To determine the antiulcer properties of Polygonum bistorta hydroethanolic extract in rats with gastric ulcers caused by pylorus ligation and indomethacin.

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Abstract

The objective of this study was to determine the protective effect of a hydroethanolic extract of Polygonum bistorta (PBE) against gastric ulcers caused by indomethacin and indomethacin combined with ligation of the pylorus in rats. Materials and Methods: Thirty-six rats were used in the investigation; they were given free water prior to the experiment but were starved for the entire night. There were six groups of animals. As a control, Group I was given regular saline. In order to cause ulcers, Group II received indomethacin (20 mg/kg, orally) for five days. Group III was treated with indomethacin and pylorus ligation. PBE was given to groups IV and V at doses of 300 and 600 mg/kg, respectively. The typical antiulcer medication (such as omeprazole, 10 mg/kg) was administered to Group VI. Every therapy was given orally. Histopathological analyses, antioxidant enzyme levels, gastric juice parameters, and ulcer index were conducted. **Results:** Treatment with PBE showed a significant, dose-dependent decrrese in ulcer index, gastric acidity, and pepsin levels, while enhancing gastric mucus production. Antioxidant analysis revealed a marked increase in SOD, CAT, and GSH levels compared to the ulcer control groups. Histopathological findings supported the biochemical results, demonstrating restoration of gastric mucosa integrity. The gastroprotective effects of **PBE** at 600 mg/kg were comparable to the standard antiulcer drug.

Conclusion: The hydroethanolic extract of Polygonum bistorta exhibits potent antiulcerogenic and antioxidant activities, suggesting its potential use in the management of gastric ulcers and related gastrointestinal disorders.

Keywords: Polygonum bistorta; Indomethacin; Pylorus ligation; Ulcer index; Gastric output.

Introduction:

Gastric ulcer remains a significant global health issue, affecting nearly 4–10% of the population, with a high prevalence in India. Although the precise cause is often uncertain, several factors such as stress, smoking, nutritional imbalances, long-term use of NSAIDs, genetic predisposition, and Helicobacter pylori infection contribute to its onset. (1) Reports also suggest that duodenal ulcer incidence is comparatively higher in Southern India. (2) The pathophysiology involves an imbalance between offensive factors (acid, pepsin, free radicals) and protective mechanisms (mucus secretion, bicarbonate, prostaglandins, blood flow). Conventional therapies include proton pump inhibitors, antacids, antagonist of H_2-receptor and anticholinergics. However, their limitations—such as adverse effects and recurrence—necessitate safer alternatives (3-5). Medicinal plants have emerged as promising candidates in this direction. Polygonum bistorta is widely distributed across Europe, Central Asia, and the Indian subcontinent, including Himalayan regions such as Ladakh and Gilgit. (6-7) Traditionally, the roots of this plant have been employed in managing various ailments such as carbuncles, dysentery, piles, acute gastroenteritis, snake envenomation, chronic respiratory disorders associated with scrofula, persistent cough, mouth ulcers, rectal bleeding, skin infections, and nasal bleeding. (8) The astringent nature of the rootstock is mainly attributed to its tannin content, which ranges between 15% and 22% and may reach up to 36%. These tannins are of mixed type, comprising catechol, phloroglucinol, gallic acid, and phlobaphene.

In addition, the rootstock has been reported to contain methyl anthraquinone, calcium oxalate (approximately 1.1%), starch (about 30%), and albumin (around 1.9%), along with small amounts of emodin. (9) "The rhizomes exhibit a range of pharmacological properties, including protection of the nervous system, liver support, stimulation of bile production, fungal inhibition, fever reduction, antioxidant effects, muscle relaxation, and diarrhoea treatment (10-12). Polygonum bistorta (P. bistorta) seems to be a plant used in traditional Chinese medicine and the Unani system of medicine. It's used for treating various conditions like venomous snake bites, bleeding issues (epistaxis, haematemesis, bleeding from haemorrhoidal), diarrhea with bloody in the stools, acute gastroenteritis, and aphthous ulcers. In Unani medicine, it's a haemostatic drug to control bleeding from different body parts. Sharbat-e-Anjbar (of P. bistorta) is used for abrasion of the intestinal tract. (13) Research The current investigation was conducted to ascertain the antiulcer properties of the P. bistorta hydroethanolic extract in light of the aforementioned. Examining the plant's in vivo antioxidant activities further supported its effects; glutathione, malondialdehyde, and other antioxidants appear to have protective functions against stomach ulcers.

