

CHARACTERIZATION OF MANGO SEED AQUEOUS EXTRACT AND ITS ADJUNCTIVE THERAPEUTIC EFFECTS IN GASTRIC ULCER

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ABSTRACT

M. indica L. seed is a by-product of the mango yield that is abundant and rich in bioactive compounds that may be used in therapeutic applications. The purpose of this study was to characterize the aqueous extract of mango seed and assess its gastroprotective action in patients suffering from gastric ulcers in a randomized controlled clinical trial. There were 60 patients in total, with half of them in the control group and the other half in the intervention group. The groups were given standard anti-ulcer treatment (omeprazole and clarithromycin) along with a modified diet, but the intervention group was also given mango seed aqueous extract (3g/day) for 12 weeks. Standard methods were used to determine the proximate composition, phytochemicals, and antioxidant activity of the extract. Pre and post-treatment clinical, endoscopic, and histopathological evaluation was done. The extract was found to have a high concentration of carbohydrates, phenolics, flavonoids, tannins, and alkaloids with high antioxidant activity ($IC_{50} = 62.18\mu\text{g/mL}$). In the intervention group, ulcer healing was significantly improved (70 vs 30%) with a decrease in ulcer size, symptom scores, and histopathological damage when compared with controls ($p < 0.05$). Endoscopic examinations also revealed improved mucosal healing. There were no serious adverse effects observed. The results indicate that mango seed aqueous extract has potent antioxidant and gastroprotective activity and can be used as a natural alternative to gastric ulcer treatment in the future without any side effects.

Keywords: *Mangifera indica*, Gastric ulcer, Antioxidant activity, Phytochemicals, Gastric inflammation.

INTRODUCTION

Mango is a tropical fruit that belongs to the genus *Mangifera* of the family Anacardiaceae, and is one of the most popular tropical fruits in the world (Rahat et al., 2026). *Mangifera indica* is the most popular species of mango due to its nutritional value, taste, and medicinal properties. Mango seeds are an agro-industrial waste of mango juice and pulp processing. A significant amount of mango seeds are generated as a waste product during juice and pulp production. They are usually discarded because of their high content of biologically active species, including polyphenols, flavonoids, tannins, mangiferin, gallic acid, and antioxidant vitamins. The use of mango extracts in recent years has garnered interest as they exhibit antioxidant, anti-inflammatory, antimicrobial, and gastroprotective properties as natural therapeutic agents. The aqueous extract of mango seed is of special importance because the extraction using water is economical, environmentally friendly, and can be used in biomedical applications (Ibrahim et al., 2025).

A gastric ulcer is a common gastrointestinal disorder characterized by erosion and inflammation of the gastric mucosa (Erfan et al., 2025). It can be caused by many things, such as excess alcohol, stress, smoking, using nonsteroidal anti-inflammatory drugs (NSAIDs) for a long period of time, an unhealthy diet, and *Helicobacter pylori* (*H. pylori*) infection. Inflammation of

the stomach may become chronic and result in severe conditions such as peptic ulcers, erosion of the mucous membranes, bleeding, or gastric cancer (ALMULLA et al., 2025). Treatment is available with anti-inflammatory and anti-ulcer medications, although prolonged use of these medications can have side effects such as diarrhea, nausea, antibiotic resistance, and liver toxicity. Plant-based therapeutic options that are safer and more effective are in demand. Medicinal plants have been a source of natural products that hold significant scientific interest due to their ability to regulate inflammatory pathways and oxidative stress. Mango seed is a promising source for such compounds. The mango seed has strong free radical scavenging activity due to the presence of phenolics and flavonoids (Choudhary et al., 2026). These phytochemicals have been shown to block lipid peroxidation, decrease oxidative damage, and prevent gastric epithelial cell damage from inflammation. Moreover, mangiferin, one of the key xanthone compounds present in mango seed, has been found to possess strong anti-inflammatory and antioxidant properties through its ability to block the release of pro-inflammatory cytokines and modulate inflammatory cell pathways.

Mango seed aqueous extract has to be characterized before it can be used to determine its chemical composition, functional groups and biological activities. Various analysis methods like phytochemical screening, Fourier-transform infrared spectroscopy (FTIR), high-performance liquid chromatography (HPLC), and antioxidant assays are usually used to assess the presence of bioactive compounds and their therapeutic benefits (Mutha et al., 2025). The physicochemical and phytochemical properties of the extract provide insight into the mechanism of action and possible pharmaceutical applications of the extract. Moreover, characterization assists in standardizing the extract for future herbal formulation and nutraceutical products.

