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INVESTIGATING THE GASTROPROTECTIVE EFFECT OF MORINA LONGIFOLIA AGAINST INDOMETHACIN-INDUCED GASTRIC ULCER

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1. INTRODUCTION

Peptic ulcer disease (PUD) can be defined as the presence of a deep destruction of the stomach lining or mucosa or duodenum, reaching beyond the muscularis mucosa, specifically to the muscle layer owing to the environmental gastric acid synthesis.[1] The primary cause of peptic ulcer is infection with Helicobacter pylori (*H. pylori*), a bacterium that weakens the protective mucosal lining of the stomach, making it susceptible to damage by stomach acid.[2] Another major cause is the prolonged use of nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin, ibuprofen, and naproxen, which interfere with the production of prostaglandins, compounds that help maintain the protective mucus barrier.[3,4] Peptic ulcer symptoms can range from mild to severe, but they usually include nausea, bloating, heartburn, searing sensation in the stomach (which is worst when the stomach is empty or at night), vomiting, and lack of appetite. Some of the complications that can develop in more severe cases include bleeding ulcers, which can cause blood in the stool and vomiting, perforation, which is characterized by severe abdominal pain caused by the ulcer creating a hole in the intestines or stomach, and gastric outlet obstruction, which is characterized by food blockage and persistent vomiting.[5] Study data suggest the prevalence rate of this disease covers four million people worldwide annually and has an estimated lifetime prevalence of 5−10% in the general population. While the overall occurrence of PUD has declined significantly over the last several decades, but the occurrence of its consequences has stayed the.[6] In 2019, the global prevalence of PUD was approximately 8.09 million, representing a 25.82% increase from 1990.[7] NSAIDs are well

documented as producing upper gastrointestinal (GI) problems, ranging from dyspeptic symptoms in up to 40% to life-threatening complex ulcers (haemorrhage, perforation, or pyloric blockage). Gastroduodenal (GD) damage associated to NSAID usage is regarded to be the most prevalent and, in aggregate, the most devastating consequence of any pharmacological treatment. The incidence of peptic ulceration in chronic NSAID users is 20–30%, with gastric ulcers roughly six times more prevalent than duodenal ulcers. The risk of hospitalization for major upper GI problems (bleeding or perforation) with NSAID usage is 1–2% per year.[8]

NSAIDs can leads to generation of ulcer through disrupting the natural stomach mucosal barrier of bicarbonate and hydrophobic mucus and it can be achieved by two mechanism. The main mechanism is caused by suppression of the constitutive cyclo-oxygenase (COX) isoenzyme, COX-1, which disrupts prostaglandin production regardless of the route of administration. Prostaglandins have a critical protective function in the stomach by preserving mucosal blood flow, promoting mucus and bicarbonate production, and controlling mucosal cell turnover and repair. The absence of prostaglandin inhibition makes the stomach more susceptible to gastric acid injury.[9] The management of NSAID-induced peptic ulcers focuses on reducing gastric acid secretion, enhancing mucosal protection. Currently several pharmacological approach includes proton pump inhibitors (PPIs), histamine H_2-receptor antagonists (H_2RAs), prostaglandin analouges, antacids, and mucosal protective agents are used in the management of this disease.[10]

Emerging trends in society for the use of natural bioactive compound in management of peptic ulcer have gained attention. Researchers focus on naturally bioactive compound that explored as alternative or adjunctive therapies for this disease due to their anti-inflammatory, antioxidant, cytoprotective, and acid-suppressing properties. Many plant-derived compounds can complement conventional treatments like PPIs, H_2RAs, and mucosal protectants, either by enhancing gastric mucosal defense or reducing gastric acid secretion. Morsy et al. demonstrated the defensive effects of Curcumin on the digestive mucosa in rat, particularly against in indomethacin-caused gastric ulcer. The study result demonstrate that Curcumin protect the rats gastric mucosa against indomethacin-induced gastric ulceration possibly, at least in part, by enhancement of the gastric mucosal barrier and reduction in acid secretory parameters in addition to antioxidant and antiapoptotic activities.[11] Similarly, Al-Zubaidy et al. demonstrated that the extract from *Capparis spinosa* showed protective effects on the stomach, potentially attributed to its ability to enhance prostaglandin E2 (PGE2). This

enhancement of PGE2 is suggested to act as anti-inflammatory agent by preventing neutrophil infiltration. These results indicate the potential utility of *C. spinosa* extract as a natural remedy for the treatment of gastric ulcer, highlighting its beneficial influence on mucosal defense mechanism within the stomach and duodenum.[12] *Morina longifolia* commonly known as the Himalayan whorlflower or long-leaved whorl flower, Considered as a flowering plant association of the family Caprifoliaceae. It is indigenous to the foothills of the Himalayas. They serve various medicinal purposes, functioning as emetic, digestive & stomachic agents, particularly in the prophylaxis of digestive disorders. It is characterized by its spiny-edged leaves and a lengthy inflorescence, which exhibit whitish pink hues. Research study on its pharmacological properties indicates that rich in phenylpropanoid glycosides, shows significant antibacterial, antitumor, antiviral, and antioxidant properties.[13]

2. MATERIAL AND METHODS

2.1 Drugs and Chemical

Indomethacin and omeprazole was purchased from a local pharmacy. Kits for assessing inflammatory markers, specifically TNFα and IL6, was obtained from Thermo Fisher Scientific. Additional chemicals, including thiobarbituric acid (TBA), trichloroacetic acid (TCA), 5,5-dithiobis(2-nitrobenzoic acid) (DTNB), and others, was procured from certified chemical suppliers (CDH, NEW DELHI).

2.2 Collection and Authentication of Plant Material

Fresh leaves of *Morina longifolia* plant was collected from the herbal garden valley of flower, National park, Uttrakhand. Proper precaution was taken during the plant collection. The collected plant parts was cleaned with normal tap water and kept in shadow cool place and sent to Botanical garden of India republic, New Delhi for authentication.

2.3 Animal Procurement

For this study, 30 animal were divided into 5 groups, each group comprise of 6 animals. After approval of study from institutional Animal Ethics Committee (IAEC) Wistar rats of weight 180 and 220 grams were obtain from All India Institute of Medical Sciences (AIIMS) New Delhi. Obtained animals were quarantine for 10 days, provided a standard diet and have access to water to ensure their nutritional needs are met. Animal were kept in a controlled environment at 25^0C temperature and 50- 60% relative humidity, maintaining a 12-hour dark/light cycle.

2.4 Extract Preparation

Leaves were washed with water to remove any dirt or contaminants. It *was* air-dried and weighed, then grounded into a fine powder using a grinder. Then the powder was shieved through 60 mesh size of shieve. The residual portion were again crushed to fine powder until these were form uniform size. Hydroalcoholic (80:20) preparation were made. All the component of Soxhlet apparatus was assembled and it was set at 70^{o} C.[14] After 7 hrs the extraction process was completed and hydroalcoholic plant extract was settled in round bottom flask. The extracted mixture was set on rotary evaporator for 2 hrs to removed excess solvent from extract. The final plant extract was obtained.

