Protective and Therapeutic Effects of an Aqueous Extract of Beetroot (*Beta vulgaris* L.) Against Indomethacin-Induced Toxicity in Rats: A Biochemical and Histopathological Study

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Abstract

The present study was conducted to evaluate the protective and therapeutic effects of an aqueous extract of beetroot (*Beta vulgaris* L.) against indomethacin-induced toxicity in laboratory rats. Thirty adult female Sprague–Dawley rats were randomly allocated into six experimental groups (n = 5/group): control, indomethacin, beetroot extract, co-treatment (indomethacin + beetroot extract), therapeutic beetroot extract, and sucralfate groups. The experiment lasted 45 days. Serum superoxide dismutase (SOD), malondialdehyde (MDA), reduced glutathione (GSH), and prostaglandin E_2 (PGE_2) levels were determined, in addition to histopathological examination of the stomach and duodenum. Indomethacin significantly decreased SOD activity (3.66 ± 0.50 vs. 6.60 ± 0.55), GSH levels (33.95 ± 2.00 vs. 90.78 ± 0.91), and PGE_2 concentrations (187.27 ± 5.60 vs. 371.16 ± 3.94), while significantly increasing MDA levels (538.48 ± 60.67 vs. 289.00 ± 4.95) compared with the control group ($P \leq 0.05$). Beetroot extracts markedly ameliorated these biochemical alterations, particularly in the co-treatment group, where SOD, MDA, GSH, and PGE_2 values improved to 5.82 ± 0.49, 338.90 ± 8.22, 69.83 ± 1.15, and 307.67 ± 8.72, respectively ($P \leq 0.05$). Histopathological examination confirmed substantial protection of the gastric and duodenal mucosa in beetroot-treated animals, whereas sucralfate produced only partial recovery. These findings indicate that aqueous beetroot extract exerts significant protective and therapeutic effects against indomethacin-induced gastrointestinal toxicity through attenuation of oxidative stress and preservation of mucosal integrity.

Keywords: *Beta vulgaris* L.; beetroot; indomethacin; oxidative stress; prostaglandin; stomach.

Introduction

Indomethacin is a widely prescribed non-steroidal anti-inflammatory drug (NSAID) that exerts its pharmacological activity primarily through inhibition of the cyclooxygenase (COX) enzymes responsible for prostaglandin biosynthesis from arachidonic acid. Although this mechanism effectively alleviates pain and inflammation, it may also compromise gastric mucosal defense, particularly following prolonged administration or the use of high doses [1].

Recent evidence indicates that indomethacin-induced toxicity extends beyond prostaglandin depletion and is closely associated with the development of oxidative stress, characterized by excessive generation of reactive oxygen species (ROS). This process is accompanied by increased lipid peroxidation, reflected by elevated malondialdehyde (MDA) levels, together with depletion of endogenous antioxidant defenses, including reduced glutathione (GSH) and superoxide dismutase (SOD). Consequently, these biomarkers are widely recognized as

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reliable indicators for assessing oxidative tissue injury and evaluating the efficacy of protective or therapeutic interventions in experimental models of drug-induced toxicity [2,3].

Experimental studies have consistently demonstrated that indomethacin induces severe gastric injury accompanied by marked biochemical and histopathological alterations. These changes are commonly associated with reduced prostaglandin E_2 (PGE_2) production, enhanced inflammatory responses, and oxidative damage. Several recent investigations have further shown that antioxidant-based interventions can attenuate these pathological changes by lowering MDA levels, restoring GSH and SOD activity, and improving oxidative homeostasis within affected tissues [3,4].

Among natural bioactive plants, beetroot (*Beta vulgaris* L.) has attracted considerable scientific interest owing to its abundance of biologically active constituents, particularly betalains, phenolic compounds, flavonoids, naturally occurring nitrates, vitamins, and essential minerals. These phytochemicals possess potent antioxidant and anti-inflammatory properties, making beetroot a promising candidate for mitigating oxidative and inflammatory tissue damage induced by pharmacological or chemical agents [5,6].

Betalains are considered the principal bioactive pigments responsible for many of the biological activities of beetroot. Recent reviews have demonstrated that these compounds modulate oxidative stress- and inflammation-related signaling pathways by scavenging free radicals and enhancing endogenous antioxidant defense systems. Such biological activities support the potential application of beetroot extract as a prophylactic and therapeutic adjunct against drug-induced tissue injury, particularly when the underlying pathogenic mechanism involves oxidative imbalance and depletion of protective prostaglandins [6].