A few experimental studies have shown that mango seed extract has gastroprotective properties, which include increased mucus secretion, decreased gastric acidity and prevention of oxidative stress-induced mucosal damage (Abdalla et al., 2007; Mahmoud et al., 2022; Khan et al., 2024). The anti-inflammatory effect of mango seed extract could also be due to the suppression of inflammatory mediators like tumor necrosis factor alpha (TNF- α), interleukin, cyclooxygenase enzymes and reactive oxygen species. These processes are responsible for the occurrence of healing and protection of gastric tissues. Therefore, further investigation is required to explore the phytochemical profile, antioxidant activity, and gastroprotective potential of mango seed aqueous extract. The present study was designed to characterize the mango seed aqueous extract and evaluate its adjunctive therapeutic effects in patients with gastric ulcers. The findings of this study may contribute to the development of natural, economical, and environmentally friendly therapeutic agents for gastric ulcer management and value-added utilization of mango processing waste

MATERIALS AND METHODS

Plant Material Collection and Storage

Fruits of *M. indica* at the edible maturity stage were collected from the local market. The seeds were manually separated from the pulp, after which all residues were carefully removed with distilled water and air-dried in the laboratory at room temperature (25 \pm 2 $^{\circ}$ C) under controlled conditions. The seeds were dried completely and stored in sterile airtight containers at 4 $^{\circ}$ C for further processing to reduce the microbial contamination and degradation of bioactive constituents.

Study Design

This study was a randomized, controlled, parallel group clinical trial in accordance with the Declaration of Helsinki and CONSORT guidelines. All participants gave written informed consent before entering the study.

Participants

Patients aged 25-60 years of either gender with endoscopically confirmed gastric ulcer were recruited from the gastroenterology outpatient department during the study period. Participants were consecutively enrolled and randomly allocated into control and intervention groups using a computer-generated randomization sequence. A total of 60 participants were enrolled in the study and were equally divided into two groups, with 30 participants in each group. Participants were excluded if they were pregnant or lactating, smokers, or currently using antioxidant or herbal supplements. Patients with diabetes mellitus, hypertension, chronic kidney disease, gastric malignancy, or participation in another clinical trial within the preceding three months were also excluded.

Randomization, Allocation Concealment, and Blinding

Participants who met the eligibility criteria were randomly allocated at a 1:1 ratio in a computer-generated randomization schedule to the control or intervention group. Sequentially numbered, opaque, sealed envelopes, prepared by an independent statistician who was unaware of participant recruitment and outcome assessment, were used to ensure allocation concealment. The study was designed as an assessor-blinded clinical trial with outcome assessors and the histopathologist being blinded to the group allocation throughout the study period, while participants and treating physicians knew of the interventions.

Sample Size Determination and Sampling Technique

The sample size was calculated using the standard formula for comparison between two groups:

$$n = (Z^{\alpha}/2 + Z\beta)^2 \times 2 \sigma^2/d^2$$

Where:

α = 1.96 at 5% level of significance,

Power = 0.84 at 80% study power,
 σ = standard deviation,
d = expected mean difference.

Based on previously published data, the minimum estimated sample size was 48 participants. To compensate for potential dropout and non-compliance, an additional 20% of participants were included, resulting in a final sample size of 60. Participants were recruited using a non-probability convenience sampling technique.

Treatment Protocol

Table 1 shows the treatment given to both groups. Both groups were treated with conventional anti-ulcer drugs (omeprazole and clarithromycin) and a fixed diet. The mango seed aqueous extract capsules, 3 g/day, divided and taken before a meal twice a day for 12 weeks, were also given to the intervention group. This dose of mango seed aqueous extract was chosen after preliminary experimental work showed that it was not toxic and was gastroprotective.

Table 1: Treatment Plan for Control and Intervention Groups

Parameter	Control Group	Intervention Group
Treatment	Conventional therapy: Omeprazole 20 mg + Clarithromycin 500 mg Modified diet	Conventional therapy: Omeprazole 20 mg + Clarithromycin 500 mg Mango seed aqueous extract capsules Modified diet
Dosage	Conventional therapy only	Mango seed aqueous extract: 3 g/day (1.5 g twice daily)
Modified Diet	1500–1600 kcal/day (52% carbohydrates, 18% protein, 30% fat)	1500–1600 kcal/day (52% carbohydrates, 18% protein, 30% fat)
Duration	12 weeks	12 weeks

Preparation of Mango Seed Aqueous Extract

The dried mango seeds were ground into a fine powder and filtered to get a uniform particle size. One kg of powdered material was macerated for 24h at room temperature with intermittent shaking in 2L of distilled water (1:2w/v). The extract was filtered twice, through muslin cloth and Whatman No. 1 filter paper. Filtrate was filtered and stored at -20°C for further analysis after being lyophilized. Extraction yield was determined as a dry-weight yield.

