doi.org/10.36721/PJPS.2023.36.5.REG.1425-1434.1

Phytochemical analysis and gastroprotective effect of *Stellaria media* (L.) Vill. methanolic extract on piroxicam-induced gastric ulcer in Wistar rats

Abdul Aleem[1], Bilal Aslam[1]*, Muhammad Bilal Alim[2], Asif Hussain[1,3], Muhammad Naeem Faisal[1] and Zia-ud-Din Sindhu[4]

[1]Institute of Physiology and Pharmacology, University of Agriculture, Faisalabad, Pakistan
[2]Faculty of Medical and Health Sciences, University of Sargodha, Sargodha,Pakistan
[3]Department of Pharmacy, Riphah International University, Faisalabad, Pakistan
[4]Department of Parasitology, University of Agriculture, Faisalabad, Pakistan

Abstract: *Stellaria media* L. has traditionally been used to treat inflammatory and gastrointestinal ailments. This study aimed to phytochemically characterize the *S. media* extract and explore its anti-ulcer efficacy against piroxicam-induced stomach lesions in Wistar rats. Phytochemical analysis was performed and antioxidant capacity of extract was determined using 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay. *In vivo*, piroxicam (30mg/kg) was administered to induce gastric ulceration. Gastroprotective effect of *S. media* extract was observed at 150, 300 and 450mg/kg, respectively. While omeprazole (20mg/kg) was used as a conventional anti-ulcer drug. After oral treatment for 14 days, stomach acidic secretions, ulcerogenic indices, hematological markers and oxidative stress parameters were assessed along with histological examination. The existence of polyphenol contents in *S. media* extract was confirmed in correlation to a marked DPPH inhibition (IC_{50} 27.94µg/mL). *S. media* extract resulted in a dose-dependent elevation in gastric pH while a decrease in acid volume, acidity and ulceration. Also, *S. media* extract administration restored the impaired hematological markers (RBCs, Hb, WBCs and PLTs) and decreased oxidative stress by reducing oxidants (TOS and MDA) while raising antioxidants (TAC and CAT). Furthermore, gastric histological results corroborated the aforementioned findings. Conclusively, *S. media* could provide a promising protective effect against drug-induced gastric ulceration.

Keywords: *Stellaria media*, antioxidant, piroxicam, stomach ulcer, oxidative stress.

INTRODUCTION

Stomach ulcer is a necrotizing and inflammatory illness that is a global health issue since a significant proportion (5-10%) of the world's population is diagnosed with stomach ulcers each year (Salari *et al*., 2022). Its main manifestations are stomach wall lesions and bleeding caused by an impaired balance between protective factors like bicarbonate, mucin, growth factors, nitric oxide, prostaglandins (PGs) and mucosal blood circulation and necrotizing factors including gastric acid and bacterial infections. In addition, prolonged intake of anti-inflammatory agents, stress, chronic alcohol use, smoking and poor dietary habits contribute to stomach ulcer etiology (Bereda, 2022).

Piroxicam, a commonly used anti-inflammatory drug, is a member of non-steroidal anti-inflammatory drugs (NSAIDs) that is useful in treating fever, pain and inflammatory conditions such as post-operative and post-traumatic inflammation and arthritis (Saganuwan, 2017). However, it is reported to cause stomach ulcers despite its therapeutic efficacy. Piroxicam non-selectively inhibits cyclooxygenase enzymes which blocks the PGs synthesis and ultimately reduces the secretion of mucus and bicarbonates and decreases blood circulation to gastric tissue and epithelial damage. Additionally, microvascular structural changes, excessive reactive oxygen species (ROS) generation and decreased antioxidant enzyme activities contribute to the pathophysiological basis of stomach ulcers (Alsinnari *et al*., 2022; Domper Arnal *et al*., 2022).

Currently available conventional medicines for the management of gastric ulceration have limitations because of their undesirable side effects and limited efficacy. Moreover, the recurrence of disease after extensive therapy has heightened interest in the quest for new and cost-effective agents that provide greater protection against stomach disorders while having fewer side effects (Alhammadi *et al*., 2022). However, studies have documented the successful application of herbs in traditional medicine with promising results in various pathological diseases (Abd-Alla *et al*., 2022).

Stellaria media (L.), known as 'Chickweed', is a member of the Caryophyllaceae family. The plant is native to Asia, Africa, Europe and North America. In ethnomedicine, *S. media* is employed to treat asthma, measles, jaundice, diarrhea and gastrointestinal ailments

*Corresponding author: e-mail: bilal.aslam@uaf.edu.pk

(Oladeji and Oyebamiji, 2020). *S. media* has been shown to have anti-microbial, anti-inflammatory, antioxidant, anti-obesity, anti-diabetic, neuroprotective and cardioprotective properties (Ahmad *et al*., 2022; Demján *et al*., 2022; Khan *et al*., 2019; Teuşdea *et al*., 2021). However, the effectiveness of *S. media* on chemical-induced gastrointestinal toxicity has yet to be explored. Therefore, this study was proposed to evaluate the protective effect of *S. media* extract against piroxicam-induced stomach ulcers in Wistar rats.

