

# Phytochemical Analysis and Assessment of Antioxidant and Anti-Gastric Ulcer Effects of *Prosopis farcta* in an Ethanol-Induced Ulcer Model

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## ABSTRACT

Peptic ulcer disease (PUD) is a common digestive tract disorder with a global impact. Conventional treatments such as Pods of *Prosopis farcta* (Banks & Sol.) J.F.Macbr. are widely used by Kurdistan residents. This study aimed to evaluate the antiulcer efficacy of its fruit pod extract in an ethanol-induced gastric ulcer model in rats. The low extract yield was obtained by ultrasonic-assisted extraction using 80% ethanol. Phytochemical analysis identified alkaloids, flavonoids, saponins, tannins, terpenoids, and cardiac glycosides. The low extract yield was obtained by ultrasonic-assisted extraction using 80% ethanol. The quantitative analysis identified a rich phenolic content ( $40.80 \pm 0.78 \mu\text{g}/\text{mg}$ ), tannins ( $31.59 \pm 0.55 \mu\text{g}/\text{mg}$ ), and flavonoids ( $8.52 \pm 1.18 \mu\text{g}/\text{mg}$ ). The extract had adequate antioxidant activity ( $IC_{50} = 74.94 \pm 0.22 \mu\text{g}/\text{ml}$ ). HPLC analysis validated ten phenolic compounds, with caffeic acid ( $114.8 \mu\text{g}/\text{ml}$ ), kaempferol ( $92.6 \mu\text{g}/\text{ml}$ ), and catechin ( $81.4 \mu\text{g}/\text{ml}$ ) being the most abundant. The acute toxicity evaluation demonstrated no toxic effects at doses up to 2000 mg/kg. In vivo, animal studies also revealed good antiulcer activity at both low (250 mg/kg) and high (500 mg/kg) doses paralleled the effectiveness of esomeprazole, with comparable improvements in ulcer healing parameters. Treatment resulted in measurable gastroprotective effects, increased intragastric pH, and reduced overall acidity parameters. Safety assessments also showed no harmful effects on the liver and kidney functions or the lipid profiles. Hence, the present study advocates that *P. farcta* fruit pod extract is a safe and efficient natural product for managing peptic ulcers.

**Keywords:** Anti-gastric ulcer, DPPH assay, HPLC, Inflammatory biomarkers, *Prosopis farcta*

### How to cite this paper

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## INTRODUCTION

Peptic ulcer ranks among the most prevalent gastrointestinal disorders worldwide. The pathophysiology involves ulcerative lesions developing in the stomach or proximal small intestinal mucosa, clinically presenting with dyspeptic symptoms ranging from mild abdominal distress to severe hemorrhagic complications [1]. The primary causes of PUD are infections with *Helicobacter pylori* and chronic administration of nonsteroidal anti-inflammatory drugs (NSAIDs), followed by alcohol consumption. The conventional treatment involves using antacids, muscarinic antagonists, histamine receptor blockers, proton pump inhibitors, and antimicrobials for *H. pylori* infection [2]. However, extended use of these medications can induce adverse effects. For instance, PPI may cause abdominal pain, nausea, diarrhea, constipation, arrhythmias, and blood disorders [3–5]. Furthermore, H2 blockers cause decreased libido and gynecomastia and increase the resistance to present antibiotics [6,7]. Medicinal plants have been utilized for centuries to promote health across various civilizations. The bioactive compounds present in them are the basis of the therapeutic properties of the medicinal plants [8]. Herbal medicines offer a hopeful alternative treatment due to their potential to minimize side effects and drug resistance, lower toxicity compared to synthetic drugs, better compatibility with the human body because of their natural origin, cost-effectiveness, ease of accessibility, and better social satisfaction [9,10]. *Prosopis* is a genus within the Fabaceae family that consists of nearly 44 species across the globe. *P. farcta*, which naturally thrives in the Americas,

Africa, and Asia tropical zones, is chiefly widespread in the Middle East [11]. *P. farcta*, the Syrian mesquite in English or Khrnuk in Kurdish, is a thorny, woody, perennial leguminous shrub typically with a height of 30–80 cm. However, it occasionally grows to 1m, which grows well in arid temperatures characterized by low and irregular rainfall, dry atmospheres, and strong winds [12,13]. There are also some reports of it being referred to as a ‘shrub tree’ that can grow between 2 and 3 m in height in favorable conditions. *P. farcta* has a well-developed root system, with rhizomes reaching 15–20 m deep into the soil [14]. The upright and spiky stems of *P. farcta* have basal and trailing branches with small yellow flowers that appear from May to August [11]. The plant produces leathery, dark brown, curved, elongated pods as fruit [15]. Traditional medicine practitioners have extensively employed this plant for managing inflammatory processes, claiming effectiveness against diverse pathologies ranging from digestive ulcers and arthritic conditions to asthma, angina, diarrheal diseases, and laryngeal inflammation [16]. In Kurdistan, *P. farcta* pods have traditionally been used to treat GUs. Previous animal studies have established its hepatoprotective effects [17]. However, *P. farcta* has also been effective in wound healing, urolithiasis, neuroprotective, antihyperlipidemic, and antidiabetic [18–22]. It also shows the property of platelet aggregation inhibition in vitro [23]. The antioxidant, antimicrobial, and anticancer effects of *P. farcta* have been confirmed [24]. Numerous medicinal plants containing high levels of phenolic and flavonoid compounds have been reported to protect the stomach lining and reduce ulcer formation. For

example, extracts of *Sideritis caesarea* have shown antioxidant and antiulcer effects of alcohol-triggered stomach injury in rodents [25]. There is a noticeable gap in studies examining the anti-gastric effect of *P. farcta* compared with standard antiulcer drugs or its influence on inflammatory markers. Therefore. This study aims to evaluate the therapeutic value of *P. farcta* pods against ethanol-induced gastric ulcers in rats. It involves phytochemical analysis to identify key bioactive constituents and assess antioxidant and anti-inflammatory activities, ulcer healing capacity, and safety profile. The study provides novel insights into the plant's pharmacological mechanisms and chemical composition, offering scientific support for its ethnobotanical use in gastric ulcer treatment

