(J I D P T S)
ISSN(O):2581-6934

ASSESSMENT OF GASTROPROTECTIVE ACTIVITY OF HERBAL EXTRACT TERMINALIA CHEBULA RETZIN ETHANOL INDUCED GASTRIC ULCER IN RATS

Dr.A. Ramesh[1], Dr.P. Rajashekar[2], Machana Bhavani[3]

Corresponding author: [1]Dr.A.Ramesh, Professor and Principal, [2]Dr.P.Rajashekar, Associate Professor,

[3]Machana Bhavani, M.Pharm.2nd year,

[1,2,3] Vishnu Institute of Pharmaceutical education and Research, Narsapur, Medak, Telangana.

ABSTRACT: Gastric ulcer is a common gastrointestinal disorder characterized by disruption of gastric mucosal integrity due to an imbalance between aggressive factors such as gastric acid, ethanol, oxidative stress, and inflammatory mediators and defensive mechanisms including mucus secretion, bicarbonate production, and antioxidant protection. The present study was designed to evaluate the gastroprotective activity of Terminalia chebula Retz. extract against ethanol-induced gastric ulcer in rats. Healthy Wistar rats were divided into five groups, including normal control, ethanol-induced ulcer control, standard drug-treated group, and Terminalia chebula extract-treated groups. Gastric ulceration was induced by oral administration of absolute ethanol, and the protective effect of the extract was evaluated by assessing ulcer index, gastric juice volume, gastric pH, free acidity, total acidity, and oxidative stress parameters. Ethanol administration produced significant gastric mucosal injury, characterized by increased ulcer index, gastric juice volume, free acidity, total acidity, and malondialdehyde (MDA) levels, along with decreased gastric pH and reduced antioxidant enzyme levels of superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH). Pretreatment with Terminalia chebula extract significantly attenuated ethanol-induced gastric damage by reducing ulcer severity, decreasing gastric acidity, lowering MDA levels, and restoring antioxidant defense mechanisms in a dose-dependent manner. The higher dose of the extract exhibited marked gastroprotective activity comparable to the standard antiulcer drug.

The protective effect of Terminalia chebula Retz. may be attributed to the presence of bioactive phytoconstituents such as tannins, flavonoids, phenolic compounds, chebulagic acid, chebulinic acid, gallic acid, and ellagic acid, which exhibit antioxidant, anti-inflammatory, and mucosal protective properties. The study demonstrates that Terminalia chebula possesses significant gastroprotective potential and may serve as a promising herbal candidate for the management of gastric ulcer associated with oxidative stress and gastric mucosal injury.

Keywords: Terminalia chebula Retz., Gastroprotective activity, Ethanol-induced gastric ulcer, Gastric mucosa, Oxidative stress, MDA, SOD, CAT, GSH, Herbal extract.

INTRODUCTION

Gastroprotective activity refers to the ability of a therapeutic agent, medicinal plant extract, or bioactive compound to prevent, reduce, or repair damage to the gastric mucosa caused by various ulcerogenic factors. The gastric mucosa is continuously exposed to aggressive factors such as hydrochloric acid (HCl), pepsin, alcohol, non-steroidal anti-inflammatory drugs (NSAIDs), stress, bacterial infections, and reactive oxygen species (ROS). Under normal conditions, the stomach maintains a balance between these damaging factors and protective mechanisms. Disturbance of this balance results in gastric mucosal injury, inflammation, erosion, and ulcer formation.

Gastroprotective agents act by strengthening the natural defense mechanisms of the stomach and reducing the effects of harmful factors. One of the major protective mechanisms involves enhancement of gastric mucus and bicarbonate secretion.

MATERIALS AND METHODS

COLLECTION AND AUTHENTICATION OF PLANT MATERIAL

The Leaves of Terminalia chebula Retzwere collected from the herbal market of Ranga Reddy dist., Plant materials were taxonomically identified and authenticated by Dr Madhavan Chetty, Associate Professor, Shree Venkateshwara University, and Tirupathi.

