DEPARTMENT OF SCIENCE LABORATORY TECHNOLOGY

GASTROPROTECTIVE AND ANTIOXIDANT POTENTIAL OF PSIDIUM GUAJAVA ON INDOMETICINE INDUCED ULCERATED WISTAR RATS.

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CERTIFICATION

This is to clarify that this seminar work presented by "**TAJUDEEN HALIMAH ABIMBOLA (HND/23/SLT/FT/0964)"** has been read, approved and submitted to the department of Science Laboratory Technology (Biochemistry unit), institute of applied science, Kwara State, Ilorin.

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DEDICATION

This project is dedicated to Almighty God, the most merciful, the most gracious, who as protected me through the completion of this academic program. May HIS name be praised forever.

Also to my parents Mr. and Mrs. TAJUDEEN for their support throughout this project and to the department of science laboratory technology (Biochemistry unit).

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Firstly I am grateful to Almighty God for giving us an opportunity to excel in our efforts to complete this project.

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ABSTRACT

Peptic ulcer remains a major gastrointestinal disorder with significant clinical impact, often induced or aggravated by non-steroidal anti-inflammatory drugs (NSAIDs) such as indomethacin. This study investigates the gastroprotective and antioxidant potential of Psidium guajava (guava) leaf extract against indomethacin-induced gastric ulcers in Wistar rats. Aqueous extracts of P. guajava leaves were administered to different groups of ulcerated rats at varying doses prior to indomethacin administration. The extent of gastric mucosal damage was assessed macroscopically and histologically, while antioxidant markers such as catalase (CAT), superoxide dismutase (SOD), and malondialdehyde (MDA) levels were measured in gastric tissues.

Results revealed that pre-treatment with P. guajava significantly reduced ulcer index and gastric lesions in a dose-dependent manner, with notable improvement in mucosal integrity. Furthermore, there was a marked elevation in antioxidant enzyme activity (CAT and SOD) and a corresponding decrease in lipid peroxidation (MDA), indicating the extract's potent free radical scavenging capacity.

These findings suggest that Psidium guajava exhibits strong gastroprotective and antioxidant properties, likely attributable to its rich phytochemical content. The study supports the traditional use of guava leaves in gastrointestinal disorders and highlights their potential as a natural therapeutic agent against NSAID-induced gastric ulceration.

CHAPTER ONE

INTRODUCTION

1.1 Background of the Study

Ulcer disease remains a significant global health concern, characterized by mucosal erosions in the stomach or duodenum caused by an imbalance between mucosal defensive mechanisms and aggressive factors such as gastric acid, pepsin, Helicobacter pylori infection, stress, smoking, alcohol intake, and particularly, the use of non-steroidal anti-inflammatory drugs (NSAIDs) (Konturek et al., 2011). and protective factors like mucus, bicarbonate, and mucosal blood flow. Among NSAIDs, indomethacin is known to be a potent ulcerogenic agent It induces ulceration primarily by inhibiting cyclooxygenase (COX) enzymes, leading to reduced synthesis of protective prostaglandins, increased gastric acid secretion, reduced bicarbonate and mucus production, and compromised mucosal blood flow (Wallace, 2008).

One of the underlying mechanisms contributing to NSAID-induced gastric injury is the generation of reactive oxygen species (ROS), which causes oxidative stress and damages cellular components such as lipids, proteins, and DNA (Gutiérrez et al., 2008). The role of oxidative stress in the pathogenesis of gastric ulcers has garnered increasing attention, highlighting the importance of antioxidants in gastroprotection. As such, plant-derived compounds with antioxidant and anti-inflammatory properties are gaining traction as potential therapeutic agents in the management of gastric ulcers. Despite the widespread use of conventional anti-ulcer drugs, such as proton pump inhibitors and H2 receptor antagonists, their side effects and potential for drug resistance necessitate the search for safer and more effective alternatives. (Biswas et al., 2003).

Medicinal plants have long been explored for their therapeutic potential, particularly in the treatment and prevention of gastrointestinal disorders. One such plant is **Psidium** guajava (commonly known as guava), is a tropical plant belonging to the Myrtaceae family and is widely known for its nutritional and medicinal benefits. Various parts of the plant, including the leaves, fruits, and bark, have been used traditionally to treat ailments such as diarrhea, wounds, cough, diabetes, and gastrointestinal disorders. The leaves of Psidium guajava are particularly rich in polyphenols, flavonoids (e.g., quercetin), tannins, saponins, essential oils, and vitamin C, all of which are bioactive compounds known to exhibit potent antioxidant and anti-inflammatory activities. These properties suggest its potential utility in mitigating oxidative stress and inflammation associated with gastric ulceration. (Arima & Danno, 2002).

Recent studies have shown that guava leaf extracts possess free radical scavenging capacity, lipid peroxidation inhibitory activity, and the ability to enhance endogenous antioxidant enzyme levels such as superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH). These properties may help in protecting the gastric mucosa from oxidative damage and facilitating ulcer healing. Additionally, Psidium guajava may exert direct cytoprotective effects by modulating gastric pH, reinforcing mucosal barriers, and influencing prostaglandin synthesis (Ojewole,2006).

Despite the traditional use of Psidium guajava in managing gastric ailments, there is still a need for scientific validation through experimental models. Utilizing indomethacin-induced ulceration in Wistar rats provides a reliable and reproducible method to assess the gastroprotective and antioxidant efficacy of this plant. The Wistar rat model also allows for the evaluation of biochemical, histological, and physiological parameters relevant to ulcer pathogenesis and healing (Laine et al., 2008).

1.2 Justification for the Study

Ulcer are common and persistent public health problem, affecting millions of people globally and contributing significantly to morbidity and healthcare costs. The condition is often exacerbated by the widespread use of non-steroidal anti-inflammatory drugs (NSAIDs) such as indomethacin, which, although effective in managing pain and inflammation, are known to compromise the gastric mucosal barrier. Indomethacin-induced gastric damage occurs primarily through the inhibition of prostaglandin synthesis, leading to increased gastric acid secretion, reduced mucus and bicarbonate production, impaired mucosal blood flow, and generation of reactive oxygen species (ROS), all of which result in mucosal injury.

Despite the availability of standard anti-ulcer medications such as proton pump inhibitors and H_2-receptor antagonists, these synthetic drugs are not without significant drawbacks. Long-term use is often associated with adverse effects including electrolyte imbalances, nutrient deficiencies, and increased susceptibility to infections such as *Clostridium difficile*. Furthermore, these drugs do not directly address the oxidative stress component of ulcerogenesis. This has prompted renewed interest in plant-based alternatives that are not only effective but also safe, accessible, and multifaceted in action.

This has led to increased interest in the use of medicinal plants as alternative or complementary therapies. They are often accessible, culturally accepted, and contain a diverse array of bioactive compounds capable of exerting multiple therapeutic effects. Among these, Psidium guajava (guava) has received growing attention for its wide range of pharmacological properties. Guava leaves are traditionally used in many cultures for the treatment of gastrointestinal ailments such as diarrhea, dysentery, and stomach pain. Scientific studies have shown that guava possesses

antioxidant, anti-inflammatory, antibacterial, and cytoprotective activities, largely attributed to its rich phytochemical profile, including flavonoids, tannins, saponins, polyphenols, and vitamin C. By employing indomethacin-induced ulceration in Wistar rats, this study provides a scientifically valid and reproducible method to assess the anti-ulcer properties of *Psidium guajava*. This model closely mimics the pathophysiology of NSAID-induced ulcers in humans, making the findings translatable and relevant to clinical scenarios.

In this context, the justification for the present study lies in:

- The need to develop safer and natural alternatives to conventional ulcer therapies.
- The lack of experimental validation of *Psidium guajava*'s traditional gastroprotective use.
- The potential of guava leaf extract to offer dual benefits: reducing oxidative stress and enhancing mucosal defense.
- The importance of generating scientific evidence to support herbal medicine integration into modern healthcare.

1.3 Objectives of the Study

General Objective

To scientifically investigate the **gastroprotective and antioxidant effects** of *Psidium guajava* (guava) leaf extract on indomethacin-induced gastric ulcers in Wistar rats, with the aim of exploring its potential as a natural therapeutic agent for ulcer prevention and management.

Specific Objectives

1. **To establish a validated animal model** of gastric ulceration by administering indomethacin to Wistar rats, thereby mimicking NSAID-induced mucosal damage as seen in clinical settings.
2. **To prepare and standardize ethanolic or aqueous extracts** of *Psidium guajava* leaves, ensuring consistency in dosage and phytochemical content for experimental administration.
3. **To evaluate the dose-dependent gastroprotective effects** of *Psidium guajava* extract by administering different concentrations to ulcer-induced rats and assessing changes in ulcer index, gastric volume, pH, and total acidity.
4. **To measure the antioxidant defense capacity** of *Psidium guajava* extract by analyzing biomarkers such as:
    - **Malondialdehyde (MDA)** – an indicator of lipid peroxidation.
    - **Superoxide dismutase (SOD)** – an enzyme that catalyzes the dismutation of superoxide radicals.
    - **Catalase (CAT)** – an enzyme that converts hydrogen peroxide into water and oxygen.
    - **Reduced glutathione (GSH)** – a major cellular antioxidant that neutralizes reactive oxygen species.
5. **To compare the therapeutic efficacy of *Psidium guajava* extract** with that of a standard anti-ulcer drug (e.g., omeprazole or ranitidine), in terms of both gastric protection and antioxidant activity.