Despite growing evidence regarding the antioxidant potential of beetroot extract, studies directly comparing its protective and therapeutic efficacy against indomethacin-induced toxicity while simultaneously correlating oxidative stress biomarkers with histopathological alterations in both the stomach and duodenum remain limited. Therefore, the present study was designed to evaluate the protective and therapeutic effects of an aqueous extract of *Beta vulgaris* L. roots against indomethacin-induced toxicity in laboratory rats. This was accomplished by determining serum levels of superoxide dismutase (SOD), malondialdehyde (MDA), reduced glutathione (GSH), and prostaglandin E_2 (PGE_2), together with histopathological examination of the stomach and duodenum, to correlate biochemical findings with tissue alterations.

Material and Methods

2.1 Plant Collection and Preparation of the Aqueous Extract

Fresh beetroot (*Beta vulgaris* L.) roots were collected from Salah Al-Din Province, Iraq, in September 2025. Botanical identification was performed at the Plant Laboratory, Department of Biology, College of Education for Pure Sciences, Tikrit University, by Assistant Professor Dr. Mohammed Adnan Hashem. The roots were thoroughly washed with tap water to remove adhering soil and impurities, sliced into uniform sections, and subjected to freeze-drying (lyophilization). The freeze-drying process involved freezing the samples at −40°C or lower, followed by dehydration under vacuum, allowing water to be removed through sublimation without passing through the liquid phase. This procedure was employed to preserve thermolabile

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bioactive compounds, particularly betalains and phenolic constituents, while maintaining the biological activity of the plant material [7].

The freeze-dried samples were subsequently ground into a fine powder and stored in airtight containers at room temperature in a dry place protected from direct light and moisture until extraction. The phytochemical characterization of the beetroot material included determination of the total phenolic content using a standard spectrophotometric method. The total phenolic content was 345.6 mg/100 g dry weight.

Exactly 50 g of beetroot powder was transferred into a 1-L glass flask containing 250 mL of distilled water. The mixture was stirred using a magnetic stirrer at 70 rpm for 1 h to ensure complete homogenization and maximize extraction efficiency. The flask was then tightly sealed with a plastic stopper, wrapped with opaque material to protect the extract from light, and incubated in a shaking incubator for 24 h [8].

Following extraction, the suspension was initially filtered through four layers of sterile medical gauze to remove coarse plant debris. The filtrate was subsequently passed through Whatman No. 1 filter paper to obtain a clear aqueous extract free of particulate impurities. The freshly prepared aqueous extract was used immediately for oral administration to the experimental animals.

2-2 Experimental Animals

A total of 30 adult female Sprague–Dawley rats, weighing 180–210 g, were used in the present study. The animals were obtained from the Animal House of the College of Veterinary Medicine, Tikrit University, Iraq. They were housed in well-ventilated plastic cages (46 × 28 × 13 cm) under standard laboratory conditions.

Before the initiation of the experiment, all animals were allowed to acclimatize to the laboratory environment for one week. During the acclimatization and experimental periods, the animals were maintained at 25 ± 2°C under a 12 h light/12 h dark photoperiod, with adequate ventilation. Standard husbandry conditions were maintained throughout the study, and the animals had ad libitum access to food and drinking water.

The rats were fed a standard laboratory diet consisting of 34% wheat, 25% yellow corn, 20% barley, 10% animal protein, 10% powdered milk, and 1% sodium chloride. The diet ingredients were thoroughly ground and mixed before the addition of vegetable oil and water to produce a homogeneous dough. The dough was cut into small portions, dried, and provided fresh to the animals daily in sufficient quantities [9].

Following the acclimatization period, the animals were randomly assigned to six experimental groups (n = 5 per group) and housed in separate cages according to the experimental design. The experiment commenced on 1 October 2025 and continued until 15 November 2025.

2.3 Experimental Design

Following the acclimatization period, the animals were randomly allocated into six experimental groups (n = 5 per group), ensuring comparable body weights among the groups. The treatment protocols were as follows:

1) G1, Control: Animals received distilled water together with the standard laboratory diet throughout the 45-day experimental period
2) G2, Indomethacin: Animals were orally administered indomethacin (5 mg/kg body weight/day) by gastric gavage for 45 consecutive days.
3) G3, Beetroot Extract: Animals received the aqueous beetroot extract at a dose

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of 1.5 mL/animal/day by oral gavage for 45 consecutive days.

4) G4, Co-treatment: Animals were simultaneously administered indomethacin (5 mg/kg body weight/day) and the aqueous beetroot extract (1.5 mL/animal/day) by oral gavage for 45 consecutive days.
5) G5, Therapeutic Beetroot Extract: Animals were first administered indomethacin (5 mg/kg body weight/day) by oral gavage for 30 days, followed by treatment with the aqueous beetroot extract (1.5 mL/animal/day) for the subsequent 15 days.
6) G6, Sucralfate: Animals received indomethacin (5 mg/kg body weight/day) by oral gavage for 30 days, followed by sucralfate (308 mg/kg body weight/day) administered orally for 15 days.