PREPARATION OF PLANT MATERIAL FOR EXTRACTION

The enough fresh leaves of Terminalia chebula Retzwere washed with water and the water was drained and allows completing dry under shade at room temperature. The dried leaves were finely powdered with mixer grinder avoiding elevation of their temperature above 40°C and powder was then passed through mesh # 40″. The powder was weighed and stored in air tight container for further use.

EXTRACTION

The process of separating active principle(s) from powdered crude drugs by using suitable solvents is called extraction. The basic principle behind extraction is the exceptional behaviour of the active principles towards the solvent. Air-dried and finely powdered of 50gm was extracted by socklation by using ethanol (1:4) as a solvent to form a c extract. The powder was immerged in the selected solvent for 7 days with occasional shaking. After days the extract was filtered by using Whatman filter paper and made dry by the help of a rotary evaporator. The extracts were stored at 4°C in the refrigerator before use in various phytochemical and pharmacological experiments.

PRELIMINARY QUALITATIVE TEST

The extracts obtained by successive solvent extraction of plant material were then subjected to qualitative tests for the identification of various constituents present in crude extracts.

Test for Carbohydrates

Molisch's Test (General test)

A few drops of α-naphthol solution in alcohol were added to 2-3 mL of the extract. This was shaken and conc. H_2SO_4 was added from the sides of the test tube. The Violet ring formed at the junction of two liquids shows the presence of carbohydrates.

Fehling's Test

The extract was added to boiling Fehling's solution (1 mL Fehling's A and 1 mL Fehling's B solutions) in a test tube. First yellow, then brick red precipitate shows the presence of reducing sugar.

Benedict's test

Equal volumes of Benedict's reagent and test solution were mixed in the test tube. This was heated in a boiling water bath for 5 minutes. The appearance of green, yellow, or red shows the presence depending on the amount of reducing sugar present in the test solution.

Barfoed's test

An equal volume of Barfoed's reagent and test solution were mixed. The solution was heated for 1-2 minutes in a boiling water bath and then it was cooled. Red precipitate shows the presence of monosaccharides.

Test for Proteins

Biuret Test (General Test)

4% NaOH solution was added to a 3 mL test solution followed by addition of few drops of

1% $CuSO_4$ solution, a violet or pink color indicates presence of protein.

Test for amino acids

Ninhydrin test (General Test)

3 mL test solution and 3 drops 5% ninhydrin solution was heated in boiling water bath for

10 minutes. Appearance of purple or bluish color shows the presence of amino acid.

Test for Steroid

Salkowaski reaction

2 mL chloroform and 2 mL conc. H_2SO_4 were added to 2 mL of the extract. This was shaken

Well. Appearance of red layer in chloroform and greenish yellow fluorescence in acid layer

Indicates the presence of steroid.

Liebermann-Burchard Reaction

Mixed 2 mL extract with chloroform and added 1-2 mL acetic anhydride. Now added 2 drops

of conc. H2SO4 from the side of test tube. First red, then blue and finally green color shows

The presence of steroid.

Liebermann's Reaction

Mixed 3 mL extract with 3 mL acetic anhydride, heated and cool the mixture. Now added few drops of conc. H2SO4. Blue color appears.

Test for Flavonoids

Shinoda test

5 mL 95% ethanol/t-butyl alcohol, few drops of conc. HCl and 0.5 g magnesium turnings were added to the extract. Orange, pink, red to purple color appears (flavanols, dihydro derivatives and xanthenes) for the flavonoids.

Sulfuric acid test

In addition of sulphuric acid (66% or 80%) flavones and flavonols were dissolved into it and given a deep yellow solution. Chalcones and aurones are given red or red-bluish solutions. Flavones given an orange to red colors.

