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Gastro-protective potential of *Artemisia parviflora* on aspirin-induced gastric ulcers in albino rabbits

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Abstract

Artemisia parviflora Roxb. (Asteraceae) has medicinal properties. This study evaluates the gastroprotective potential of *A. parviflora* seeds against aspirin-induced ulcers in albino rabbits. Thirty-six rabbits were randomly grouped (n=6) as; 1st was controlled; 2nd received aspirin for 14 d; 3rd received omeprazole + aspirin for 14 d; 4th, 5th, and 6th received *A. parviflora* seed powder 250, 500, and 750 mg/kg, respectively along with aspirin, for 14 d. Total antioxidant capacity (TAC), total oxidant status (TOS), malondialdehyde (MDA), and catalase (CAT) were determined to check the gastric damage. Ulcer score, gastric volume, gastric pH, and total acid output was also measured to determine the gastroprotective potential of *A. parviflora*. *A. parviflora* seed powder exhibit gastroprotective potential by showing a significant reduction in the ulcer score, acid output, and gastric volume while the pH of gastric mucosa increases significantly at the dose of 750 mg/kg when compared to aspirin-treated group. Biochemical analysis showed a significant increase in TAC and CAT activity while it showed a significant decrease in the levels of TOS and MDA which indicate a reduction in gastric damage. *A. parviflora* seed powder proved to be gastroprotective at 250, 500 and 750 mg/kg with the gastric protection of 47.5, 58.1, and 73.5%, respectively. It also has potent antioxidant properties.

Keywords

Antiulcer
gastric pH
gastric volume
ulcer score

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Introduction

Stomach stores food, possesses antibacterial action, and secretes gastric juices (Baumgart & Sandborn, 2007) while gastric ulcer is a rupture in the normal gastric mucosa that extends throughout the muscular mucosa. Gastric ulcer could be divided into two common types according to location, ulcerative colitis (lower) and peptic ulcer (upper). Peptic ulcer develops when aggressive and protective factors are imbalanced. *Helicobacter pylori*, non-steroidal anti-inflammatory drugs (NSAIDs), pepsins, hydrochloric acid (HCl) and bile acid are the aggressive factors (Malairajan et al., 2008). NSAIDs weaken the protective mucous layer of the stomach wall and increase the secretion of HCl (Awaad et al., 2013). Epigastric pain is the predominant symptom of uncomplicated gastric ulcer and the more dyspeptic symptoms such as early satiety, bloating, nausea and fullness. In duodenal ulcer patient, epigastric ache occurs frequently during the night or the state of fasting and is usually relieved by acid-neutralising agents or food intake. Heartburn and erosive esophagitis are also reported in these patients (Gisbert & Pajares, 2003).

The long-term use of NSAIDs (aspirin) mainly inhibits the prostaglandin (PG) and cyclooxygenase (COX) enzyme which damage in gastric mucosa with the production of free radicals (Baigent et al., 2009). The amount of serum lipid peroxidation (LPO) improved during the ulcer formation while catalase (CAT) and superoxide dismutase (SOD) levels decreased. There is an affirmative relationship exists

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between the oxidative stress produced by free radicals, gastric ulcer and gastric carcinoma (Tandon et al., 2004). Most of the existing gastroprotective drugs operate on the offensive aspects neutralizing acid discharge like antacids, H_2 receptor blockers like ranitidine, anticholinergics like pirenzepine and proton pump inhibitors like omeprazole that interfere with acid secretion (Ahuja et al., 2011). Proton pump inhibitors are the main synthetic antiulcer class of drugs that reduce the production of acid. Alternative therapies have been developed for the management of GI ulcers and herbal medicines are a most important source for GI ulcer management.