2.5 Pre-liminary examination of extract

Several test were performed for the confirmation of phytoconstituent including triterpenoids, alkaloids, carbohydrates, and flavonoids.[15]

2.6 Experimental design

The study design comprise of 5 group consisting of 6 animal were placed in each group. Group 1 considered as normal control that received normal saline *2 ml/kg, orally* p.o. for 15 days. Group 2 were considered as diseased control that received single dose Indomethacin (40mg/kg, orally) for 15 alternate days to induce ulcer. Group 3 were considered as treatment group 1 that received extract of *Morina longifolia* (200 mg/kg, orally) + Single dose Indomethacin (40mg/kg, orally) p.o. for 15 days. Group 4 were considered as treatment group 2 that received extract of *Morina longifolia* (400 mg/kg, orally) + Single dose Indomethacin (40mg/kg, orally) for 15 days. Group 5 were considered as standard group that received Omeprazole (20 mg/kg, orally) + Single dose Indomethacin (40mg/kg, orally) for 15 days.

Plant extract was dissolved in DMSO solution and administered orally for 15 days according to the body weight of animal. The body weight of all the animals were recorded at every 7th day. After the completion of the study i.e 15th day, the rat were anesthetized by giving thiopental (40 mg/kg, i.p.) injection in order to obtain blood sample through retro-orbital route to prepare serum. The collected blood was centrifuged at 3000 rpm for 15 minute to get serum. The obtained serum was used for the evaluation of inflammatory markers such as TNF-α & IL-6. After that all the animal were scarified by decapitation and stomach from all animal from all groups (n=30) were excised and stomach content was collect in clean centrifuge tube. One stomach sample from each group (n=5) were stored in 10% formalin solution for histopathological analysis & Ulcer index measurement. The remaining sample were used to prepare tissue homogenate for the biochemical estimation such as superoxide dismutase

(SOD), malondialdehyde (MDA), catalase (CAT), reduced glutathione (GSH), glutathione reductase (GR) and glutathione peroxidase level (GPx).

2.7 Measurement of Gastric pH

The contents of each stomach was extracted by opening along the greater curvature, and the gastric fluid will be collected into a centrifuge tube. Subsequently, collected samples will undergo centrifugation at 1000 rpm for 10 minutes, and used for pH measurement.

2.8 Tissue Homogenate Preparation

Homogenate of the isolated stomach were prepared for the study of molecular antioxidant parameters. Homogenate was made in 10% homogenization buffer. The separated stomach was placed into homogenization tube containing 10 ml of prepared buffer and homogenize tissue at 800-1000 rpm for 5 minute. Following that, supernatant was transferred into a centrifuged tube and utilized to estimate LPO level and remaining supernatant was again homogenize at at 3000-4000 xg for 20 minute at a maintained temperature of 4^{o}C to get post mitochondrial supernatant (PMS). The PMS was then utilized to measure GSH, GPx, GR, SOD, & CAT level.

2.9 Biochemical Oxidative Parameters

Firstly protein content of each sample was estimated through the procedure followed by Lowry et al.[16] Lipid peroxidation assay was carried out in tissue homogenate by methodology describe by ohkhawa et al.[17] The GSH level was determined by procedure described by Jollow et al.[18] The Mohandas et al. approach was used to calculate the GR.[19] The Marklund approach was used to quantify SOD activities[20], whereas the Claiborne method was used to measure the amount of CAT.[21]

2.10 Inflammatory Cytokines Markers (TNF-α, IL-6)

Evaluation of inflammatory cytokines like TNF-α, IL-6 was done through the ELISA kit as per instruction given by manufacturer for the experiment.

2.11 Ulcer Index Measurement

The average ulcer score for each group was determined by calculating the mean number of ulcers of one stomach of one rat in each group. Using these scores, an Ulcer Index (UI) was then derived by multiplying the ulcer score of each group by 100. Following this, the net preventive index was computed by using the formula: 100% × (UI of the ulcer-only group −

UI of the treated group) / UI of the ulcer-only group.

2.12 Histopathological analysis

The isolated stomach samples was preserved on a paraffin block and by using microtome, 3-5 µm thickness of stomach tissue section were prepared. The slides of these sections were employing hematoxylin and eosin (H&E) dye & prepared for further histopathological analysis using a 40x magnification microscope.

2.13 *Statistical Analysis*

Result interpretation was done by using GraphPad Prism software (version 10.2). in this software for the analysis and comparison of results way, ANOVA was used followed by Tukey's post hoc test to determine statistical significance. The analysed results were compared and reported as ± standard error mean (SEM). $P<0.05$ was set minimum criteria for the results to be statistically significant.

3. RESULTS

3.1 Pre-liminary phytoconstituent assessment

Result of Phytoconstituent assessment of *Morina longifolia* extract described in table 1.

Phytoconstituent	Test	Colour formation	Hydroalcoholic Extract
Alkaloids	Mayers test	Creamy white precipitate	+
Flavonoids	Alkaline reagent test	yellow tint turns colourless	+
Tannins	Ferric chloride test	Brownish colour, blue-black	±
Saponins	Froth test	Froth (foam)	±
Glycosides	Keller -Kailani test	Violet or bluish-green	±
Phenolics	Ferric chloride test	green or bluish tint	±
Terpenoids	Salkowski test	reddish-brown	+++
Steroids	Liebermann-Burchard test	Blue or green tint	+++

Keywords: (+) Indicates presence, (±) indicates trace amounts, (++) indicates high presence, (+++) indicates very high presence, (-) Indicates absence ± Trace amount.

3.2 Effect on Gastric pH

Administration of indomethacin at dose of 40 mg/kg cause a reduction in gastric pH of group-2 animals. Administration of plant extract at dose of 200 mg/kg in group-3 slightly increase the gastric pH and Administration of plant extract at dose of 400 mg/kg in group-4 significantly increase the gastric pH whereas the omeprazole standard drug administration in group-5 also increases the gastric pH at optimum level.

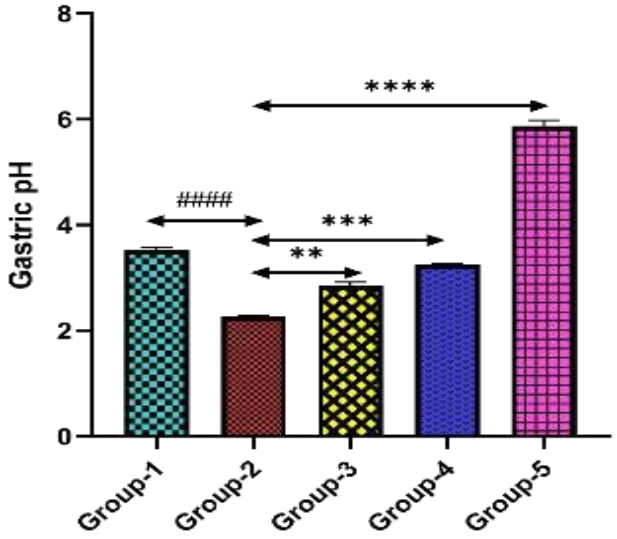

Fig. 3.1. Represent the gastric pH level. Group-2 shows→ ####*p*<0.0001 when compared it with group-1. Group-3 shows→ ***p*<0.01 when compared it with group-2. Group-4 shows→ ****p*<0.001 when compared it with group-2. Group-5 standard treatment shows→ *****p*<0.0001 when compared it with group-2.