Proximate Analysis, Phytochemical and Antioxidant Analysis

The proximate composition was conducted using the standard methods of AOAC (2012) for moisture, ash, crude protein, crude fat, and crude fiber, with the difference used to determine the nitrogen-free extract (NFE) content. The phytochemical analyses carried out included determination of total phenolic contents (TPC) and total flavonoid contents (TFC) by the use of the Folin–Ciocalteu and aluminium chloride colorimetric method, respectively. The standard spectrophotometric procedures were used to determine the amount of alkaloids and tannins. The antioxidant activity of the extract was determined by DPPH radical scavenging assay at various concentrations of the extract. The IC₅₀ value was determined and then compared with that of ascorbic acid as a reference antioxidant standard.

Clinical and Endoscopic Assessment

A baseline and 12 weeks after the intervention, endoscopic evaluations were conducted. A complete re-epithelialization of the gastric mucosa was considered as a complete healing of ulcers. The sizes of the ulcer were determined by measuring the diameter with the standard measurement tools in endoscopy in millimeters. Histopathological examination of the gastric biopsy was performed from the edges of the ulcers.

Histopathological Evaluation

Biopsies were fixed in 10% buffered formalin, processed in a standard manner and stained with hematoxylin and eosin (H&E). The histopathological evaluation was done by a blinded pathologist. Inflammation, cell infiltration, mucosal damage, oedema and haemorrhage were each graded on a semi-quantitative scale of 0 to 3, with 0 being the absence of the change and 3 being the most severe change. The total histopathological score was between 0 and 12.

Statistical Analysis

SPSS version 25.0 (IBM Corp., Armonk, NY, USA) was used for statistical analyses. Normality of data was assessed by the Shapiro–Wilk test. Continuous variables were reported as mean ± SD, while categorical variables were reported as frequencies and percentages.

Intergroup comparisons used an independent-samples t-test, and intragroup comparisons used a paired t-test between baseline and post-treatment data. The chi-square test was used for the categorical variables. A p-value of <0.05 was deemed statistically significant.

RESULTS

A total of 60 patients with endoscopically confirmed gastric ulcers were enrolled and randomized equally into control and intervention groups. All participants completed baseline assessment, and follow-up evaluation was performed after 12 weeks of treatment (Figure 1). There was no significant loss to follow-up in either group. Table 2 shows the baseline demographic and clinical parameters of study participants. There were no significant differences in baseline scores between the control and intervention groups ($p > 0.05$).