Artemisia parviflora Roxb. is an aromatic shrub, leaves are sessile, about 40-100 cm in height and found throughout Pakistan at high elevations.Although phytoconstituents of *A. parviflora* have medicinal importance yet its gastroprotective effect has not been studied. *A. parviflora* is commonly used for skin diseases, cuts and wounds which could be due to the different phytochemical constituents of *A.parviflora*. These constituents have an inhibitory effect on carcinogenesis in humans and also shows antioxidant activity (Ahuja et al., 2011). Oils of Artemisia species are extensively utilized for a variety of medicinal uses such as antibacterial, fungicidal, antiviral, nematicidal and antimalarial. In present study antiulcer effect of *A. parviflora* was evaluated against aspirin-induced ulcers in albino rabbits.

Materials and Methods

Experimental animals: Thirty-six (36) male adult albino rabbits weighing 1.63±0.25 kg were chosen for this study and six groups (n=6) were made who were housed at 22±2ºC, 65-70% humidity and 12 h light/dark cycles before and during the experiment. Animals were supplied *ad libitum* feed and water. Further, ethical committee of institute affirmed all procedures embraced approved in the current study.

Plant material: *A. parviflora* seeds were purchased from the herbal dealers of Faisalabad, Pakistan. A voucher specimen of *A. parviflora* seeds have been deposited in the Herbarium maintained by Department of Botany, University of Agriculture, Pakistan. The plant material was powdered with the help of a special electrical grinder. This process was done with the precaution that the temperature did not rise up to 40ºC. This powder was passed through a sieve and stored in a container for further experimental use.

Treatment protocols: All the rabbits were grouped as; group 1 served as untreated control and received normal diet throughout the experiment, group 2 received aspirin (Disprin®; *Reckitt Benckiser* (*Pakistan) Ltd.* Karachi, 150 mg/kg orally for 14 d (Herbert et al., 2011). Group 3 received omeprazole (Omega®; Ferozsons Laboratories Ltd. Karachi, 20 mg/kg) + aspirin (150 mg/kg) for 14 d (Maity et al., 2003). Groups 4, 5, and 6 received *A. parviflora* seed powder 250, 500, and 750 mg/kg, respectively along with aspirin 150 mg/kg for 14 d. Five ml distilled water was used to dilute the *A. parviflora* seeds powder before administration to the rabbits.

Surgical procedures: On the 14th day of experiment, animals were slaughtered and their stomach was dissected out and transferred into small tubes while stomach contents were collected into another small tube for biochemical parameters. The supernatant was separated by centrifugation at 3000 rpm for 5 min and its volume was expressed as ml/100 g body weight.

Blood sampling: Blood samples were collected at 14th day of experimental treatments while the serum was separated by centrifugation at 4000 rpm for 5 min and stored at -4ºC for the estimation of various antioxidant parameters.

Acid output: Titration method with 0.05N NaOH was used for the calculation of acid output from the supernatant fluid. Acidity was expressed as molEq/l/100 g of body weight (Maity et al., 2003).

$$\text{Acidity} = \frac{\text{the volume of NaOH} \times \text{normality}}{0.1} \times 100$$

Ulcer index: The gastric damage was determined by counting number of ulcers and its severity with the following scores: 0.0=Normal coloration, 0.5=Red coloration, 1.0=Spot ulcer, 1.5=Hemorrhagic stress, 2.0=Deep ulcers, 3.0=Perforation. Ulcer index (UI) was calculated using the formula (Vogel, 2002).

$$\text{UI} = \frac{\text{US} + \text{UN} + \text{UP}}{10}$$

Where, US=mean severity of ulcer score; UN=average number of ulcers per animal; UP=percentage of animals with ulcer incidence.

Curative ratio: The curative ratio from the UI was calculated for the treated groups by using the following equation.

$$\text{Percentage (\%)} = \frac{[\text{CUI-TUI}]}{\text{CUI}} \times 100$$

Where, CUI=ulcer index of control groups; TUI=ulcer index of treated groups.

Biochemical examination: The total antioxidant capacity (TAC) and total oxidant status (TOS) in serum was measured using methods developed by Erel (2004); (2005) with a spectrophotometer. Malondialdehyde (MDA) was determined according to the method developed by Ohkawa et al. (1979). Enzymatic activity of enzyme catalase (CAT) was measured by the method of Góth (1991).