MATERIALS AND METHODS

Chemicals

Piroxicam was purchased from Pfizer®, Pakistan and omeprazole was obtained from Getz Pharma®, Pakistan. Other chemicals of analytic grade including gallic acid, ascorbic acid, catechin, 1,1-diphenyl-2-picrylhydrazyl (DPPH), Folin-Ciocalteu reagent and aluminum chloride were purchased from Sigma-Aldrich®, USA.

Plant collection

Whole plant of *S. media* was procured from Punjab Forestry Research Institute Gatwala Faisalabad (31º28′12″N, 73º12′39″E), Pakistan. A taxonomist of Department of Botany, University of Agriculture, Faisalabad, Pakistan, verified the plant specimen and allotted a voucher no. 283-1-22.

Plant extraction

S. media methanolic extract was prepared using the maceration technique. The plant was properly cleaned, dried and then coarsely powdered. The powdered material (100g) was soaked in 1L of methanol for three days and filtered through a muslin cloth and filter paper (Whatman® no. 1). A rotary evaporator (Heizbad Hei-VAP®, Germany) was used to evaporate the excessive solvent at 55ºC. The obtained extraction yield was 13.62% w/w (Yang *et al*., 2022)

Phytochemical screening

Phytochemical tests were done to qualitatively detect different phytoconstituents of *S. media* extract according to previously described methods (Aslam and Hussain, 2021).

Total phenolic (TPC) and flavonoid (TFC) contents

The Folin-Ciocalteu method was implicated to quantify the TPC of *S. media* extract. The sample was prepared using the procedure described by Sultana *et al*. (2009) and absorbance of prepared sample was measured at 765 nm with a spectrophotometer. TPC was calculated using the gallic acid calibration curve (R^2 = 0.998, y = 0.011x+0.008) and presented in mgGAE/g of *S. media* extract. The TFC of extract was quantified spectrophotometrically using the aluminum chloride method (Sultana *et al*., 2009). The prepared sample's absorbance was taken at 510 nm and content was calculated using the catechin calibration curve (R^2 = 0.999, y=0.040x+0.009). The TFC was mentioned in mgCE/g of *S. media* extract.

HPLC characterization

The polyphenol content of extract was determined by HPLC analysis. For chromatographic analysis, HPLC equipment (Shimadzu®, Japan) with a UV-Vis detector and C_{18} column was used. To prepare the sample, 25mg of dried extract was combined with 20mL of methanol (60% v/v), acidified with HCl and heated at 90ºC for 2 hours. The mobile phase was composed of 6% acetic acid (pH 2.27) and absolute acetonitrile with gradient elution: 15%, 45% and 100% of each combination for 15 minutes. The injection port was used to inject 20µL of the sample. During the analysis, HPLC parameters such as flow rate (1mL/min), column temperature (27ºC) and absorbance at 280 nm were maintained. The phytoconstituents were quantified using the obtained retention times and concentrations (Hussain *et al*., 2021).

FT-IR analysis

For infrared spectroscopic analysis, sample was prepared using 10mg of extract (Aslam *et al*., 2023) and analyzed with an FT-IR spectrometer of Spectrum Two™, Germany. Analysis conditions including a resolution of 4 cm^{-1} with a scan range of 4000 to 500 cm^{-1} were set to acquire the FT-IR spectrum.

In vitro antioxidant activity

Antioxidative potential of extract was determined through assessing its potential to scavenge DPPH radicals. In brief, varied concentrations (3.125-50µg/mL) of extract and ascorbic acid were prepared using the ethanolic solutions of extract and ascorbic acid (standard antioxidant). Then, 500µL of each sample was combined with 1000µL of ethanolic solution of DPPH (0.2mg/mL) and incubated for 30 min. As a blank solution, a mixture containing all of the aforementioned chemicals except extract/standard was employed. Absorbance of samples at 517 nm was taken in triplicates and percentage inhibition results were derived using the provided formula by Subhan *et al*. (2021).

$$\% \text{ DPPH inhibition} = \left[\frac{AB - AT}{AB}\right] x\ 100$$

Here, AB is absorbance of blank solution and AT is absorbance of test sample.

Animals and ethical approval

Thirty-six female Wistar rats, weighing an average of 150 to 190g and varying in age from 6 to 8 weeks, were acquired and kept at Institute of Microbiology, University of Agriculture, Faisalabad, Pakistan. All rats were acclimatized and conditions such as light/dark cycle (12 hours), temperature (25±2ºC), humidity (40-60%), standard pellet chow feed and free access to fresh water were maintained throughout the study. The Institutional

Bioethical Committee (IBC) of University of Agriculture, Faisalabad, Pakistan approved the study protocols (letter No. 2006/ORIC).