Throughout the experimental period, all animals were monitored daily for general health status, clinical signs, behavioral changes, and any adverse effects. Body weights were recorded at the beginning and at the end of the experiment for all groups to evaluate changes in body weight and for subsequent statistical analysis.

2.4 Dose Selection

2.4.1 Selection of the Experimental Dose of Beetroot Extract

A preliminary dose-selection study was conducted to determine the optimal experimental dose of the aqueous extract of beetroot (*Beta vulgaris* L.). Twenty-five adult female Sprague–Dawley rats (180–200 g) were randomly assigned into five groups (n = 5 per group). The control group received 1 mL of distilled water orally, whereas the remaining four groups were administered the aqueous beetroot extract at doses of 0.5, 1.0, 1.5, and 2.0 mL/animal, respectively, by oral gavage.

At the end of the treatment period, blood samples were collected from the retro-orbital venous plexus, and serum glucose concentrations were determined using a spectrophotometric method. Based on the dose–response relationship, the dose of 1.5 mL/animal produced the most favorable biological response compared with the other tested doses, without any observable adverse effects during the experimental period. Therefore, this dose was selected as the experimental dose and was used throughout the subsequent experiments.

2.4.2 Selection of Therapeutic Doses Used in the Experiment

The therapeutic doses of indomethacin and sucralfate were calculated according to the human-to-animal dose conversion method described by Nair and Jacob [10], which is based on body surface area (BSA) normalization. This method estimates equivalent doses for laboratory animals using species-specific body surface area conversion factors (Km values)

- **Indomethacin**

The standard human therapeutic dose of indomethacin (50 mg/day) was used as the reference dose. Assuming an average adult body weight of 60 kg, the human equivalent dose was calculated as follows

$$\text{Human Equivalent Dose (HED)} = \frac{50\ \text{mg (active drug dose)}}{60\ \text{kg (average human body weight)}} = 0.8\ \text{mg/kg}$$

the equivalent rat dose was then calculated according to the body surface area conversion equation

$$\text{Rat Equivalent Dose} = 0.8 \times \frac{\text{Human Km factor (37)}}{\text{Rat Km factor (6)}} = 5\ \text{mg/kg}$$

Accordingly, an experimental dose of 5 mg/kg body weight/day was selected for the study.

- **Sucralfate**

For sucralfate, the standard human therapeutic dose (3000 mg/day) was used as the reference dose.

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The human equivalent dose was calculated

$$\text{Human Equivalent Dose} = \frac{3000\ \text{mg (active drug dose)}}{60\ \text{kg (average human body weight)}} = 50\ \text{mg/kg}$$

The equivalent rat dose was calculated using the same conversion method

$$\text{Rat dose (mg/kg)} = 50 \times \frac{37}{6} = 308\ \text{mg/kg}$$

Therefore, 308 mg/kg body weight/day was selected as the therapeutic dose of sucralfate. For oral administration, 1000 mg of sucralfate was dissolved in 16 mL of distilled water immediately before dosing.

2.5 Animal Sacrifice and Sample Collection

At the end of the experimental period, the animals were fasted for 12 h, while water was provided ad libitum. Subsequently, the rats were deeply anesthetized by inhalation of chloroform, after which blood samples were collected by cardiac puncture using sterile syringes.

The collected blood samples were transferred into serum separator tubes (gel tubes) and incubated at 37°C for 30 min to allow complete clot formation. The samples were then centrifuged at 3,000 rpm for 15 min, and the resulting serum was carefully separated using micropipettes and transferred into sterile Eppendorf tubes. Serum samples were stored at −20°C until biochemical analyses were performed.

Serum biochemical analyses included the determination of prostaglandin E_2 (PGE_2), reduced glutathione (GSH), superoxide dismutase (SOD) activity, and malondialdehyde (MDA) levels.

2.6 Statistical Analysis

Data were analyzed using GraphPad Prism software (version 10.2.3). The results are presented as the mean ± standard deviation (Mean ± SD). Statistical differences among experimental groups were evaluated using one-way analysis of variance (one-way ANOVA), followed by Duncan's multiple range test for post hoc multiple comparisons. A value of $P \leq 0.05$ was considered statistically significant [11]

Results and Discussion

3.1 Biochemical Findings

Table 1 summarizes the serum levels of superoxide dismutase (SOD), malondialdehyde (MDA), reduced glutathione (GSH), and prostaglandin (PGE_2) in the experimental groups, expressed as mean ± standard deviation (Mean ± SD). Statistical analysis revealed significant differences among the experimental groups ($P \leq 0.05$).