## MATERIAL AND METHODS

### Chemicals

Sulfuric acid 98% (Biochem, France), Hydrochloric acid 37% (Chemolab, Belgium), Absolute Ethanol (Chemolab, Belgium), Glacial acetic acid (Scharlau, Spain), Chloroform (Scharlau, Spain), Fehling's reagent (Scharlau, Spain), Phenolphthalein indicator (Scharlau, Spain), Ferric chloride (Scharlau, Spain), Aluminum chloride (AlCl<sub>3</sub>) (Scharlau, Spain), Sodium chloride (NaCl) (Scharlau, Spain), Ammonium hydroxide (NH<sub>4</sub>OH) (Scharlau, Spain), Picric acid (Thomas Baker Pvt. Limited, India), Sodium carbonate (Thomas Baker Pvt. Limited, India), Dragendorff reagent (Biochem, France), Gallic acid powder (Biochem, France), Lead acetate trihydrate (Biochem, France), Potassium hydroxide (Biochem, France), Iodine (Biochem, France), Potassium iodide (Biochem, France), Sodium hydroxide (Biochem, France), Quercetin Dihydrate 97% (Thermo Fisher Scientific, Germany), Folin's reagent (Merck, Germany), Ethyl Acetate 99.5% (Chemolab, Belgium), acetonitrile (Scharlau, Spain), trifluoroacetic acid (Scharlau, Spain), DPPH (Merck, Germany), Alpha-tocopherol (Sigma-Aldrich, USA), Petroleum ether (Chemolab, Belgium), Formaldehyde 37% (Chemolab, Belgium), Normal Saline 0.9% NaCl (Pioneer Pharmaceuticals, Iraq), Ninhydrin (Scharlau, Spain), and esomeprazole 20mg (AstraZeneca, Switzerland), Ketamine 10% and Xylazine 2% Injectable Solution (Alfasan, Holland)

### Collection of Plant Material

Mature fruit pods of *P. farcta* were gathered on September 30, 2024, from Rwandiz in the Erbil province of the Kurdistan Region, Iraq. Botanical authentication was carried out at the College of Agricultural Sciences, Salahaddin University. The pods were thoroughly rinsed with distilled water to remove surface debris and then air-dried in a shaded, well-ventilated area at ambient temperature (approximately 30 ± 3 °C) for seven days. After drying, the seeds were carefully separated, and the pods were pulverized into a uniform powder using an automated grinding device. The powdered material was transferred into sealed containers and preserved in a temperature-controlled, light-protected area until the study commenced. A voucher specimen (H-10) has been deposited in the Department of Pharmaceutical Chemistry and Pharmacognosy, College of Pharmacy, Hawler Medical University, Erbil.

### Extraction of Plant Material

Ground *P. farcta* pods were processed using an ultrasonic-assisted technique. Ethanol 80% was used as the extraction solvent. A 1:10 weight-to-volume ratio of plant material to solvent was maintained. The mixture was treated in an ultrasonic bath (Labtech Power Sonic

405, South Korea) at 40 °C for 60 minutes to enhance compound release. Upon completion, the solution was filtered under a vacuum using a Büchner funnel (Vacuubrand GmbH + Co. KG, Germany) to remove solid residues. The resulting liquid was passed through Whatman filter paper (Whatman Ltd., UK) for further purification. The clarified extract was then measured, labeled with extraction parameters, and stored at 4 °C until it was used for further experimental analysis [26].

### Qualitative Phytochemical Testing

The ethanolic extract of *P. farcta* fruit pods was examined for the presence of various phytochemicals, including alkaloids, flavonoids, phenols, cardiac glycosides, anthraquinone glycosides, saponins, reducing sugars, terpenoids, amino acids and proteins applying standard procedures [27,28].

### Quantification of Phytochemical Constituents

#### Total Phenolic Content (TPC)

Using the Folin-Ciocalteu (F-C) method, which was based on the process of Vala *et al.*, the amount of phenolic compounds was measured [29]. With this procedure, a volume of 0.5 mL from the plant extract was mixed with the F-C reagent. Two milliliters of a 7.5% (w/v) solution of sodium bicarbonate were added following a five-minute waiting period, and distilled water was added to bring the level up to ten milliliters. The mixture was left to stand away from light for half an hour. Calculations were made using a gallic acid calibration curve (20–100 µg/ml). Using a Shimadzu 1900i UV-visible spectrophotometer, absorbance readings were recorded at a wavelength of 760 nm and quantified in terms of gallic acid equivalents per milligram of sample.

#### Total Flavonoid Content (TFC)

Flavonoid concentration in the extract was measured by color reaction with aluminum chloride, following a method described by Aveen [26]. A 5 ml sample of the 80% ethanol extract was combined with 5 ml aluminum chloride at 13% dilution. This mixture was held under room condition for one hour. The concentration was interpolated using a quercetin calibration range of 20 to 100 µg/ml. Absorbance was measured at 415 nm with a Shimadzu 1900i spectrophotometer, and the results were reported as micrograms of quercetin per milligram of extract.

#### Total Tannin Content (TTC)

As outlined by CI *et al.*, the F-C method was used to determine the extract's tannin content [30]. One milliliter of a 35% sodium carbonate solution, 7.5 milliliters of water, 0.5 milliliters of F-C reagent, and 0.1 milliliters of the extract were combined in a 10-milliliter flask. After that, distilled water was added to the mixture until it reached 10 mL and thoroughly mixed. The absorbance was recorded at 725 nm following a 30-minute incubation at ambient temperature. The tannin content was measured using a standard gallic acid curve (20–100 µg/ml) and expressed as micrograms of gallic acid per milligram of extract.

### Chromatographic Evaluation of Key Phytochemicals in *P. farcta* Pods

The phytochemical composition of *P. farcta* fruit pods was analyzed using a modified high-performance liquid chromatography (HPLC) method adapted from Ngamsuk *et al.* [31]. The analysis employed a SYKAM HPLC (Germany) equipped with a C18-ODS column (250 mm × 4.6 mm, 5 µm particle size). A 100 µL portion of the extract was injected into the column.