Study design

Rats were divided into six groups (six rats in each group) and treated orally for 14 days: Normal control was given normal saline (3mL/kg) and Ulcer control was administered with 30mg/kg of piroxicam (Abdeen *et al*., 2019). Omeprazole at 20 mg/kg was co-administered with piroxicam (Berezi *et al*., 2017). *S. media* extract at 150, 300 and 450mg/kg plus piroxicam was administered in three groups (Khan *et al*., 2019).

Collection of blood and organ samples

On the 15th day, blood was withdrawn by a heart puncture under ketamine anesthesia and preserved for hematological and biochemical analyses. Further, all animals were decapitated and their stomachs were taken, sliced along the greater curve and collected gastric contents were preserved. Small portions of stomachs were kept in a 10% v/v formalin buffer solution for histopathological examinations.

Gastric acid secretion indices

Stomach contents were combined with 5mL of distilled water and centrifuged at 5,000 rpm for 5 minutes. The collected supernatants were transferred into a measuring cylinder to measure the acid volume. A digital pH meter was used to assess the pH of the supernatants. The titration method of Adefisayo *et al*. (2017) was adopted to measure the gastric free and total acidity using 0.01 N NaOH solution, Topfer's reagent and phenolphthalein (indicator). Results were expressed as mEq/L.

Gastric ulcer scoring parameters

Each stomach's inner mucosal lining was inspected with a magnifying lens and mucosal lesions were rated using the 0-3 grading scale (Peskar *et al*., 2002). Ulcer score was determined for each rat by multiplying the severity factor by total number of lesions. The ulcer index was calculated following the formula provided by Sattar *et al*. (2019). Further, the extent of ulcer inhibition was calculated (Akhtar and Kamal, 1995).

Hematological parameters

Whole blood samples preserved in EDTA tubes were used to assess Red blood cells (RBCs) count, concentration of hemoglobin (Hb), white blood cells (WBCs) and platelet (PLTs) counts with the help of hematology autoanalyzer of Boule Medical AB®, Sweden.

Estimation of oxidative stress markers

Blood samples stored in gel clot activator tubes were allowed to clot and centrifuged at 3,000 rpm for 10 minutes to separate sera. Total antioxidant capacity (TAC) was determined as described by Erel (2004). The method of Goth (1991) was used to measure catalase (CAT) activity. Serum levels of total oxidant status (TOS) and malondialdehyde (MDA) were analyzed according to previously devised methods (Erel, 2005; Hassan *et al*., 2022).

Histopathological examination

Stomach tissues preserved in a 10% formalin buffer solution were dehydrated using graded alcohols, cleaned with xylene and embedded in paraffin. Tissues were cut into 5µm slices and hematoxylin and eosin (H&E) staining was done. Histopathological alterations were detected using a light microscope (Olympus PM-10ADS, Japan) and images were captured at 10×10 magnification.

STATISTICAL ANALYSIS

SPSS software (v23.0) was used for data analysis and graphs were created using GraphPad Prism® software (v6.01). The one-way ANOVA was applied followed by Duncan's multiple-range (DMR) test. Results were provided as mean±SEM with a significance level of $p<0.05$.

RESULTS

Phytochemical analysis

Phytochemical tests of *S. media* extract revealed the presence of flavonoids, phenols, tannins, glycosides, alkaloids, quinones, fixed oils, carbohydrates and proteins.

TPC and TFC of S. media extract

The TPC of *S. media* extract was found 68.12±0.10 mgGAE/g, determined using Folin-Ciocalteu method. Whereas, 41.81±0.07 mgCE/g of TFC was quantified according to aluminum chloride method.

HPLC analysis of S. media extract

Fig. 1 and table 1 indicate the significant quantities of identified polyphenols including gallic acid, chlorogenic acid, hydroxybutyric acid, kaempferol, vanillic acid, coumarins, salicylic acid and rutin in *S. media* extract.

FT-IR analysis of S. media extract

Infrared spectroscopic analysis of *S. media* extract indicated the presence of flavonoids, phenols, lipids, alcohols and aromatic and halogenated compounds, as presented in fig. 2 and table 2.

DPPH scavenging activity of S. media extract

The DPPH assay was used to investigate the free radical scavenging capability of *S. media* extract compared to ascorbic acid, as shown in fig. 3. At the highest concentration (50µg/mL), the extract resulted in 62.27±2.18% DPPH inhibition. An IC_{50} value of 27.94µg/mL of *S. media* extract was found compared to ascorbic acid (9.35µg/mL).

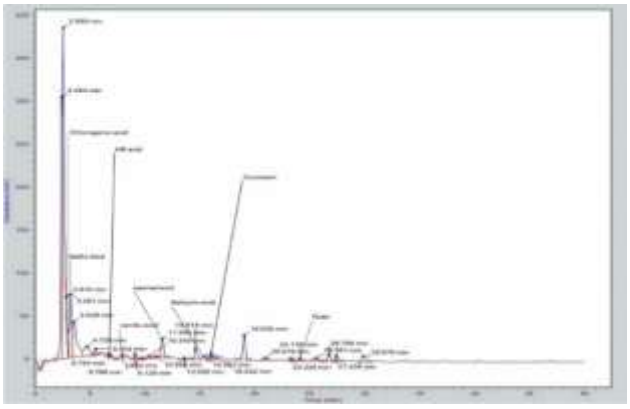

Fig. 1: HPLC chromatogram indicating polyphenols of *S. media* extract.