Regarding SOD activity, the indomethacin-treated group (G2) exhibited a significant reduction compared with the control group (G1). In contrast, animals treated with beetroot extract, either alone (G3) or in combination with indomethacin (G4), showed significantly higher SOD activity than the indomethacin group. Partial restoration of SOD activity was also observed in the therapeutic beetroot (G5) and sucralfate (G6) groups, although their values remained lower than those of the control group.

For MDA, a significant increase was observed in the indomethacin-treated group (G2) compared with the control group (G1). Administration of beetroot extract significantly reduced MDA levels in both the preventive (G4) and therapeutic (G5) groups. Sucralfate (G6) also reduced MDA concentrations compared with the indomethacin-treated group, although to a lesser extent than beetroot extract

Regarding reduced glutathione (GSH) levels, the indomethacin-treated group (G2) exhibited a significant decrease compared with the control group (G1). In contrast, administration of beetroot extract alone (G3) maintained GSH levels close to those of the control group. Both the co-

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treatment (G4) and therapeutic beetroot extract (G5) groups showed significant improvement in GSH levels compared with the indomethacin group, although the values remained lower than those observed in the control group. The sucralfate-treated group (G6) also exhibited a partial restoration of GSH levels relative to the indomethacin-treated group.

Regarding prostaglandin (PGE_2) levels, the indomethacin-treated group (G2) exhibited a marked reduction compared with the control group (G1). Administration of beetroot extract, either alone (G3) or in combination with indomethacin (G4), significantly restored PGE_2 levels. The therapeutic beetroot extract group (G5) and the sucralfate-treated group (G6) also demonstrated improved prostaglandin concentrations relative to the indomethacin-treated group, although complete restoration to control values was not achieved.

The biochemical findings were supported by histopathological observations in the stomach and duodenum, as presented below

3.2 Histological results

3.2.1 Stomach

Histopathological examination of the gastric tissue revealed distinct differences among the experimental groups (Figure 2). The control group (G1) exhibited normal gastric architecture with intact mucosal, submucosal, muscular, and serosal layers, together with well-defined gastric pits. In contrast, the indomethacin-treated group (G2) showed extensive necrosis of the gastric mucosa accompanied by marked disruption of the normal tissue architecture.

The beetroot extract-treated group (G3) maintained normal histological features comparable to those observed in the control group, with preservation of the gastric mucosa and underlying tissue layers. In the co-treatment group (G4), gastric tissue exhibited partial preservation of the mucosal architecture, although focal necrotic areas and increased gastric gland secretions were still evident .

The therapeutic beetroot extract group (G5) demonstrated partial restoration of the gastric tissue architecture, with noticeable improvement in mucosal organization compared with the indomethacin-treated group, despite the persistence of mild histopathological alterations. Similarly, the sucralfate-treated group (G6) showed moderate improvement in gastric histology, characterized by partial recovery of the gastric wall architecture with residual alterations remaining mainly within the submucosal layer.

3.2.2 Duodenum

Histopathological examination of the duodenum revealed marked differences among the experimental groups (Figure 3). The control group (G1) exhibited normal duodenal architecture with intact mucosal, submucosal, muscular, and serosal layers. In contrast, the indomethacin-treated group (G2) showed prominent histopathological alterations characterized by mucosal necrosis, pyknosis of epithelial cell nuclei, and increased Brunner's gland secretions

The beetroot extract-treated group (G3) maintained normal duodenal histology comparable to that of the control group, with preservation of the normal tissue architecture. In the co-treatment group (G4), the duodenal tissue exhibited partial preservation of the histological architecture, accompanied by increased intestinal gland secretions and moderate improvement compared with the indomethacin-treated group**.**

the therapeutic beetroot extract group (G5) demonstrated marked restoration of

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the normal duodenal architecture, with improved organization of the intestinal layers and more evident intestinal glands. Likewise, the sucralfate-treated group (G6) showed partial recovery of the duodenal tissue architecture, with preservation of the mucosal and submucosal layers despite the persistence of mild histopathological alterations

4. Discussion

4.1 Biochemical Findings

The findings of the present study demonstrated that indomethacin administration markedly disrupted oxidative homeostasis, as evidenced by enhanced lipid peroxidation and impaired antioxidant defense mechanisms, resulting in significant alterations in all investigated biochemical parameters. This disturbance is primarily attributable to the excessive generation of reactive oxygen species (ROS) following the suppression of prostaglandin synthesis and impairment of gastric mucosal integrity, leading to depletion of endogenous antioxidant defenses and progressive cellular injury. In contrast, treatment with beetroot (Beta vulgaris L.) extract effectively restored oxidative balance and attenuated cellular damage, most likely owing to its high content of betalains, phenolic compounds, and other bioactive phytochemicals with potent antioxidant properties. These protective effects were reflected in the concurrent improvement of the investigated biochemical biomarkers