MATERIALS AND METHODS

Medicines and Substances:

For the study's evaluation, conventional medicines like Omeprazole obtained from SD Fine-Chem Limited , acetic acid (Rankem Ltd), ethanol (Fisher Scientific), indomethacin (Jagsonpal), 5,5-dithiobis-2-nitrobenzoic acid (Sigma-Aldrich), Alcian Blue, and albumin were sourced from SD Fine-Chem Limited. All the buffers and chemicals used were of AR grade, and buffer solutions were freshly prepared before use.

Plant Extract Preparation:

The plants used in this study were purchased from the neighborhood market, Hamdard Dawakhana, which is situated in AminaBaad Lucknow and was verified by the herbalist and the Faculty of Pharmacy's authentication office.Polygonum bistorta Linn root, Integral University Lucknow (voucher number: IU/PHAR/HRB/25/05). First, petroleum ether (60–80°C) was used to defatten the powdered root sections of P. bistorta. After drying in the shade to obtain a dry mass, the defatted marc was extracted using Soxhlet extraction with 70% hydroethanolic ethanol and water. This process was carried out for two days at room temperature with sporadic shaking. After filtering, the solvent was concentrated on a rotavapor (Buchi, USA). After being weighed and its yield percentage (21.95% w/w) determined, the finished extract was kept in a cold location. [11] Diterpene dimers, including those found in animals: We purchased Wister rats weighing between 200 and 250 grammes from the Animal House Facility at Acharya Narendra Dev College of Pharmacy in Babhnan, GondaUnder typical laboratory circumstances, each of the six animals was kept in a polypropylene cage with a 12-hour light/dark cycle, a temperature and relative humidity of 22 ± 2°C and 50 ± 15%, respectively, and unrestricted access to a standard pellet meal.(kapila pashu ahar Gorakhpur Industries, India) and unlimited drinking water. The animals were divided into experimental and control groups at random. The Institutional Animal Ethical Committee (IAEC), Regd., granted ethical approval. No. 1585/Po/Re/S/11/CPCSEA.

Antiulcer activity study: Six groups were used to examine Polygonum bistorta's antiulcer activity**.** 1% CMC (1 milliliter/kg, p.o.) was administered for five days to the first group, which was the negative control; 1% CMC (1 milliliter/kg, p.o.) was administered to the second, positive control group for five days, along with pylorus ligation [14] on the sixth day under anaesthesia; and indomethacin (20 mg/kg) was administered for five days along with pylorus ligation on the sixth day under anaesthesia. The 70% hydroethanolic extract of P. bistorta was given to the fourth and fifth groups at doses of 300 and 600 mg/kg/day, respectively. The sixth group received 10 mg/kg/day of omeprazole. The animals were all denied food (but not water) for a full day before they were put through ulcerogenic compounds.

Ulcer Index: The score system of [14] was used to determine the Ulcer Index. [(UI control−UI treated)/UI control] × 100 was the formula used to determine the protection percentage, and the ulcer index (UI) was determined using the lesions of each stomach.

Calculate the amount of gastric mucus: The stomach tissues were promptly submerged in 10 millilitres of a 0.1% w/v alcian blue solution. The mucus was washed twice at 15 and 45 minutes using a 250 mM sucrose solution. Using 10 millilitres of a 500 mM magnesium chloride solution, mucus and dye complexes were extracted. The mixture was shaken once every 30 minutes for two hours. The resultant solution was centrifuged for 10 minutes at 3000 r.p.m. after being combined with diethyl ether in an equal volume. 580 nm was used to measure absorbance. The amount of mucus was measured using conventional alcian blue curves, which ranged from 20 µg/10 ml. The data were expressed in µg of alcian blue/g tissue [15].