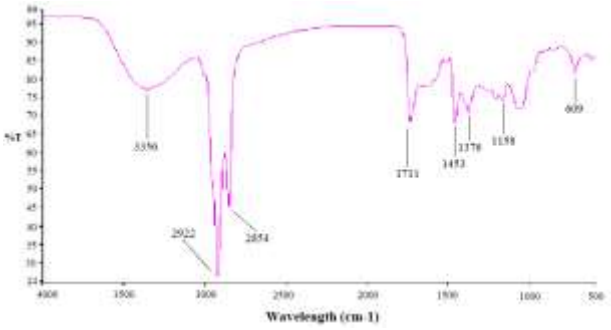

Fig. 2: FT-IR spectrum showing functional groups of phytocompounds of *S. media* extract.

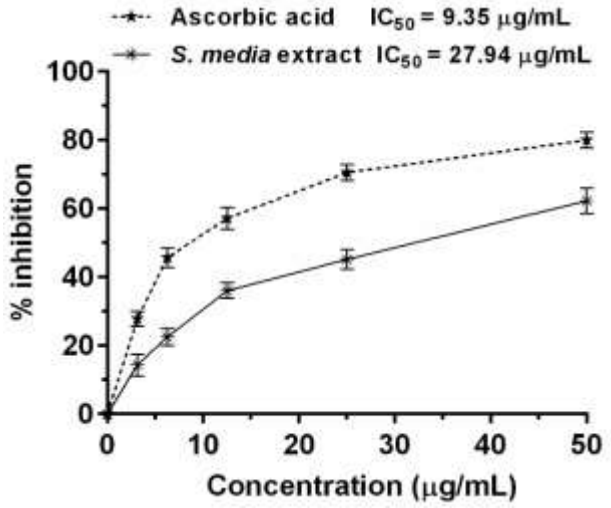

Fig. 3: DPPH radical scavenging activity of *S. media* extract at graded concentrations. Triplicate values are mentioned as mean±SEM (n=3).

S. media extract lowered gastric acid secretions

As indicated in fig. 4A, piroxicam caused a significant (p<0.05) elevation in stomach acid volume of ulcer control rats in comparison to the normal rats. *S. media* extract or omeprazole in combination with piroxicam considerably (p<0.05) reduced acid volume in comparison to ulcer control. In contrast to ulcer control, the stomach pH of *S. media* extract treated rats was found significantly (p<0.05) higher (fig. 4B). Furthermore, *S. media* extract or omeprazole plus piroxicam considerably (p<0.05) reduced free and total acidity (fig. 4C, D). Overall, *S. media* extract caused a mark reduction in stomach acid output induced by piroxicam.

S. media extract reduced gastric ulcer indicators

As demonstrated in table 3, rats given graded doses of *S. media* extract had a considerably (p<0.05) lower ulcer score and index than the ulcer control. The highest ulcer inhibitory effect was observed in rats treated with *S. media* extract at 450mg/kg dose (68.48±1.54%), which was approximately identical to that of omeprazole (72.02±1.78%).

S. media extract alleviated hematological parameters

Fig. 5 showing the ameliorating effect of *S. media* extract on hematological parameters in ulcerated rats. In contrast to normal rats, piroxicam alone markedly (p<0.05) reduced RBCs count and Hb concentration (fig. 5A, B). *S. media* extract administration for 14 days resulted in a dose-dependent rise in RBCs count and Hb concentration. Moreover, rats were given *S. media* extract and piroxicam together, they considerably (p<0.05) recovered WBCs and PLTs counts in comparison to ulcer control (fig. 5C, D). Furthermore, *S. media* extract (300 and 450mg/kg) improved hematological indices more than *S. media* extract (150mg/kg).

S. media extract attenuated oxidative stress

As shown in fig. 6, results showed that piroxicam significantly impaired oxidant and antioxidant indicators in rat sera. Fig. 6(A, B) depicts that oxidants (TOS and MDA) were considerably (p<0.05) higher in rats given only piroxicam, as compared to normal rats. The co-treatment of *S. media* extract with piroxicam substantially (p<0.05) lowered these parameters. When compared to the normal rats, ulcer control rats had significantly (p<0.05) reduced antioxidants (TAC and CAT). However, combined treatment with *S. media* extract or omeprazole with piroxicam markedly increased the antioxidants to normal levels (fig. 6C, D). Furthermore, *S. media* extract at 300 and 450mg/kg showed better attenuation of oxidative stress markers than at 150mg/kg.

Histopathological findings

Fig. 7 indicating histology images of stomachs from the normal, ulcer control, and *S. media* extract treated rats. Stomach histo-structures, including epithelial and submucosal linings, were intact in the normal control (fig. 7A). Piroxicam alone administration showed significant degenerative alterations in stomach histology including epithelial erosion and glandular destruction as well as infiltration of mononuclear cells (fig. 7B).