4.1.1 Superoxide Dismutase (SOD)

The present study demonstrated a significant reduction in superoxide dismutase (SOD) activity in the indomethacin-treated group compared with the control group, indicating impairment of the enzymatic antioxidant defense system as a consequence of oxidative stress. These findings are consistent with those reported by [2,12], who likewise observed a marked decline in SOD activity following indomethacin administration. In contrast, treatment with beetroot (Beta vulgaris L.) extract significantly restored SOD activity, suggesting that its antioxidant constituents contribute to strengthening endogenous antioxidant defenses and mitigating oxidative damage.

4.1.2 Malondialdehyde (MDA)

A significant elevation in malondialdehyde (MDA) levels was observed in the indomethacin-treated group, reflecting increased lipid peroxidation and membrane damage. These findings are in agreement with those reported by[13,12] who similarly documented elevated MDA levels following indomethacin administration. Conversely, treatment with beetroot (Beta vulgaris L.) extract significantly reduced MDA concentrations compared with the indomethacin-treated group, indicating its protective role in limiting oxidative membrane damage and preserving cellular integrity.

4.1.3 Reduced Glutathione (GSH)

A significant depletion of reduced glutathione (GSH) was observed in the indomethacin-treated group, indicating consumption of one of the major non-enzymatic antioxidants during the cellular response to oxidative stress. These findings are consistent with those reported by [14,15] who likewise documented a marked reduction in GSH levels following indomethacin administration. Treatment with beetroot (Beta vulgaris L.) extract significantly restored GSH levels, demonstrating its ability to re-establish redox homeostasis and reinforce the endogenous antioxidant defense system.

4.1.4 Prostaglandin E_2 (PGE_2)

A significant reduction in prostaglandin E_2 (PGE_2) levels was observed in the indomethacin-treated group, primarily as a result of cyclooxygenase-1 (COX-1) and

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cyclooxygenase-2 (COX-2) inhibition, which compromised the protective mechanisms of the gastric mucosa. These findings are consistent with those reported by [16,3]. In contrast, treatment with beetroot (Beta vulgaris L.) extract significantly restored PGE_2 levels compared with the indomethacin-treated group, suggesting its beneficial role in preserving gastric mucosal integrity and reducing tissue injury associated with oxidative stress and inflammation.

Collectively, the biochemical findings indicate that indomethacin markedly disrupted redox homeostasis, whereas beetroot extract effectively restored this balance by enhancing antioxidant defense, reducing lipid peroxidation, and maintaining PGE_2 levels. These coordinated biochemical improvements provide a plausible explanation for the protective and therapeutic effects of beetroot extract against indomethacin-induced toxicity observed in the present study.

4.2 Histopathological Findings

4.2.1 Stomach

The histopathological alterations observed in the stomach following indomethacin administration are consistent with the well-established mechanism of NSAID-induced gastric injury. Inhibition of cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) suppresses the synthesis of cytoprotective prostaglandins, thereby compromising gastric mucosal defense and increasing tissue susceptibility to oxidative injury. These mechanisms have been extensively documented by [4,3] whose findings closely parallel the histopathological changes observed in the present study.

Administration of beetroot (Beta vulgaris L.) extract effectively ameliorated gastric tissue injury, with the preventive regimen producing a more pronounced protective effect than the therapeutic regimen. This difference may be attributed to the ability of beetroot bioactive constituents to limit oxidative and inflammatory damage before irreversible tissue injury develops, whereas post-injury administration primarily facilitates tissue recovery rather than complete prevention of damage. These observations are in agreement with the findings of [6,17] , who reported comparable gastroprotective effects of beetroot-derived phytochemicals.

Although sucralfate improved gastric histological recovery compared with indomethacin treatment alone, its effect was less pronounced than that observed with beetroot extract. This difference may reflect the distinct mechanisms of action of the two treatments, as sucralfate primarily acts by forming a protective barrier over the damaged mucosa, whereas beetroot extract appears to provide broader cytoprotective effects through attenuation of oxidative injury and improvement of the cellular environment required for tissue repair.

4.2.2 Duodenum

The histopathological findings in the duodenum closely paralleled those observed in the gastric tissue, confirming that indomethacin-induced gastrointestinal injury extends beyond the stomach to involve the small intestine. This widespread tissue damage is consistent with the known adverse effects of non-steroidal anti-inflammatory drugs (NSAIDs), which impair mucosal defense mechanisms and increase susceptibility to intestinal injury. Similar histopathological observations have been reported by [4,3] in experimental models of NSAID-induced intestinal damage.