The mobile phase comprised solvent A (95% acetonitrile) and solvent B (0.01% trifluoroacetic acid in water), delivered at a flow

rate of 1 mL per minute. The gradient elution was programmed as follows: 10% B during the first 5 minutes, 25% B from 5 to 7 minutes, and 40% B from 7 to 13 minutes before returning to initial conditions. Detection was performed at 278 nm using a UV-visible detector. Identification and quantification of phenolic constituents were achieved by comparing retention times with standard reference compounds.

### ***In vitro* Antioxidant Activity**

The extract's ability to neutralize free radicals was evaluated using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) technique. To avoid photodegradation, different quantities of the extract were separately treated with an ethanolic DPPH solution and stored without light. The decrease in absorbance at 517 nm was measured spectrophotometrically after the incubation period. Alpha-tocopherol was used as a common comparison to assess the extract's effectiveness. Using the formula % inhibition =  $[(Ac - As) / Ac] \times 100$ , the concentration that produced 50% scavenging activity (IC50) was utilized to represent the antioxidant power of the sample. The extent of DPPH radical scavenging was determined as a percentage. Where % inhibition =  $[(Ac - As) / Ac] \times 100$ . Here, As denotes the absorbance of the test extract, and Ac refers to that of the control [32].

### ***In-Vivo* Animal Study**

#### **Experimental Animals**

Adult Wistar rats weighing between 180-250 grams were used in this investigation. The rats were acquired from Hawler Medical University's College of Pharmacy's Animal House. The subjects were housed in polypropylene cages with regulated conditions, such as a 12-hour light/dark cycle, a room temperature of  $24 \pm 2$  °C, and a humidity of  $57 \pm 3\%$ . The rats had complete access to water and pellet food. NIH guidelines for the care and use of laboratory animals (NIH publication No. 85-23, amended 1996) were followed in all animal operations. Ethical consent for the study was granted by the College of Pharmacy, Hawler Medical University (Approval No. 29162024-46).

#### **Acute Toxicity Test**

Twenty-four healthy, non-pregnant female Wistar rats participated in an acute toxicity investigation. In compliance with OECD Guidelines 425, random allocation was used to assign rats into four groups (n=6), with one group as the vehicle control. Oral 0.9% normal saline has been administered to the normal control group (CG).

Conversely, the obtained extract was administered orally in single doses to the treatment groups at 1000, 1500, and 2000 mg/kg of body weight. All rats were given unfettered access to water and fasted for a full day before the administration. At specified time points within the first 30 minutes, at 4 hours, and then at 24-hour intervals over 14 days, all rats were observed for indications of toxicity, including changes in fur and color of the skin, vision, urination, fecal consistency, respiration, decreased activity, lethargy, seizures, and mortality [33].

#### **Antiulcer Activity**

##### **Study Design**

The study was conducted with minor adjustments to agree with Omar et al. [34]. The thirty male Wistar rats used in this investigation were split up into five groups, each consisting of six rats. To induce gastric ulcers, rats received absolute ethanol at a dose of 5 mL/kg via oral gavage [35]. Treatment started after ulcer induction and was administered for one month. Rats were randomly divided into five groups (n=6):

Normal control (distilled water), negative control (ethanol only), positive control (esomeprazole, 20 mg/kg), low-dose extract (250 mg/kg), and high-dose extract (500 mg/kg). At the end of the treatment period, all the animals were sedated with an intraperitoneal dose of Ketamine 10% and Xylazine 2% Injectable Solution. Blood samples were collected by heart puncture for biochemical examination, and stomachs were probed for additional research. For safety evaluations, lipid profile renal and hepatic functions were evaluated after the one-month treatment period.

#### **Macroscopic Evaluation**

The larger curvature of the stomachs was cut, and distilled water was used to remove all gastric contents, including blood clots, completely. The size and development of ulcers were then rated macroscopically by attaching each stomach to a corkboard. The number of ulcers in each stomach was recorded, and a ruler was used to measure the lesion diameters in millimeters. To measure the severity of the ulcers, a scale from 0 to 5 was used: Firehun and Nedi define the following criteria: 0 = Normal mucosa; 1 = Mucosal edema and petechiae; 2 = 1–5 tiny ulcers (1-2 mm); 3 = More than five small or intermediate ulcers (3–4 mm); 4 = Two or more intermediate ulcers or one gross ulcer (>4 mm); and 5 = Perforation. The ulcer index (UI) was calculated using the formula:  $UI = (UP + UN + US) / 10$ , where UI denotes the UI, UP represents the proportion of animals having ulcers, UN indicates the number of ulcers per animal, and US means the ulcer severity score per animal. The cure rate was determined using the formula:  $(UI_{control} - UI_{test}) / UI_{control} \times 100$  [36].

#### **Assessment of Gastric pH and Total Acidity**

Gastric juice was obtained from each stomach and centrifuged at 3000 rpm for 10 minutes to isolate solid particles, yielding a clear supernatant. The pH of the gastric juice was measured using a calibrated digital pH meter (Sartorius, Germany) by submerging the electrode in the diluted supernatant inside a clean tube, guaranteeing stable readings before recording. To ascertain the sample's acidity, 1 mL of gastric juice was diluted with 1 mL of distilled water, then supplemented with 2–3 drops of phenolphthalein indicator. The resultant mixture was titrated with 0.01 N sodium hydroxide (NaOH) until a stable light pink endpoint was attained [37].

The volume of NaOH used was documented, and the overall acidity was computed using the relevant formula: Total Acidity = (Volume of NaOH) times (Normality of NaOH)  $\times (100/0.1)$ .

#### **Anti-Inflammatory Activity**

Serum levels of interleukin-1 beta (IL-1 $\beta$ ) and tumor necrosis factor-alpha (TNF- $\alpha$ ) were measured using ELISA kits from Sunlong Biotech Co., Ltd., China, with the desire to figure out the anti-inflammatory abilities of *P. farcta* extract. The application procedures were completed to comply with the directions given by the manufacturer [34].