Animals

Wistar albino rats, weighing 100-150 g were purchased from the, Jeeva life sciences, Hyderabad. Animals were housed 5 per cage, allowed access to water and food, ad libitum, and maintained at a constant temperature of 22 ± 2°C and humidity of 50-55% and 12 h of light/dark cycle. All experimental procedures were carried out by the Institutional Animal Ethics Committee affiliated with CPCSEA.

Induction of Ethanol-Induced Gastric Ulcer Model:

Healthy Wistar rats weighing 150–250 g is selected and acclimatized under standard laboratory conditions for 7 days before the experiment. The animals are fasted for 18–24 hours prior to ulcer induction, with free access to water. The animals are randomly divided into different experimental groups, including normal control, ethanol-induced ulcer control, standard drug-treated, and Terminalia chebula extract-treated groups. The treatment groups receive the respective doses of Terminalia chebula extract and standard antiulcer drug according to the study protocol. Gastric ulceration is induced by oral administration of absolute ethanol (1 mL/kg body weight, p.o.) to the ulcer control and treatment groups. After ethanol administration, animals are maintained for 1–4 hours to allow the development of gastric lesions. The animals are then euthanized, and the stomachs are removed, opened along the greater curvature, and washed with normal saline. The gastric mucosa is examined for ulcerative lesions, and the severity of gastric damage is assessed by calculating the ulcer index and percentage ulcer protection.

Experimental grouping

Group I: Normal Control Vehicle-treated normal rats Vehicle (normal saline) 1 mL/kg, p.o.

Group II: Ulcer Control Ethanol-induced gastric ulcer Absolute ethanol 1 mL/kg, p.o.

Group III: Standard Group Omeprazole + ethanol-induced ulcer Omeprazole 20 mg/kg, p.o. + Ethanol 1 mL/kg, p.o.

Group IV: Terminalia chebula extract + ethanol-induced ulcer Terminalia chebula extract 200 mg/kg, p.o. + Ethanol 1 mL/kg, p.o.

Group V: Terminalia chebula extract + ethanol-induced ulcer Terminalia chebula extract 400 mg/kg, p.o. + Ethanol 1 mL/kg, p.o.

Quantitative analysis of ulceration

Ulcer scoring:

Twenty-four hours after the induction of gastric ulcer, the stomach was opened along greater curvature and washed with normal saline. Gastric mucosal lesions were expressed in terms of ulcer index (U.I.) according to Peskar et al. which depends on the calculation of a lesion index by using a 0–3 scoring system based on the severity of each lesion. The severity factor was defined according to the length of the lesions. Severity factor

0= no lesions;

1= lesions < 1 mm length;

2 =lesions 2–4 mm length and

3= lesions > 4 mm length.

The lesions/ulcer score for each rat was calculated as the number of lesions in the rat multiplied by their respective severity factor. The mean ulcer index (UI) was calculated by the method of Raji et al.

$$Ulcer\ index\ (UI) = Mean\ group\ of\ ulceration \times \frac{\%\ of\ group\ of\ ulceration}{100}$$

The percentage inhibition (P.I.) of a given drug was calculated by the equation of Hano et al.100.

$$Percentage\ of\ Inhibition = \frac{U.I.of\ aspirin\ group\ -\ U.I.of\ treated\ group}{U.I.of\ aspirin\ group} \times 100$$

$$\%\ of\ Ulceration\ = \frac{No.of\ ulcered\ rat\ -\ no.of\ non-ulcered\ rat}{No.of\ rat\ in\ group} \times 100$$

Measurement of gastric acid secretion

Twenty-four hours after the induction of gastric ulcer, the rats were sacrificed under ketamine hydrochloride; the abdomen was opened to remove the stomach. The stomach was opened along the greater curvature and gastric content was drained into a centrifuge tube. Five ml of distilled water was added and the resultant solution was centrifuged at 3000 rpm for 10 min. From the supernatant, an aliquot (1 mL of each) was taken and diluted with 1 mL of water, and the pH of the fluid was measured using a pH meter.