Administration of beetroot (Beta vulgaris L.) extract preserved normal duodenal histology when administered alone and markedly improved tissue recovery in both

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the preventive and therapeutic treatment groups. The more pronounced restoration observed following therapeutic administration suggests that beetroot extract not only limits tissue injury but also promotes the regenerative processes required for mucosal repair. These findings are in agreement with those of [6,18], who highlighted the protective and restorative potential of beetroot-derived bioactive compounds in gastrointestinal tissues.

Although sucralfate also enhanced duodenal tissue recovery compared with indomethacin treatment alone, complete restoration of the normal histological architecture was not achieved within the experimental period. In comparison, beetroot extract produced a more comprehensive histological response, supporting its potential as a natural therapeutic agent for reducing indomethacin-induced intestinal injury and facilitating mucosal healing.

These findings further suggest that the protective effect of beetroot extract is not solely attributable to its antioxidant activity. Indomethacin-induced inhibition of cyclooxygenase (COX-1 and COX-2) reduces prostaglandin E_2 (PGE_2) synthesis, thereby impairing mucus and bicarbonate secretion, decreasing mucosal blood flow, and increasing susceptibility to inflammatory injury. Restoration of PGE_2 levels following beetroot extract administration may therefore contribute to preserving mucosal integrity by supporting both antioxidant defenses and physiological mechanisms involved in gastric and duodenal mucosal protection. This integrated effect may explain the close association observed between the biochemical improvements and the histopathological recovery in the present studyOverall, the biochemical and histopathological findings were highly consistent in explaining both the toxic effects of indomethacin and the protective and therapeutic actions of beetroot (Beta vulgaris L.) extract. The histological alterations observed in the stomach and duodenum were closely associated with disturbances in oxidative stress biomarkers, whereas the restoration of tissue architecture paralleled improvements in antioxidant status and prostaglandin E_2 (PGE_2) levels. This close association between biochemical and histopathological outcomes provides strong evidence that the beneficial effects of beetroot extract extend beyond the attenuation of tissue injury to the modulation of the underlying biological mechanisms involved in oxidative stress and mucosal protection. Collectively, these findings support the potential application of beetroot extract as a promising natural adjunctive agent for the prevention and management of indomethacin-induced gastrointestinal toxicity.

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Table 1. Effects of beetroot extract, indomethacin, and sucralfate on serum oxidative stress biomarkers and prostaglandin E_2 (PGE_2) levels in experimental rats.

Groups	SOD(ng/mL)	MDA(ng/mL)	GSH(µg/mL)	**PGE** (pg/mL)
G1	6.60 ± 0.55 a	289.00 ± 4.95 e	90.78 ± 0.91 a	371.16 ± 3.94 a
G2	3.66 ± 0.50 c	538.48 ± 60.67 a	33.95 ± 2.00 f	187.27 ± 5.60 d
G3	6.38 ± 0.47 a	266.43 ± 15.99 f	81.90 ± 2.21 b	369.39 ± 6.06 a
G4	5.82 ± 0.49 a	338.90 ± 8.22 d	69.83 ± 1.15 c	307.67 ± 8.72 b
G5	5.60 ± 0.14 a	438.15 ± 8.79 b	61.00 ± 2.26 d	263.18 ± 4.81 c
G6	5.11 ± 0.15 b	411.18 ± 6.40 c	52.95 ± 2.34 e	314.66 ± 4.59 b

- Data are presented as mean ± standard deviation (Mean ± SD). Different superscript letters (a–f) within the same column indicate statistically significant differences according to Duncan's multiple range test at $P \leq 0.05$.

G1= Control, G2= Indomethacin, G3= Beetroot Extract, G4=Indomethacin + Beetroot Extract, G5=Therapeutic Beetroot Extract, G6= Sucralfate.