6. **To perform histopathological analyses** of gastric tissues to evaluate microscopic changes in mucosal architecture, inflammation, necrosis, and healing across experimental groups.
7. **To investigate possible correlations** between oxidative stress levels and ulcer severity in both treated and untreated groups, to better understand the mechanism of action of *Psidium guajava*.
8. **To identify the phytochemical constituents** (e.g., flavonoids, tannins, saponins, alkaloids, phenolic compounds) of *Psidium guajava* extract that may contribute to its observed biological activities.
9. **To provide scientific evidence** supporting the traditional use of *Psidium guajava* in the treatment of gastrointestinal disorders, and to explore its potential application in modern natural medicine.
10. **To investigate potential cytoprotective mechanisms** of action, including:
    - Enhancement of endogenous antioxidant enzyme systems.
    - Stimulation of prostaglandin synthesis or mucin secretion.
    - Suppression of neutrophil infiltration and pro-inflammatory cytokine production.
11. **To provide scientific validation of the ethnopharmacological use of *Psidium guajava* in gastrointestinal disorders**, and generate preclinical evidence for future clinical trials.
12. **To administer *Psidium guajava* extract in different doses** and investigate its ability to:
    - Modulate pH and volume of gastric secretions
    - Improve survival and general condition of ulcerated animals
13. **To analyze dose-dependency and safety margin**, determining the lowest effective dose and monitoring for any signs of toxicity, hepatotoxicity, or adverse reactions through liver and kidney function markers (AST, ALT, urea, creatinine).

14. **To provide direction for future translational research**, including

- Standardization of plant extracts for clinical formulation
- Integration into phytopharmaceutical pipelines
- Basis for human clinical trials in ulcer therapy

15. **To investigate inflammatory modulation** by assessing:

    - Levels of pro-inflammatory cytokines (e.g., TNF-α, IL-1β, IL-6)
    - Neutrophil infiltration and myeloperoxidase (MPO) activity
    - Histopathological indicators of mucosal inflammation

CHAPTER TWO

2.0 ULCER

An ulcer is an open sore or break in the lining of an organ that impedes its normal function. Most commonly, ulcers occur in the digestive tract, such as the stomach, small intestine, or esophagus. An ulcer is a sore on the lining of an organ, most commonly the stomach or small intestine, caused by acid damage and infection, leading to pain and sometimes bleeding.

Peptic ulcer disease is when the inner part of the stomach's gastric mucosa (lining of the stomach), the first part of the small intestine, or sometimes the lower esophagus, gets damaged. An ulcer in the stomach is called a gastric ulcer, while one in the first part of the intestines is a duodenal ulcer. The most common symptoms of a duodenal ulcer are waking at night with upper abdominal pain, and upper abdominal pain that improves with eating. With a gastric ulcer, the pain may worsen with eating. The pain is often described as a burning or dull ache. Other symptoms include belching, vomiting, weight loss, or poor appetite.About a third of older people with peptic ulcers have no symptoms. Complications may include bleeding, perforation, and blockage of the stomach. Bleeding occurs in as many as 15% of cases.

Common causes include infection with Helicobacter pylori and non-steroidal antiinflammatory drugs (NSAIDs). Other, less common causes include tobacco smoking, stress as a result of other serious health conditions, Behçet's disease, Zollinger– Ellison syndrome, Crohn's disease, and liver cirrhosis. Older people are more sensitive to the ulcer-causing effects of NSAIDs. The diagnosis is typically suspected due to the presenting symptoms with confirmation by either endoscopy or barium swallow. H. pylori can be diagnosed by testing the blood for antibodies, a urea breath test, testing the stool for signs of the bacteria, or a biopsy of the stomach. Other conditions that produce similar symptoms include stomach cancer, coronary heart disease, and inflammation of the stomach lining or gallbladder inflammation.

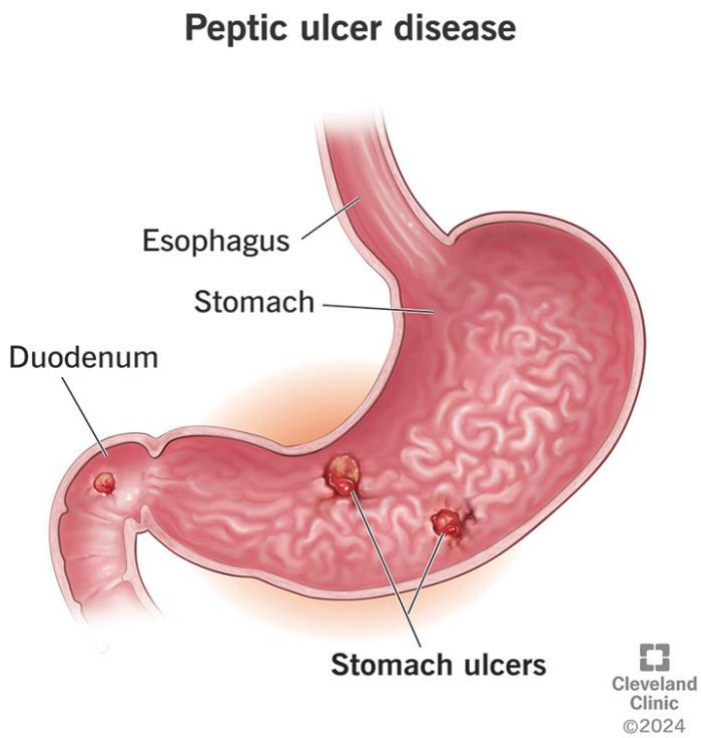

Figure 2.0 ulcer disease

Reference: Emmanuel 2022

Diet does not play an important role in either causing or preventing ulcers.

Treatment includes stopping smoking, stopping use of NSAIDs, stopping alcohol, and taking medications to decrease stomach acid. The medication used to decrease acid is usually either a proton pump inhibitor (PPI) or an H2 blocker, with four weeks of treatment initially recommended. Ulcers due to H. pylori are treated with a combination of medications, such as amoxicillin, clarithromycin, and a PPI. Antibiotic resistance is increasing and thus treatment may not always be effective. Bleeding ulcers may be treated by endoscopy, with open surgery typically only used in cases in which it is not successful.

Peptic ulcers are present in around 4% of the population. New ulcers were found in around 87.4 million people worldwide during 2015. About 10% of people develop a peptic ulcer at some point in their life. Peptic ulcers resulted in 267,500 deaths in 2015, down from 327,000 in 1990. The first description of a perforated peptic ulcer was in 1670, in Princess Henrietta of England. H. pylori was first identified as causing peptic ulcers by Barry Marshall and Robin Warren in the late 20th century, a discovery for which they received the Nobel Prize in 2005.

2.1 SIGNS AND SYMPTOMS OF ULCER

Signs and symptoms of a peptic ulcer can include one or more of the following: abdominal pain, classically epigastric, strongly correlated with mealtimes. In case of duodenal ulcers, the pain appears about three hours after taking a meal and wakes the person from sleep; bloating and abdominal fullness; waterbrash (a rush of saliva after an episode of regurgitation to dilute the acid in esophagus, although this is more associated with gastroesophageal reflux disease); nausea and copious vomiting; loss of appetite and weight loss, in gastric ulcer; weight gain, in duodenal ulcer, as the pain is relieved by eating; hematemesis (vomiting of blood); this can occur due to bleeding

directly from a gastric ulcer or from damage to the esophagus from severe/continuing vomiting.melena (tarry, foul-smelling feces due to presence of oxidized iron from hemoglobin); rarely, an ulcer can lead to a gastric or duodenal perforation, which leads to acute peritonitis and extreme, stabbing pain,[13] and requires immediate surgery.

A history of heartburn or gastroesophageal reflux disease (GERD) and use of certain medications can raise the suspicion for peptic ulcer. Medicines associated with peptic ulcer include NSAIDs (non-steroidal anti-inflammatory drugs) that inhibit cyclooxygenase and most glucocorticoids (e.g., dexamethasone and prednisolone.

The timing of symptoms in relation to the meal may differentiate between gastric and duodenal ulcers. A gastric ulcer would give epigastric pain during the meal, associated with nausea and vomiting, as gastric acid production is increased as food enters the stomach. Pain in duodenal ulcers would be aggravated by hunger and relieved by a meal and is associated with night pain. Also, the symptoms of peptic ulcers may vary with the location of the ulcer and the person's age. Furthermore, typical ulcers tend to heal and recur, and as a result the pain may occur for few days

and weeks and then wane or disappear. Usually, children and the elderly do not develop any symptoms unless complications have arisen. A burning or gnawing feeling in the stomach area lasting between 30 minutes and 3 hours commonly accompanies ulcers. This pain can be misinterpreted as hunger, indigestion, or heartburn. Pain is usually caused by the ulcer, but it may be aggravated by the stomach acid when it comes into contact with the ulcerated area. The pain caused by peptic ulcers can be felt anywhere from the navel up to the sternum, it may last from few minutes to several hours, and it may be worse when the stomach is empty. Also, sometimes the pain may flare at night, and it can commonly be temporarily relieved by eating foods that buffer stomach acid or by taking anti-acid medication. However, peptic ulcer disease symptoms may be different for everyone.

2.2 COMPLICATIONS OF ULCER

Gastrointestinal bleeding is the most common complication.

Sudden large bleeding can be lifethreatening. It is associated with 5% to 10% death rate. Perforation (a hole in the wall of the gastrointestinal tract) following a gastric ulcer often leads to catastrophic consequences if left untreated. Erosion of the gastrointestinal wall by the ulcer leads to spillage of the stomach or intestinal contents into the abdominal cavity, leading to an acute chemical peritonitis. The first sign is often sudden intense abdominal pain, as seen in Valentino's syndrome. Posterior gastric wall perforation may lead to bleeding due to the involvement of gastroduodenal artery that lies posterior to the first part of the duodenum. The death rate in this case is 20%.Penetration is a form of perforation in which the hole leads to and the ulcer continues into adjacent organs such as the liver and pancreas.

Gastric outlet obstruction (stenosis) is a narrowing of the pyloric canal by scarring and swelling of the gastric antrum and duodenum due to peptic ulcers. The person often presents with severe vomiting. Cancer is included in the differential diagnosis (elucidated by biopsy), Helicobacter pylori as the etiological factor making it 3 to 6 times more likely to develop stomach cancer from the ulcer. The risk for developing gastrointestinal cancer also appears to be slightly higher with gastric ulcers.