Assessment of free acidity and total acidity

Reagents used:

1. 0.01N oxalic acid solution
2. 0.01 N sodium hydroxide solution: Prepared by solubilizing ~4mg of NaOH in 100mL of Milli-Q water.
3. Topfer's reagent: It is a commercially available reagent containing 0.5% of di-methyl amino benzene in absolute ethanol
4. 1% phenolphthalein solution: Prepared by diluting the commercially available reagent with absolute ethanol.

All the above reagents used were prepared freshly on day of experiment.

Experimental procedure:

1. Aliquot ~1mL of gastric juice to a 50 mL conical flask, to this added little quantity of Topfer's reagent followed by titration using 0.01 N NaOH up to endpoint (i.e. till all the traces of red color vanishes and becomes yellowish orange).
2. The quantity of 0.01N NaOH added to achieve the endpoint was noted which represents the free acidity.
3. Further, to the above solution added little quantity of phenolphthalein solution followed by continuing the titration with 0.01 N NaOH till a distinct red tinge re-emerges.
4. The quantity of 0.01N NaOH added was recorded which represents the total acidity. Acidity was computed employing the below-mentioned formula:

$$Acidity\ = \frac{vol\ of\ NaOH\ \times\ Normality\ of\ NaOH\ \times\ 100\ mEq/L}{0.1}$$

Assessment of total proteins

Protein estimation was done as per the method described by Lowry. The principle of the method involves the establishment of a colored composite between the proteins and Folin Ciocalteau reagent, which can be assessed calorimetrically at 610nm. BSA was employed as a standard.

Reagents required:

1. Alkaline reagent solution: Prepared by solubilizing ~20gm of Sodium carbonate in one liter of 0.1N NaOH solution.
2. Alkaline mixture solution: Prepared by adding 1mL of 4% aqueous copper sulphate solution to 100mL of the alkaline reagent solution.
3. Phenol reagent: Commercially available reagent thinned with an equal volume of water before use and stored at 2-80C.
4. 0.1N NaOH solution: Prepared by solubilizing ~40mg of sodium hydroxide in 100 mL of Milli-Q water.
5. 90% alcohol
6. 0.08 % of standard bovine albumin solution: Prepared by solubilizing ~ 8mg of standard bovine albumin in 10 ml of Milli-Q water.

All the above reagents used were prepared freshly on the day of the experiment.

Experimental Procedure:

1. Aliquot ~100µL of gastric juice to an eppendroff tube, to this added 900µL of alcohol followed by centrifugation at 4000rpm for ten min. The supernatant was disposed and the precipitant was solubilized in 1000µL of 0.1N NaOH solution.
2. Aliquot ~50µL of the above solution to a test tube into which added 4mL of alkaline mixture solution and set aside for 10 minutes.
3. Ten minutes later, to the above reaction mixture added 400µL of phenol reagent and again set aside for another ten minutes for accomplishing the reaction.

4. The absorbance was assessed at 610nm using Milli-Q water as blank.
5. Aliquot ~100µL of standard bovine albumin solution into an eppendroff tube and processed as noted in steps 1-3.

The quantity of protein was computed employing the below-mentioned formula:

$$Protein = \frac{O.D.of\ sample \times final\ volume \times dilution\ factor \times con.of\ std.\ (mg/ml)}{O.D.of\ standard}$$

RESULTS:

Percentage of yield

$$\text{Percentage of yield} = \frac{\text{Weight of crude extract}}{\text{Weight of dried material}} \times 100$$

$$\text{Percentage of yield} = \frac{18g}{50g} \times 100 = 36\ \%$$

Table 1: Preliminary Phytochemical test results

Phytochemical Constituents	Result
Alkaloids	+
Flavonoids	+
Phenolic compounds	+
Tannins	+++
Saponins	+