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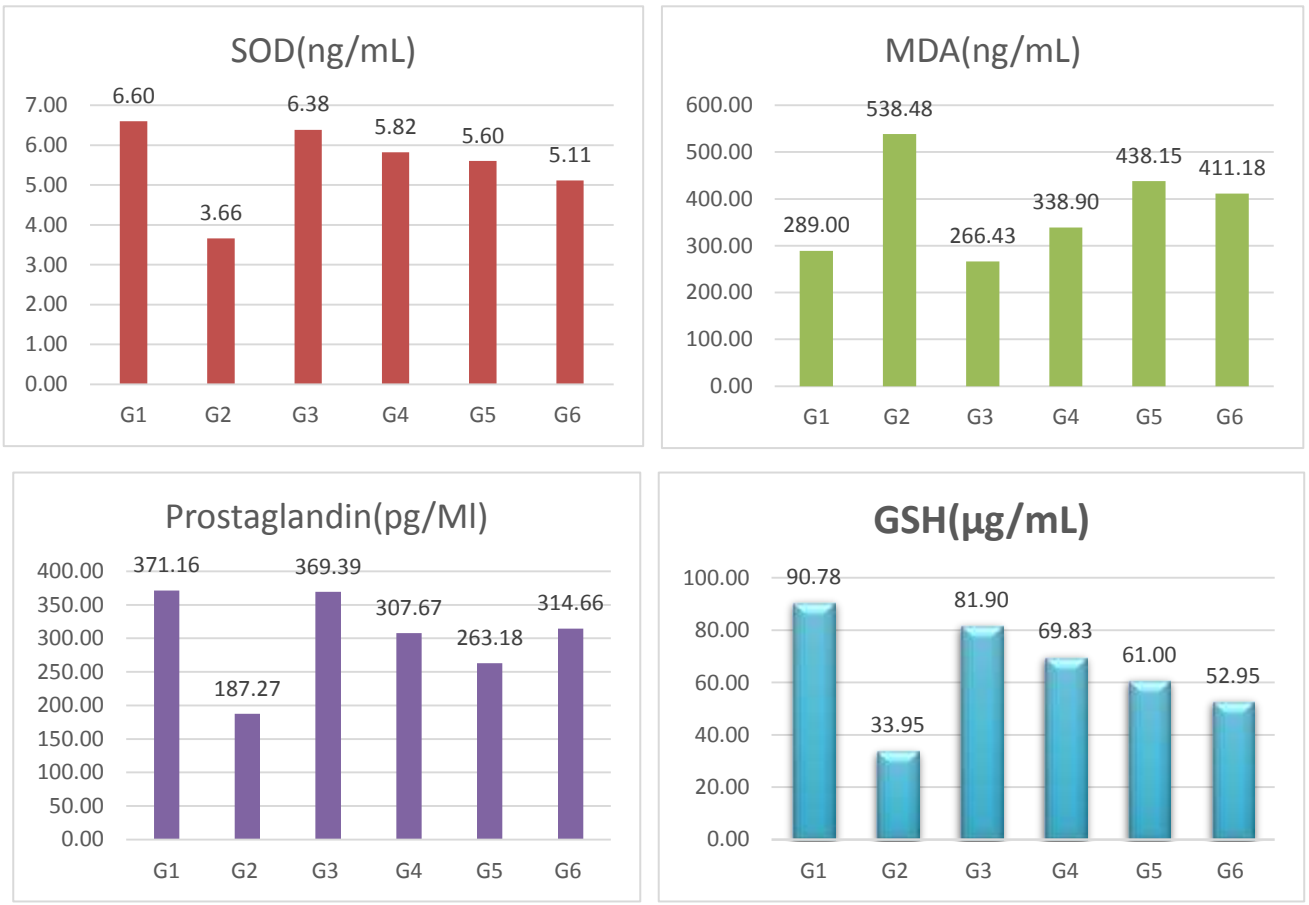


figure 1. Effects of beetroot extract, indomethacin, and sucralfate on serum superoxide dismutase (SOD), malondialdehyde (MDA), reduced glutathione (GSH), and prostaglandin levels in experimental rats. G1= Control, G2= Indomethacin, G3= Beetroot Extract , G4=Indomethacin + Beetroot Extract , G5=Therapeutic Beetroot Extract ,G6= Sucralfate

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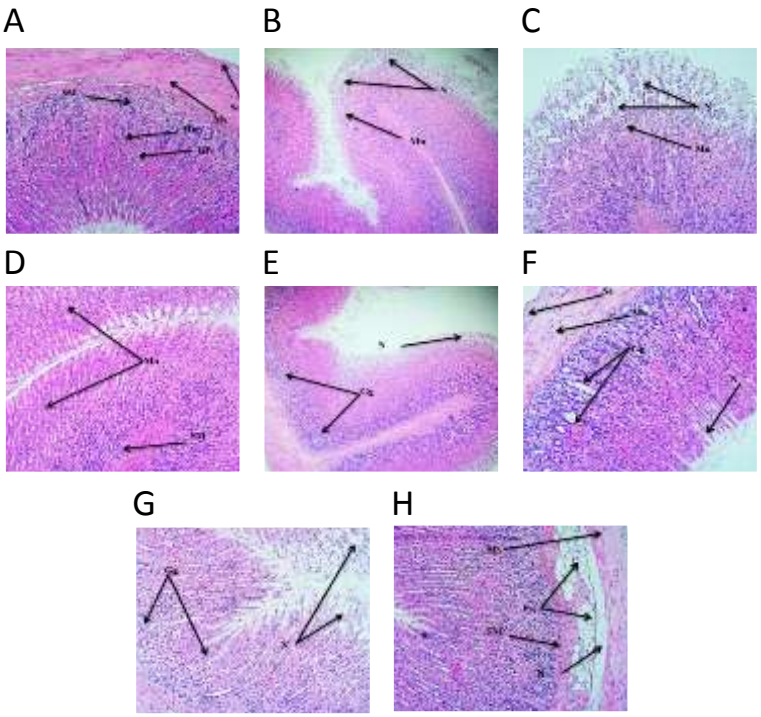