Calculating Reactive Substances of Thiobarbituric Acid (TBARS): Washing, scraping, weighing, and homogenising the stomach tissue in a 0.15 M KCl solution (1:10, w/v) were all done. Add 0.5 ml of 30% TCA and 0.5 ml of 0.8% TBA reagent to 1 ml of solution. The aforementioned solution was put into a test tube, wrapped in aluminium foil, and placed in a water bath at 80°C for 30 minutes. It was then chilled in ice-cold water for 30 minutes, then it was centrifuged for 15 minutes at 3000 rpm. At 540 nanometres, the organic layer's absorbance was measured [16].

Estimate of Tissue Glutathione: 10 millilitres of 200 mM potassium phosphate buffer (pH 6.5) were used to homogenise 500 mg of tissue. After vortexing the aliquot homogenate for 10 minutes and adding 50% trichloroacetic acid, it is centrifuged at 6000 rpm. 0.4 M Tris buffer and 0.01 M DTNB were added to the supernatant after it had been removed. A measurement of the supernatant's absorbance was made at 415 nm [17].

Free acidity and total acidity measurement:

Ten millilitres of distilled water are used to dilute one millilitre of gastric juice. Two drops of Topfer's reagent are then added, and 0.01 N sodium hydroxide is titrated until the end point is reached. The amount of NaOH used is equivalent to the amount of free acidity. Then, the

titration was carried on until the colour turned red once more when two to three drops of phenolphthalein reagent were added [18].
Total acidity is equal to the total amount of sodium hydroxide. The following formula was used to determine acidity:NaOH Volume * NaOH Normality * 100/0.1 mEq/L/100 grammes = Acidity. Estimation of Gastric pH: A digital pH meter was used to determine the pH based on the previously collected gastric content [19].

Stomach Pepsin Activity Estimation: Based on this, each rat test and blank received 0.2 ml of centrifuged stomach juice with 3 ml of 3% albumin. To halt enzyme activity, 10 millilitres of 6% trichloroacetic acid were then added to the blank. The test and blank tubes were incubated for 30 minutes at 37°C in a water bath. After that, test tubes were filled with 10 millilitres of trichloroacetic acid, well shaken, and filtered. Optical density at 280 wavelengths was used to spectrometrically measure proteolytic activity. Standard curve extrapolation was used to determine the pepsin content [20].

The stomach tissue was sliced and rinsed with cold saline at the conclusion of the trial. Buffering formalin solution (10%) was used to repair the tissue. Figure 2 displays the slides after they were examined under a light microscope and photographed. The results of the statistical study were presented as mean ± SEM. Using multiple comparisons between the groups, the student t-test was used to examine the data. The statistical significance threshold was set at a P value of 0.05.

RESULTS

Extractive value Phytochemical test:

Soxhlet extraction was used to create the hydroethanolic extract. In the identical case, the yield was 21.95% w/w. An ulcer index An indicator of gastric mucosal lesions, the ulcer index, can be used to assess the anti-ulcer capability of the new medications. Drug- or ulcerate-induced stomach injury was identified by varying-sized mucosal lesions and spots. Comparing group II rats with pylorus ligation to group I rats, the ulcer index increased significantly ($P < 0.001$). When IND+PL group III rats were given 300 and 600 mg/kg PBE extract, their ulcer index significantly increased ($P < 0.001$ & $P < 0.05$ and $P < 0.001$) in comparison to group II rats. The ulcer index was considerably lower in PBE-treated groups IV, V, and VI ($P<0.01$) than in groups II and III animals, respectively. In contrast, PBE-treated groups at a dose of 600 mg/kg had significantly higher levels of stomach mucus ($P<0.001$) than group II animals. PBE treatment at 600 mg/kg resulted in a substantial decrease in GSH levels ($P<0.001$) and an increase in gastric mucus ($P<0.001$) in groups V and VI compared to control group I. Rats in group III exhibited a small drop in GSH levels and a large increase in TBARS levels in comparison to group II. When compared to group II at the 300 and 600 mg/kg doses, respectively, the TBARS levels in groups IV and V were significantly lower ($P < 0.05$). When compared to group III animals, the TBARS levels in group IV and V animals treated with doses of 300 and 600 mg/kg are significantly lower ($P < 0.05$, $P < 0.01$). The TBARS level was much lower ($P < 0.001$) in the standard-treated group VI than in the animals in groups II and III. In comparison to group II, the rats in groups IV