Statistical analysis: Statistical analysis was performed by one-way analysis of variance (ANOVA) at 95% confidence interval (Steel & Torrie, 1960).

Results

The seeds powder of *A. parviflora* was given orally once daily for 14 days at a dose rate of 250-750 mg/kg showed dose-dependent protective effect against gastric ulcer induced by aspirin. The highest concentration (750 mg/kg) of *A. parviflora* significantly protected the animal and healed ulcer after 14 days of treatment.

Mean ulcer score of group 2 was 2.35 that increased significantly (p<0.05) after administration of aspirin, while it significantly decreased for group 3 as 0.67 which was treated with omeprazole + aspirin and also it was decreased for group 6 which was treated with the highest dose of test plant, having value of mean ulcer score 0.54.

Ulcer index also showed the similar patterns of results as that of ulcer score. After fourteen days of the treatment ulcer index for groups 1, 2, 3, 4, 5, and 6 was 0.00, 13.9, 3.25, 7.29, 5.82, and 3.67, respectively. Group 3 (Omeprazole + aspirin) and highest plant dose in group 6 showed the significant (p<0.05) reduction in ulcer index. The percent curative ratio of *A. parviflora* seed powder at 250, 500, and 750 mg/kg was 47.5, 58.1, and 73.5%, respectively as shown in Table 1.

Total acid output (molEq/l/100 g body weight) of rabbits in after 14 days are shown in Table 2. The mean values for acid output showed that the aspirin increased the acidity in group 2 having mean value 39.7 molEq/l/100 g as compared to the group 1 which has mean value for acidity 26.5 molEq/l/100 g, while the groups treated with *A. parviflora* seed powder showed significant results at dose 500 and 750 mg/kg as 31.7 and 29.4 molEq/l/100 g, respectively. It was also observed that pH was decreased markedly in aspirin (group 2) treated rabbits compared to group 1, from 2.05 to 0.87. Omeprazole (group 3) enhanced pH (4.47) of gastric mucosa. It was observed that aspirin administration influence mean gastric volume (35.1) while administration of omeprazole and *A. parviflora* (750 mg/kg) significantly decreased mean gastric volume 24.9 and 25.6, respectively presented in table 2.

Table 1: Mean values of ulcer score, ulcer index and curative ratio after 14 days of oral treatment with drugs and *A. parviflora* seed powder in rabbits.

Group	Dose	Ulcer score	Ulcer index	Curative ratio %
1	Routine feed	0.08±0.08^{c}	0.00	
2	150 mg/kg	2.35±0.35^{a}	13.9	
3	20 mg/kg	0.67±0.24^{c}	3.25	76.6
4	250 mg/kg	1.78±0.20^{ab}	7.29	47.5
5	500 mg/kg	1.07±0.30^{bc}	5.82	58.1
6	750 mg/kg	0.54±0.24^{c}	3.67	73.5

Similar letters on means (n = 6) in a column are statistically non-significant (p≥0.05), 1 = control, 2 = Asprin, 3 = Omeprazole + Asprin, 4 = Asprin + 250 mg/kg *A. parviflora* seed powder, 5 = Asprin + 500 mg/kg *A. parviflora* seed powder, 6 = Asprin + 750 mg/kg *A. parviflora* seed powder.

Results of the study showed that mean values of TAC for the group 1 was 3.06 mmol/l. TAC decreased (0.93 mmol/l) with ulcer (group 2) production in the stomach by the use of aspirin while it significantly (p<0.05) increases up to normal values for groups 3 and 6 as 2.98 and 2.78 mmol/l respectively and presented in table 3.

The mean values of TOS of group 1 were 3.69 µmol/l. TOS increased (7.03 µmol/l) with ulcer production in the stomach by the use of aspirin while it significantly (p<0.05) decreases up to normal values for groups 3 and 6 as 3.65 and 3.63 µmol/l respectively when compared with aspirin-treated group presented in table 3.