3.3 Biochemical Oxidative Stress Parameter

3.3.1 MDA Estimation

MDA level was increased in group-2 (Diseased control) when equated it to Group-1 (Normal control). Whereas administration of extract at 200 mg/kg in Group-3 (Treatment control-1) significantly reduce MDA level when equated with Group-2. Administration of extract at dose of 400 mg/kg in Group-4 (Treatment control-2) significantly reduce the MDA level) equated with Group-2. Omeprazole administration at dose of 20 mg/kg in Group-5(Standard control) significantly showed lowers level of MDA.

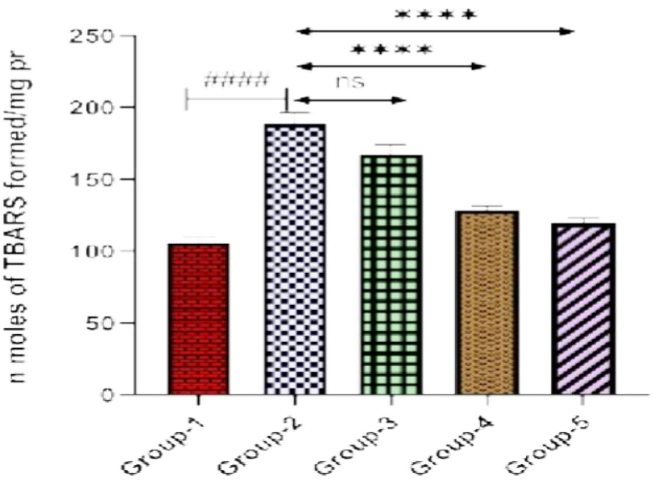

Fig. 3.2: Represent the effect of extract on MDA level against indomethacin induced gastric ulcer in Wister rat. Group-2 when equated with Group-1 shows →$^{####}$*p*<0.001.

Group-3 when equated with Group-2 shows→ ns *p*>0.05. Group-4 when equated with Group-2→***p*<0.0001. Group-5 when equated with Group-2 shows →*****p*<0.0001.**

3.3.2 SOD Estimation

Figure 3.3 Demonstrates the SOD level in the tissue homogenate of Group-1, Group-2, Group-3, 4, and 5. Group-2 shows reduction in level of SOD as equated to the group-1. plant extract administration at dose of 200 mg/kg in Group-3 significantly elevate the SOD level as equated with Group-2. Similarly, plant extract administration → 400 mg/kg in groups-4 significantly elevate the SOD level as equated to the Group-2. Omeprazole administration on Group-5 → 20 mg/kg shows significantly elevation in the SOD level as equated to the Group-2.

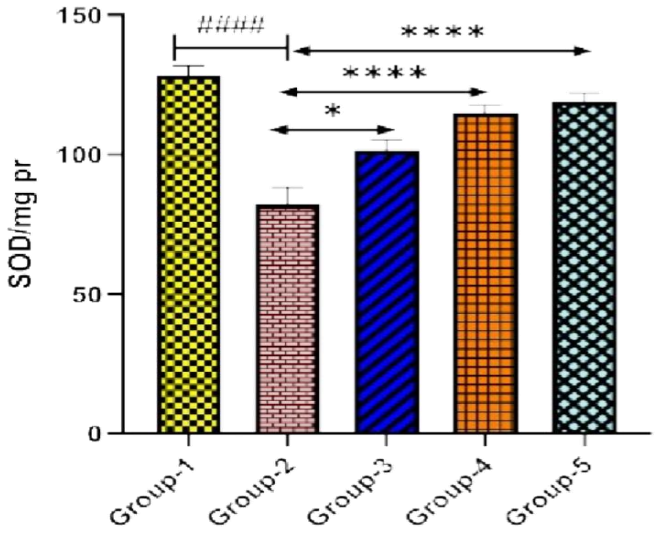

Fig. 3.3: Represent the effect of extract on SOD level against gastric ulcer in Wister rat. Group- 2 when equated with Group-1 shows →$^{\#\#\#\#}$*p*<0.001. Group-3 when equated with Group-2 shows →p*<0.01. Group-4 when equated with Group-2→*****p*<0.0001. Group-5 when equated with Group-2 shows →*****p*<0.0001.**

3.3.3 Catalase (CAT) Estimation

Figure 3.4 Demonstrate the CAT level in the tissue homogenate of Group-1, Group-2, Group-3, 4, and 5. Group-2 shows reduction in level of CAT as equated to the group-1. Plant extract administration at dose of 200 mg/kg in Group-3 significantly elevate the CAT level as equated with Group-2. Similarly, plant extract administration → 400 mg/kg in groups-4 significantly elevate the CAT level as equated to the Group-2. Omeprazole administration on Group-5 → 20 mg/kg shows significantly elevation in the CAT level as equated to the Group-2.

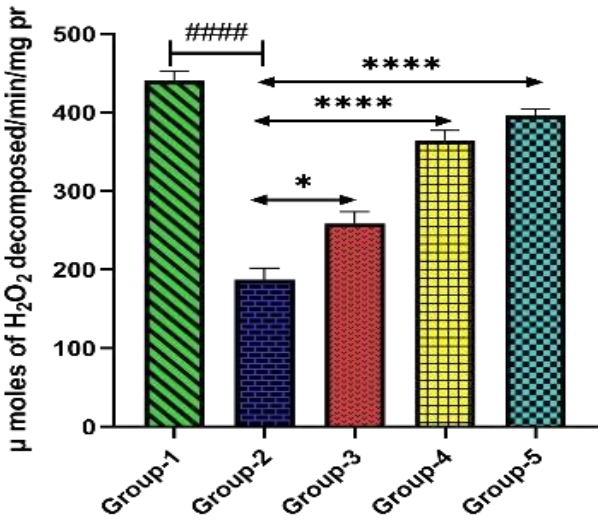

Fig. 3.4: Represent the effect of extract on CAT level against gastric ulcer in Wister rat. Group- 2 when equated with Group-1 shows →$^{####}p$<0.001. Group-3 when equated with Group-2 shows →*p<0.01. Group-4 when equated with Group-2 →**p<0.0001. Group-5 when equated with Group-2 shows →****p<0.0001.**

3.3.4 GSH Estimation

GSH level was decreased in Group-2 when equated it to Group-1. Whereas administration of extract at 200 mg/kg in Group-3 significantly elevate GSH level when equated with Group-2. Administration of extract at dose of 400 mg/kg in Group-4 significantly elevate the GSH level equated with Group-2. Omeprazole administration at dose of 20 mg/kg in Group-5 significantly showed elevated level of GSH.