and V showed a substantial increase in GSH ($P < 0.05$ and $P < 0.01$) after receiving doses of 300 and 600 mg/kg of PBE. When animals were dosed with 300 and 600 mg/kg of PBE, their GSH levels were found to be significantly higher ($P < 0.01$) than those of group III animals. The GSH levels of the animals in group VI, who received the conventional medication, were significantly higher than those in groups T-II and III ($P < 0.01$).

Titrable acidity and pH determination:

The marked rise in pH and fall in acidity seen in ulcer-induced animals that had received PBE prior to treatment. Rats treated in groups II and III had lower pH values ($P < 0.001$) than control group I rats; however, group IV showed a substantial increase in pH ($P < 0.01$) at the dose of 300 mg/kg compared to groups II and III rats, respectively. The pH is substantially higher in group V ($P < 0.001$) than in animals in groups II and III, respectively. When compared to animals in groups II and III, the pH of the standard-treated group VI is significantly higher ($P < 0.001$). Rats treated with IND+PL and in group II had higher levels of free acidity ($P < 0.01$, $P < 0.001$) than rats in control group I. When treated with PBE group IV animals, group II did not exhibit a discernible increase in acidity in comparison to groups III and IV. When compared to group III rats, the PBE-treated group IV rats at 300 mg/kg showed a substantial decrease in free acidity ($P < 0.05$). In contrast, group V's free acidity was considerably lower ($P < 0.01$) after receiving 600 mg/kg of PBE than group II and group III animals. Comparing group VI to group II and group III animals, respectively, reveals a significant decrease in free acidity ($P < 0.01$ and $P < 0.001$). In comparison to the control group of rats, the rats in groups II and III had higher levels of total acidity ($P < 0.01$). Rats in PBE treatment group V (600 mg/kg) had lower total acidity ($P < 0.05$) than rats in control group II. Comparing group IV and V animals to group III, the PBE treatment at 300 and 600 mg/kg resulted in a substantial decrease in total acidity ($P < 0.05$ and $P < 0.01$). Comparing the standard-treated group VI to the animals in groups II and III, however, reveals a significant decrease in total acidity ($P < 0.01$).

The activity of gastric pepsin:

In comparison to the control group of rats, the rats in groups II and III exhibited a notable rise in pepsin activity ($P < 0.001$) (fig. 4). When compared to control group III rats, pylorus ligation group II rats exhibited a significant increase in pepsin activity ($P < 0.01$). Pepsin activity, on the other hand, was considerably lower in the PBE-treated groups IV and V rats at 200 and 400 mg/kg and in the standard-treated group VI than in the groups II and III, respectively ($P < 0.001$). The drug was found to lower pepsin concentrations to almost normal levels when taken prior to therapy; the effect was similar to that of omeprazole, a common medication.