#### **Statistical Analysis**

Data analyses were directed using Microsoft Excel 2019 and SPSS version 26. Results are shown as mean  $\pm$  standard deviation (SD). A one-way analysis of variance (ANOVA) was used to ascertain significant differences across experimental groups. A post hoc Bonferroni test determined specific group differences in multiple comparisons. The criterion for statistical significance was set at  $P < 0.05$ .

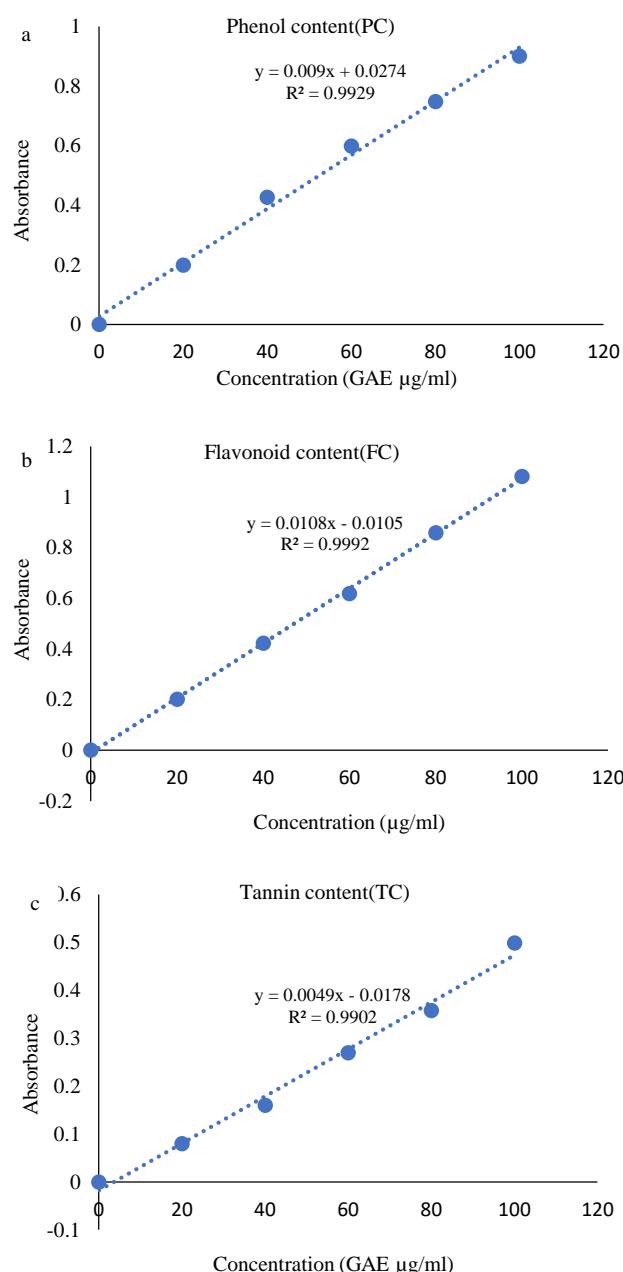
## RESULTS

### Extraction and Phytochemical Constituents

The ultrasonic-assisted extraction of *P. farcta* pods has yielded 12.5% hydroalcoholic extract (Table 1). The identified compounds comprised carbohydrates, proteins, tannins, flavonoids, saponins, alkaloids, cardiac glycosides, and terpenoids. While anthraquinone glycosides were absent. The standard calibration curves for gallic acid (GAE) and quercetin (QE) demonstrated strong linearity, as shown in Figure 1, proving the reliability of the quantification method. Quantitative findings further indicated that phenolic compounds were the most predominant in the extract, with tannins and flavonoids in lesser quantity (Table 2).

**Table 1** Percentage yield and appearance of Pod extract

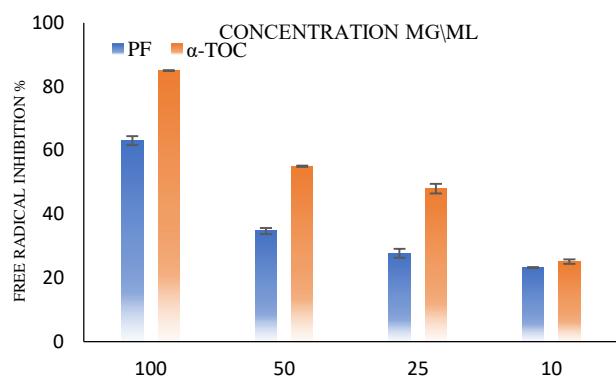
Sample	Method	Yield percentage	Color	Consistency
<i>P. farcta</i>	Ultrasonication	12.5%	Reddish-brown	Solid



**Fig. 1** a. Calibration curve of gallic acid equivalents to PC; b. quercetin equivalents to FC; c. gallic acid equivalents to TC