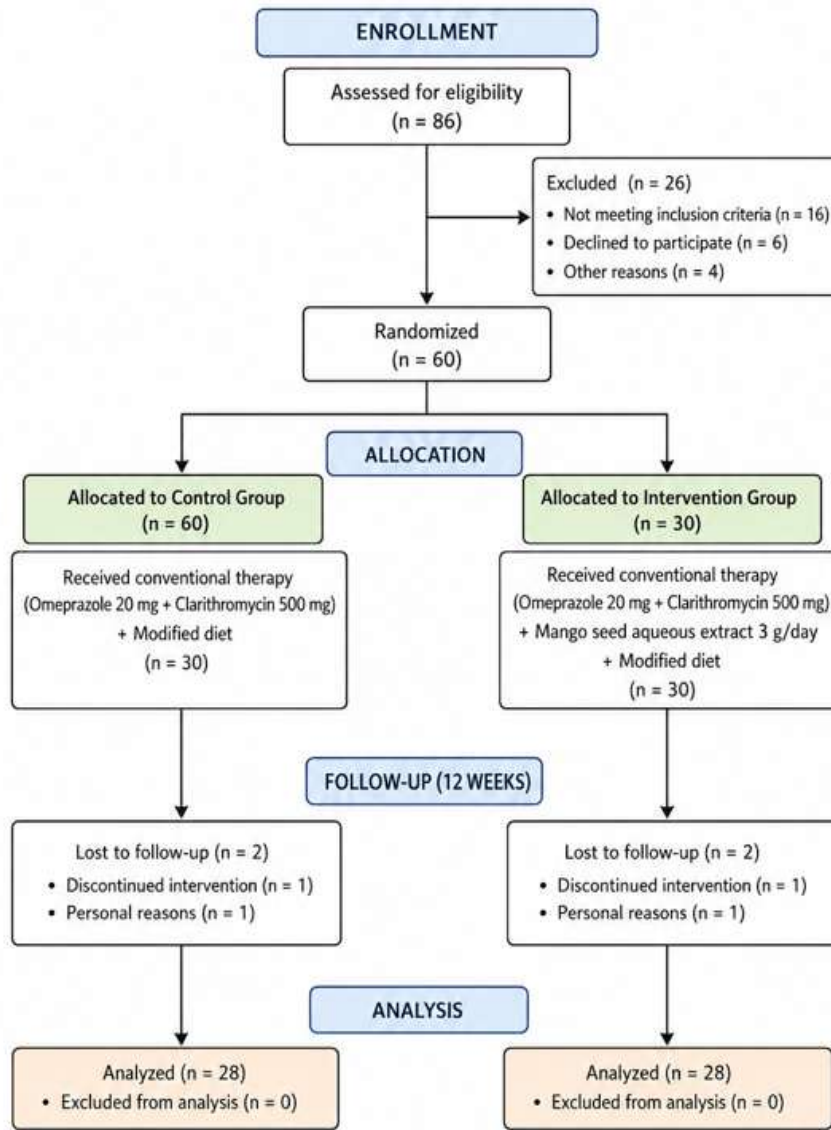


Figure 1: CONSORT flow diagram of participant recruitment, randomization, allocation, follow-up, and analysis in the randomized controlled clinical trial evaluating mango seed aqueous extract in gastric ulcer patients.

Table 2: Baseline Demographic and Clinical Characteristics of Study Participants

Parameter	Control Group	Intervention Group	p-value
Age (years)	42.3±8.1	41.7±7.9	0.74
Male/Female	16/14	15/15	0.81
BMI (kg/m ²)	25.8±2.4	26.1±2.1	0.66
Baseline ulcer size (mm)	6.4±1.2	6.2±1.4	0.58

Proximate Composition

The proximate composition of mango seed extract is presented in Table 3. The analysis demonstrated high carbohydrate content along with moderate fiber levels, suggesting potential nutritional and gastroprotective properties.

Table 3: Proximate Composition of Mango Seed Extract

Parameter	Value (% ± SD)
Moisture	10.82±0.24
Ash	3.91± 0.07
Crude Protein	5.74 ± 0.15
Crude Fat	3.12 ± 0.10
Crude Fiber	9.28 ± 0.22
NFE	67.13 ± 0.41

Phytochemical Composition

Quantitative phytochemical screening confirmed the presence of bioactive compounds with potential therapeutic relevance, as shown in Table 4.

Table 4: Phytochemical Profile of Mango Seed Extract

Compound	Concentration (mg/100g ± SD)
Tannins	3.18 ± 0.31
Alkaloids	6.45 ± 0.52

Total Phenolic and Flavonoid Content

The extract exhibited high concentrations of polyphenolic compounds, indicating substantial antioxidant capacity (Table 5).

Table 5: Total Phenolic and Flavonoid Contents of Mango Seed Aqueous Extract

Parameter	Value
Total Phenolic Content	214.56 ± 10.82 mg GAE/g
Total Flavonoid Content	132.44 ± 7.91 mg QE/g

Antioxidant Activity

The mango seed extract demonstrated concentration-dependent DPPH radical scavenging activity. The percentage inhibition at different concentrations is presented in Table 6. The extract exhibited an IC₅₀ value of 62.18 ± 4.07 µg/mL, indicating marked antioxidant potential.

Table 6: DPPH Radical Scavenging Activity of Mango Seed Extract

Concentration (µg/mL)	Inhibition (% ± SD)
20	18.92 ± 1.88
40	39.45 ± 2.76
60	55.63 ± 3.21
80	71.28 ± 3.67
100	84.90 ± 2.95

Endoscopic Outcomes

Endoscopic findings after 12 weeks of treatment are summarized in Table 7. The intervention group demonstrated significantly improved mucosal healing and reduced ulcer-associated abnormalities compared with the control group.

Table 7: Comparative Endoscopic Outcomes in Control and Intervention Groups After 12 Weeks of Treatment

Parameter	Control (%)	Intervention (%)
Persistent ulcer	56.7	23.3
Mucosal edema	50.0	16.7
Fold distortion	46.7	13.3

H. pylori Serological Markers

Baseline serological markers of H. pylori infection are presented in Table 8. These markers were interpreted as supportive indicators rather than definitive diagnostic parameters.

Table 8: Baseline Serological Markers of H. pylori Infection in Study Participants

Marker	Value ± SD	Interpretation
IgG	28.67 ± 3.92	Positive
IgM	2.21 ± 0.38	Positive

Changes in Serological Markers

Significant reductions in serum IgG and IgM levels were observed in the intervention group following treatment, as presented in Table 9.

Table 9: Changes in H. pylori Serological Markers Following 12 Weeks of Treatment

Parameter	Mean Difference ± SD	t-value	p-value
IgG	18.34 ± 4.85	21.12	<0.001
IgM	1.32 ± 0.49	14.76	<0.001

Clinical and Histopathological Outcomes

Clinical and histopathological outcomes are summarized in Table 10. Participants receiving mango seed extract showed significantly improved clinical recovery, reduced ulcer size, and lower histopathological scores compared with the control group. Representative endoscopic findings of gastric mucosa in both control and intervention groups are presented in Figure 2.

