alcoholic extracts were well tolerated by the experimental animals. No mortality or significant treatment-related behavioral or neurological abnormalities were observed during the observation period at the tested doses. The absence of observable toxicity at the higher tested dose provides preliminary evidence of the safety of the extracts and supported their subsequent evaluation in the anti-ulcer studies. However, detailed chronic and sub-chronic toxicity studies would be required to establish the long-term safety profile of the plant extracts [18].

Alcohol-induced gastric ulceration is a widely used experimental model for evaluating cytoprotective and gastroprotective agents. Ethanol causes direct injury to the gastric mucosa through disruption of the epithelial barrier, depletion of protective mucus, vascular disturbances, oxidative stress, and generation of reactive oxygen species. These events can result in increased lipid peroxidation, membrane damage, hemorrhage, and formation of gastric lesions. In the present study, administration of alcohol produced prominent hemorrhagic lesions in the glandular portion of the stomach, confirming successful induction of gastric mucosal injury. Pretreatment with both aqueous and alcoholic extracts of *Salvadora indica* reduced the severity of gastric lesions compared with the ulcer-control group. The alcoholic extract showed comparatively greater protection than the aqueous extract. The observed increase in gastric mucus content in the treated animals further suggests that enhancement of the mucosal defensive barrier may contribute to the gastroprotective effect of the extracts. The presence of flavonoids, tannins, phenolic compounds, and other secondary metabolites may contribute to antioxidant and mucosal protective effects [19].

The paracetamol-induced ulcer model was employed to investigate the protective effect of *Salvadora indica* against chemically induced gastric mucosal damage. Ulcerogenic drugs can disturb gastric mucosal integrity through several mechanisms, including impairment of endogenous protective factors, oxidative stress, and alteration of prostaglandin-mediated mucosal defense. In the present study, administration of the ulcerogenic agent produced a marked increase in the ulcer index in the ulcer-control animals.

Treatment with both aqueous and alcoholic extracts significantly reduced the ulcer index compared with the ulcer-control group. The alcoholic extract demonstrated comparatively greater protection, while the standard anti-ulcer drug produced substantial inhibition of ulcer formation. These findings indicate that *Salvadora indica* may strengthen gastric mucosal resistance against chemically induced injury. The protective activity may be associated with preservation of mucus, reduction of oxidative damage, and maintenance of the integrity of the gastric epithelial lining [20-22].

Stress is another important contributing factor in the development and aggravation of gastric ulceration. The pathophysiology of stress-induced gastric injury is complex and involves alterations in gastric blood flow, increased gastric acid secretion, impairment of mucosal defense, oxidative stress, and disturbances in the normal protective mechanisms of the stomach. In the present study, water-immersion stress produced significant gastric lesions in the ulcer-control animals. Pretreatment with aqueous and alcoholic extracts of *Salvadora indica* markedly reduced the ulcer index compared with the ulcer-control group. The alcoholic extract again demonstrated comparatively greater protective activity than the aqueous extract, although the standard drug produced the highest level of protection. These findings suggest that *Salvadora indica* may protect the gastric mucosa against stress-induced injury by enhancing mucosal defense and possibly reducing gastric secretory and oxidative damage [23].

The overall findings obtained from the different experimental models demonstrate that *Salvadora indica* possesses significant gastroprotective potential. The protective effect observed in alcohol-, paracetamol-, and stress-induced ulcer models indicates that the activity of the extracts may involve more than one mechanism. The reduction in ulcer index suggests an overall decrease in mucosal damage, while improvement in mucus content supports a possible cytoprotective mechanism. The findings from gastric secretion-related parameters, where available, may additionally indicate an antisecretory component of the activity. Therefore, the gastroprotective effect of *Salvadora indica* may be attributed to a combination of **cytoprotective, mucus-enhancing, antioxidant, and antisecretory mechanisms** [24].