### In vitro Antioxidant Activity

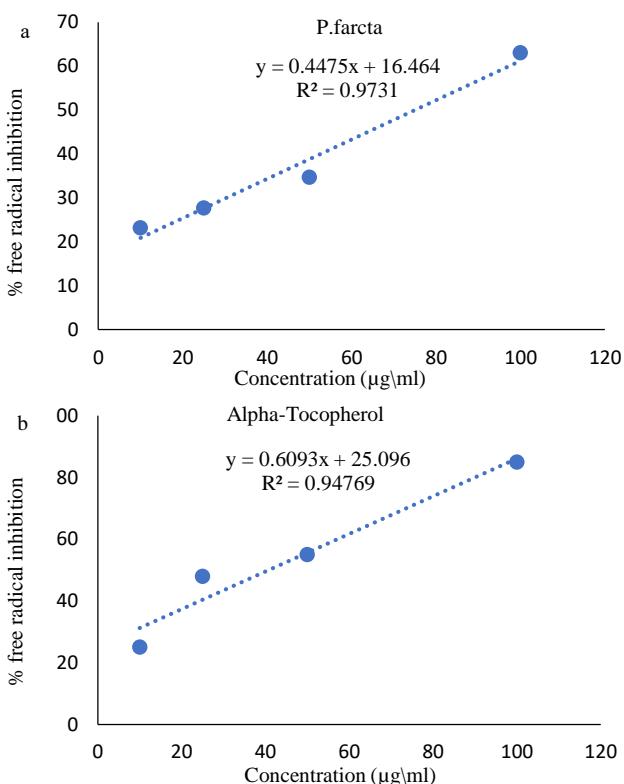
In the DPPH test, *P. farcta* gradually increased the percentage of inhibition with increasing concentration. The maximum inhibition observed was 63.05% at a dose of 100  $\mu$ g/ml (Fig. 2). In contrast, the standard reference ( $\alpha$ -tocopherol) exhibited a significantly greater percentage of inhibition, reaching a maximum of 85% at the same concentration. The  $IC_{50}$  value was the concentration necessary to counteract 50% of free radicals. It was calculated from the dose-response curve (Fig. 3). The  $IC_{50}$  value for *P. farcta* was determined to be  $74.94 \pm 0.22 \mu$ g/ml, indicating a moderate level of antioxidant activity in comparison to  $\alpha$ -tocopherol, which had an  $IC_{50}$  of  $40.87 \pm 0.35 \mu$ g/ml.



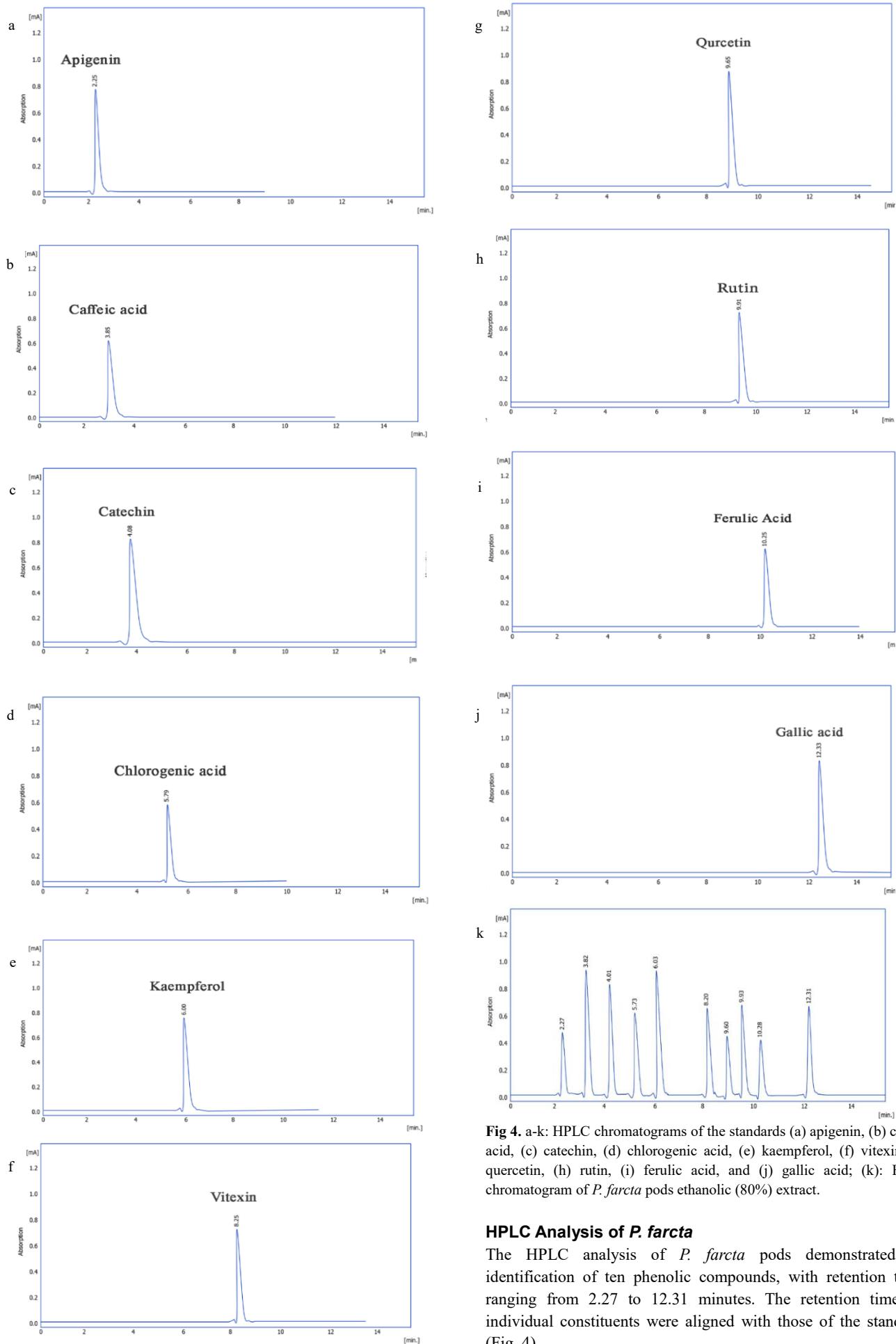
**Fig. 2** DPPH radical scavenging activity of *P. farcta* pods ethanolic extract and  $\alpha$ -tocopherol at a concentration range (10–100  $\mu$ g /mL) stated as a percentage (n = 3).

**Table 2** Quantitative Phytochemical study (n=3) Values expressed as mean  $\pm$  SD

Sample a	TPC b (GAE $\mu$ g/mg)	TFC b (QE $\mu$ g/mg)	TTC b (GAE $\mu$ g/mg)
<i>P. farcta</i> pods	$40.80 \pm 0.78$	$8.52 \pm 1.18$	$31.59 \pm 0.55$



**Fig. 3** Concentration-Dependent curve; a. *P. farcta* pods; b. alpha-Tocopherol. The regression lines and corresponding  $R^2$  values reflect the relationship between concentration and percentage inhibition, which were applied to estimate the  $IC_{50}$  values.