2.3 CAUSE OF ULCER

H. pylori (Helicobacter pylori) is one of the major causative factors of peptic ulcer disease. It secretes urease to create an alkaline environment, which is suitable for its survival. It expresses blood group antigen-binding adhesin (BabA) and outer inflammatory protein adhesin (OipA), which enables it to attach to the gastric epithelium. The bacterium also expresses virulence factors such as CagA and PicB, which cause stomach mucosal inflammation. The VacA gene encodes for vacuolating cytotoxin, but its mechanism of causing peptic ulcers is unclear. Such stomach mucosal inflammation can be associated with hyperchlorhydria (increased stomach acid secretion) or hypochlorhydria (reduced stomach acid secretion). Inflammatory cytokines inhibit the parietal cell acid secretion. H. pylori also secretes certain products that inhibit hydrogen potassium ATPase; activate calcitonin gene-related peptide sensory neurons, which increases somatostatin secretion to inhibit acid production by parietal cells; and inhibit gastrin secretion. This reduction in acid production causes gastric ulcers. On the other hand, increased acid production at the pyloric antrum is associated with duodenal ulcers in 10% to 15% of H. pylori infection cases. In this case, somatostatin production is reduced and gastrin production is increased, leading to increased

histamine secretion from the enterochromaffin cells, thus increasing acid production. An acidic environment at the antrum causes metaplasia of the duodenal cells, causing duodenal ulcers.

Human immune response toward the bacteria also determines the emergence of peptic ulcer disease. The human IL1B gene encodes for Interleukin 1 beta, and other genes that encode for tumour necrosis factor (TNF) and Lymphotoxin alpha also play a role in gastric inflammation.

2.3.1 NSAIDs

Taking nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin. can increase the risk of peptic ulcer disease by four times compared to non-users. The risk of getting a peptic ulcer is two times for aspirin users. Risk of bleeding increases if NSAIDs are combined with selective serotonin reuptake inhibitor (SSRI), corticosteroids, antimineralocorticoids, and anticoagulants. The gastric mucosa protects itself from gastric acid with a layer of mucus, the secretion of which is stimulated by certain prostaglandins. NSAIDs block the function of cyclooxygenase 1(COX-1), which is essential for the production of these prostaglandins. Besides this, NSAIDs also inhibit stomach mucosa cells proliferation and mucosal blood flow, reducing bicarbonate and mucus secretion, which reduces the integrity of the mucosa. Another type of NSAIDs, called COX-2 selective anti-inflammatory drugs (such as celecoxib), preferentially inhibit COX-2, which is less essential in the gastric mucosa. This reduces the probability of getting peptic ulcers; however, it can still delay ulcer healing for those who already have a peptic ulcer. Peptic ulcers caused by NSAIDs differ from those caused by H. pylori as the latter's appear as a consequence of inflammation of the mucosa (presence of neutrophil and submucosal edema), the former instead as a consequence of a direct damage of the NSAID molecule against COX enzymes, altering the hydrophobic state of the mucus, the permeability of the lining epithelium and mitochondrial machinery of the cell itself.

In this way NSAID's ulcers tend to complicate faster and dig deeper in the tissue causing more complications, often asymptomatically until a great portion of the tissue is involved.

2.3.2 STRESS

physical stress can directly cause stress ulcers, while psychological stress mainly acts as a contributing factor that aggravates or increases the risk of peptic ulcers by affecting acid levels, immune response, and health behaviors. Physiological (not psychological) stress due to serious health problems, such as those requiring treatment in an intensive care unit, is well described as a cause of peptic ulcers, which are also known as stress ulcers. While chronic life stress was once believed to be the main cause of ulcers, this is no longer the case. It is, however, still occasionally believed to play a role. This may be due to the well-documented effects of stress on gastric physiology, increasing the risk in those with other causes, such as H. pylori or NSAID use.

2.3.3 DIET

Dietary factors, such as spice consumption, were hypothesized to cause ulcers until the late 20th century, but have been shown to be of relatively minor importance.Caffeine and coffee, also commonly thought to cause or exacerbate ulcers, appear to have little effect. Similarly, while studies have found that alcohol consumption increases risk when associated with H. pylori infection, it does not seem to independently increase risk. Even when coupled with H. pylori infection, the increase is modest in comparison to the primary risk factor.

Diet itself does not directly cause ulcers. The main causes of stomach ulcers are Helicobacter pylori infection and prolonged use of NSAIDs (nonsteroidal anti-inflammatory drugs) that damage the stomach lining.

However, diet can influence ulcer symptoms and healing. Spicy foods were once blamed for ulcers, but research shows they do not cause ulcers and may even stimulate protective mechanisms in the stomach. Still, if spicy foods cause discomfort, they should be limited.

Highly processed, fatty, salty, or sugary foods can worsen symptoms and slow healing, so avoiding these may help reduce discomfort. Some foods rich in antioxidants and probiotics—such as berries, broccoli, cabbage, yogurt, kefir, and fermented foods—may help fight H. pylori infection and support ulcer healing.Fiber-rich foods like apples, pears, and whole grains may lower stomach acid and ease symptoms.

Certain foods like chocolate, coffee, alcohol, and citrus can irritate the stomach lining and worsen symptoms, so they are often recommended to be limited during ulcer treatment.

2.3.4 OTHER CAUSES OF ULCER

Other causes of peptic ulcer disease include gastric ischaemia, drugs, metabolic disturbances, cytomegalovirus (CMV), upper abdominal radiotherapy, Crohn's disease, and vasculitis. Gastrinomas (Zollinger–Ellison syndrome), or rare gastrin-secreting tumors, also cause multiple and difficult-to-heal ulcers. It is still unclear whether smoking increases the risk of getting peptic ulcers.

The diagnosis of Helicobacter pylori can be made by: Urea breath test (noninvasive and does not require EGD); Direct culture from an EGD biopsy specimen; this is difficult and can be expensive. Most labs are not set up to perform H. pylori cultures; Direct detection of urease activity in a biopsy specimen by rapid urease test; Measurement of antibody levels in the blood (does not

require EGD). It is still somewhat controversial whether a positive antibody without EGD is enough to warrant eradication therapy; Stool antigen test;

Histological examination and staining of an EGD biopsy. The breath test uses radioactive carbon to detect H. pylori.[38] To perform this exam, the person is asked to drink a tasteless liquid that contains the carbon as part of the substance that the bacteria breaks down. After an hour, the person is asked to blow into a sealed bag. If the person is infected with H. pylori, the breath sample will contain radioactive carbon dioxide. This test provides the advantage of being able to monitor the response to treatment used to kill the bacteria.

The possibility of other causes of ulcers, notably malignancy (gastric cancer), needs to be kept in mind. This is especially true in ulcers of the greater curvature of the stomach; most are also a consequence of chronic H. pylori infection. If a peptic ulcer perforates, air will leak from inside the gastrointestinal tract (which always contains some air) to the peritoneal cavity (which normally never contains air). This leads to "free gas" within the peritoneal cavity. If the person stands, as when having a chest X-ray, the gas will float to a position underneath the diaphragm. Therefore, gas in the peritoneal cavity, shown on an erect chest X-ray or supine lateral abdominal X-ray, is an omen of perforated peptic ulcer disease.