The phytochemical findings provide a possible explanation for the pharmacological activity observed in the present investigation. Flavonoids and phenolic compounds are known to possess antioxidant properties and may help protect gastric tissues from oxidative damage. Tannins may contribute to mucosal protection by promoting protein precipitation and formation of a protective layer over the gastric mucosa. Saponins and other secondary metabolites may also influence mucosal defense and tissue repair. Alkaloids, glycosides, steroids, and other constituents identified in the extracts may contribute synergistically to the overall pharmacological response. Nevertheless, preliminary phytochemical screening alone cannot establish which individual constituent is responsible for the anti-ulcer effect. Further isolation, characterization, and mechanistic studies are therefore necessary.

The comparatively greater activity observed with the alcoholic extract in several experimental models may indicate that

certain gastroprotective constituents are extracted more efficiently in alcohol than in water. However, this observation should be interpreted cautiously because the biological activity of a crude extract depends on the concentration, extraction method, chemical composition, and interaction of multiple constituents. Standardization of the extract and quantitative estimation of the major active phytochemicals would therefore be valuable for future studies.

In conclusion, the present investigation provides experimental evidence supporting the **gastroprotective and anti-ulcer potential of *Salvadora indica* leaf extracts** in different experimental models of gastric ulceration. Both aqueous and alcoholic extracts demonstrated protective effects, with the alcoholic extract generally showing comparatively stronger activity. The observed effects may be associated with enhancement of gastric mucosal defense, preservation of mucus, reduction of oxidative injury, and possible modulation of gastric acid secretion. These findings support the traditional and pharmacological relevance of *Salvadora indica* as a potential source of gastroprotective agents. However, further investigations involving **dose-response studies, chronic toxicity evaluation, isolation and characterization of active constituents, antioxidant assays, gastric acid secretion studies, molecular investigations, and detailed histopathological evaluation** are necessary to establish the precise mechanisms responsible for its anti-ulcer activity and to determine its potential for further development as a plant-derived gastroprotective agent.

CONCLUSION

The present study demonstrated that the aqueous and alcoholic extracts of *Salvadora indica* leaves possess significant anti-ulcer and gastroprotective activity against experimentally induced gastric ulcers in rats. The extracts were evaluated using paracetamol-, alcohol-, and stress-induced ulcer models, which represent different mechanisms of gastric mucosal injury. The observed reduction in ulcer index and improvement in gastric mucosal protection indicate that *Salvadora indica* can effectively counteract several ulcerogenic factors.

The alcohol-induced ulcer model demonstrated that the extracts protected the gastric mucosa against ethanol-induced injury, which is mainly associated with oxidative stress, lipid peroxidation, and disruption of the gastric epithelial barrier. The reduction in lesion formation suggests a possible cytoprotective and antioxidant effect of the plant extracts. Similarly, the extracts significantly reduced gastric injury in the paracetamol-induced ulcer model, indicating their ability to protect the gastric mucosa against chemically induced damage. In the stress-induced ulcer model, treatment with *Salvadora indica* extracts resulted in a significant reduction in ulcer index and improvement in gastric defensive parameters. The extracts also showed favorable effects on gastric volume, acidity, and pH, suggesting a possible antisecretory component in their gastroprotective action. Overall, the findings indicate that the extracts may act by strengthening gastric mucosal defense while reducing aggressive factors such as excessive acid secretion and oxidative damage [25].

Preliminary phytochemical screening revealed the presence of flavonoids, tannins, phenolic compounds, alkaloids, saponins,

steroids, carbohydrates, and glycosides in the extracts. Among these constituents, flavonoids and phenolic compounds may play an important role because of their reported antioxidant and gastroprotective properties. The anti-ulcer activity of *Salvadora indica* may therefore be attributed to the combined action of these phytoconstituents through enhancement of mucosal protection, antioxidant activity, mucus preservation, and reduction of gastric acidity.