Table 2: Effect of Terminalia chebula Extract on Gastric Parameters

Groups	Gastric Juice Volume (mL/100 g)	Gastric pH	Free Acidity (mEq/L)	Total Acidity (mEq/L)
Normal Control	1.85 ± 0.12	3.92 ± 0.15	38.45 ± 2.10	62.30 ± 3.25
Ulcer Control (Ethanol)	3.95 ± 0.18	2.10 ± 0.12	78.65 ± 3.45	118.40 ± 4.20
Omeprazole (20 mg/kg)	2.05 ± 0.14	3.75 ± 0.16	42.30 ± 2.35	68.50 ± 3.10
T. chebula Extract (200 mg/kg)	3.10 ± 0.16	2.85 ± 0.14	61.20 ± 2.85	92.40 ± 3.60
T. chebula Extract (400 mg/kg)	2.45 ± 0.13	3.35 ± 0.18	50.25 ± 2.50	76.80 ± 3.35

Table 3: Ulcer Scoring Results of Terminalia chebula Retz. Extract in Ethanol-Induced Gastric Ulcer Model

Groups	Treatment	Ulcer Score	Ulcer Index	Ulcer Protection (%)
Group I	Normal Control	0.45 ± 0.10	0.45 ± 0.08	—
Group II	Ethanol-induced Ulcer Control	12.80 ± 0.55	8.65 ± 0.35	—
Group III	Omeprazole (20 mg/kg) + Ethanol	2.15 ± 0.20	1.75 ± 0.15	79.76%
Group IV	Terminalia chebula Extract (200 mg/kg) + Ethanol	7.25 ± 0.40	5.20 ± 0.25	39.88%
Group V	Terminalia chebula Extract (400 mg/kg) + Ethanol	4.10 ± 0.30	3.15 ± 0.20	63.58%

The ulcer control group showed a significant increase in ulcer score and ulcer index due to ethanol-induced gastric mucosal injury. Treatment with Terminalia chebula Retz. extract significantly decreased ulcer severity compared with the ulcer control group. The 400 mg/kg dose exhibited greater ulcer protection than the 200 mg/kg dose, suggesting a dose-dependent gastroprotective effect. The reduction in ulcer formation may be attributed to the presence of tannins, flavonoids, and phenolic compounds in Terminalia chebula, which enhance mucosal defense, reduce oxidative damage, and promote gastric tissue repair. The protective effect was comparable to the standard antiulcer drug omeprazole, confirming the gastroprotective potential of the extract.

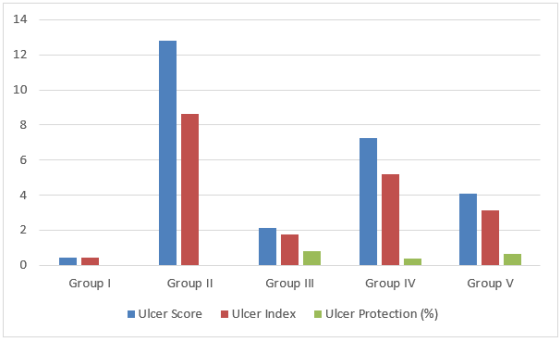

Table 4: Effect on Oxidative Stress Parameters

Groups	MDA (nmol/mg protein)	SOD (U/mg protein)	CAT (µmol/min/mg protein)	GSH (µg/mg protein)
Normal Control	1.85 ± 0.10	8.75 ± 0.35	62.40 ± 2.80	7.65 ± 0.30
Ulcer Control (Ethanol)	5.90 ± 0.25	3.85 ± 0.20	28.50 ± 1.60	3.25 ± 0.18
Omeprazole (20 mg/kg)	2.10 ± 0.12	8.15 ± 0.32	59.80 ± 2.60	7.20 ± 0.28
T. chebula Extract (200 mg/kg)	4.05 ± 0.20	5.90 ± 0.28	42.60 ± 2.10	5.25 ± 0.22
T. chebula Extract (400 mg/kg)	2.75 ± 0.15	7.35 ± 0.30	54.80 ± 2.40	6.65 ± 0.25