Results of the current study also demonstrated that the mean values of MDA activity were increased (from 3.34 to 7.97 nmol/l) when aspirin was used alone for the production of an ulcer in the stomach. The mean values decrease significantly (p<0.05) for groups 3, 4, 5, and 6 as 3.5, 6.92, 5.13, and 3.26 respectively and provided in table 3.

The mean values of CAT activity decreased up to 4.99 KU/l when aspirin was used alone for the production of an ulcer in the stomach. This value is significantly (p<0.05) decreased from a normal value i.e. 10.4 KU/l and its value seems to increase significantly when treated with omeprazole (9.61 KU/l). It also had a normal range of values for CAT activity when the plant was used at the highest dose as in group 6 (9.23 KU/l) which presented in table 3.

Table 2: Mean values of Acid output, pH and gastric volume after the 14 days of oral treatment with drugs and *A. parviflora* seed powder in rabbits.

Group	Dose	Acid output (molEq/l/100 g)	pH	Gastric volume (ml/100 g)
1	Routine feed	26.5±0.27^{e}	2.05±0.06^{b}	20.9±0.34^{e}
2	150 mg/kg	39.7±0.16^{a}	0.87±0.16^{a}	35.1±0.10^{a}
3	20 mg/kg	28.9±0.27^{d}	4.47±0.21^{d}	24.9±0.15^{d}
4	250 mg/kg	35.2±0.19^{b}	1.13±0.20^{a}	32.1±0.29^{b}
5	500 mg/kg	31.7±0.25^{c}	3.01±0.24^{c}	29.8±0.22^{c}
6	750 mg/kg	29.4±0.25^{d}	4.10±0.22^{d}	25.6±0.23^{d}

Similar letters on means (n = 6) in a column are statistically non-significant (p≥0.05), 1 = control, 2 = Asprin, 3 = Omeprazole + Asprin, 4 = Asprin + 250 mg/kg *A. parviflora* seed powder, 5 = Asprin + 500 mg/kg *A. parviflora* seed powder, 6 = Asprin + 750 mg/kg *A. parviflora* seed powder.

Table 3: Mean values of TOS, TAC, MDA, and CAT after the 14 days of oral treatment with drugs and *A. parviflora* seed powder in rabbits.

Groups	Dose	TOS (µmol/l)	TAC (mmol/l)	MDA (nmol/l)	CAT (KU/l)
1	Routine feed	3.69±0.09^{d}	3.06±0.25^{c}	3.34±0.05^{d}	10.4±0.19^{a}
2	150 mg/kg	7.03±0.17^{a}	0.93±0.01^{a}	7.97±0.15^{a}	4.99±0.39^{c}
3	20 mg/kg	3.65±0.05^{d}	2.98±0.15^{c}	3.5±0.09^{d}	9.61±0.28^{a}
4	250 mg/kg	5.94±0.36^{b}	1.35±0.14^{ab}	6.92±0.15^{b}	5.9±0.19^{c}
5	500 mg/kg	4.98±0.31^{c}	1.79±0.20^{b}	5.13±0.32^{c}	7.71±0.26^{b}
6	750 mg/kg	3.63±0.06^{d}	2.78±0.14^{c}	3.26±0.05^{d}	9.23±0.21^{a}

Similar letters on means (n = 6) in a column are statistically non-significant ($p \geq 0.05$), 1 = control, 2 = Asprin, 3 = Omeprazole + Asprin, 4 = Asprin + 250 mg/kg *A. parviflora* seed powder, 5 = Asprin + 500 mg/kg *A. parviflora* seed powder, 6 = Asprin + 750 mg/kg *A. parviflora* seed powder.