Table 10: Comparative Clinical and Histopathological Outcomes in Control and Intervention Groups After 12 Weeks of Treatment

Parameter	Control	Intervention	p-value
Complete healing (%)	30.0	70.0	<0.01
Ulcer size (mm)	4.21 ± 1.18	2.03 ± 0.74	<0.001
Symptom score	4.11 ± 1.32	1.89 ± 0.81	<0.001
Histopathology score	5.42 ± 1.21	2.78 ± 0.92	<0.001

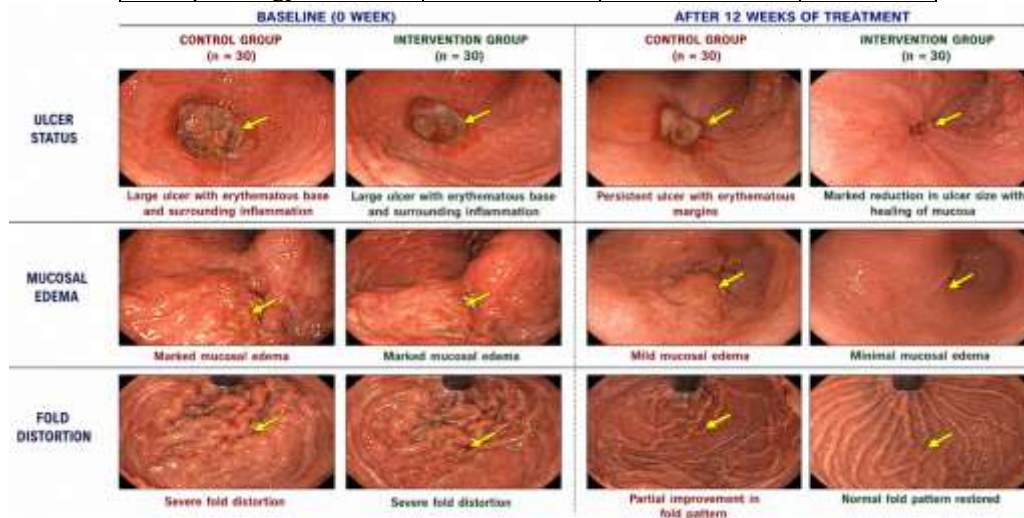


Figure 2: Endoscopic findings in gastric ulcer patients showing comparative changes between control and mango seed extract-treated groups at baseline and after 12 weeks of treatment.

Baseline images demonstrate large gastric ulcers with marked mucosal edema and fold distortion in both groups. After 12 weeks, the control group shows persistent ulceration with mild improvement, whereas the intervention group receiving mango seed aqueous extract shows marked ulcer healing, reduced mucosal inflammation, decreased edema, and restoration of normal gastric fold architecture.

Safety Profile

The incidence of adverse events observed during the study period is summarized in Table 11. No serious adverse events were reported, and the intervention group demonstrated favorable tolerability of the mango seed extract.

Table 11: Incidence of Adverse Events in Control and Intervention Groups During the 12-Week Treatment Period

Event	Control n (%)	Intervention n (%)
Nausea	6 (20.0)	4 (13.3)
Diarrhea	3 (10.0)	2 (6.7)
Constipation	2 (6.7)	1 (3.3)
Headache	5 (16.7)	3 (10.0)
None	14 (46.7)	20 (66.7)

DISCUSSION

The present study, mango seed aqueous extract, was chemically characterized and clinically tested as an adjunct in the management of gastric ulcer using a randomized controlled clinical design. The extent of the antioxidant activity and the

presence of substantial bioactive phytochemicals were confirmed, the results of which showed the extract to be effective in the clinical and histopathological improvement of patients who also had a conventional anti-ulcer treatment. Based on these observations, the mango seed, which is an underutilized agro-industrial waste product, can be considered as a new functional ingredient with gastroprotective properties in the near future. From the proximate composition analysis, it was found that mango seed extract contained a high content of NFE ($67.13 \pm 0.41\%$), which suggests that there is a good carbohydrate content in the extract, and moderate crude fiber ($9.28 \pm 0.22\%$) and crude protein ($5.74 \pm 0.15\%$). These findings are similar to what has been reported as the carbohydrate-rich plant material (Soong & Barlow, 2004; Jahurul et al., 2015) with potential nutritional and functional applications. Dietary fiber has been established as a dietary component that has a beneficial effect on gastrointestinal health through its ability to enhance gastrointestinal motility and the balance of intestinal flora. Recent evidence also suggests that plant-derived bioactive compounds contribute to gastrointestinal health by modulating the gut microbiota and reducing inflammation and oxidative stress. Although the present study did not evaluate gut microbial composition, these mechanisms may partly explain the observed gastroprotective effects of mango seed extract (Khan et al., 2026).