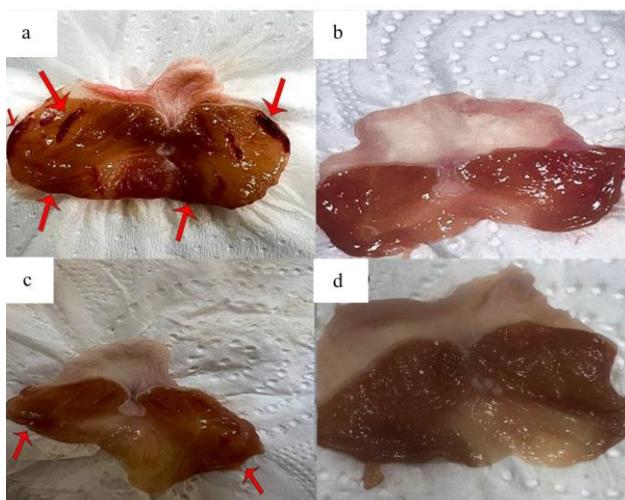


**Fig 4.** a-k: HPLC chromatograms of the standards (a) apigenin, (b) caffeic acid, (c) catechin, (d) chlorogenic acid, (e) kaempferol, (f) vitexin, (g) quercetin, (h) rutin, (i) ferulic acid, and (j) gallic acid; (k): HPLC chromatogram of *P. farcta* pods ethanolic (80%) extract.

#### HPLC Analysis of *P. farcta*

The HPLC analysis of *P. farcta* pods demonstrated the identification of ten phenolic compounds, with retention times ranging from 2.27 to 12.31 minutes. The retention times of individual constituents were aligned with those of the standards (Fig. 4).

The concentrations of the individual phenolic compounds were quantified using standard curve calibration, which involved comparing the peak areas of the samples to those of authentic references under consistent chromatographic conditions. The total amount of each phenolic component was determined by comparing the peak area of the standard to that of the sample under similar separation conditions. Table (3) explains the types and concentrations of phenolic compounds in *P. farcta*.



**Fig. 5** Gross structure of the stomach mucosa; a. Negative CG; b. Positive CG; c. Low dose *P. farcta*; d. High dose *P. farcta*

#### Acute toxicity test and safety of Ethanolic extract of *P. farcta* pods

In the acute toxicity test of *P. farcta*, there were no deaths or other signs of toxicity at the highest dose of 2000 mg/kg, which means that it is relatively safe. There were no apparent changes in the test animals' behavior, activity, and general health. From the safety

analysis of *P. farcta*, 250 and 500 mg/kg doses were chosen for the experimental study. No notable changes were detected in the levels of liver function markers, kidney function indicators, and lipid profile parameters in the animals following the administration of *P. farcta* at doses of 250 and 500 mg/kg for a month, relative to the CG, with no notable differences observed ( $P > 0.05$ ), as presented in table (4).

#### *In vivo* anti-gastric ulcer

##### Macroscopic evaluation

Macroscopic examination revealed substantial mucosal lesions, marked by extended hemorrhagic streaks and many tiny spots along the longitudinal axis of the glandular portion of the stomach in the negative CG (Fig. 5). In contrast, the animals treated with *P. farcta* had fewer and less severe lesions than the negative control. The UI experienced a significant reduction in the groups treated with *P. farcta*. The curative rate of *P. farcta* extract on the UI shows a dose-dependent curative effect. Specifically, the treatment with 250 mg/kg had a curative rate of 56.60%, which indicated that it has a moderate capacity to promote ulcer healing. Conversely, the 500 mg/kg dose had a higher curative rate of 79.88%, almost as good as the positive CG (80.62%), as highlighted in Table (5).

#### Assessment of gastric pH and acidity

Administering *P. farcta* extracts over a month led to a reduction in total acidity and an elevation in gastric pH. Total acidity decreased from  $70.4 \pm 1.13$  mEq/l in the negative CG to  $40.83 \pm 0.75$  mEq/l with 250 mg/kg and  $33 \pm 2.15$  mEq/l with 500 mg/kg of *P. farcta*, closely matching esomeprazole. Similarly, at a dosage of 250 mg/kg, there was an increase in gastric pH compared to the CG (significant at  $P < 0.5$ ) while at 500 mg/kg. This increase was even more evident, demonstrating high significance (highly significant, at  $P < 0.01$ ), which was not far from that of esomeprazole, as made known in Table (5).

**Table 3** HPLC analysis of ethanolic extract of *P. farcta* pod

No	Compound name	Wave length [nm]	Retention time [min]	Area [mAU.s] <sup>a</sup>	Height [mAU]	Concentration (ppm) <sup>b</sup>
1	Apigenin	278	2.27	3205.44	430.21	62.1
2	Caffeic acid	278	3.82	9854.07	947.14	114.8
3	Catechin	278	4.01	7741.00	813.45	81.4
4	Chlorogenic acid	278	5.73	4562.14	620.31	54.9
5	Kaempferol	278	6.03	8752.09	950.14	92.6
6	Vitexin	278	8.20	5621.45	710.12	74.5
7	Quercetin	278	9.60	3269.80	430.11	58.7
8	Rutin	278	9.93	4123.65	611.12	68.7
9	Ferulic acid	278	10.28	3387.41	385.14	41.6
10	Gallic acid	278	12.31	5120.25	620.33	70.6