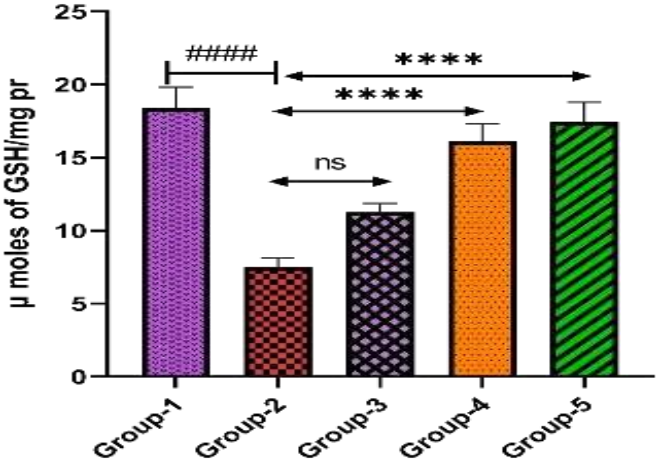

Fig. 3.5: Represent the effect of extract on GSH level against gastric ulcer in Wister rat. Group- 2 when equated with Group-1 shows →$^{####}p$<0.001. Group-3 when equated with Group-2 shows →ns p>0.05. Group-4 when equated with Group-2 →**p<0.0001. Group-5 when equated with Group-2 shows →****p<0.0001.**

3.4 Inflammatory Cytokines Estimations

3.4.1 TNF-α level

TNF-α level was increase in Group-2 when equated it to Group-1. Whereas administration of extract at 200 mg/kg in Group-3 significantly reduce TNF-α level when equated with Group-2. Administration of extract at dose of 400 mg/kg in Group-4 significantly lowers the TNF-α level equated with Group-2. Omeprazole administration at dose of 20 mg/kg in Group-5 significantly showed reduction in level of TNF-α.

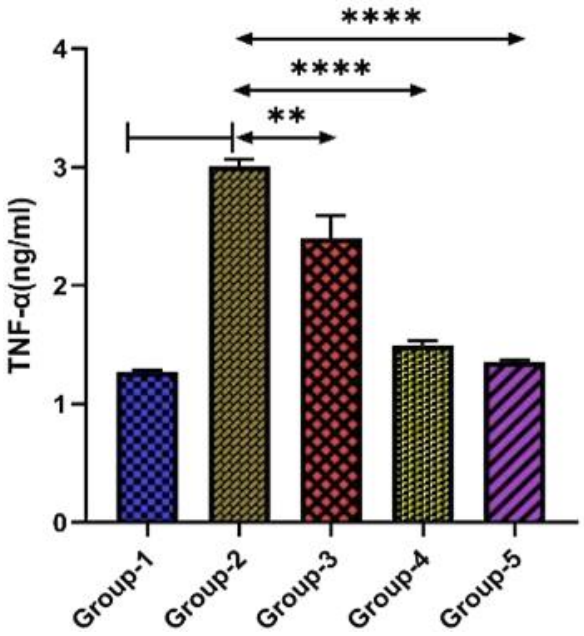

Fig. 3.6. Represent the effect of extract on TNF-α level against indomethacin induced gastric ulcer in Wister rat. Group-2 when equated with Group-1 shows →$^{####}$*p*<0.001. Group-3 when equated with Group-2 shows →*p*<0.01. Group-4 when equated with Group-2→*****p*<0.0001. Group-5 when equated with Group-2 shows →*****p*<0.0001.**

3.4.2 IL-6 Level

IL-6 level was increased in Group-2 when equated it to Group-1. Whereas administration of extract at 200 mg/kg in Group-3 reduce IL-6 level when equated with Group-2. Administration of extract at dose of 400 mg/kg in Group-4 significantly reduce the IL-6 level equated with Group-2. Omeprazole administration at dose of 20 mg/kg in Group-5 significantly showed reduction in level of IL-6.

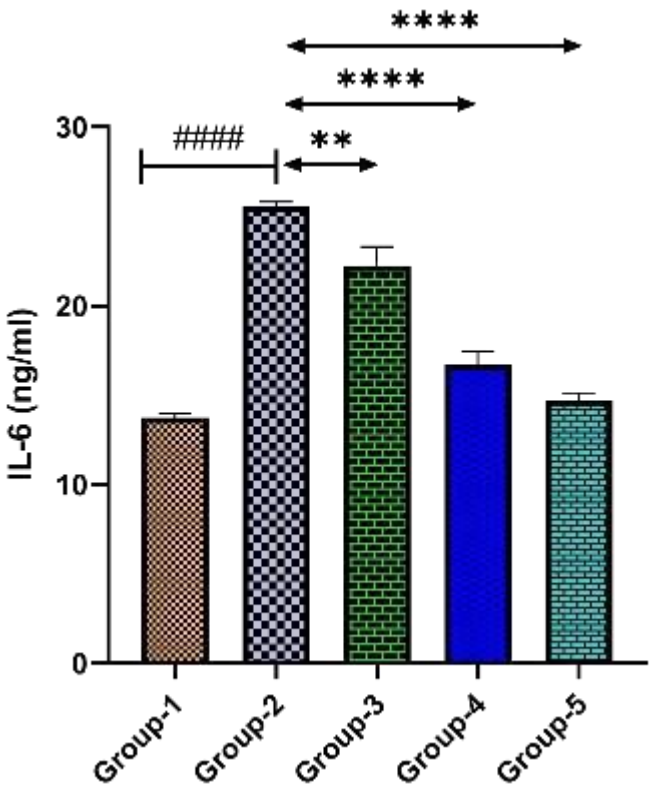

Fig. 3.7: Represent the effect of extract on IL-6 level against indomethacin induced gastric ulcer in Wister rat. Group-2 when equated with Group-1 shows →$^{####}$*p*<0.001. Group-3 when equated with Group-2 shows →*p*<0.01. Group-4 when equated with Group-2 →*****p*<0.0001. Group-5 when equated with Group-2 shows →*****p*<0.0001**.

3.5 Ulcer Index Measurement

The findings reveal a decrease in the ulcer scores of *Morina longifolia* treated groups in comparison to that of the indomethacin only group. At the time of survey, the ulcer score of group- 3 was (3.2 ± 1.0) and group-4 (2.8 ± 0.7) as compared to group-2 (7.5 ± 1.2), indicating a significant reduction in ulcer severity *Morina longifolia* (p<0.05).