2.4 CLASSIFICATION OF ULCERS

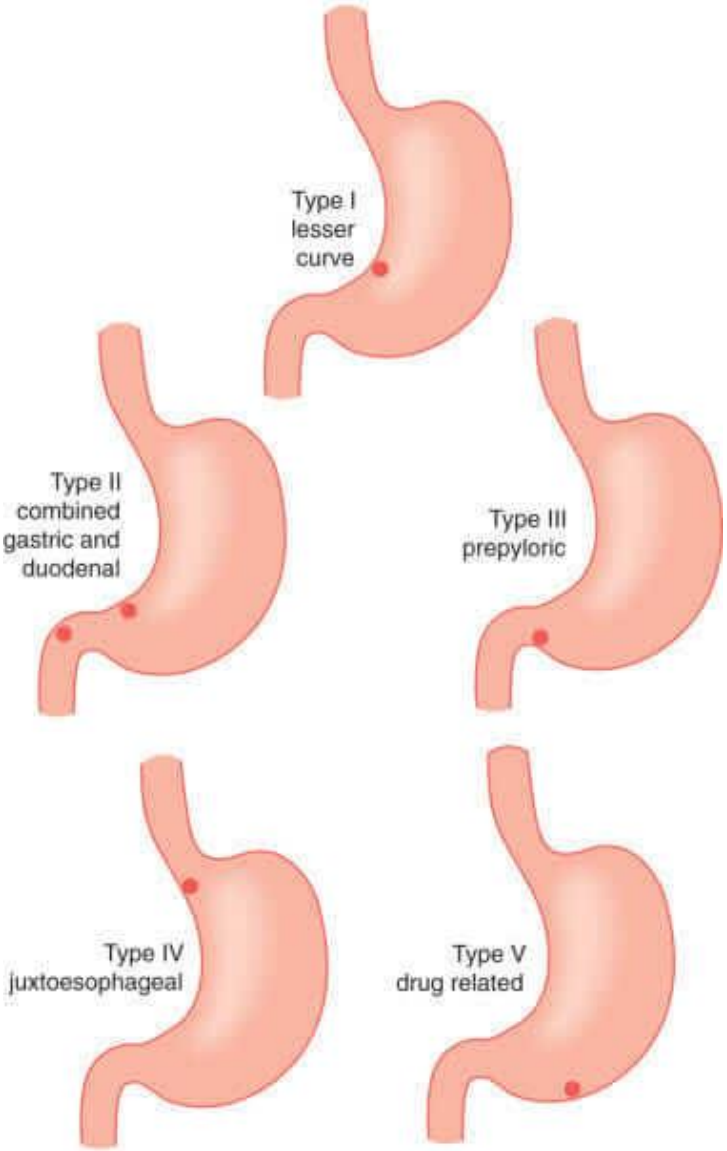

Figure 2.2 Classification of ulcer

Reference: Ijioma 2019

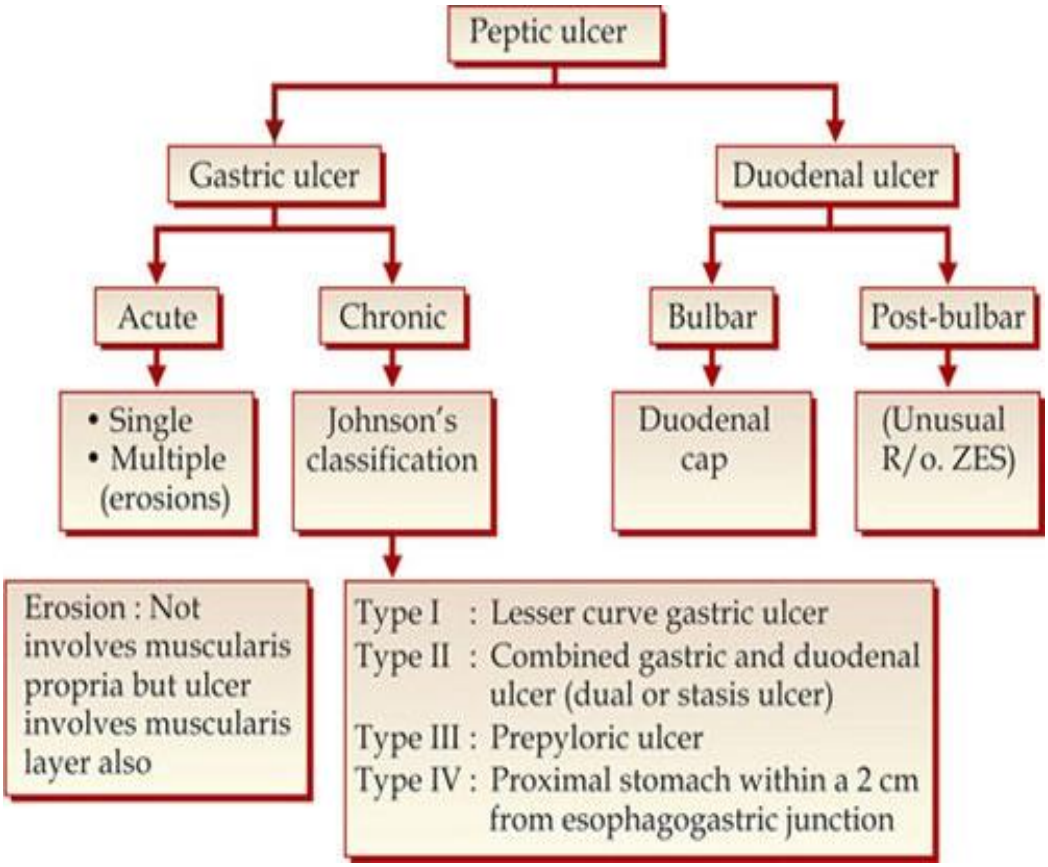

Figure 2.3 classification of ukcer

Reference: ijioma 2019

2.4,1 Classification of ulcer by location

Duodenum (called duodenal ulcer) Esophagus (called esophageal ulcer)

Stomach (called gastric ulcer)

Meckel's diverticulum (called Meckel's diverticulum ulcer; is very tender with palpation)

2.4.2 Classification of ulcer Modified Johnson

Type I: Ulcer along the body of the stomach, most often along the lesser curve at incisura angularis along the locus minoris resistantiae. Not associated with acid hypersecretion.

Type II: Ulcer in the body in combination with duodenal ulcers.

Associated with acid oversecretion.

Type III: In the pyloric channel within 3 cm of pylorus. Associated with acid oversecretion.

Type IV: Proximal gastroesophageal ulcer.

Type V: Can occur throughout the stomach. Associated with the chronic use of NSAIDs (such as ibuprofen).

2.5 GASTRIC ULCER

Gastric ulcer A sore that develops on the lining of the oesophagus, stomach or small intestine. Gastric ulcers are most often localized on the lesser curvature of the stomach. The ulcer is a round to oval parietal defect ("hole"), 2–4 cm diameter, with a smooth base and perpendicular borders. These borders are not elevated or irregular in the acute form of peptic ulcer, and regular but with elevated borders and inflammatory surrounding in the chronic form. In the ulcerative form of gastric cancer, the borders are irregular. Surrounding mucosa may present radial folds, as a consequence of the parietal scarring.

A gastric peptic ulcer is a mucosal perforation that penetrates the muscularis mucosae and lamina propria, usually produced by acid-pepsin aggression. Ulcer margins are perpendicular and present chronic gastritis. During the active phase, the base of the ulcer shows four zones: fibrinoid necrosis, inflammatory exudate, granulation tissue and fibrous tissue. The fibrous base of the ulcer may contain vessels with thickened wall or with thrombosis.

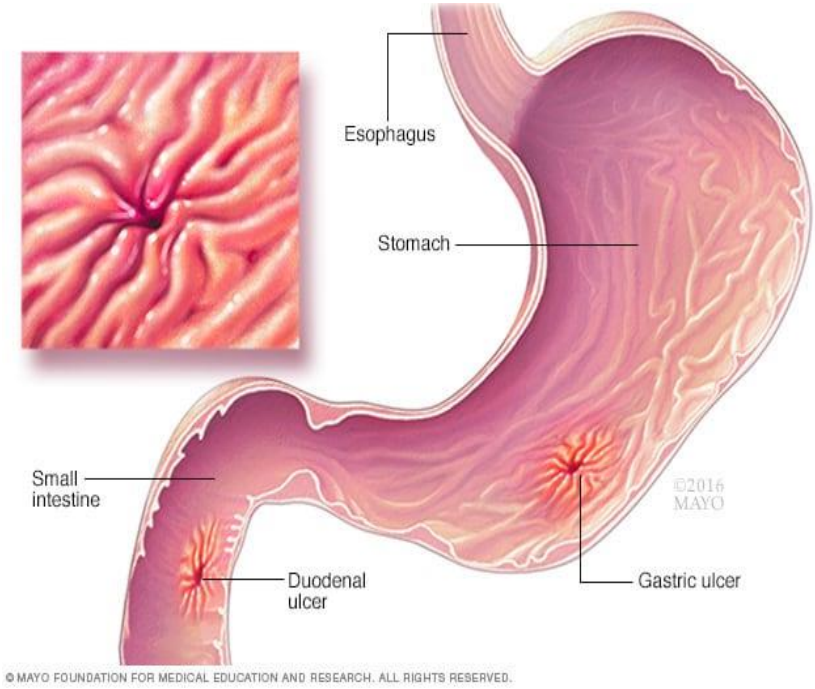

Figure 2.4 Gastric ulcer

Reference: Ibrahim 2017

2.6;Symptoms of gastric ulcer

pain or discomfort in the upper part of your abdomen, anywhere between your belly button and breastbone

feeling full too soon while eating a meal

feeling uncomfortably full after eating a meal

nausea and vomiting

bloating

belching

Burning or dull stomach pain, often in the upper abdomen between the belly button and breastbone. This pain can worsen with eating and may last from minutes to hours.

Pain may be worse between meals or at night, sometimes waking a person from sleep.

Indigestion, bloating, belching, and nausea.

Feeling full quickly or uncomfortably full after eating.

Loss of appetite and weight loss.

Vomiting, which may sometimes contain blood or look like coffee grounds, indicating bleeding.

Black or tarry stools, a sign of bleeding in the stomach.

In severe cases, sudden sharp abdominal pain, dizziness, fainting, or shock symptoms may occur, signaling complications

Abdominal pain is the most common symptom of a peptic ulcer. The pain may be dull or burning and may come and go over time. For some people, the pain may occur when the stomach is empty or at night, and it may go away for a short time after they eat. For other people, eating may make the pain worse.

Many people who have peptic ulcers don't have any symptoms. They may not develop symptoms until an ulcer leads to complications.

2.7 PREVENTION OF GASTRIC ULCER

Prevention of peptic ulcer disease for those who are taking NSAIDs (with low cardiovascular risk) can be achieved by adding a proton pump inhibitor (PPI), an H2 antagonist, or misoprostol.[15] NSAIDs of the COX-2 inhibitors type may reduce the rate of ulcers when compared to non-selective NSAIDs.[15] PPI is the most popular agent in peptic ulcer prevention.[15] However, there is no evidence that H2 antagonists can prevent stomach bleeding for those taking NSAIDs.[15] Although misoprostol is effective in preventing peptic ulcer, its properties of promoting abortion and causing gastrointestinal distress limit its use.[15] For those with high cardiovascular risk, naproxen with PPI can be a useful choice. Otherwise, low-dose aspirin, celecoxib, and PPI can also be used.