The effect of Terminalia chebula Retz. extract on oxidative stress parameters was evaluated by estimating malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH) levels in gastric tissue homogenates. Ethanol administration significantly increased oxidative stress in the ulcer control group, as evidenced by a marked elevation in MDA levels (5.90 ± 0.25 nmol/mg protein) compared with the normal control group (1.85 ± 0.10 nmol/mg protein). The increased MDA level indicates enhanced lipid peroxidation and gastric mucosal damage caused by ethanol-induced free radical generation. Treatment with Terminalia chebula extract significantly reduced MDA levels in a dose-dependent manner, with the 400 mg/kg dose showing greater reduction (2.75 ± 0.15 nmol/mg protein) compared with the 200 mg/kg dose (4.05 ± 0.20 nmol/mg protein), indicating protection against oxidative injury.

DISCUSSION

The present study was undertaken to evaluate the gastroprotective activity of Terminalia chebula Retz. extract against ethanol-induced gastric ulcer in rats. Gastric ulcer is a multifactorial gastrointestinal disorder caused by an imbalance between aggressive factors such as gastric acid, pepsin, alcohol, oxidative stress, and inflammatory mediators, and protective factors including mucus secretion, bicarbonate production, prostaglandins, and antioxidant defense mechanisms. Ethanol-induced gastric ulcer is a commonly used experimental model because it rapidly produces gastric mucosal injury through direct cytotoxic effects, disruption of the gastric mucus layer, increased vascular permeability, inflammation, and excessive generation of reactive oxygen species (ROS). In the present study, administration of ethanol produced significant gastric mucosal injury, as evidenced by an increase in ulcer index and ulcer score compared with the normal control group. Ethanol penetrates the gastric mucosa and damages epithelial cells by solubilizing membrane lipids, causing mucosal erosion, hemorrhage, and loss of gastric barrier function. The increased ulcer formation in the ethanol-treated group confirms the successful induction of gastric ulcer. Pretreatment with Terminalia chebula extract significantly reduced ulcer severity and provided protection against ethanol-induced gastric damage. The higher dose of the extract exhibited greater ulcer protection compared with the lower dose, indicating a dose-dependent gastroprotective effect.

CONCLUSION:

The present study concludes that Terminalia chebula Retz. extract exhibits significant gastroprotective activity against ethanol-induced gastric ulcer in rats. Ethanol administration produced marked gastric mucosal damage, which was evidenced by increased ulcer index, gastric juice volume, free acidity, and total acidity, along with decreased gastric pH and impaired antioxidant defense mechanisms. Treatment with Terminalia chebula extract significantly reduced gastric lesions and improved gastric parameters in a dose-dependent manner. The extract effectively reduced oxidative stress by decreasing malondialdehyde (MDA) levels and restoring the activities of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH). The gastroprotective effect of Terminalia chebula may be attributed to its rich phytochemical constituents, particularly tannins, flavonoids, and phenolic compounds, which possess antioxidant, anti-inflammatory, and mucosal protective properties. The findings indicate that Terminalia chebula Retz. protects gastric mucosa by reducing gastric acid secretion, enhancing mucosal defense, inhibiting lipid peroxidation, and improving endogenous antioxidant status. The higher dose of the extract showed better protective activity, suggesting a dose-dependent response. Therefore, Terminalia chebula Retz. can be considered a promising herbal therapeutic agent for the prevention and management of gastric ulcer disorders, although further studies are required to explore its molecular mechanisms and clinical applications.

REFERENCES:

[1]. Malfertheiner P, Megraud F, Rokkas T, Gisbert JP, Liou JM, Schulz C, et al. Management of Helicobacter pylori infection: the Maastricht VI/Florence consensus report. Gut. 2022;71(9):1724-1762.