Table 1: Concentrations and retention times of polyphenols identified in *S. media* extract using HPLC analysis.

Phytocompounds	Retention time (min)	Area (mV.s)	Concentration (mg/g)
Chlorogenic acid	2.91	589,546.9	76.64
Gallic acid	3.26	861,904.3	75.84
Hydroxybutyric acid	6.78	59,856.4	9.58
Vanillic acid	7.99	68,617.0	5.33
Kaempferol	11.59	341,065.4	13.91
Salicylic acid	15.35	110,439.9	41.64
Coumarin	16.03	92,755.0	11.31
Rutin	24.13	34,906.4	3.94

Table 2: Functional groups detected in *S. media* extract using FT-IR analysis.

Wave number (cm^{-1})	Functional group	Phytochemicals
3356	H-bonded, O-H str.	Phenols, Alcohols
2922	Asymmetric str. of $–CH(CH_2)$	Lipids
2854	Symmetric str. of $–CH(CH_2)$	Fatty acids, lipids
1711	C=O str.	Lipids, flavonoids
1453	C=C, C-H str.	Aromatic compounds, flavonoids
1376	O-H bend.	Tertiary alcohols, phenols
1158	C-OH bend., C-O str.	Lipids, Alcohols
609	C-I, C-Cl str.	Alkyl halides, halogens (iodo-/chloro-compounds)

Str.: stretching, Bend.: bending

Table 3: Effect of *S. media* extract on gastric ulcer score, ulcer index and ulcer inhibition in piroxicam-induced stomach lesions in rats.

Groups	Ulcer score	Ulcer index	Ulcer inhibition (%)
Normal control	---	---	---
Ulcer control	$5.67±0.33^{a}$	$5.29±0.30^{a}$	---
Omeprazole (20mg/kg)	$1.50±0.24^{d}$	$1.36±0.11^{d}$	$72.02±1.78^{a}$
S. media extract (150mg/kg)	$4.61±0.42^{b}$	$4.38±0.31^{b}$	$20.86±1.46^{c}$
S. media extract (300mg/kg)	$2.50±0.23^{c}$	$2.32±0.22^{c}$	$59.25±1.17^{b}$
S. media extract (450mg/kg)	$1.83±0.31^{cd}$	$1.57±0.19^{cd}$	$68.48±1.54^{a}$

Values are mentioned as Mean±SEM (n=6). Dissimilar alphabets indicate a significant ($p<0.05$) difference.

Rats given a combination of *S. media* extract and/or omeprazole plus piroxicam showed considerable improvement when compared to ulcer control (fig. 7C-F). Moreover, *S. media* extract at 450mg/kg exhibited higher gastroprotective efficacy against the harmful effects of piroxicam which was comparable to omeprazole.

DISCUSSION

Piroxicam is a popular antipyretic, analgesic and anti-inflammatory agent. Despite its therapeutic value, long-term piroxicam usage has been linked to oxidative stress-linked stomach injury (Abd-Alla *et al*., 2022). Excessive NSAIDs use is considered to be responsible for 20-30% of gastric ulcer cases (McEvoy *et al*., 2021). Several reports have found that natural products can help to prevent NSAIDs-induced stomach lesions (Bari *et al*., 2021; Kim *et al*., 2022; Nworah *et al*., 2022). As a result, this study sought to investigate the gastro-protective effect of *S. media* extract on piroxicam-induced stomach lesions in an animal model.

In our study, piroxicam substantially lowered stomach pH while a notable increase in acid volume and acidity was observed, as seen in a recent study (de Oliveira *et al*., 2022). Administration of graded doses of *S. media* extract showed a significant rise in gastric acid pH and markedly reduced gastric acid volume and acidity. In addition, ulcer score and index were significantly decreased with *S. media* extract treatment as comparable to omeprazole-treated rats. Histological examination of *S. media* extract or omeprazole-treated groups revealed the protection of gastric mucosal lining disruption and lesions with hemorrhage caused by piroxicam. *S. media* extract therapy suppressed gastric acid production in a dose-dependent manner. Our findings also imply that *S. media* extract may have reduced the formation of gastric ulcers by inhibiting histamine-induced gastric acid production influenced by piroxicam.