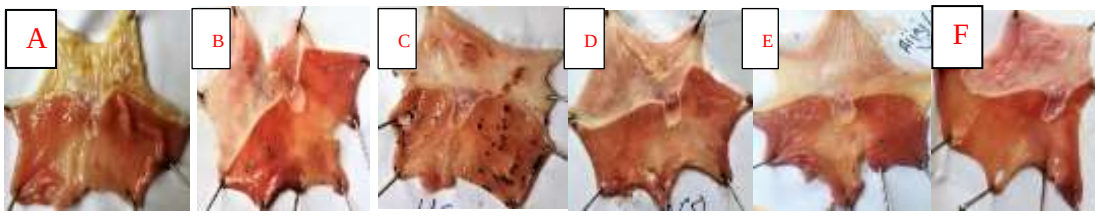
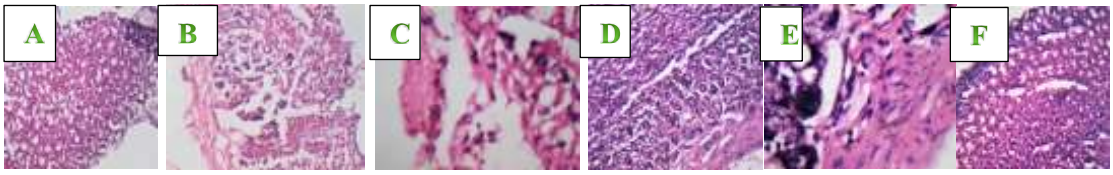


Fig1;(A) A normal group displaying its typical look. (B) First control group: ulcer caused by pylorus ligation. (C) Second control group: pylorus ligation + stomach ulcer brought on by indomethacin. (D) Pylorus ligation plus PBE 300 mg/kg is used as a pretreatment for stomach ulcers caused by indomethacin. (E) Gastric ulcers caused by indomethacin and pylorus ligation: PBE 600 mg/kg was administered beforehand. (F) Pylorus ligation plus gastric ulcer caused by indomethacin: pre-treated with omeprazole (10 smg/kg).



Fig;2 Histopathological structure of stomach (A) The mucosal lining of the flattened epithelial cells is intact in the slice of normal group I. Compactly packed mucosal glands are made up of cells with vesicular nuclei, nucleoli, and copious amounts of eosinophilic cytoplasm. (B and C In groups II and III, the pylorus ligation-induced ulcer and the indomethacin plus pylorus ligation-induced gastric ulcer exhibit lining epithelium denudation, inflammatory cell infiltration with pigment-laden macrophages, intracellular and interstitial cell oedema, and degenerative changes in sglandular epithelial cells. (D) Group IV's intact mucosal lining of flattened epithelial cells is demonstrated after pretreatment with PBE 300 mg/kg. Thin fibroconnective tissue strands divide glands. The basement membrane is sturdy and undamaged. There are sporadic blood vessels and few bundles of fibrous tissue. You can see mucosal glands. densely packed cells with vesicular nuclei, nucleoli, and copious amounts of eosinophilic cytoplasm. (E) Group V, which was pre-treated with PBE 600 mg/kg, exhibits gland separation caused by thin fibro connective tissue strands. intact epithelial cell mucosal lining that has been flattened. The basement's membrane is sturdy and thick. There are sporadic blood arteries and a few bundles of fibrous tissue. Compactly arranged mucosal glands are made up of cells with vesicular nuclei and nucleoli. (F) Group VI pre-treated with omeprazole 20 mg/kg exhibits inflammatory cell infiltration, pigment-laden macrophages, degenerative cell alterations, and denudation of lining epithelium sites of haemorrhage. Cell degeneration and intracellular and interstitial cell oedema in glandular epithelial cells.