[2]. Laine L, Takeuchi K, Tarnawski A. Gastric mucosal defense and cytoprotection: bench to bedside. Gastroenterology. 2008;135(1):41-60.

[3]. Hoogerwerf WA, Pasricha PJ. Agents used for control of gastric acidity and treatment of peptic ulcers and gastroesophageal reflux disease. In: Brunton LL, Hilal-

Dandan R, Knollmann BC, editors. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 13th ed. New York: McGraw-Hill; 2018.

[4]. Wolfe MM, Soll AH. The physiology of gastric acid secretion. N Engl J Med. 1988;319(26):1707-1715.

[5]. Wallace JL. Prostaglandins, NSAIDs, and gastric mucosal protection: why doesn't the stomach digest itself? Physiol Rev. 2008;88(4):1547-1565.

[6]. Sostres C, Gargallo CJ, Lanas A. Nonsteroidal anti-inflammatory drugs and upper and lower gastrointestinal mucosal damage. Arthritis Res Ther. 2013;15(Suppl 3): S3.

[7]. Bjarnason I, Scarpignato C, Holmgren E, Olszewski M, Rainsford KD, Lanas A. Mechanisms of damage to the gastrointestinal tract from nonsteroidal anti-inflammatory drugs. Gastroenterology. 2018;154(3):500-514.

[8]. Hunt RH, Camilleri M, Crowe SE, El-Omar EM, Fox JG, Kuipers EJ, et al. The stomach in health and disease. Gut. 2015;64(10):1650-1668.

[9]. Kusters JG, van Vliet AHM, Kuipers EJ. Pathogenesis of Helicobacter pylori infection. Clin Microbiol Rev. 2006;19(3):449-490.

[10]. Peek RM Jr, Blaser MJ. Helicobacter pylori and gastrointestinal tract malignancies. Nat Rev Cancer. 2002;2(1):28-37.

[11]. Konturek SJ, Konturek PC, Brzozowski T. Gastric and duodenal ulcers: mechanisms of development and healing. J Physiol Pharmacol. 2005;56(Suppl 5):5-31.

[12]. Tarnawski AS. Cellular and molecular mechanisms of gastrointestinal ulcer healing. Dig Dis Sci. 2005;50(Suppl 1): S24-S33.

[13]. Takeuchi K. Pathogenesis of NSAID-induced gastric damage: importance of cyclooxygenase inhibition and beyond. Curr Med Chem. 2012;19(1):1-13.

[14]. Suzuki T, Tsutsumi S, Fujita K, et al. Role of oxidative stress in gastric mucosal injury induced by ethanol and NSAIDs. World J Gastroenterol. 2012;18(33):4543-4551.

[15]. Repetto MG, Llesuy SF. Antioxidant properties of natural compounds used in gastric ulcer therapy. Life Sci. 2002;71(9):1023-1033.

[16]. Borrelli F, Izzo AA. The plant kingdom as a source of anti-ulcer remedies. Phytother Res. 2000;14(8):581-591.

[17]. Bigoniya P, Singh K. Ulcer protective potential of standardized hydroalcoholic extract of Bauhinia purpurea. J Ethnopharmacol. 2010;128(3):603-608.

[18]. Al Rashdi KS, Salama SM, Alkiyumi SS, et al. Mechanisms of gastroprotective effects of natural products. Evid Based Complement Alternat Med. 2012; 2012:1-15.

[19]. Sumbul S, Ahmad MA, Mohd A, Aftab S. Role of phenolic compounds in the prevention of gastric ulcer. J Ethnopharmacol. 2011;134(2):351-356.

[20]. Khazaei M, Salehi H. Protective effect of Ficus carica extract on ethanol-induced gastric ulcer in rats. Iran J Pharm Res. 2006;5(1):43-48.