2.8 MANAGEMENT OF GASTRIC ULCER

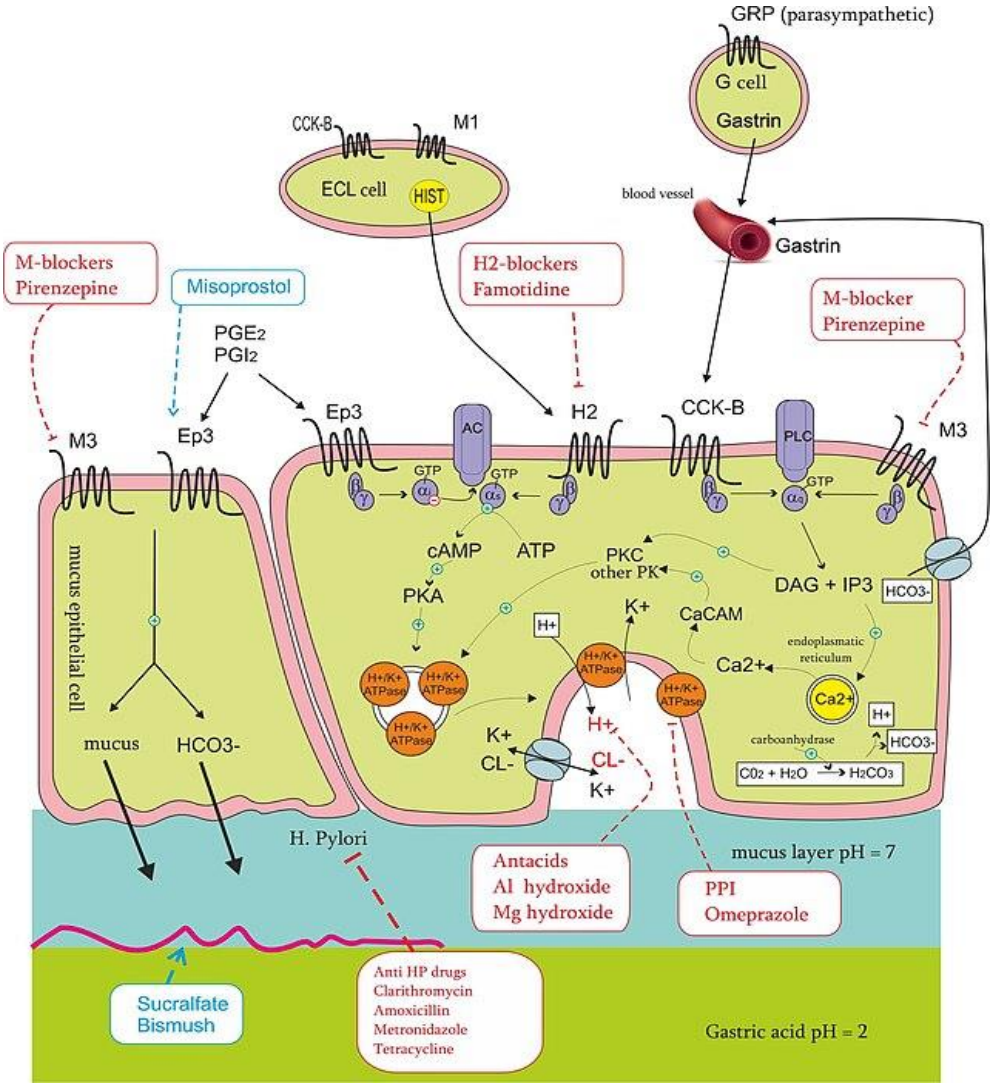

Figure 2.5 management of gastric ulcer

Reference Emmanuel, 2021

2.9 ERADICATION THERAPY OF GASTRIC ULCER

Once the diagnosis of H. pylori is confirmed, the first-line treatment would be a triple regimen in which pantoprazole and clarithromycin are combined with either amoxicillin or metronidazole. This treatment regimen can be given for 7–14 days. However, its effectiveness in eradicating H. pylori has been reducing from 90% to 70%. However, the rate of eradication can be increased by doubling the dosage of pantoprazole or increasing the duration of treatment to 14 days. Quadruple therapy (pantoprazole, clarithromycin, amoxicillin, and metronidazole) can also be used. The quadruple therapy can achieve an eradication rate of 90%. If the clarithromycin resistance rate is higher than 15% in an area, the usage of clarithromycin should be abandoned. Instead, bismuth-containing quadruple therapy can be used (pantoprazole, bismuth citrate, tetracycline, and metronidazole) for 14 days. The bismuth therapy can also achieve an eradication rate of 90% and can be used as second-line therapy when the first-line triple-regimen therapy has failed.

2.9.1 NSAIDs-induced ulcers

NSAID-associated ulcers heal in six to eight weeks provided the NSAIDs are withdrawn with the introduction of proton pump inhibitors (PPI).

2.9.2 Bleeding

For those with bleeding peptic ulcers, fluid replacement with crystalloids is sometimes given to maintain volume in the blood vessels. Maintaining haemoglobin at greater than 7 g/dL (70 g/L) through restrictive blood transfusion has been associated with reduced rate of death. Glasgow-Blatchford score is used to determine whether a person should be treated inside a hospital or as an outpatient. Intravenous PPIs can suppress stomach bleeding more quickly than oral ones. A neutral stomach pH is required to keep platelets in place and prevent clot lysis. Tranexamic acid and antifibrinolytic agents are not useful in treating peptic ulcer disease.

Early endoscopic therapy can help to stop bleeding by using cautery, endoclip, or epinephrine injection. Treatment is indicated if there is active bleeding in the stomach, visible vessels or an adherent clot Endoscopy is also helpful in identifying people who are suitable for hospital discharge. Prokinetic agents such as erythromycin and metoclopramide can be given before

endoscopy to improve endoscopic view. Either high- or low-dose PPIs are equally effective in reducing bleeding after endoscopy. High-dose intravenous PPI is defined as a bolus dose of 80 mg followed by an infusion of 8 mg per hour for 72 hours—in other words, the continuous infusion of PPI of greater than 192 mg per day. Intravenous PPI can be changed to oral once there is no high risk of rebleeding from peptic ulcer.

For those with hypovolemic shock and ulcer size of greater than 2 cm, there is a high chance that the endoscopic treatment would fail. Therefore, surgery and angiographic embolism are reserved for these complicated cases. However, there is a higher rate of complication for those who underwent surgery to patch the stomach bleeding site when compared to repeated endoscopy. Angiographic embolisation has a higher rebleeding rate but a similar rate of death to surgery.

2.9.3 Anticoagulants

According to expert opinion, for those who are already on anticoagulants, the international normalized ratio (INR) should be kept at 1.5. For aspirin users who required endoscopic treatment for bleeding peptic ulcer, there is two times increased risk of rebleeding but with ten times reduced risk of death at eight weeks following the resumption of aspirin. For those who were on double antiplatelet agents for indwelling stent in blood vessels, both antiplatelet agents should not be stopped because there is a high risk of stent thrombosis. For those who were under warfarin treatment, fresh frozen plasma (FFP), vitamin K, prothrombin complex concentrates, or recombinant factor VIIa can be given to reverse the effect of warfarin. High doses of vitamin K should be avoided to reduce the time for rewarfarinisation once the stomach bleeding has stopped. Prothrombin complex concentrates are preferred for severe bleeding. Recombinant factor VIIa is reserved for life-threatening bleeding because of its high risk of thromboembolism.[15] Direct oral anticoagulants (DOAC) are recommended instead of warfarin as they are more effective in preventing thromboembolism. In case of bleeding caused by DOAC, activated charcoal within four hours is the antidote of choice.