Table 3.2: Represent the Ulcer index.

GROUP	Ulcer Score	Ulcer Index
Normal control	0.0 ± 0.0	--
Disease control	7.5 ± 1.2	750
Disease control +Morina longifolia 200 mg/kg	3.2 ± 1.3	320
Disease control +Morina longifolia 400 mg/kg	2.8 ± 0.7	280
Disease control + Omeprazole 20 mg/kg	1.8 ± 0.4	180

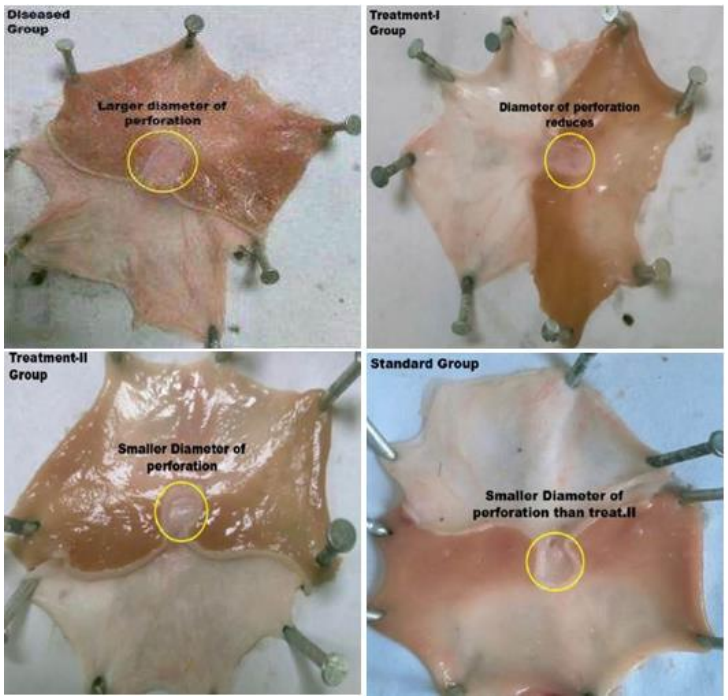

Fig. 3.8: Represent the ulcer diameter in group 2,3,4&5.

3.6 Histopathological Analysis

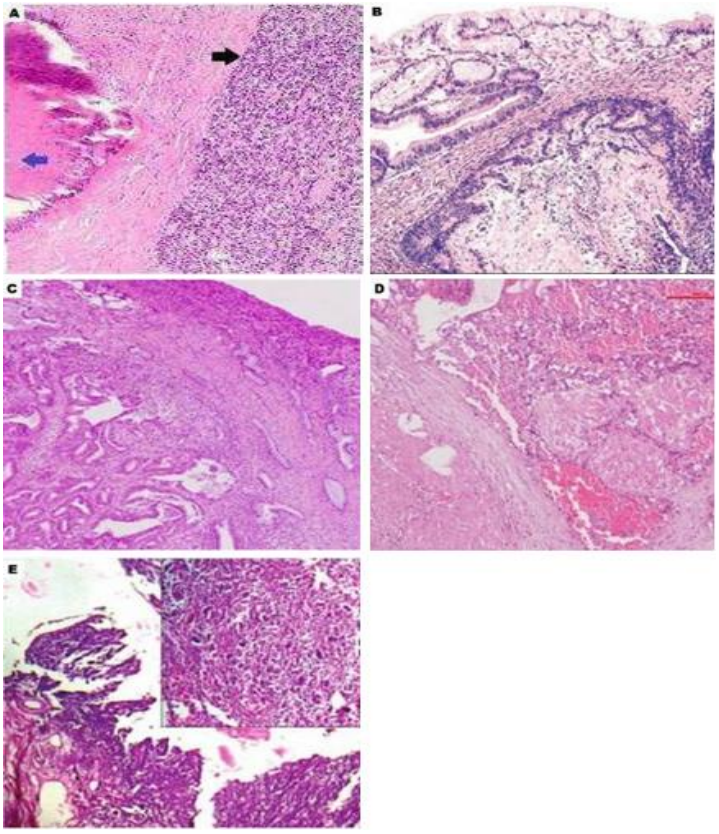

Fig. 3.9: Represent the histopathological structural change inside the stomach in normal, diseased, treatment & standard control group. (A) Stomach histology of normal control group shows normal microscopic architecture with normal lumen and glands,

without any sign of abnormalities. On the other hand, (B) Diseased group shows severe inflammatory reaction, manifested by submucosal edema with local mononuclear leucocytic infiltration (mainly lymphocytes and few eosinophiles) in the layers of stomach. (C) Administration of plant at dose of 200 mg/kg in treatment control-I shows reduction in inflammation and edema and tissue turns to recover into normal cell architecture. (D) Administration of plant at dose of 400 mg/kg in treatment control-II shows very mild inflammation and lesser edema in stomach tissue which demonstrate the gastroprotective potential of *morina longifolia* plant extract. (E) Standard drug omeprazole administration with a dose of 20 mg/kg in group-5 shows recovery of ulcerative stomach tissue to the normal.

4. DISCUSSION

A peptic ulcer is a sore that forms on the lining of the stomach, the upper part of the small intestine, or occasionally the oesophagus. It occurs when the protective mucous layer of the digestive tract is eroded, allowing stomach acid to damage the tissue.[22] Common causes include infection with *Helicobacter pylori* bacteria and prolonged use of nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin and ibuprofen.[23,24] Symptoms of a peptic ulcer can include a burning pain in the abdomen, bloating, nausea, and in severe cases, vomiting blood or dark stools. Nonsteroidal anti-inflammatory drugs (NSAIDs) can cause peptic ulcers by disrupting the protective mechanisms of the stomach and duodenal lining, primarily through inhibition of prostaglandin synthesis and direct local irritation.[25,26] NSAIDs work by inhibiting the activity of cyclooxygenase (COX) enzymes, which are responsible for the synthesis of prostaglandins from arachidonic acid. Prostaglandins are critical in maintaining the integrity of the gastric mucosa. They Stimulate the production of protective mucus and bicarbonate, which form a barrier against stomach acid. Promote mucosal blood flow, which helps maintain tissue repair and barrier integrity. Prostaglandins are also involved in promoting the healing and repair of the gastric mucosa. When their synthesis is inhibited, healing of minor injuries caused by stomach acid is impaired, making the mucosa more susceptible to ulceration. Prostaglandins promote vasodilation in the gastric mucosa, ensuring adequate blood supply to maintain healthy tissue. NSAID use reduces mucosal blood flow, leading to ischemia (reduced oxygen supply), which impairs the ability of the stomach lining to repair itself and increases the risk of ulcer formation.[27-29]