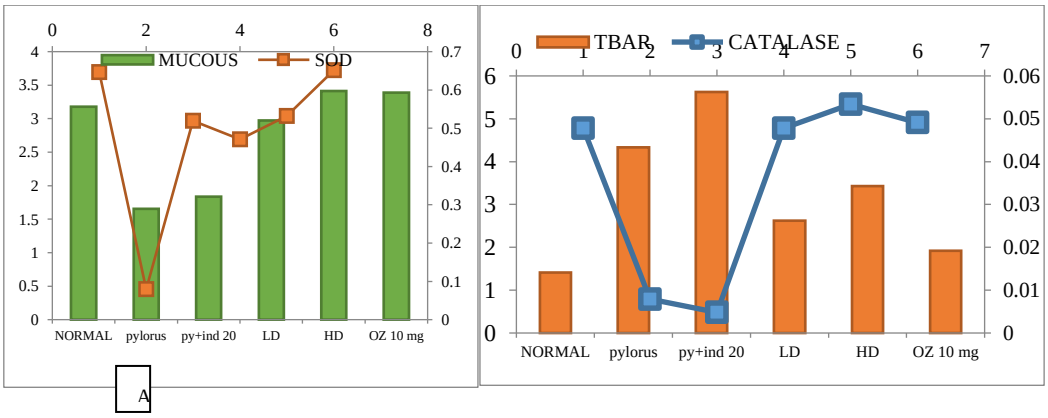


Figure 3: A.TBARS and Catalase levels in the experimental and control groups are affected by 70% hydroethanolic Polygonum bistorta extract.creatures Indomethacin plus Pylorus Ligation is PL+IND. Values are expressed as the mean ± SEM of six rats per group. P-value: $

Figure B: Effects of 70% hydroethanolic extract of Polygonum bistorta on SOD and mucous barrier in experimental and control groups of animals. Indomethacin plus pylorus ligation is PL+IND. Values are expressed as the mean ± SEM of six rats per group. P-value: $

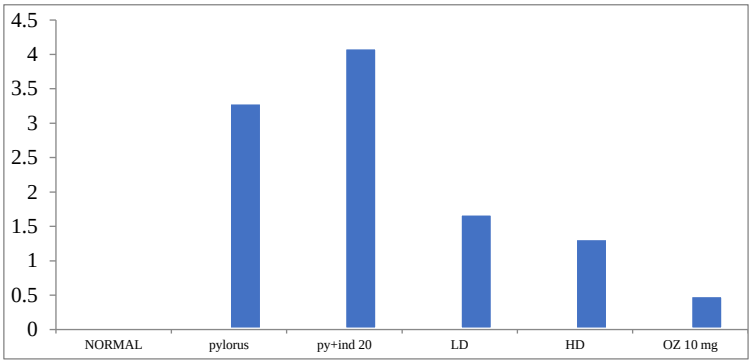


Figure 4: Impact of Polygonum bistorta 70% hydroethanolic extract on ulcer index in experimental and control animal groups. PL+indomethacin plus pylorus ligation is IND. Mean ± SEM of six rats in each group is used to express values. P value: $

DISCUSSION:

The present peptic ulcer treatment is costly, which restricts its use, and it also has adverse consequences. Therefore, finding a more affordable, nontoxic, and effective antiulcer medication is a difficult undertaking. An excellent source of novel medications is medicinal plants. The community uses Polygonum bistorta, a medicinal plant, extensively to treat stomach issues. Their effectiveness as a treatment for stomach issues is also supported by literature reviews. Thus, this study's primary goal is to confirm the hydroethanolic extract of Polygonum bistorta antiulcer properties. Prostaglandins, mucosal blood flow, nitric oxide, mucus and HCO_3^- secretion, and the equilibrium between protective factors and HCl pepsin and protective factors are all necessary for the integrity of the gastric mucosa [21]. In order to prevent damage to the epithelium, the primary treatment guidelines focus on producing more protective factors for the stomach mucosa in addition to blocking the secretion of acid [22]. By reducing ulcer formation, the current study demonstrates Polygonum bistorta's preventive impact. Due to the presence of pepsin and acid in the abdomen [14], pylorus ligation starts, which causes the stomach mucosa to autodigest and the gastric mucosal barrier to break down [23]. This work used a well-established indomethacin-induced paradigm from the literature [24]. The repression of NSAID-induced prostaglandin synthesis causes an increase in mucosal lesions. because prostaglandins have a protective impact on the stomach mucosa, stimulate bicarbonate secretion, maintain mucosal blood flow, and promote healing [25]. Therefore, in order to cause severe ulceration in rats, we employed the indomethacin plus pylorus ligation model. The study demonstrates that PBE dramatically reduced the amount of gastric content, pH, and overall acidity in gastric ulcers caused by indomethacin + pylorus ligation. PBE reduces ulcer index and score at doses of 300 and 600 mg/kg. The pre-treated experimental rats exhibit a significant reduction in the severity of gastric mucosal damages ($p < 0.001$) in a gradient fashion as a result of the phenolic compound present in PBE [26-27]. Phenolic chemicals have an anti-inflammatory effect and increase mucus formation because of their antioxidant and free-radical scavenging capabilities [28]. An imbalance between defensive and aggressive elements can result in a stomach lesion and ulcer development.