The ash content ($3.91 \pm 0.07\%$) suggested the presence of essential minerals, which may play a role in the enzymatic and metabolic functions, while the moisture content ($10.82 \pm 0.24\%$) was relatively low, which would increase the storage stability of the dried extract. Results of phytochemical analysis revealed biologically active secondary metabolites such as alkaloids (6.45 ± 0.52 mg/100 g) and tannins (3.18 ± 0.31 mg/100 g). These compounds are known to have antimicrobial, antioxidant and anti-inflammatory properties (Cushnie et al., 2014; Khan et al., 2026). Tannins are especially noted to precipitate proteins, and provide protection to damaged mucosal surfaces, and therefore are also known to be involved in the healing of ulcers and protection of mucosal surfaces. The same applies to alkaloids, which are known to modulate inflammatory pathways and decrease the oxidative tissue injury. The presence of these phytochemicals gives a biological rationale for the therapeutic activity found in the present study. The mango seed extract also exhibited high values of total phenolic content (214.56 ± 10.82 mg GAE/g) and total flavonoid content (132.44 ± 7.91 mg QE/g), which reveals a high polyphenolic profile. Mango seed kernels are recognized to contain various bioactive phenolic compounds, including mangiferin, gallic acid derivatives, gallotannins, and flavonoid compounds with potent antioxidant and anti-inflammatory properties (Dorta et al., 2014; Lauricella et al., 2017). The main protective biological effect of polyphenols is attributed to their ability to scavenge free radicals, inhibit lipid peroxidation and chelate metal ions (Scalbert et al., 2005). The high phenolic and flavonoid content found in this study could have played a significant role in the gastroprotective activity of the extract, as oxidative stress is one of the most important factors that cause gastric mucosal injury and the pathogenesis of gastric ulcers. The results from the DPPH radical scavenging assay further showed the concentration-dependent radical scavenging activity of the extract, with an IC_{50} value of 62.18 ± 4.07 μ g/mL. The antioxidant activity was found to be less than that of ascorbic acid, but the scavenging activity of free radicals was still significant for a crude extract of an aqueous plant extract. The antioxidant activity may be due to the synergic interactions between phenolic compounds that are able to donate hydrogen atoms or electrons to the neutralization of reactive oxygen species. Oxidative stress has been shown to play a crucial role in the development of gastric ulcer by inducing lipid peroxidation, epithelial cell injury, disruption of the mucosal defense systems, and activation of inflammation (Bhattacharyya et al., 2014). As a result, mango seed extract possesses antioxidant activity, which can play a significant role in the preservation of gastric mucosal integrity and improvement of gastric ulcer healing. In a clinical study, the treatment group that received mango seed aqueous extract in addition to conventional therapy achieved better therapeutic results than the control group. The 70.0% in the intervention group had complete healing of their ulcers, while the 30.0% in the control group did not. In addition, the ulcer size was significantly smaller, and the symptom scores and histopathological results were better in the intervention group after treatment. The endoscopic findings also showed a decrease in mucosal edema and distortion of folds, and remaining ulcerative lesions, in the intervention group. Based on these results, it can be concluded that mango seed extract can be effective as an adjunctive treatment to promote gastric mucosal recovery. The positive clinical results achieved in the present study could be attributed to the various biological mechanisms of action of mango seed phytochemicals. Polyphenolic compounds like mangiferin and flavonoids have been reported to have anti-oxidative, anti-inflammatory, gastric mucoprotective and vasoregulatory effects (Borrelli & Izzo, 2000; Sumbul et al., 2011). These mechanisms combine to promote gastric mucosal defence and promote tissue repair processes. In this study, direct measurement of inflammatory cytokines and oxidative parameters were not performed, but the observed amelioration of the clinical and histopathological parameters suggest Treatment also led to a decrease in *H. pylori* serological markers in the intervention group. Serological assays cannot confirm eradication of bacteria as antibodies may remain after infection, but decreased levels of both IgG and IgM might be a reflection of decreased antigenic stimulation and better gastric inflammatory status. *H. pylori* inhibitory effect of polyphenols from plants has been previously reported, such as disruption of bacterial cell membrane, inhibition of urease activity and interference with the adhesion of bacteria to gastric epithelial cells (Chatterjee et al., 2004). The synergistic effect of these mango seed phytochemicals on the therapeutic effects of conventional anti-ulcer medications is thus possible. The protection observed by mango seed extract was also corroborated by the histopathological findings. The intervention group showed less histological scoring and less damage to the mucosa, edema, hemorrhage, and infiltration of inflammatory cells than the control group. These findings are consistent with recent evidence demonstrating that

bioactive therapeutic agents can promote tissue repair through antioxidant and anti-inflammatory mechanisms. Roy et al. (2026) reported that chemically synthesized nickel nanoparticles significantly enhanced wound healing and tissue regeneration by reducing oxidative damage and microbial burden, supporting the importance of antioxidant-mediated mucosal repair observed in the present study.