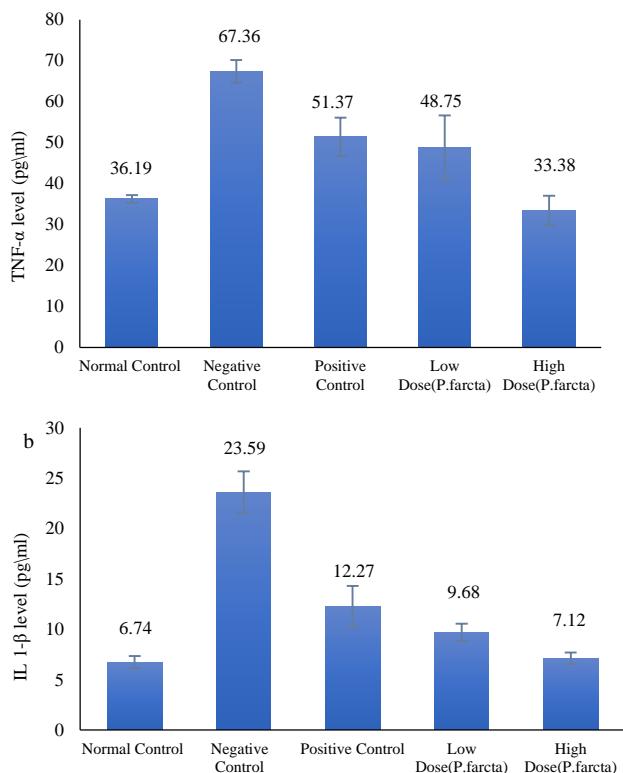
a. Milli absorbance units multiply by seconds to measure the area under the curve.

b. Results are presented as part per million (μg/ml).

**Table 4** Safety of *P. farcta* extract

Parameters	Healthy animals	<i>P. farcta</i> 250 mg/kg	<i>P. farcta</i> 500 mg/kg
alanine aminotransferase (U/l)	$40.36 \pm 1.25$	$41.47 \pm 3.17$	$38.97 \pm 5.33$
aspartate aminotransferase (U/l)	$71.56 \pm 6.41$	$65.89 \pm 4.39$	$69.12 \pm 7.01$
alkaline phosphatase (U/l)	$136.47 \pm 6.98$	$139.6 \pm 9.98$	$135.99 \pm 8.93$
Total bilirubin (mg/dl)	$0.35 \pm 0.25$	$0.3 \pm 0.1$	$0.57 \pm 0.21$
Direct bilirubin (mg/dl)	$0.1 \pm 0$	$0.2 \pm 0$	$0.3 \pm 0$
Urea (mg/dl)	$30.15 \pm 3.25$	$30.80 \pm 8.62$	$29.7 \pm 7.2$
Creatinine (mg/dl)	$0.445 \pm 0.017$	$0.57 \pm 0.3$	$0.495 \pm 0.019$
Uric acid (mg/dl)	$2.9 \pm 0.8$	$3.45 \pm 0.49$	$3.3 \pm 0.57$
Triglyceride (mg/dl)	$49.3 \pm 5.9$	$51.65 \pm 4.03$	$48.65 \pm 8.56$
Cholesterol (mg/dl)	$70.9 \pm 1.4$	$69.2 \pm 6$	$66.1 \pm 5.23$
Low Density Lipoprotein (mg/dl)	$63 \pm 7$	$55.5 \pm 4.53$	$61.79 \pm 1.70$
High Density Lipoprotein (mg/dl)	$40.64 \pm 3.11$	$37.69 \pm 8.59$	$35.43 \pm 5.82$

Results were presented as mean  $\pm$  SD; Insignificance difference ( $P > 0.05$ ) for both doses of extract compared with healthy rats.



**Fig. 6** a. serum level of TNF- $\alpha$ ; b. serum level of IL-1 $\beta$ . The low-dose extract has a substantial difference from the negative CG ( $P < 0.05$ ), while the high dose has a considerable difference from both the negative CG ( $P < 0.01$ ) and the positive CG ( $P < 0.05$ ).

#### Anti-inflammatory effect of *P. farcta* pods

As presented in Figure (6), absolute ethanol increases the level of inflammatory markers. *P. farcta* pod extract suppressed inflammation by decreasing the level of TNF- $\alpha$  and IL-1 $\beta$  in serum. IL-1 $\beta$  was reduced to a low level by both doses of *P. farcta* compared to the negative CG, thus exhibiting an extreme anti-inflammatory action irrespective of the dose. A little TNF- $\alpha$  was reduced by esomeprazole, *P. farcta* 250mg/kg dose improved it, and 500 mg/kg dose had the best effect. The 500 mg/kg dose of *P. farcta* was even more effective than esomeprazole in decreasing IL-1 $\beta$  ( $P < 0.05$ ) and TNF- $\alpha$  ( $P < 0.01$ ).

**Table 5** The effect of *P. farcta* extract on the UI, curative rate pH of the stomach, and total acidity in the stomach (n = 6)

Groups	Ulcer Index c	Curative Rate c	Gastric pH	Total Acidity c (mEq/l)
Negative CG	9.03 $\pm$ 0.21	-	1.96 $\pm$ 0.035	70.4 $\pm$ 1.13
Positive CG	1.75 $\pm$ 0.20	80.62%	5 b $\pm$ 1	31.50 $\pm$ 1.05
Low dose extract	3.73 $\pm$ 0.47	56.60%	3.50 a $\pm$ 0.27	40.83 $\pm$ 0.75
High dose extract	1.82 $\pm$ 0.12	79.88%	4.80 b $\pm$ 0.30	33 $\pm$ 2.15

a: different from negative CG statistically ( $P < 0.05$ ). b: different from negative CG statistically ( $P < 0.01$ ).

c: different from negative CG statistically ( $P < 0.001$ ).