Mucus on the tissue was thus measured, and the outcome demonstrates that PBE increases mucus production in a dose-dependent way [29-30]. As a result, PBE may help enhance mucosal protection against experimental ulcers and resistance to stomach acid .[31]. Abdominal illness and peptic ulcers are among the inflammatory disorders whose pathophysiology is linked to increased production of reactive oxygen metabolites. The current study's findings demonstrated that PBE-pretreated groups of rats considerably reduced the increase in TBARS levels in rats with indomethacin + pylorus ligation. This may be because the PBE prevents lipid peroxidation during ulcer development. In experimental animals, PBE has been demonstrated to increase antioxidant potential. The anti-lipid peroxidative action seen in this study is attributed to flavonoids, including quercetin, biochanin A, and formononetin, which are abundant in the PBE [32]. Glutathione is a key component of the intracellular defence system against oxidative stress and other harmful stimuli. Oxidative tissue damage of the gastric mucosa is caused by excessive free radical production (radicals of oxygen in the extracellular environment and glutathione exhaustion) facilitated by glutathione peroxidase inhibition [33-34]. In our study, rats pre-treated with a hydro-ethanolic extract of Polygonum bistorta exhibited a significant increase in glutathione levels, while control groups II and III showed significant decreases in glutathione concentrations. This suggests that the extracts prevent the depletion of non-protein Indomethacin and pylorus ligation treatment-induced sulfhydryl groups [35]. The main cause of gastric ulcers in the pylorus is increased gastric hydrochloric acid output, which damages the mucosal barrier and causes the stomach mucosal layer to autodigest. Proton pump inhibitors (PPIs), which work by reducing the activity of the H+ K+ ATPase enzyme, may be part of the recommended treatment for this illness [36]. Analysis of Polygonum bistorta's hydroethanolic extract revealed a notable inhibitory effect on both free and total acidity. [37] supports our findings as well:PBE prevents ulcers by modulating H+/K+ ATPase activity and/or maintaining mucin. Acid and pepsin levels significantly rise in animals with ulcers [38], and indomethacin also raises the secretion of pepsinogen . According to this study, pepsin activity significantly increases following pylorus ligation and indomethacin injection. Compared to omeprazole, pretreatment with PBE results in a decrease in pepsin levels. The reduction in both total and free acidity indicated that the PBE possesses anti-inflammatory qualities. Additionally, by increasing mucus wall thickness and antioxidant activity, the PBE provides cytoprotection. PBE's action on defensive mucosal components may be the primary cause of its stomach prophylactic and therapeutic actions. One of the key elements influencing PBE's activity may be its innate antioxidant capacity.

CONCLUSION:

In rats with or without indomethacin, the current study clearly showed that a 70% hydro-ethanol extract of Polygonum bistorta has significant substantial gastroprotective effect in gastric ulcers caused by pylorus ligation that is dosage dependant by restoring the imbalanced antioxidant activity, strengthening the gastric mucosa, and lowering the acidity of gastric juice and pepsin activity. These results may at least partially support the ethnomedical application of this herb in the treatment of stomach issues. The results of this experimental investigation may result in additional pharmacological action and isolation of ulcer-fighting chemicals.

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