2.10 EPIDEMIOLOGY OF ULCER

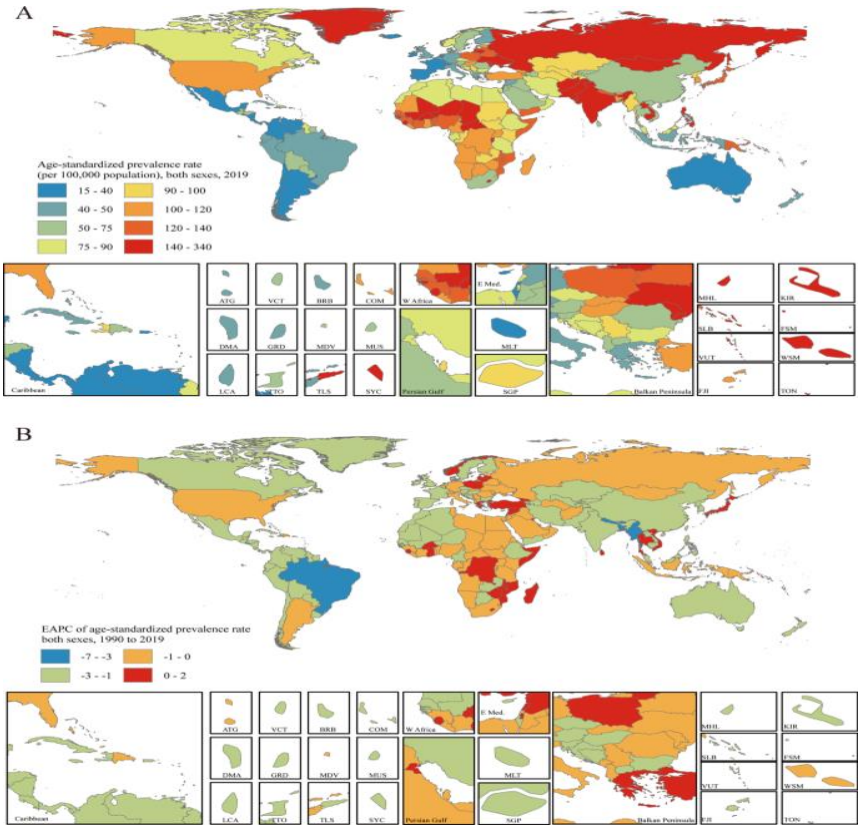

Figure 2.6 The global, national and regional burden of peptic ulcer

Reference Emmanuel, 2021

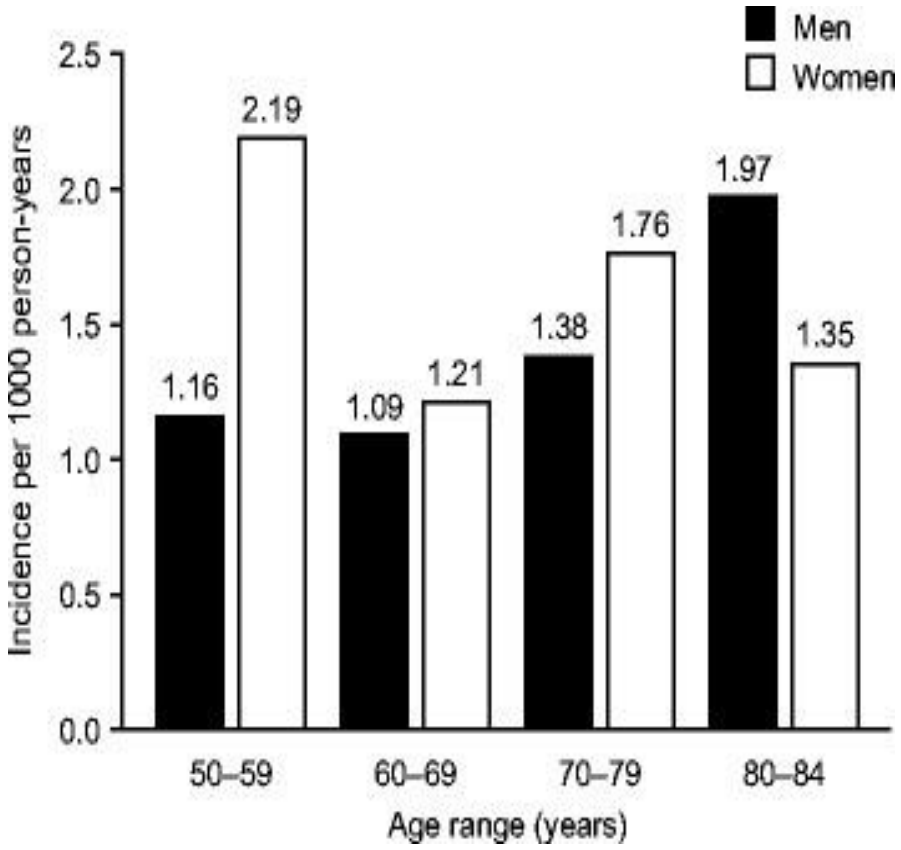

Figure2.7 Incidence of uncomplicated ulcer by age and sex

Reference cassarett, 2018

2.11 INCIDENCE OF UNCOMPLICATED ULCER BY AGE AND SEX

The lifetime risk for developing a peptic ulcer is approximately 5% to 10% with the rate of 0.1% to 0.3% per year. Peptic ulcers resulted in 301,000 deaths in 2013, down from 327,000 in 1990.

In Western countries, the percentage of people with H. pylori infections roughly matches age (i.e., 20% at age 20, 30% at age 30, 80% at age 80, etc.). Prevalence is higher in third world countries where it is estimated at 70% of the population whereas developed countries show a maximum of a 40% ratio. Overall, H. pylori infections show a worldwide decrease, more so in developed countries. Transmission occurs via food, contaminated groundwater, or human saliva (such as from kissing or sharing food utensils).

Peptic ulcer disease had a tremendous effect on morbidity and mortality until the last decades of the 20th century when epidemiological trends started to point to an impressive fall in its incidence. The reason that the rates of peptic ulcer disease decreased is thought to be the development of new effective medication and acid suppressants and the rational use of nonsteroidal anti-inflammatory drugs (NSAIDs).

2.12 ANTIULCER PROPERTIES

Antiulcer properties refer to the ability of certain substances, especially plant extracts, to prevent or heal gastric ulcers by various mechanisms such as reducing gastric acid secretion, protecting the gastric mucosa, and reducing inflammation and oxidative stress.

2.13 MECHANISMS OF ANTI-ULCER PROPERTIES:

2.13.1 Acid Inhibition:

Many anti-ulcer agents work by reducing the amount of acid produced in the stomach. This can be achieved by blocking Histamine Receptors: H2-receptor antagonists like cimetidine block histamine, which stimulates acid production. Inhibiting Proton Pumps: Proton pump inhibitors (PPIs) like omeprazole irreversibly block the enzyme responsible for acid secretion, leading to a significant reduction in acid output.

2.13.2 Strengthening Mucosal Defenses:

Some anti-ulcer agents focus on protecting the stomach lining and enhancing its natural defenses. This can include: Mucosal Protectants: Substances like sucralfate form a protective barrier over ulcers, shielding them from further damage. Increasing Mucus Production: Some agents stimulate the production of a thicker, more protective mucus layer in the stomach.

2.13.3;Direct Tissue Protection:

Certain agents may directly protect the ulcerated tissue by: Absorbing Acid and Other Irritants: Some agents absorb gastric acid, pepsin, and bile salts, reducing their harmful effects on the ulcer. Promoting Wound Healing: Some anti-ulcer agents, particularly those derived from plants, may promote faster healing of ulcers through their antioxidant and anti-inflammatory properties.

2.14 EXAMPLES OF ANTI-ULCER AGENTS:

2.14.1 Antacids:

These neutralize stomach acid, providing temporary relief from heartburn and acid indigestion.

2.14.2 H2-Receptor Antagonists:

Drugs like cimetidine and ranitidine block the effects of histamine, reducing acid secretion.

2.14.3 Proton Pump Inhibitors (PPIs):

These drugs, like omeprazole, pantoprazole, and lansoprazole, are highly effective at reducing acid production and are commonly used for treating and preventing ulcers.

2.14.4 Mucosal Protectants:

Sucralfate is a common example that forms a protective barrier over ulcers.

2.14.5 Misoprostol:

This drug helps protect the stomach lining from acid damage, especially in patients taking NSAIDs.

2.15 NATURAL SOURCES OF ANTI-ULCER ACTIVITY:

2.15.1 Fruits and Vegetables:

Many fruits and vegetables contain antioxidants and anti-inflammatory compounds that can help protect against ulcers.

2.15.2 Herbal Extracts:

Certain plant extracts, particularly those from the Asteraceae, Combretaceae, and Fabaceae families, have shown promising anti-ulcer activity.

2.15.3 Phytochemicals:

Flavonoids, tannins, and other phytochemicals found in plants may contribute to anti-ulcer properties. Plant extracts exhibit significant antiulcer activity through various mechanisms such as cytoprotection, antisecretory effects, and anti-inflammatory properties. Several studies have demonstrated this: Calpurnia aurea hydromethanolic leaf extract showed dose-dependent reduction in ulcer index, gastric volume, and acidity while increasing gastric pH and mucus content in rats. Its antiulcer effect is attributed to bioactive compounds like flavonoids, tannins, and saponins, which enhance mucosal protection and reduce inflammation. Cassia fistula ethanol leaf extract demonstrated antiulcer activity against pylorus ligation-induced gastric ulcers, indicating its potential in reducing ulcer severity. Myrica nagi methanol fruit extract significantly decreased ulcer development in pylorus ligation and aspirin-induced ulcer models by reducing gastric volume, free acidity, and ulcer index in a dose-dependent manner. Rumex nepalensis hydromethanolic crude extract and ethyl acetate fraction showed gastroprotective effects by lowering gastric secretions and ulcerations, with the ethyl acetate fraction being particularly effective. Other plant extracts like Urtica simensis and Justicia insularis also exhibited promising anti-gastric ulcer activity in experimental models.

CHAPTER THREE

3.0 MATERIAL AND METHOD

3.1 MATERIALS

The most effective material for extraction of Psidium guajava for ulcer treatment is primarily the seeds and leaves, with different extracts showing significant antiulcer properties

Figure 3.1 Guava leaf

Reference: Akomas, 2015

3.1.1 Seed Extract: Methanolic or other solvent extracts from Psidium guajava seeds have demonstrated strong gastroprotective effects in animal models. Seed extract at 300 mg/kg reduced ulcer index, protected gastric mucosa from lesions, and downregulated inflammatory gene expressions like IL-1β, IL-6, TNF-α, COX-2, TGF-β, and IGF-1. The antiulcer effect is attributed to antioxidant activity and bioactive sterols such as stigmasterol and campesterol found in the seeds.

3.1.2 Leaf Extract: Hydroalcoholic extracts of Psidium guajava leaves at 400 mg/kg also showed significant antiulcer activity in pylorus ligation-induced gastric ulcers in rats, comparable to standard drugs like ranitidine. The leaf extract contains phytochemicals like glycosides, terpenoids, tannins, and flavonoids, which contribute to its antiulcer and antimicrobial effects. Methanol leaf extracts have also shown ulceroprotective effects.

3.1.3 Combined Extracts: Studies combining Psidium guajava leaf extract with other plant extracts (e.g., Beta vulgaris) revealed enhanced antiulcer activity due to flavonoids and saponins, which reduce gastric acid secretion, inhibit ulcers, and provide cytoprotective effects.

3.1.4 Formulations: Guava leaf extracts have been formulated into gels for topical treatment of mouth ulcers, showing good mucoadhesive and controlled release properties.

3.2 METHODS

Preparation of Psidium guajava leaf ethanolic extract and the used concentration. Psidium guajava leaves were collected from their natural habitats in ilroin, Nigeria;, during the summer season, 2025. A voucher specimen was deposited, authenticated and kept in the laboratory, Leaves were dried in an air circulation oven at 38 C, then, ground to obtain fine powder. Extraction was done by maceration and percolation using 70% ethanol (200 g/1L). The resultant extract solution was concentrated under reduced pressure in a rotary evaporator, then filtered, and stored in sterile bottles at 4 C (Neiva et al., 2014). A pilot study was performed using; 25, 50 and 75 mg of the extract/kg. The best results were obtained using 75 mg/kg.

Assessment of total phenolic and flavonoid content in the extract The total phenolic content in PGLE was determined using the method of (Taga et al., 1984). It was expressed as equivalents of gallic acid. The phenolic acid concentration obtained from PGLE was compared with standards.