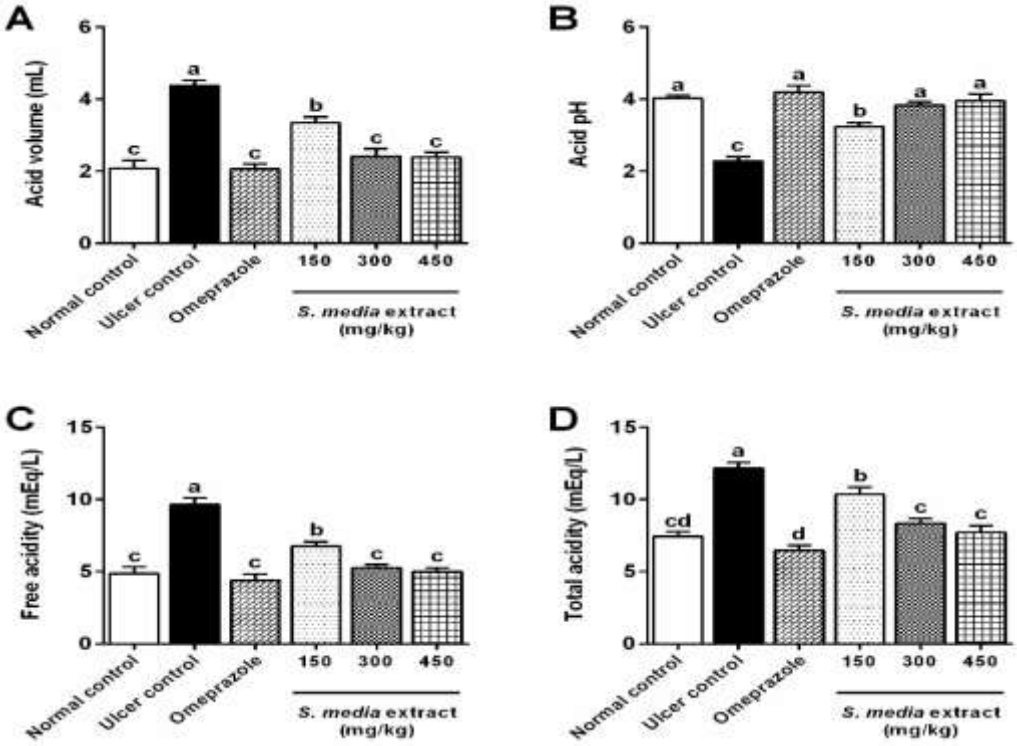

Fig. 4: Effect of graded doses of *S. media* extract on (A) gastric acid volume (mL), (B) acid pH, (C) free acidity (mEq/L) and (D) total acidity (mEq/L) in rats. Values are presented as mean±SEM (n=6). Dissimilar alphabets indicate a significant (p<0.05) difference.

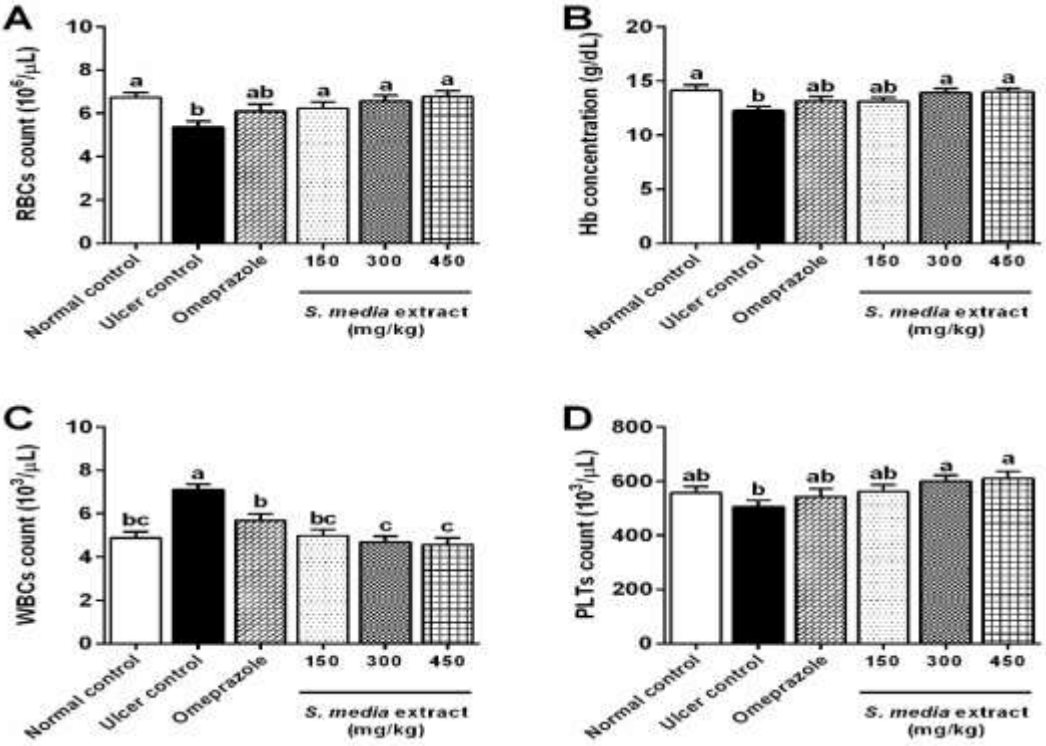

Fig. 5: Dose dependent effect of *S. media* extract on (A) RBCs count (10^6/µL), (B) Hb concentration (g/dL), (C) WBCs count (10^3/µL) and (D) PLTs count (10^3/µL) in rats. Values are presented as mean±SEM (n=6). Dissimilar alphabets indicate a significant (p<0.05) difference.