Figure 2. Representative photomicrographs of gastric tissues from the experimental groups stained with hematoxylin and eosin (H&E). G1: Control; G2: Indomethacin; G3: Beetroot extract; G4: Indomethacin + Beetroot extract; G5: Therapeutic beetroot extract; G6: Sucralfate. The arrows indicate the principal histopathological features observed in each group

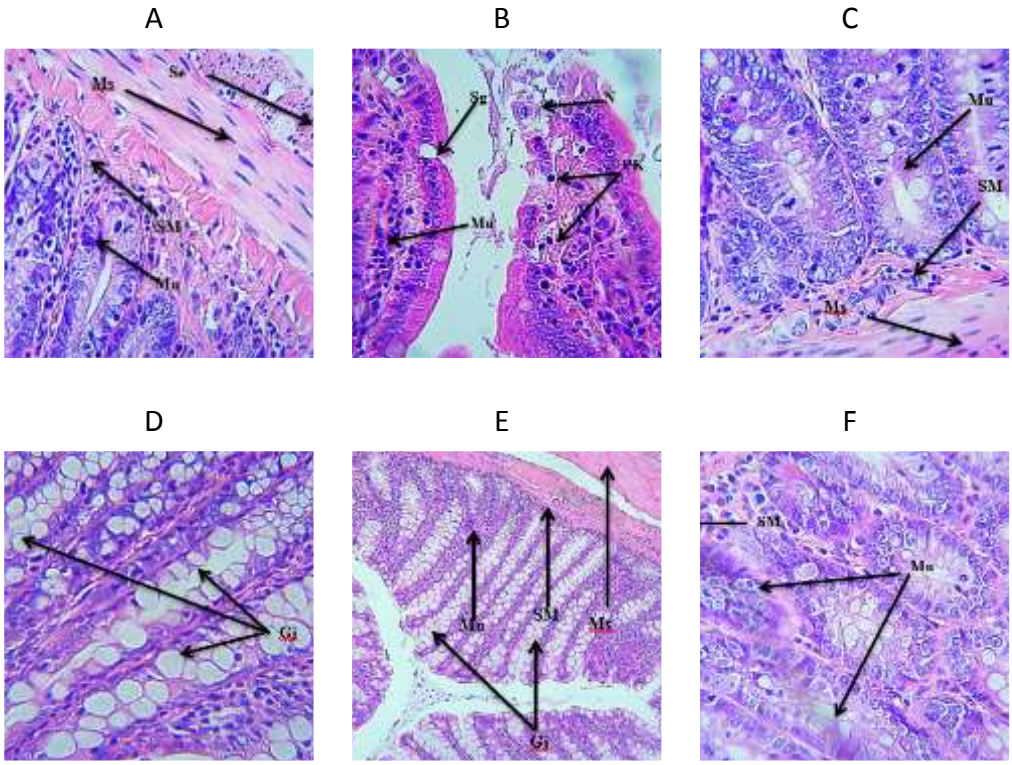


Figure 3. Representative photomicrographs of duodenal tissues from the experimental groups stained with hematoxylin and eosin (H&E). G1: Control; G2: Indomethacin; G3: Beetroot extract; G4: Indomethacin + Beetroot extract; G5: Therapeutic beetroot extract; G6: Sucralfate. Arrows indicate mucosal necrosis, pyknosis, increased glandular secretions, and restoration of the normal.

Conclusion

1. Indomethacin induced marked oxidative stress and histopathological damage in both the stomach and duodenum of experimental rats.
2. Beetroot (*Beta vulgaris* L.) extract exhibited a favorable safety profile when administered alone, with no detectable adverse biochemical or histopathological effects.
3. Beetroot extract demonstrated both preventive and therapeutic effects by improving oxidative stress biomarkers and attenuating histopathological damage induced by indomethacin.

The therapeutic efficacy of beetroot extract was comparable to, and in some parameters exceeded, that of sucralfate, supporting its potential as a promising natural adjunctive agent for reducing indomethacin-induced gastrointestinal toxicity.

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