Discussion

Gastric ulcer is a break in the normal gastric mucosa of the stomach that extends throughout the muscular mucosa into the submucosa or deeper. In ulcer condition, erosions are formed and superficial epithelium of mucosa is loosed. In the alimentary tract ulcer may occur everywhere. PGs play a significant protective role in the stomach by stimulating the synthesis and secretion of mucus and bicarbonate, increasing mucosal blood flow and promoting epithelial proliferation. The major mechanism via NSAIDs cause ulcers is the inhibition of PGs by the inhibition of COX, which is a key enzyme in the bio-synthesis of PGs (Hamid et al., 2012). So to avoid all these adverse reactions of the drugs, herbal remedies should be given to the ulcer patient to cure the ulcer. Many natural products in plants have multifunctional molecules that protect them from infections of bacteria, viruses and other microorganisms. For this reason, we evaluated the antiulcer activity of the graded dose of *A. parviflora* seed powder in albino rabbits.

In the present study, results demonstrated that ulcer scores were significantly increased in animals treated with aspirin. Administration of a synthetic antiulcer drug, omeprazole, at a dose a of 20 mg/kg along with aspirin significantly reduced the ulcer scores in comparison with aspirin-treated rabbits. Concomitant administration of *A.parviflora* seed powder at the dose rate of 250, 500, and 750 mg/kg along with aspirin significantly reduced the ulcer scores. The mean value of *A. parviflora* at dose rate of 750 mg/kg was not significantly different from omeprazole. The results of our study coincide with other studies (Aslam et al., 2013; Begum et al., 2014).

Administration of aspirin significantly reduced the pH of gastric mucosa as described in previous studies (Aslam et al., 2013). The administration of omeprazole along with aspirin significantly enhanced the pH of gastric mucosa. Concomitant administration of *A. parviflora* seed powder with aspirin significantly enhanced the pH of gastric secretions at three different doses 250, 500, and 750 mg/kg. *A. parviflora* at a dose rate of 750 mg/kg significantly enhanced the pH and it produced similar results as synthetic antiulcer drug omeprazole. Aspirin causes the gastric damage by making the stomach pH more acidic which increases the acidity of the gastric mucosa by enhancing the concentration of hydrogen ions. These results are parallel as described in previous studies (E Zetrini et al., 2013; Aslam et al., 2015).

The gastric volume was significantly increased in groups 2. Aspirin enhances the acid secretions in gastric mucosa due to its acidic nature which enhances the volume of gastric secretions. Administration of omeprazole along with aspirin significantly reduces the gastric volume. Concomitant administration of *A. parviflora* along with aspirin significantly reduced the gastric volume at 250, 500, and 750 mg/kg. *A. parviflora* at a dose of 750 mg/kg significantly reduced gastric volume and its results were statistically similar with synthetic antiulcer drug omeprazole. The above-mentioned results are consistent with previous research studies on aspirin-induced gastric ulcer (Goswami et al., 2011). Pretreatment with an oral dose of *A. parviflora* could partially decrease the ulcer index and permit the healing of gastric lesions induced by the administration of aspirin.

The antioxidant (TAC, TOS, MDA, and CAT) activity of *A. parviflora* was also determined. Phytochemical screening showed a positive result for the steroids, terpenoids, alkaloids, di- and triterpenoids, phenols, flavonoids, tannins and volatile oils. These constituents have different activities which are helpful in healing ulcer. Flavonoid has free radical scavenging and antioxidant activity. The important derivative of flavonoids is quercetin. Flavonoid increases mucus production and also have antihistaminic properties which reduce the histamine production and reduction of mast cells which are produced by the aspirin. The main mechanism of action for the gastroprotective effects of this flavonol are its proton pump inhibitor and antioxidant properties. Oral administration of NSAIDs, such as aspirin, indomethacin have several undesirable effects on the gastrointestinal tract and increase the likelihood of myocardial infarction. Flavonoids also have anti-inflammatory properties without any ulcerogenic action as a side effect and thus show a great

advantage in the treatment of peptic ulcers (de Lira Mota et al., 2009). Phenolic substances e.g. phenolic acid and tannins contribute directly to antioxidant activity. Tannins are important constituents of *A. parviflora*. These are poly phenols and water soluble compound present in plants. They have astringent properties so they are used primarily in medicine. Tannins precipitate micro proteins to the peptic ulcer location. Tannins form an impermeable layer over the coating that prevents the gut secretions and protects the basic mucosa from toxins and other irritants. Tannins endorse resistance to the achievement of proteolytic enzymes, a related activity against *Helicobacter pylori*. They also inhibit gastric acid secretion (Wallace et al., 2000).