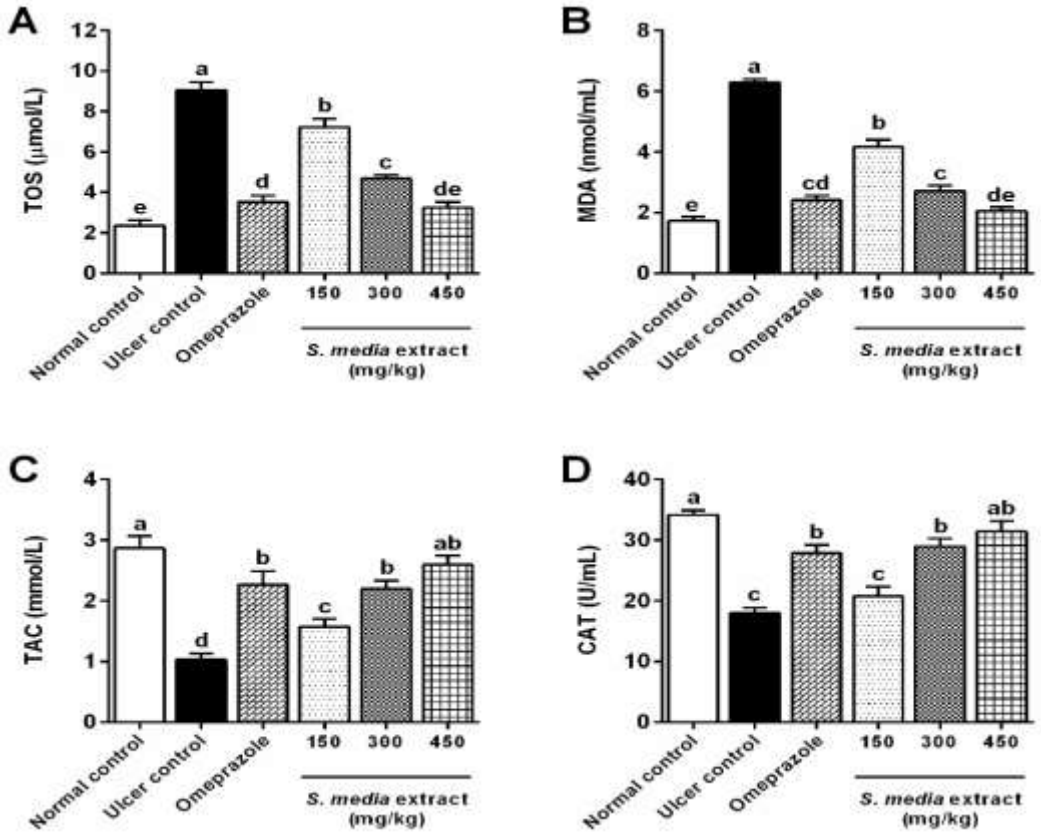

Fig. 6: Effect of different doses of *S. media* extract on serum levels of (A) total oxidant status (TOS), (B) malondialdehyde (MDA), (C) total antioxidant capacity (TAC) and (D) catalase activity (CAT) in rats. Values are presented as mean±SEM (n=6). Dissimilar alphabets indicate a significant (p<0.05) difference.