Based on the present findings, it can be concluded that *Salvadora indica* leaves possess promising gastroprotective and anti-ulcer properties and may serve as a potential natural source for the development of safer and cost-effective anti-ulcer agents. However, further investigations are necessary to identify and isolate the active constituents, establish their precise mechanisms of action, evaluate long-term toxicity, and confirm the therapeutic potential through well-designed pharmacological and clinical studies.

RECOMMENDATIONS

The findings of the present investigation provide a basis for further research on *Salvadora indica* and other medicinal plants with potential gastroprotective activity. Further studies may include screening of additional plant extracts, evaluation of combinations of medicinal plants for possible synergistic effects, standardization of active extracts, and investigation of suitable herbal or polyherbal formulations. Appropriate clinical studies will also be required to establish the safety, efficacy, dosage, and therapeutic applicability of such formulations in humans.

FUTURE SCOPE OF THE RESEARCH

The present study provides preliminary scientific evidence supporting the gastroprotective potential of *Salvadora indica*. Future research should focus on the isolation and structural characterization of the active phytoconstituents, particularly flavonoids and phenolic compounds, followed by evaluation of their individual anti-ulcer activity. Detailed studies on antioxidant activity, gastric acid secretion, mucus production, prostaglandin pathways, inflammatory mediators, and oxidative stress markers may help clarify the precise mechanism of action. Sub-chronic and chronic toxicity studies are also required to establish long-term safety. Further pharmacological investigations, formulation development, standardization, and appropriately designed clinical trials may determine the potential of *Salvadora indica* as a safe, effective, affordable, and plant-derived gastroprotective agent.

AUTHOR CONTRIBUTIONS

Both authors contributed to equally.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Hemadharsni P, Sivanesan M, Sivasakthi S, Sivasakthi Balan M, Sriashok Kumar M, Kannan S, et al. Evaluation of in-vitro anti-ulcer potential of aerial parts of *Crossandra infundibuliformis* Linn. J Pharm Res Int. 2026;38(3):23-35.
2. Uwaeme UF, Osigwe CC, Okokon JE. Antiulcer activity of *Justicia insularis* leaf extract on experimentally-induced ulcers in rats. Asian J Biochem Genet Mol Biol. 2025;17(4):49-57.
3. Johnson DB, Moganthan R, Swarnabala S. Evaluation of anti-ulcer activity of *Calycopteris floribunda* Lams leaf extract in Wistar rats. Res J Pharmacogn Phytochem. 2024;16(4):277-282.
4. Zade A, Vyas J, Paithankar V, Wankhede A. Evaluation of antiulcer activity of herbal drugs on experimental animal: *Myrica nagi* (Myricaceae). GSC Biol Pharm Sci. 2022;20(2):138-144.
5. Adane H, Atnafie SA, Kifle ZD, Ambikar D. Evaluation of in vivo antiulcer activity of hydro-methanol extract and solvent fractions of the stem bark of *Ficus thonningii* (Moraceae) on rodent models. Biomed Res Int. 2021;2021:6685395.
6. Mekonnen AN, Atnafie SA, Atta MAW. Evaluation of antiulcer activity of 80% methanol extract and solvent fractions of the root of *Croton macrostachyus* Hochst. ex Delile (Euphorbiaceae) in rodents. Evid Based Complement Alternat Med. 2020;2020:2809270.
7. Ukwuani-Kwaja AN, Zakari A. Antiulcer activity of methanolic seed extract of *Citrullus lanatus* in albino rats. J Pharmacogn Phytochem. 2018;7(2):1254-1256.
8. Mostofa R, Ahmed S, Begum MM, Rahman MS, Begum T, Ahmed SU, et al. Evaluation of anti-inflammatory and gastric anti-ulcer activity of *Phyllanthus niruri* L. (Euphorbiaceae) leaves in experimental rats. BMC Complement Altern Med. 2017;17:1-10.
9. Abebaw M, Mishra B, Gelayee DA. Evaluation of anti-ulcer activity of the leaf extract of *Osyris quadripartita* Decne. (Santalaceae) in rats. J Exp Pharmacol. 2017;9:1-11.
10. Bhajoni PS, Meshram GG, Lahkar M. Evaluation of the antiulcer activity of the leaves of *Azadirachta indica*: an experimental study. Integr Med Res. 2016;5(1):16-20.
11. Sahoo SK, Sahoo HB, Priyadarshini D, Soundarya G, Kishore Kumar C, Usha Rani K. Antiulcer activity of ethanolic extract of *Salvadora indica* (W.) leaves on albino rats. J Clin Diagn Res. 2016;10(9):FF07-FF10.
12. Prabhu K, Rajan S. Assessment of antiulcer activity of ethanolic extract of *Mangifera indica* seed kernel using acid ethanol induced ulcer model. Int J Curr Microbiol Appl Sci. 2015;4(4):854-860.
13. Wasicky A, Hernandez LS, Vetore-Neto A, Moreno PRH, Bacchi EM, Kato ETM, et al. Evaluation of gastroprotective activity of *Passiflora alata*. Rev Bras Farmacogn. 2015;25:407-412.