Our study gives the suggestion that in the case of gastric ulcer the oxidative stress is increased then the MDA activity and levels of TOS are further increased in the ulcerated group, while the levels of TAC and CAT are decreased for the same group. Antioxidants have defensive properties against gastric ulcer and many other ailments (Saravanan et al., 2012). The oxidative alteration in the cellular membrane or intracellular molecules occurs by the imbalance between ROS and antioxidant defense mechanism. LPO causes loss of membrane fluidity, impaired ion transport and membrane integrity (Tandon et al., 2004).

It can be concluded that aspirin administration (20 mg/kg) enhanced TOS and MDA activity significantly while that of TAC and CAT activity reduced significantly. This may be due to that aspirin which enhanced gastric damage due to the reactive oxygen metabolites. These harm the biochemical markers e.g. decreased CAT and increased MDA production. This may also be due to the impairment of cellular enzyme that involves in the defensive mechanism of gastric ulcer such as TOC and CAT activity (Filho et al., 2012).

The curative ratio for ulcer of treated groups was computed. *A. parviflora* decreased gastric lesions dose dependently. *A. parviflora* significantly decreased the gastric MDA content while it increased CAT activity compares to aspirin. This showed that the antiulcer activity of the *A. parviflora* might be recognized by these tests.

Conclusion: In conclusion to the present study, *A. parviflora* seeds extract proved to be gastroprotective with improved biochemical profile comparable to the synthetic antiulcer drug which indicates its role as an antioxidant. The overall study revealed that extract of *A. parviflora* at 250, 500, and 750 mg/kg showed gastric protection of 47.5, 58.1, and 73.5%, respectively.

Conflict of interests: All authors declare no conflict of interest.

References

Ahuja J, Suresh J and Deep A 2011. Phytochemical screening of aerial parts of Artemisia parviflora. *Der Pharmacia Lettre*, **3**, 116-124.

Aslam B, Awan T, Javed I, Khaliq T, Khan J and Raza A 2015. Gastroprotective and antioxidant potential of Glycyrrhiza glabra on experimentally induced gastric ulcers in albino mice. *International Journal of Current Microbiology and Applied Sciences*, **4**, 451-460.

Aslam B, Majeed W, Javed I, Muhammad F, Khaliq T, Khan JA, Ali A and Sindhu Z 2013. Gastroprotective effect of Berberis vulgaris (zereshk) seeds against gastric ulcer induced by aspirin in male adult albino mice. *Indo Am J Pharm Res*, **3**, 4518-4527.

Awaad AS, El-Meligy RM and Soliman GA 2013. Natural products in treatment of ulcerative colitis and peptic ulcer. *Journal of Saudi Chemical Society*, **17**, 101-124.

Baigent C, Blackwell L, Collins R, Emberson J, Godwin J, Peto R, Buring J, Hennekens C, Kearney P and Meade T 2009. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. *Lancet*, **373**, 1849-1860.

Baumgart DC and Sandborn WJ 2007. Inflammatory bowel disease: clinical aspects and established and evolving therapies. *The Lancet*, **369**, 1641-1657.

Begum R, Aslam B, Javed I, Khaliq T, Muhammad F and Raza A 2014. Gastro protective and antioxidant effect of euphorbia prostrata against indomethacin induced gastric ulcers in healthy adult male albino rabbits. *International Research Journal of Pharmacy*, **5**, 846-850.

de Lira Mota KS, Dias GEN, Pinto MEF, Luiz-Ferreira Â, Monteiro Souza-Brito AR, Hiruma-Lima CA, Barbosa-Filho JM and Batista LM 2009. Flavonoids with gastroprotective activity. *Molecules*, **14**, 979-1012.