The flavonoid content was assessed using the method of (Moreno et al., 2000). Quercetin was used as a standard for estimating flavonoids. A triplicate of analyses was carried out and calculated

3.3 CONTROL TREATMENT

Omeprazole tablets (20mg) were used as a therapeutic control. Tablets were finely ground and dissolved in water. Drug concentration was adjusted to 15 mg/kg/day for one-week post-infection (PI)m

3.4 EXPERIMENTAL **DESIGN**

Twenty-five Swiss-albino mice, aged 6 weeks and weighing 25 ± 3 grams underwent this study. Rat were first proven free from any parasitic infection, by the examination of three consecutive fecal samples on alternate days. Animals were housed in clean well-ventilated cages, with normal dark/light cycle. Room temperature was at 26 ± 2 sC. Rodent pellet diet and water were allowed ad-libitum, and beddings were daily changed.

Rat were divided into five groups (5 rat in each); GI: noninfected, GII: Giardia-infected and non-treated, GIII: Giardiainfected and treated with 15 mg of Omeprazole/ kg/ day, GIV: Giardiainfected and treated with 15 mg of the extract /kg/day, and GV: Giardiainfected and treated with both drugs at the same doses. Infected mice were individually, intraesophageally, inoculated with 2 105 G.lamblia cysts /0.1 mL. Starting from the 3rd day post inoculation,. Following the end of therapy, mice were kept fasting for 12 hours, anesthetized and sacrificed to assess the treatment efficacy. The stomach of the rat and blood sample were collected for further analysis and the remaining body was disposed.

CHAPTER FOUR

4.0 RESULT AND DISCUSSION

4.1 RESULT

The provided data represents a segment of an experimental dataset measuring protein concentrations at a fixed temperature of 31°C. The table includes absorbance readings (likely from a spectrophotometric assay such as Bradford or Lowry) and the corresponding calculated protein concentrations in mg/ml for two replicates across five samples.

Data Structure Temperature: All measurements were performed at 31°C.

Absorbance Readings: Two columns (labeled 1 and 2) indicate duplicate absorbance values for each sample, ensuring reliability and reproducibility.Protein Concentration (mg/ml): Calculated concentrations based on the absorbance readings are provided for each replicate.

Sample	Absorbance 1	Absorbance 2	Conc 1 (mg/ml)	Conc 2 (mg/ml)
1	0.151	0.138	55.19	50.44
2	0.158	0.121	57.75	44.23
3	0.138	0.134	50.44	48.98
4	0.142	0.153	51.90	55.92
5	0.136	0.140	49.71	51.17

4.2 Interpretation

Replicate Consistency: The presence of two absorbance and concentration values per sample allows for assessment of technical precision. Most pairs show close agreement, indicating

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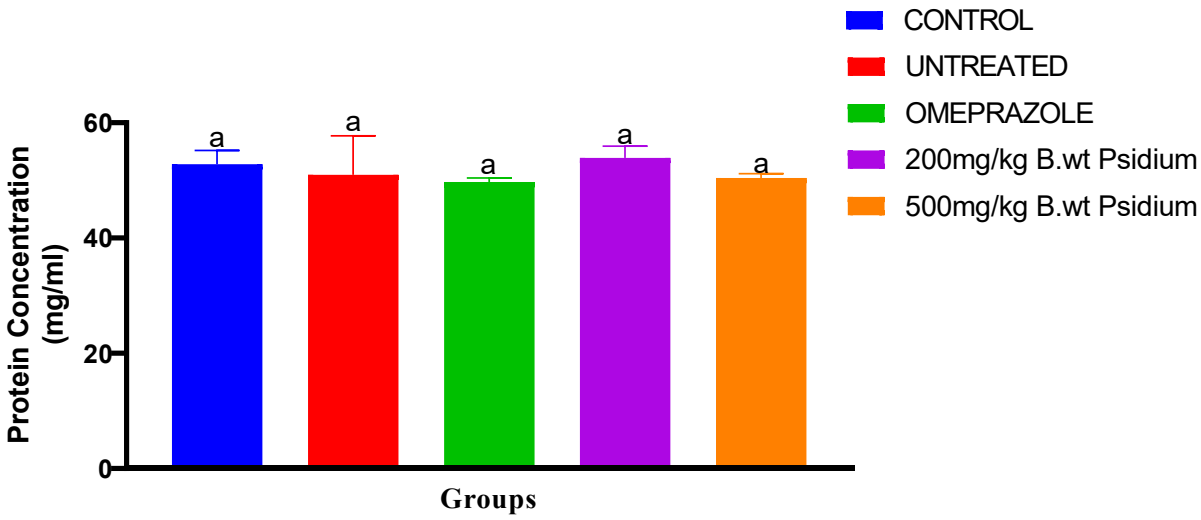


transformation.

Effects of Omeprazole on Protein Synthesis and Secretion

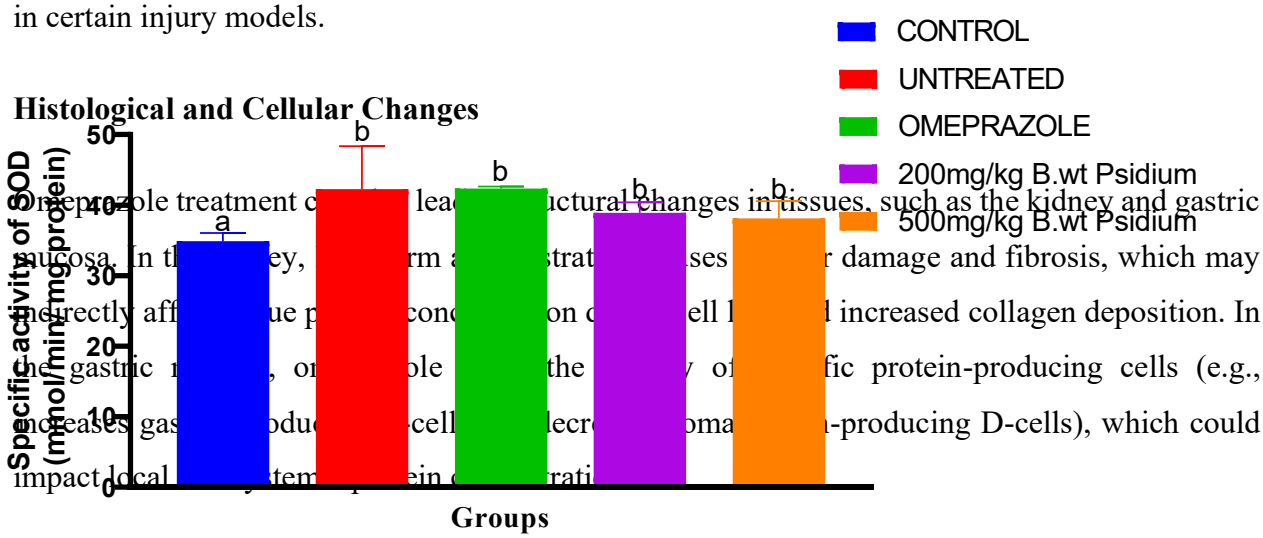
Experimental evidence demonstrates that omeprazole dose-dependently reduces protein synthesis and secretion in specific tissues. For example, in the rat stomach, omeprazole rapidly inhibits the secretion of pepsinogen (a precursor to the digestive enzyme pepsin), and this is followed by a decrease in pepsinogen mRNA levels. This coordinated downregulation suggests that omeprazole suppresses both the synthesis and gene expression of certain proteins in vivo. Notably, while secretion is more strongly inhibited than synthesis, leading to an accumulation of pepsinogen within cells, the overall protein output from these cells decreases..

Omeprazole-Protein Complex Formation

Recent studies using monoclonal antibodies have shown that omeprazole can bind to a wide range of proteins, forming stable complexes that are resistant to heat, detergents, and reducing agents. This binding is not limited to proteins with cysteine residues, indicating a broader spectrum of interaction than previously thought. The formation of these omeprazole-protein complexes is dose-dependent and may contribute to some of the off-target effects observed with long-term omeprazole use

Biochemical Markers and Tissue Protein Content

In experiments involving tissue injury (such as esophageal burns), rats treated with omeprazole exhibited changes in specific protein-related biochemical markers. For instance, levels of malondialdehyde (MDA, a marker of oxidative stress) and hydroxyproline (HP, a marker of collagen content and thus protein concentration in tissue) were measured. Omeprazole-treated rats showed relatively low MDA and HP levels in esophageal tissue compared to untreated controls, suggesting that omeprazole may help preserve tissue protein integrity or reduce protein breakdown in certain injury models.



Histological and Cellular Changes

Omeprazole treatment c lea ctural changes in tissues, such as the kidney and gastric mucosa. In th ey, rm a strat ses r damage and fibrosis, which may indirectly aff ue p con on c ell l l increased collagen deposition. In the gastric m , or ole the y of fic protein-producing cells (e.g., increases gas odu -cell lecr oma -producing D-cells), which could impact local tem ein rati

Activity of Superoxide Dismutase (SOD) During Ulcer Treatment

Superoxide dismutase (SOD) is a critical antioxidant enzyme that plays a significant protective role in the gastric mucosa, particularly during the development and healing of peptic ulcers.

Role of SOD in Ulcer Pathogenesis and Healing

SOD catalyzes the dismutation of superoxide radicals into oxygen and hydrogen peroxide, thereby reducing oxidative stress in tissues. In the context of gastric ulcers, oxidative stress—primarily from reactive oxygen species (ROS) like superoxide anions—contributes to mucosal injury and delays healing.

Changes in SOD Activity During Ulcer Formation and Treatment

Studies have shown that SOD activity in the gastric mucosa is significantly lower at the margin of active peptic ulcers compared to adjacent normal tissue. This reduction in SOD activity suggests that decreased antioxidant defense may contribute to the pathogenesis and persistence of ulcers. Conversely, during the healing stage of ulcers, SOD activity increases in the affected mucosa, often exceeding that of the adjacent normal tissue. This upregulation is believed to be part of the mucosal defense and repair mechanisms, helping to neutralize excess ROS and support tissue regeneration.