It is compatible with the previous experimental studies indicating that antioxidant properties of plant extracts can help to decrease inflammatory responses and prevent oxidative tissue damage that is associated with gastric mucosal damage. The mucosal architecture is preserved as seen in the present study which supports the histological evidence of the healing of ulcers seen in the present study. The safety profile seen during the study was good. There were no serious adverse events reported during intervention and the incidence of minor gastrointestinal complaints (nausea, diarrhea, constipation and headache) was less in the intervention group than in controls. The results obtained indicate that mango seed aqueous extract was well tolerated with the standard anti-ulcer treatment for 12 weeks duration. Aqueous extraction can also help to ensure safety, avoiding potential residual organic solvent toxicity with certain extraction methods. While the results of the present study are encouraging, there are some limitations. First, the number of subjects was fairly small, and participants were from a single clinical center, potentially limiting the generalizability of results. Second, the length of the study was fairly brief, with no assessment of long-term therapeutic results. Third, detailed mechanistic biomarkers such as inflammatory cytokines, parameters of oxidative stress, and molecular signaling pathways were not examined. Furthermore, serological H pylori testing is not able to distinguish between past exposure and current infection. In order to confirm the therapeutic efficacy and safety of mango seed extract in the treatment of gastric ulcer, further clinical trials with larger patient populations, longer follow-up period and mechanistic studies should be carried out in the future on a multi-center basis. Future multicenter clinical trials with larger patient populations, extended follow-up periods, and detailed mechanistic investigations are warranted. In addition, future research may explore nanoparticle-based delivery systems for mango seed bioactive compounds to improve their stability, bioavailability, controlled release, and targeted delivery to gastric tissues, thereby enhancing their therapeutic efficacy (Khan et al., 2026).

CONCLUSION

The present work shows that in gastric ulcer, the mango seed aqueous extract is in a position to provide substantial gastroprotective action when as adjunct therapy to conventional medicines. The extract contains a rich amount of phenolic and flavonoid compounds, which are responsible for its strong antioxidant and anti-inflammatory properties. These bioactive components are likely to have a significant effect in reducing oxidative stress, inhibiting mucosal inflammation and inducing gastric tissue repair. The endoscopic healing, ulcer size, symptom control, and histopathological findings were improved in the patients who received the extract versus the control group. Importantly, the intervention was well tolerated and did not have serious adverse effects, supporting its safety for short-term use. The study highlights the importance of mango seed waste as a low-cost, eco-friendly therapeutic source. But, it requires larger multicenter trials and mechanistic studies in order to further validate its efficacy and elucidate its molecular pathways during gastric ulcer healing.

DECLARATIONS

Author contributions: Saira Rehman, Muhammad Usman, Sadaf Naz, Shaheer Ahmad, Naila Riaz, Azman Abdullah, and Muhammad Zulfiqah Sadikan contributed equally to this work and approved the final version of the manuscript.

Funding: The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Data availability: Although adequate data have been provided in the form of tables and figures.

Conflict of interest: No conflict of interest

Acknowledgment: No Acknowledgment

REFERENCES

1. Abdalla AE, Darwish SM, Ayad EH, El-Hamahmy RM. (2007). Egyptian mango by-product 2: Antioxidant and antimicrobial activities of extract and oil from mango seed kernel. *Food Chem* 103: 1141–1152. <https://doi.org/10.1016/j.foodchem.2006.10.026>
2. Almulla AE, Albahri AH, Alsuwailim MA, Almreded A, Al Ibrahim AA, Abdulal MA, et al. (2025). A comprehensive review of gastritis clinical manifestation and treatment. *TPM Test Psychom Methodol Appl Psychol* 32(S3): 37–40.
3. Choudhary P, Dawange SP, Bidyalakshmi T, Kasana RC, Narsaiah K, Ghodki BM. (2026). Investigating the antioxidant potential of mango seed kernel polyphenols: extraction and optimization strategies. *Foods* 15(1): 173.
4. Erfan IA, Ghattas MH, Mesbah N, Wahba AS. (2025). Gastric ulcer: an overview of pathophysiology, diagnosis, and management. *Rec Pharm Biomed Sci* 9(1): 162–186.
5. Ibrahim IA, Ebeid HMM, Heikal YAER, Elhariry HM. (2025).