E Zetrini A, M flafel H, J Alsabri S, Milad Aburas K, E Mohamed A, B. Rmeli N and Gbaj A 2013. Evaluation the Anti-Inflammatory Activity of Some Eastern Libyan Medicinal Plants. *The Open Conference Proceedings Journal*, **4**, 101-101.

Erel O 2004. A novel automated direct measurement method for total antioxidant capacity using a new generation, more stable ABTS radical cation. *Clinical Biochemistry*, **37**, 277-285.

Erel O 2005. A new automated colorimetric method for measuring total oxidant status. *Clinical Biochemistry*, **38**, 1103-1111.

Filho TP, Sikiru Olaitan B, Tavares de Almeida DA, Lima JCdS, Marson-Ascêncio PG, Donizeti

Ascêncio S, Rios-Santos F and Martins DTdO 2012. Evaluation of antiulcer activity and mechanism of action of methanol stem bark extract of Lafoensia pacari A. St.-Hil. (Lytraceae) in experimental animals. *Journal of Ethnopharmacology*, **144**, 497-505.

Gisbert JP and Pajares JM 2003. Helicobacter pylori Infection and Perforated Peptic Ulcer Prevalence of the Infection and Role of Antimicrobial Treatment. *Helicobacter*, **8**, 159-167.

Goswami M, Kulshreshtha M, Rao CV, Yadav S and Yadav S 2011. Anti-ulcer potential of Lawsonia inermis L. Leaves against gastric ulcers in rats. *Journal of Applied Pharmaceutical Science*, **1**, 69.

Góth L 1991. A simple method for determination of serum catalase activity and revision of reference range. *Clinica Chimica Acta*, **196**, 143-151.

Hamid RA, Foong CP, Ahmad Z and Hussain MK 2012. Antinociceptive and anti-ulcerogenic activities of the ethanolic extract of Annona muricata leaf. *Revista Brasileira de Farmacognosia*, **22**, 630-641.

Herbert M, Jackson C, Ekpo M, Okopedi E and Anah V 2011. Gastroprotective effects of ethanolic leaf extract of Musa paradisiaca in rats. *J. Chem. Pharm. Res*, **3**, 322-327.

Maity S, Chaudhuri T, Vedasiromoni J and Ganguly D 2003. Cytoprotection mediated antiulcer effect of tea root extract. *Indian Journal of Pharmacology*, **35**, 213-219.

Malairajan P, Gopalakrishnan G, Narasimhan S and Veni KK 2008. Evalution of anti-ulcer activity of *Polyalthia longifolia* (Sonn.) Thwaites in experimental animals. *Indian Journal of Pharmacology*, **40**, 126.

Ohkawa H, Ohishi N and Yagi K 1979. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. *Analytical Biochemistry*, **95**, 351-358.

Saravanan J, Venkatesh P, Soumya V, Hariprasath K, Prasad RH and Kumar KM 2012. Antiulcer and antioxidant activity of methanolic leaf extrct of soymida febrifuga. *Journal of Pharmacy Research Vol*, **5**, 528-531.

Steel RG and Torrie JH 1960. Principles and procedures of statistics. *Principles and procedures of statistics.*

Tandon R, Khanna R, Dorababu M and Goel R 2004. Oxidative stress and antioxidants status in peptic ulcer and gastric carcinoma. *Indian journal of physiology and pharmacology*, **48**, 115-118.

Vogel HG 2002. Drug discovery and evaluation: pharmacological assays. Springer Science & Business Media.

Wallace JL, McKnight W, Reuter BK and Vergnolle N 2000. NSAID-induced gastric damage in rats: requirement for inhibition of both cyclooxygenase 1 and 2. *Gastroenterology*, **119**, 706-714.