Indomethacin is a nonsteroidal anti-inflammatory drug (NSAID) used to reduce inflammation, pain, and fever. It is commonly prescribed for conditions such as arthritis, gout, and tendonitis, as well as to relieve pain from minor injuries or surgeries. Indomethacin works by inhibiting the production of prostaglandins, chemicals in the body that contribute to inflammation and pain. While effective, it can cause side effects such as gastrointestinal irritation, including ulcers, heartburn, and in some cases, bleeding.[30] Long-term use may also increase the risk of cardiovascular events like heart attack or stroke. It is usually prescribed under careful medical supervision, particularly in patients with a history of gastrointestinal or heart issues. Indomethacin, ability to induce peptic ulcers, particularly due to its strong inhibition of both COX-1 and COX-2 enzymes.[31] As a non-selective cyclooxygenase inhibitor, indomethacin significantly reduces the production of protective prostaglandins in the gastrointestinal (GI) tract, leading to decreased mucus and bicarbonate secretion, increased gastric acid production, and impaired mucosal blood flow.[32] These effects compromise the protective barrier of the stomach and duodenum, making them more vulnerable to damage by gastric acid. Additionally, indomethacin has a high propensity to cause direct local irritation of the gastric mucosa, further contributing to ulcer formation. The risk of indomethacin-induced peptic ulcers is particularly high in patients using the drug for long-term management of chronic conditions like arthritis, and the likelihood of complications increases with higher doses.[33] Symptoms may include abdominal pain, bloating, nausea, and in severe cases, gastrointestinal bleeding or perforation, requiring careful monitoring and protective measures like co-administration of proton pump inhibitors (PPIs) or misoprostol.[34] Apart from this, Natural products have gained attention for their potential role in managing and treating peptic ulcers, especially due to their accessibility and fewer side effects compared to conventional medications. Many plant-based and traditional remedies offer gastroprotective, anti-inflammatory, and antioxidant properties that may aid in healing peptic ulcers or preventing their occurrence. Flavonoids, found in many fruits, vegetables, and teas, are potent antioxidants known to promote mucosal protection. For instance, *Glycyrrhiza glabra* (licorice) contains a flavonoid called glabridin, which helps in reducing inflammation, increasing mucus secretion, and improving the integrity of the stomach lining.[35] Flavonoids also help inhibit *Helicobacter pylori*, a bacteria commonly associated with peptic ulcers. In our research study *morina longifolia* plant was chosen after a complete literature review about their phytoconstituent for gastroprotection.

The role of pH in indomethacin-induced peptic ulcers is critical, as the drug's effects are closely tied to the acidic environment of the stomach. Indomethacin is a nonsteroidal anti-

inflammatory drug (NSAID) that inibits cyclooxygenase (COX) enzymes, specifically COX-1 and COX-2.[36] COX-1 plays an essential role in maintaining the protective mucosal lining of the stomach by promoting the production of prostaglandins. These prostaglandins stimulate mucus and bicarbonate secretion, which help to neutralize stomach acid and maintain an optimal pH level, protecting the stomach lining from damage.[37] Indomethacin disrupts this process by decreasing prostaglandin production, which weakens the mucosal barrier and reduces bicarbonate secretion, thus lowering the stomach's ability to buffer its acidic environment. The stomach's pH is naturally low (highly acidic, around pH 1.5-3.5) to aid in digestion, but without sufficient protection from the mucosal layer, this acidic environment can easily lead to erosion of the stomach lining, creating peptic ulcers. In our study we also found that indomethacin treatment in Group-2 animals shows low level of stomach pH when it is compared with group-1 animals. However, plant extract administration in group-3 and 4 at dose of 200 and 400 mg/kg significantly elevate the pH of stomach and has a potential to prevent stomach lining from degradation. Furthermore, Presence of *H. pylori* and metabolites of indomethacin cause generation of ROS. These ROS leads to cellular damage via oxidative stress.

Lipid peroxidation is a process in which free radicals, particularly reactive oxygen species (ROS), attack the lipids containing carbon-carbon double bonds in cell membranes, leading to oxidative degradation of these lipids. This process results in the formation of lipid radicals and hydroperoxides, which further propagate damage to the cell membrane and other cellular components**.** Lipid peroxidation compromises the structural integrity of cell membranes, disrupts cellular functions, and can trigger cell death.[38] Malondialdehyde (MDA) and 4-hydroxynonenal (4-HNE) are common by-products of lipid peroxidation and serve as biomarkers for oxidative stress. Antioxidants play a significant role in managing peptic ulcers by protecting the stomach lining from neutralizing these ROS. The result of our study revealed the, indomethacin administration in group-2 shows a high level of MDA when compared it with group-1. Administration of *morina longifolia* plant extract reduce the level of MDA in Group-3 and 4 that shows the antioxidant potential of plant extract. Standard drug omeprazole administration in group-5 also has a potential to reduce MDA content. One of the most essential enzymes in the body's defense against oxidative stress is superoxide dismutase (SOD) and catalase (CAT). It converts superoxide radicals into hydrogen peroxide or regular molecular oxygen which further broken down by glutathione peroxidase and catalase, among other antioxidant enzymes.[39] SOD aids in preventing oxidative damage to cellular

components, including DNA, proteins, and lipids, by reducing the damaging effects of superoxide radicals. Alteration in the SOD and CAT level in stomach tissue after indomethacin administration causes an imbalance in the level of superoxide radical and hydrogen peroxide or regular molecular oxygen that ultimately leads to cellular damage through ROS. Administration of *morina longifolia* plant extract reduce the level of SOD & CAT in Group-3 and 4 that shows the antioxidant and gastroprotective potential of plant extract. GSH, also known as reduced glutathione, is a powerful antioxidant in almost all human cells. It is essential for maintaining the redox equilibrium and shielding cells from oxidative damage. Its main role is to counteract ROS and free radicals, which may harm cells. GSH is also necessary for immune system support, liver detoxification of toxic chemicals, and the regeneration of other antioxidants, including vitamins C and E.[40] The ROS generated after the introduction of indomethacin reduces the GSH level in the cell, ultimately resulting in imbalance between the oxidant and antioxidant mechanisms of the cell. Administration of *morina longifolia* plant extract reduce the level of GSH in Group-3 and 4 that shows the antioxidant and gastroprotective potential of plant extract. In addition to cellular oxidative stress, activations of inflammatory pathways also play a big role in the pathophysiology of indomethacin-induced peptic ulcer. Tacrolimus produces ROS, which ultimately leads to oxidative stress inside the cell**.** High ROS generation can potentially harm cellular constituents and trigger nuclear factor kappa B (NF-κB), a transcriptional regulator of inflammation. An inflammatory response is promoted by NF-κB activation, which stimulates the transcription of pro-inflammatory cytokines like IL-6 & TNF- α. TNF-α is a major pro-inflammatory cytokine. Indomethacin causes a rise in TNF-α, which promotes inflammation and tissue damage by recruiting immune cells (like neutrophils) to the site of injury. It also increases the permeability of blood vessels, allowing further infiltration of immune cells into the gastric mucosa. IL-6 is released in response to tissue injury and inflammation. It helps promote the inflammatory process and is associated with both acute and chronic inflammation seen in peptic ulcers. Our study found that rats given indomethacin had considerably elevated levels of TNF-α and IL-6, indicating the presence of inflammatory cytokines that cause injury to stomach cells.[41] Fascinatingly, the levels of these inflammatory markers decrease after plant extract administration. This decrease in the levels of inflammatory cytokines indicates the gastroprotective potential of *morina longifolia* against indomethacin- induced peptic ulcer. Histopathological study revealed the structural change inside the stomach in normal, diseased, treatment & standard control group. Histology of normal control group shows normal microscopic architecture with normal lumen and glands, without any sign of