14. Paguigan ND, Castillo DHB, Chichioco-Hernandez CL. Anti-ulcer activity of Leguminosae plants. Arq Gastroenterol. 2014;51(1):64-69.
15. El-Shinnawy NA, Abd-Elmageid SA, Alshailabi EMA. Evaluation of antiulcer activity of indole-3-carbinol and/or omeprazole on aspirin-induced gastric ulcer in rats. Eur J Pharmacol. 2012;697(1-3):140-147.
16. Dashputre NL, Naikwade NS. Evaluation of anti-ulcer activity of methanolic extract of *Abutilon indicum* Linn. leaves in experimental rats. Int J Pharm Sci Drug Res. 2011;3(2):97-100.
17. Dhasan PB, Jegadeesan M, Kavimani S. Antiulcer activity of aqueous extract of fruits of *Momordica cymbalaria* Hook f. in Wistar rats. Pharmacogn Res. 2010;2(1):58-61.
18. Muralidharan P, Srikanth J. Antiulcer activity of *Morinda citrifolia* Linn. fruit extract. J Sci Res. 2009;1(2):345-352.
19. Malairajan P, Gopalakrishnan G, Narasimhan S, Veni KJK. Evaluation of anti-ulcer activity of *Polyalthia longifolia* (Sonn.) Thwaites in experimental animals. Indian J Pharmacol. 2008;40(3):126-128.
20. Chaturvedi A, Kumar MM, Bhawani G, Chaturvedi H, Kumar M, Goel RK. Effect of ethanolic extract of *Eugenia jambolana* seeds on gastric ulceration and secretion in rats. Indian J Physiol Pharmacol. 2007;51(2):131-140.
21. Jamal A, Farah S, Siddiqui A, Aslam M, Javed K, Jafri MA. Antiulcerogenic activity of *Elettaria cardamomum* Maton and *Amomum subulatum* Roxb. seeds. Indian J Tradit Knowl. 2005;4(3):298-302.
22. Beil W, Birkholz W, Sewing KF. Effects of flavonoids on parietal cell acid secretion, gastric mucosal prostaglandin production and *Helicobacter pylori* growth. Arzneimittelforschung. 1995;45:697-700.
23. Goso Y, Ogata Y, Ishihara K, Hotta K. Effects of traditional herbal medicine on gastric mucin against ethanol-induced gastric injury in rats. Comp Biochem Physiol C. 1996;113(1):17-21.
24. Maity S, Chaudhuri T, Vedasiromoni JR, Ganguly DK. Cytoprotection mediated antiulcer effect of tea root extract. Indian J Pharmacol. 2003;35:213-219.
25. Rafatulla S, Tariq M, Alyahya MA. Evaluation of turmeric (*Curcuma longa*) for gastric and duodenal antiulcer activity in rats. J Ethnopharmacol. 1990;29(1):25-34.