- Sustainable valorization of mango peel waste by extracting bioactive compounds for functional applications. *Sci Rep* 15: 43283.
6. Khan N, Khushtar M, Rahman MA, Kaish M, Ajmal M. (2024). Amelioration of gastric ulcer using a hydro-alcoholic extract of *Mangifera indica* in Sprague Dawley rats by prevention of muco-oxidative stress. *Pharmacol Res Mod Chin Med* 11: 100442.
 7. Mahmoud MF, Nabil M, Hasan RA, El-Shazly AM, El-Ansari MA, Sobeh M. (2022). Pentagalloyl glucose, a major compound in mango seed kernel, exhibits gastroprotective effects in indomethacin-induced gastropathy in rats via modulating NO/eNOS/iNOS signaling pathway. *Front Pharmacol* 13: 800986.
 8. Mutha RE, Kalaskar M, Khan ZG. (2025). Modern analytical techniques for quality control and chemical identification of phytochemicals. In: *Pharmacognosy and Phytochemistry: Principles, Techniques, and Clinical Applications*. pp. 167–188.
 9. Rahat M, Shuja S, Zafar N, Talib S, Kanwal SS, Farooqi SS, et al. (2026). *Mangifera indica* L.: A miracle plant – a review. *J Pharm Biomed* 4: 69–79.
 10. Bhattacharyya A, Chattopadhyay R, Mitra S, Crowe SE. (2014). Oxidative stress in gastrointestinal mucosal diseases. *Physiol Rev* 94: 329–354. <https://doi.org/10.1152/physrev.00040.2012>
 11. Borrelli F, Izzo AA. (2000). The plant kingdom as a source of anti-ulcer remedies. *Phytother Res* 14: 581–591. <https://doi.org/10.1002/1099-1573>
 12. Chatterjee A, Yasmin T, Bagchi D, Stohs SJ. (2004). Inhibition of *Helicobacter pylori* by plant extracts. *Mol Cell Biochem*.
 13. Cushnie TPT, Cushnie B, Lamb AJ. (2014). Alkaloids: an overview of their antibacterial, antibiotic-enhancing and anti-virulence activities. *Int J Antimicrob Agents*.
 14. Dorta E, Lobo MG, González M. (2014). Optimization of factors affecting extraction of antioxidants from mango seed. *Food Bioprocess Technol* 7: 1067–1081. <https://doi.org/10.1007/s11947-013-1130-1>
 15. Jahurul MHA, Zaidul ISM, Ghafoor K, Al-Juhaimi FY, Nyam KL, Norulaini NAN, Sahena F, Mohd Omar AK. (2015). Mango (*Mangifera indica* L.) by-products and their valuable components: a review. *Food Chem* 183: 173–180. <https://doi.org/10.1016/j.foodchem.2015.03.046>
 16. Lauricella M, Lo Galbo V, Cernigliaro C, et al. (2017). Multifaceted health benefits of *Mangifera indica* L. *Nutrients* 9: 525. <https://doi.org/10.3390/nu9050525>
 17. Scalbert A, Johnson IT, Saltmarsh M. (2005). Polyphenols: antioxidants and beyond. *Am J Clin Nutr*.
 18. Soong YY, Barlow PJ. (2004). Antioxidant activity and phenolic content of selected fruit seeds. *Food Chem* 88: 411–417. <https://doi.org/10.1016/j.foodchem.2004.02.003>
 19. Sumbul S, Ahmad MA, Asif M, Akhtar M. (2011). Role of phenolic compounds in peptic ulcer. *J Pharm Bioallied Sci* 3: 361–367. <https://doi.org/10.4103/0975-7406.84437>
 20. Roy, D., Nazeer, N., Khudoykulova, Z., Raj, P. B., Eshmetov, R. J., Smerat, A., ... & Shu, P. (2026). Chemical Reduction-Derived Nickel Nanoparticles as Multifunctional Antimicrobial and Wound Healing Agents: Mechanistic, Biocompatibility, and Computational Insights. *Biological Trace Element Research*, 1-22.
 21. Khan, A. A., Arooj, S., Shabbir, S., Errum, A., Virk, R., & Rahmat, S. A. (2026). The role of gut microbiota in kidney health and disease. *International Journal of Drug Delivery Technology*, 16(21s), 62–73. <https://doi.org/10.25258/ijddt.16.21s.7>
 22. Khan, A., Waheed, M., Bangash, S., Gupta, A., & Ismailov, O. (2026). Targeted drug delivery systems using nanoparticles. *International Journal of Drug Delivery Technology*, 16(36S). <https://doi.org/10.25258/ijddt.16.36s.59>
 23. Khan, A. A., Fatima, H., Alkhasaky, A., Bobokulov, N., Riaz, N., Sadikan, M. Z., & Abdullah, A. (2026). In Silico Design and Evaluation of CRISPR-Cas9 Guide RNAs Targeting the HTT Gene for Huntington's Disease Therapy. *Therapy*, 16(25s), 23-31.