abnormalities. On te other hand, Diseased group shows severe inflammatory reaction,manifested by submucosal edema with local mononuclear leucocytic infiltration (mainly lymphocytes and few eosinophiles) in the layers of stomach. Administration of plant at dose of 200 mg/kg in treatment control-I shows reduction in inflammation and edema and tissue turns to recover into normal cell architecture. Administration of plant at dose of 400 mg/kg in treatment control-II shows very mild inflammation and lesser edema in stomach tissue which demonstrate the gastroprotective potential of *morina longifolia* plant extract.

5. CONCLUSION

The investigation into the gastroprotective effects of *Morina longifolia* plant extract against indomethacin-induced gastric ulcers demonstrates promising therapeutic potential. Indomethacin, an NSAID, disrupts gastric mucosal integrity by inhibiting prostaglandin synthesis and triggering oxidative stress and inflammatory responses, leading to ulceration. However, treatment with *Morina longifolia* extract significantly reduced ulcer formation, suggesting its protective role. The study indicates that the extract may exert its gastroprotective effects through multiple mechanisms, including antioxidant activity, reduction of inflammatory markers like TNF-α and IL-6, and enhancement of mucosal defense. By scavenging free radicals and potentially boosting prostaglandin levels, *Morina longifolia* mitigates the damage caused by indomethacin, preserving the gastric lining.

These findings support the traditional use of *Morina longifolia* for treating gastric ailments and open the door for further studies to isolate active compounds and elucidate their pharmacological actions. Thus, *Morina longifolia* extract could serve as a natural alternative or adjunct therapy for preventing NSAID-induced gastric ulcers.

REFERENCES

1. TUORKEY M, KAROLIN K. Anti-ulcer Activity of Curcumin on Experimental Gastric Ulcer in Rats and Its Effect on Oxidative Stress/Antioxidant, IL-6 and Enzyme Activities. *Biomedical and Environmental Sciences,* 2009; 22(6): 488-495. doi:10.1016/S0895-3988(10)60006-2.
2. Sonnenberg A. Review article: historic changes of *Helicobacter pylori* -associated diseases. *Aliment. Pharmacol. Ther*., 2013; 38(4): 329-342. doi:10.1111/apt.12380.
3. Drina M. Peptic ulcer disease and non-steroidal anti-inflammatory drugs. *Aust Prescr*. 2017; 40(3): 91- 93. doi:10.18773/austprescr.2017.037
4. Lee SP, Sung IK, Kim JH, Lee SY, Park HS, Shim CS. Risk Factors for the Presence of

Symptoms in Peptic Ulcer Disease. *Clin. Endosc*., 2017; 50(6): 578-584. doi:10.5946/ce.2016.129.

5. Almadi MA, Lu Y, Alali AA, Barkun AN. Peptic ulcer disease. *The Lancet*. 2024; 404(10447): 68-81. doi:10.1016/S0140-6736(24)00155-7
6. Abbasi-Kangevari M, Ahmadi N, Fattahi N, et al. Quality of care of peptic ulcer disease worldwide: A systematic analysis for the global burden of disease study 1990–2019. *PLoS One*. 2022; 17(8): e0271284. doi:10.1371/journal.pone.0271284
7. Xie X, Ren K, Zhou Z, Dang C, Zhang H. The global, regional and national burden of peptic ulcer disease from 1990 to 2019: a population-based study. *BMC Gastroenterol*. 2022; 22(1): 58. doi:10.1186/s12876-022-02130-2
8. Hawkins C, Hanks GW. The Gastroduodenal Toxicity of Nonsteroidal Anti-Inflammatory Drugs. A Review of the Literature. *J. Pain. Symptom. Manage*., 2000; 20(2): 140-151. doi:10.1016/S0885- 3924(00)00175-5
9. Drina M. Peptic ulcer disease and non-steroidal anti-inflammatory drugs. *Aust Prescr*. 2017; 40(3): 91-93. doi:10.18773/austprescr.2017.037
10. Lad R, Armstrong D. Management of Nonsteroidal Anti-Inflammatory Drug-Induced Gastroduodenal Disease by Acid Suppression. *Can J Gastroenterol Hepatol*., 1999; 13(2): 135-142. doi:10.1155/1999/715703
11. Morsy MA, El-Moselhy MA. Mechanisms of the Protective Effects of Curcumin against Indomethacin- Induced Gastric Ulcer in Rats. *Pharmacology*. 2013; 91(5-6): 267-274. doi:10.1159/000350190
12. Al-Zubaidy AA, Khalil AM. Gastroprotective Effect of Capparis spinosa on Indomethacin-induced Gastric Ulcer in Rats. *Arch. Razi. Inst*., 2022; 77(4): 1437-1445. doi:10.22092/ARI.2022.357514.2053
13. Yousuf S, Kumar Bachheti R, Joshi A, Article R, Bachheti RK, Bhat MUD. *Evaluation of Antioxidant Potential and Phytochemicals of Morina Longifolia IN VITRO ANTIBACTERIAL SCREENING OF DIFFERENT EXTRACTS OF MORINA LONGIFOLIA ON PATHOGENIC MICROORGANISMS*.; 2014. https://www.researchgate.net/publication/267035861
14. Garmus TT, Kopf SFM, Paula JT, et al. ETHANOLIC AND HYDROALCOHOLIC EXTRACTS OF PITANGA LEAVES (Eugenia uniflora L.) AND THEIR FRACTIONATION BY SUPERCRITICAL TECHNOLOGY. *Brazilian Journal of Chemical Engineering*, 2019; 36(2): 1041-1051. doi:10.1590/0104-6632.20190362s20180159