#### DISCUSSION

The results indicate that *P. farcta* pod extract confers protective effects against ethanol-induced gastric ulceration, likely through mucosal defense enhancement, free radical scavenging, and inflammatory modulation. These outcomes reflect the complex interplay of its bioactive constituents and suggest a promising role for this extract in ulcer therapy. The extraction yield in this study was higher than the 8.23% (w/w) yield of ethanolic extract reported

by Jahromi *et al.* in Iran [38]. Thus, ultrasonic extraction is more productive than conventional maceration [39]. Phytochemical screening confirmed the presence of phytoconstituents, similar to that described by Safari *et al.* [40]. Furthermore, the existence of terpenoids and cardiac glycosides in *P. farcta* fruit pod extract was validated in our study. The amount of phenols aligns with the data reported by Poudineh *et al.* in Iran. At the same time, flavonoids showed a decrease compared to the recorded data in Kurdistan by another research group [41,42]. DPPH assay exhibited a lower scavenging effect, and the IC<sub>50</sub> value for *P. farcta* was higher than that shown by Jahromi *et al.* [38], probably due to differences in extraction technique or chemical compositions. HPLC detections from our study align with research conducted on *Prosopis* species regarding the presence of phenolic compounds with some variations in their profiles and concentrations [43]. Nevertheless, the partitioning of flavonoids and phenolic acids in the pods of *P. farcta* differs from the finding by Khosravi *et al.* for other parts of the plant [44]. This difference indicates that the composition of phenolics is influenced by the part of the plant being examined. Also, previous studies suggested that the phenolic content of *P. farcta* roots and branches differ by ethnic origin and location, indicating that environmental conditions might play a role in phenolic biogenesis [45]. Acute toxicity study observations of our research imply that *P. farcta* is well tolerated, even at doses as high as 2000 mg/kg. This can be likened to *P. africana*, which demonstrated no impacts at 5000 mg/kg and had an LD<sub>50</sub> surpassing this dosage [46]. Compared to the normal control CG, there were no liver and kidney damage signs. The absence of changes in lipid parameters means that the substance did not disturb lipid metabolism or cause disorders associated with dyslipidemia, such as cardiovascular diseases [47]. Several studies now demonstrate that hemorrhagic damage and mucosal erosion in the foregut are common outcomes of alcohol consumption [48]. The ethanol-stimulated gastric ulcers model is used frequently to investigate the pathophysiology of stomach ulceration and the gastric healing effects of several drugs and natural products [48]. Ethanol directly harms the mucosa by damaging the mucus bicarbonate layer, increasing mucosal permeability, and exposing epithelial cells to stomach acid. In addition, to that point, ethanol causes a decrease in blood flow to the stomach lining, leading to delayed tissue repair due to reduced oxygen supply and increased acidity levels in the stomach that can worsen injury conditions reported in studies [49]. Treating the subjects with *P. farcta* decreased ulcer severity compared to the control group not treated with *P. farcta* doses during our study period. The cured rate for those lesions was appreciably higher in the test groups, and it stood out as an improved recovery of stomach ulcers in a way that depended on the dosage given. Thus, our study revealed that *P. farcta* can effectively adjust the stomach environment by lowering acidity levels and mucous secretion mechanisms. The standard treatment exhibited outcomes in reductio PH and total acidity values approximately similar to *P. farcta*, which agrees with the former finding of [50]. There is an association between ethanol-induced ulcer development and inflammation. The inflammatory response is provoked by ethanol, which causes macrophages to secrete many cytokines, such as IL-1 $\beta$ , IL-6, and TNF- $\alpha$ . These cytokines draw neutrophils to the site of inflammation, disrupting the mucosal hindrance and causing connexin to collapse. This results in stress by producing oxygen species (ROS), which leads to lipid peroxidation and cell apoptosis. Oxidative stress also triggers Nuclear Factor kappa B (NF kappa B). This transcription factor boosts the overgeneration of inflammatory cytokines and the

decrement of intrinsic antioxidants such as superoxide dismutase, glutathione, and catalase [51]. Our results proved that ethanol increases cytokine levels, and they are in line with earlier research which verified that ethanol ingesting raised IL-1 $\beta$  and TNF- $\alpha$  levels and downregulated with ingesting of Licorice, which is a plant belonging to Fabaceae family [52]. The effectiveness of *P. farcta* in reducing cytokine levels is due to its abundance of phytochemicals such as flavonoids, phenols, and tannin with known antioxidant and anti-inflammatory properties; likewise, it could contain other phyto ingredients such as alkaloids saponins and terpenoids that synergistically augment the efficacy [53]. More precisely, catechin, quercetin, rutin, gallic acid, and apigenin are responsible for the antiulcer efficacy in treating ethanol-formed ulcers [54, 55]. Earlier animal studies demonstrated the protective activity of kaempferol on the stomach in ethanol-induced ulcers, and this may come from the preservation of gastric mucous glycoproteins, the blockade of neutrophil infiltration, and myeloperoxidase (MPO) activities, pro-inflammatory cytokines, and increase in nitric oxide (NO) levels [56]. Caffeic acid could also contribute to the gastroprotective effects in alcohol-provoked gastric lesions model by tapering unstable oxygen molecules and decreasing lipid peroxidation due to enhanced activity of cell-derived antioxidant enzymes such as superoxide dismutase (SOD) and glutathione (GSH). It decreases the activity of myeloperoxidase (MPO), which indicates neutrophil infiltration and tissue inflammation and restricts inflammatory tissue damage caused by excessive leukocyte recruitment. It suppresses the secretion of protective mucus from the gastric lining, which serves as a defensive buffer. Further, it increases the attachment of epithelial cells of the stomach, thus helping to heal ulcerated tissues more quickly. It helps spare gastric mucosal cells by membrane stabilization and promoting cellular mitosis [57]. Our study ensures the attendance of these constituents that contribute to the antiulcer property of *P. farcta* by HPLC.

## CONCLUSION

This research provides logical evidence that endorses the conventional application of *P. farcta* pods in treating GUs. The extract demonstrated a notable healing effect when administered in a model of ulcers stimulated by alcohol. The antiulcer properties were ascribed to its significant antioxidant activity observed in vitro and its anti-inflammatory effects demonstrated *in vivo*. The HPLC analysis confirmed the existence of elevated concentrations of phenolic compounds. These bioactive compounds may contribute to its therapeutic effect. The research findings indicated that the attenuation of inflammatory responses and the neutralization of oxidative stress are the primary processes behind the ulcer-healing efficacy of *P. farcta*. This discovery proposes that it may serve as a natural alternative for treating GUs, necessitating further research to elucidate its mechanism of action and clinical applications fully.

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## Competing Interests

The authors have revealed no possible conflicts of interest.

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