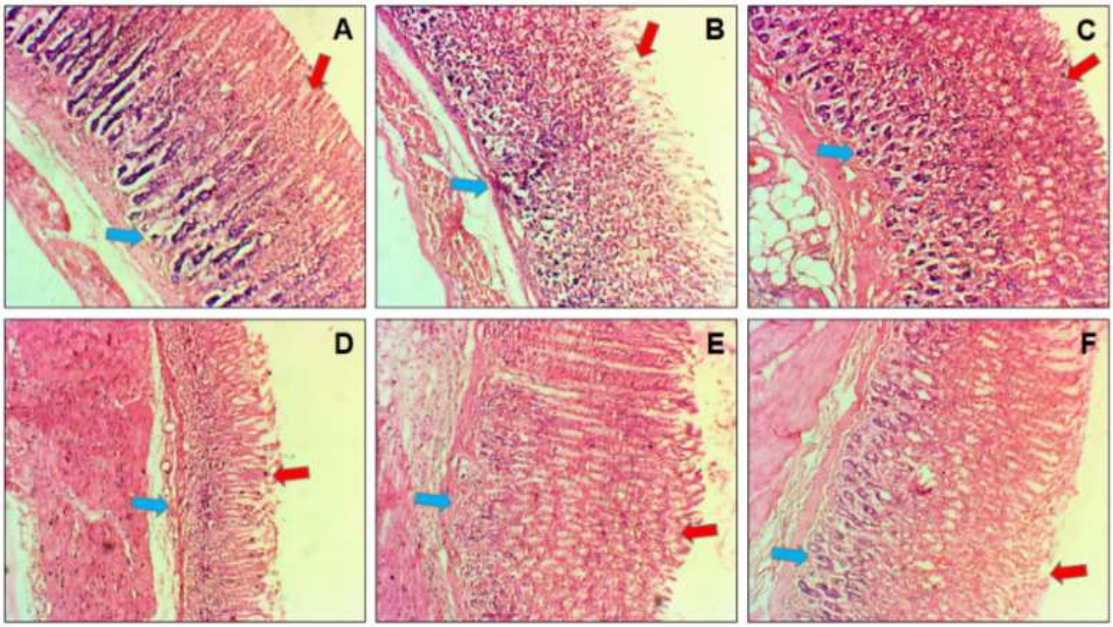

Fig. 7: H&E stained stomach histology images showing a protective effect of *S. media* extract against piroxicam-induced stomach ulcer in rats (x100 magnification). (A) Normal control, (B) ulcer control, (C) omeprazole plus piroxicam and (D-F) *S. media* extract at 150, 300 and 450mg/kg plus piroxicam treated groups. Red arrow: stomach epithelium, Blue arrow: stomach submucosal lining.

It might possibly be attributed to piroxicam's decreasing inhibitory action on PGs formation which normalized blood flow to stomach mucosa (de Veras *et al*., 2021).

Phytochemical analysis of *S. media* extract indicated the presence of polyphenols, tannins, glycosides, alkaloids, and quinones. Flavonoids in *S. media* may protect the stomach mucosa by reducing oxidative stress and increasing mucosal secretions *via* PGs production (Abou Baker, 2022). The addition of tannins in *S. media* may have decreased gastric acid output. Tannin has the ability to precipitate mucosal proteins exposed at the lesion site, forming a covering layer that protects the stomach mucosa from irritation. It can also reduce stomach acid secretion *via* inhibiting H^+-K^+ ATPase by binding at ATP hydrolysis site (Hossain *et al*., 2021). Our results are further supported by stomach histological observations of rats treated with *S. media* extract along with piroxicam which revealed better gastric histoarchitecture as compared to the ulcer control.

Piroxicam has been related to gastrointestinal tract injury which results in acute or persistent bleeding. This study demonstrated that piroxicam resulted in a considerable reduction in RBCs count and Hb concentration, as previously reported by Oraebosi *et al*., (2020). It might signify the anemia onset and a decrease in oxygen-carrying potential of blood. *S. media* extract significantly increased the RBCs count and Hb concentration, suggesting that *S. media* extract has the ability to prevent piroxicam-associated blood toxicity. In addition, WBCs and PLTs counts were found considerably impaired in piroxicam alone treated rats, indicating impaired host immunity (Oraebosi *et al*., 2020). *S. media* extract restored the WBCs to normalcy which may be attributable to significantly improved host immunity. A substantial increase in PLTs count was seen in *S. media* extract-treated group, indicating its potential to stimulate the blood clotting pathway *via* boosting thrombopoietin synthesis (Abdeen *et al*., 2020).

A continual balance between the generation of ROS and scavenging of free radicals is required for cell or tissue integrity and normal functioning. However, an impairment of it generates oxidative stress and affects normal cellular activities (Rehman *et al*., 2021; Widowati *et al*., 2022). In current investigation, a considerable rise in TOS and MDA levels and a reduction in TAC and CAT levels indicated excessive ROS formation. Piroxicam-induced toxicity may be exacerbated by increased ROS generation and decreased antioxidant activity. In animal models, NSAIDs have been found to impair antioxidant mechanisms and subsequently cause oxidative gastric injury (Abdeen *et al*., 2020). However, *S. media* extract caused a considerable drop in oxidative stress which suggest the potent antioxidative action of *S. media*. Our findings are in accordance with previous research that found the key roles of antioxidant and anti-inflammatory activities of medicinal plants against NSAID-induced stomach ulcers (Abd-Alla *et al*., 2022; Sattar *et al*., 2019).

S. media has been proven to have potent antioxidant activity (Ahmad *et al*., 2022; Teușdea *et al*., 2021). This antioxidant activity of *S. media* on stomach mucosa might have contributed to its gastroprotective properties against gastric lesions induced by piroxicam administration. Along with antioxidant action, phytocompounds found in *S. media* may have prevented stomach ulceration through several mechanisms. Our findings showed that *S. media* protected against the harmful effects of piroxicam by inhibiting lipid peroxidation and stimulating antioxidant enzymes. However, *S. media* requires further characterization to completely understand its phytochemical composition. Also, the possibility of protective effect of a single or combination of phytocompounds *via* multiple pathways cannot be ruled out and necessitates additional studies.

CONCLUSION

Results of our study showed that *S. media* extract markedly protected against piroxicam-induced gastric ulceration and oxidative stress, reversed hematological changes and improved gastric histological abrasions in rats. Antioxidant and gastroprotective actions of *S. media* could be attributed to the presence of bioactive phytocompounds. Overall, our findings indicated the efficiency of *S. media* in reducing NSAID-induced stomach lesions, suggesting that it may be employed as an alternate way to treat stomach ulcers.

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