15. Shaikh JR, Patil M. Qualitative tests for preliminary phytochemical screening: An overview. *Int. J. Chem. Stud*., 2020; 8(2): 603-608. doi:10.22271/chemi.2020.v8.i2i.8834
16. Waterborg JH. The Lowry Method for Protein Quantitation. In; 2009: 7-10. doi:10.1007/978-1- 59745-198-7_2
17. Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. *Anal Biochem,* 1979; 95(2): 351-358. doi: 10.1016/0003-2697(79)90738-3
18. Jollow DJ, Mitchell JR, Zampaglione N, Gillette JR. Bromobenzene-Induced Liver Necrosis. Protective Role of Glutathione and Evidence for 3,4-Bromobenzene Oxide as the Hepatotoxic Metabolite. *Pharmacology,* 1974; 11(3): 151-169. doi:10.1159/000136485
19. Mohandas J, Marshall JJ, Duggin GG, Horvath JS, Tiller DJ. *Low Activities of Glutathione-Related Enzymes as Factors in the Genesis of Urinary Bladder Cancer1*. Vol. 44; 1984. http://aacrjournals.org/cancerres/article-pdf/44/11/5086/2417416/cr0440115086.pdf
20. MARKLUND S, MARKLUND G. Involvement of the Superoxide Anion Radical in the Autoxidation of Pyrogallol and a Convenient Assay for Superoxide Dismutase. *Eur. J. Biochem*., 1974; 47(3): 469-474. doi:10.1111/j.1432-1033.1974.tb03714.x
21. Claiborne A, Fridovich I. Purification of the o-dianisidine peroxidase from Escherichia coli B. Physicochemical characterization and analysis of its dual catalatic and peroxidatic activities. *Journal of Biological Chemistry*, 1979; 254(10): 4245-4252. doi:10.1016/s0021-9258(18)50722-5
22. Jabri MA, Rtibi K, Tounsi H, et al. Fatty acid composition and mechanisms of the protective effects of myrtle berry seed aqueous extract in alcohol-induced peptic ulcer in rat. *Can J. Physiol. Pharmacol*., 2017; 95(5): 510-521. doi:10.1139/cjpp-2016-0094
23. Kavitt RT, Lipowska AM, Anyane-Yeboa A, Gralnek IM. Diagnosis and Treatment of Peptic Ulcer Disease. *Am J. Med*., 2019; 132(4): 447-456. doi:10.1016/j.amjmed.2018.12.009
24. Cohen H. Peptic Ulcer and Helicobacter Pylori. *Gastroenterol Clin. North Am*., 2000; 29(4): 775-789. doi:10.1016/S0889-8553(05)70146-1
25. Kavitt RT, Lipowska AM, Anyane-Yeboa A, Gralnek IM. Diagnosis and Treatment of Peptic Ulcer Disease. *Am. J. Med*., 2019; 132(4): 447-456. doi:10.1016/j.amjmed.2018.12.009
26. Shim YK, Kim N. Nonsteroidal Anti-inflammatory Drug and Aspirin-induced Peptic Ulcer Disease. *The Korean Journal of Gastroenterology*. 2016; 67(6): 300.

doi:10.4166/kjg.2016.67.6.300

27. Day RO, Graham GG. The vascular effects of COX-2 selective inhibitors. *Aust. Prescr*., 2004; 27(6): 142-145. doi:10.18773/austprescr.2004.119
28. Brater DC, Harris C, Redfern JS, Gertz BJ. Renal Effects of COX-2-Selective Inhibitors. *Am. J. Nephrol*., 2001; 21(1): 1-15. doi:10.1159/000046212
29. Bindu S, Mazumder S, Bandyopadhyay U. Non-steroidal anti-inflammatory drugs (NSAIDs) and organ damage: A current perspective. *Biochem. Pharmacol*., 2020; 180: 114147. doi:10.1016/j.bcp.2020.114147
30. Jafari A, Andishfar N, Esmaeilzadeh Z, Khezri MR, Ghasemnejad-Berenji M. Gastroprotective effect of topiramate on indomethacin-induced peptic ulcer in rats: Biochemical and histological analyses. *Basic Clin. Pharmacol. Toxicol*., 2022; 130(5): 559-568. doi:10.1111/bcpt.13718
31. Feng L, Bao T, Bai L, et al. Mongolian medicine formulae Ruda-6 alleviates indomethacin-induced gastric ulcer by regulating gut microbiome and serum metabolomics in rats. *J. Ethnopharmacol*., 2023; 314: 116545. doi:10.1016/j.jep.2023.116545
32. Chauhan RS, Nautiyal MC, Tava A, Cecotti R. Essential oil composition of *Morina longifolia* Wall. ex DC. from the Himalayan region. *Journal of Essential Oil Research*. 2012; 24(5): 461-463. doi:10.1080/10412905.2012.703500
33. Jia B, Zhao L, Liu P, Li M, Tian Z. Limonin ameliorates indomethacin-induced intestinal damage and ulcers through Nrf2/ARE pathway. *Immun. Inflamm. Dis*., 2023; 11(2). doi:10.1002/iid3.787
34. Shim YK, Kim N. Nonsteroidal Anti-inflammatory Drug and Aspirin-induced Peptic Ulcer Disease. *The Korean Journal of Gastroenterology*, 2016; 67(6): 300. doi:10.4166/kjg.2016.67.6.300
35. Wahab S, Annadurai S, Abullais SS, et al. Glycyrrhiza glabra (Licorice): A Comprehensive Review on Its Phytochemistry, Biological Activities, Clinical Evidence and Toxicology. *Plants*, 2021; 10(12): 2751. doi:10.3390/plants10122751
36. Reda Abdelaleem E, Abdelwahab MF, Mohamed Abdel-Wahab N, et al. Apple extract protects against indomethacin-induced gastric ulcers in rats by suppressing oxidative stress – The implication of Nrf-2/HO-1 signaling pathway: In silico and in vivo studies. *J. Funct., Foods*, 2024; 112: 105926. doi:10.1016/j.jff.2023.105926
37. Nørregaard R, Kwon TH, Frøkiær J. Physiology and pathophysiology of cyclooxygenase-

2 and prostaglandin E2 in the kidney. *Kidney Res. Clin. Pract*., 2015; 34(4): 194-200. doi:10.1016/j.krcp.2015.10.004

38. Iqbal M, Dubey K, Anwer T, Ashish A, Pillai KK. *Protective Effects of Telmisartan against Acute Doxorubicin-Induced Cardiotoxicity in Rats*; 2008.
39. Bansal Y, Singh R, Saroj P, Sodhi RK, Kuhad A. Naringenin protects against oxido-inflammatory aberrations and altered tryptophan metabolism in olfactory bulbectomized-mice model of depression. *Toxicol. Appl. Pharmacol*., 2018; 355: 257-268. doi:10.1016/j.taap.2018.07.010
40. Alam MF, Hijri SI, Alshahrani S, et al. Zingerone Attenuates Carfilzomib-Induced Cardiotoxicity in Rats through Oxidative Stress and Inflammatory Cytokine Network. *Int. J. Mol. Sci*., 2022; 23(24): 15617. doi:10.3390/ijms232415617
41. Anwer T, Alshahrani S, Somaili AMH, et al. Nephroprotective Effect of Diosmin against Cisplatin- Induced Kidney Damage by Modulating IL-1β, IL-6, TNFα and Renal Oxidative Damage. *Molecules*, 2023; 28(3): 1302. doi:10.3390/molecules28031302