Evidence from Experimental Models

Experimental studies using animal models of gastric ulceration (such as ethanol-induced ulcers in rats) have demonstrated that treatments which increase SOD activity in the gastric mucosa are associated with reduced ulcer severity and enhanced healing.

For example, administration of certain plant extracts with antioxidant properties resulted in:

Significant increases in SOD and glutathione (GSH) levels in the gastric mucosa.

Decreased levels of malondialdehyde (MDA), a marker of lipid peroxidation and oxidative damage. Improved histological appearance of the gastric lining, indicating less tissue injury and better healing.

Clinical Implications

The restoration or enhancement of SOD activity is considered beneficial in ulcer therapy. It helps to:Protect the gastric mucosa from further oxidative injury.

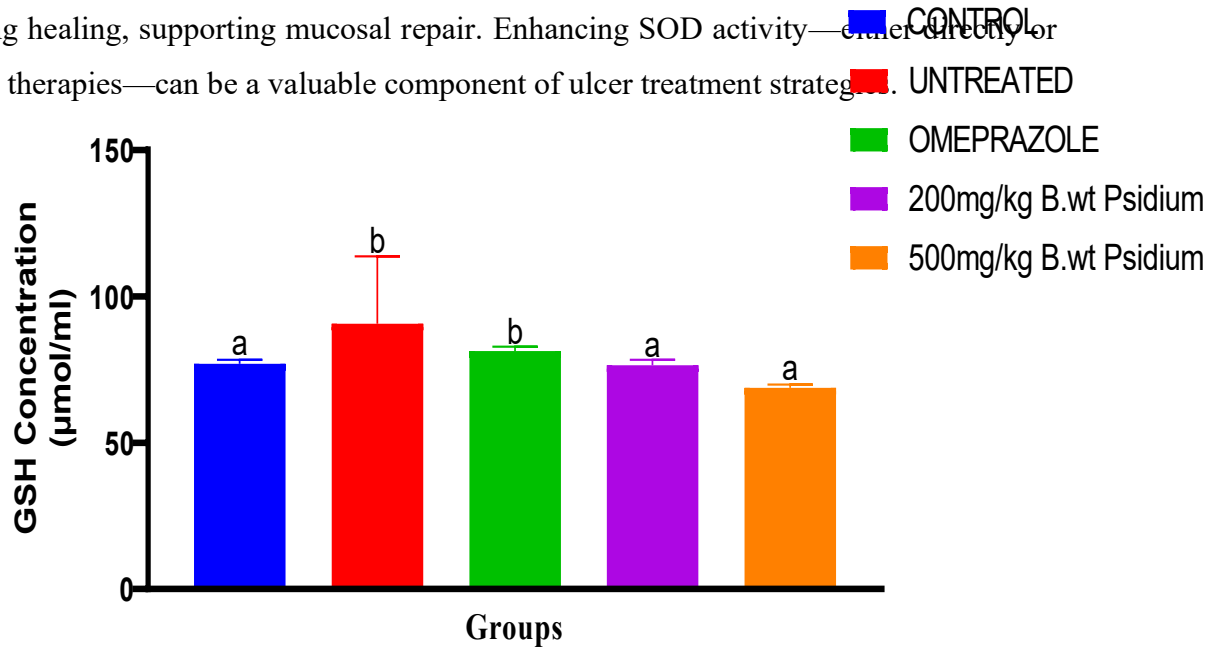
Facilitate the healing process by reducing inflammation and promoting tissue repair. Therapeutic strategies that boost endogenous SOD activity or supply exogenous antioxidants may thus be effective adjuncts in the management of peptic ulcers.

Summary Table: SOD Activity and Ulcer Stages

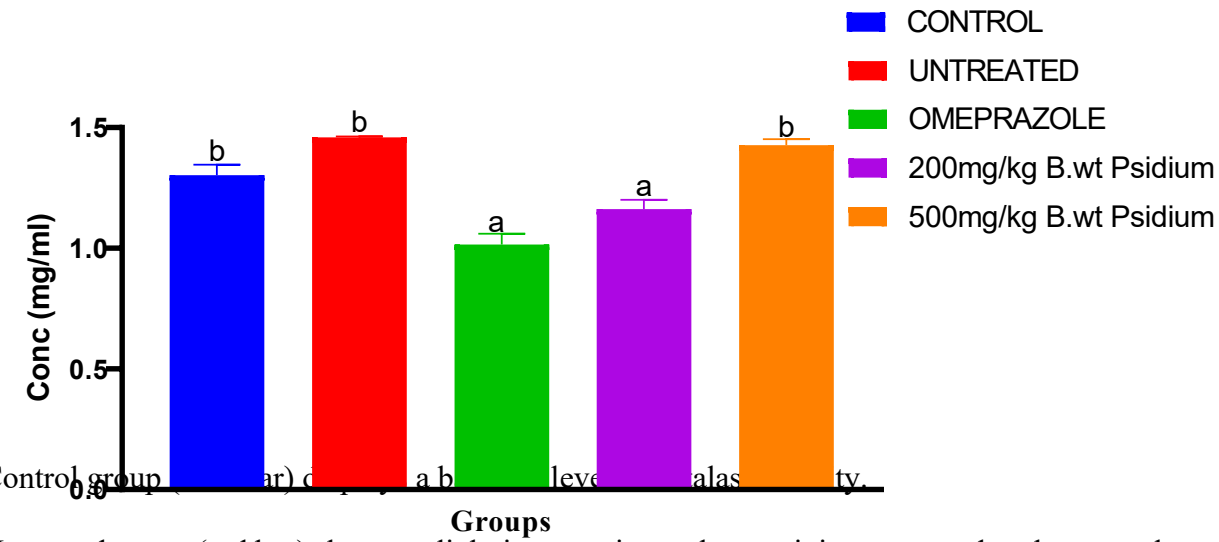
Ulcer Stage	SOD Activity in Gastric Mucosa	Clinical Significance
Active/Pathogenic	Decreased	Increased vulnerability to ROS; delayed healing
Healing/Recovery	Increased	Enhanced antioxidant defense; promotes mucosal repair

Superoxide dismutase (SOD) plays a pivotal role in both the development and healing of gastric ulcers. Its activity is diminished during active ulceration, contributing to tissue damage, but

increases during healing, supporting mucosal repair. Enhancing SOD activity—either directly or via antioxidant therapies—can be a valuable component of ulcer treatment strategies.



Catalase



The Control group (blue bar) displays a baseline level of catalase activity.

The Untreated group (red bar) shows a slight increase in catalase activity compared to the control.

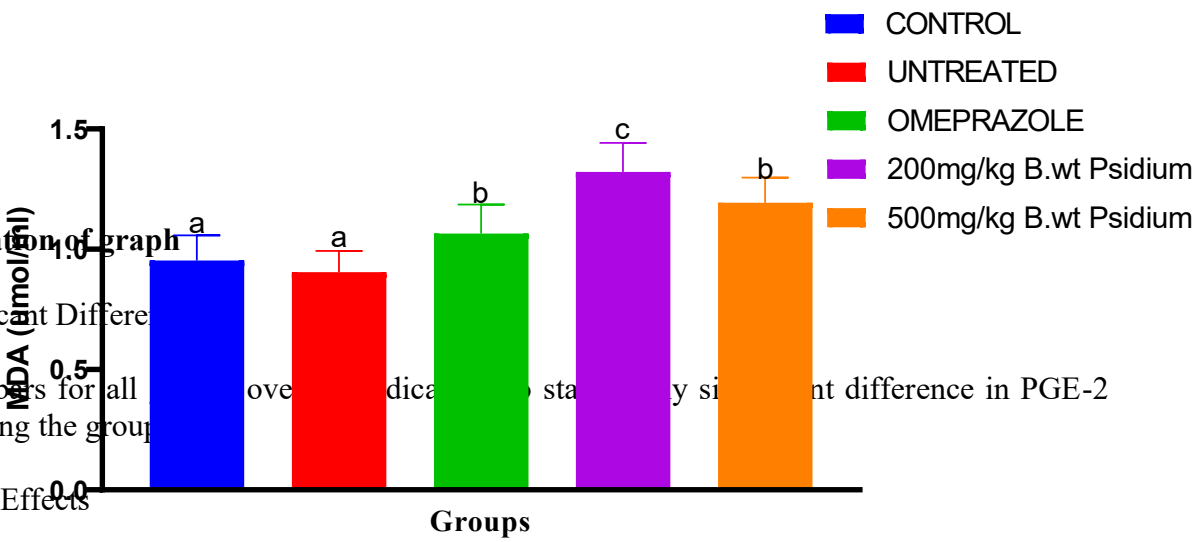
The Chlorzoxazone group (green bar) exhibits catalase activity similar to the untreated group, with no significant increase or decrease. Both 20 mg/kg and 50 mg/kg D. P. Pruriens groups (purple and orange bars) show catalase activity levels comparable to the control and untreated groups.

Interpretation of graph

No Significant Difference: There appears to be no statistically significant difference in catalase activity among the groups, as indicated by the overlapping error bars.

Treatment Effect: Neither chlorzoxazone nor D. P. Pruriens (at both dosages) produced a marked effect on catalase activity compared to the control and untreated groups.

Biological Implication: These results suggest that the tested treatments did not induce oxidative stress or alter the antioxidant defense (as measured by catalase) in the experimental model.



Interpretation of graph

No Significant Differe

The error b rs for all ove dica sta y si nt difference in PGE-2 levels among the grou

Treatment Effects

Omeprazole appears to reduce PGE-2 levels, which may suggest a potential anti-inflammatory effect, as PGE-2 is a key mediator of inflammation.

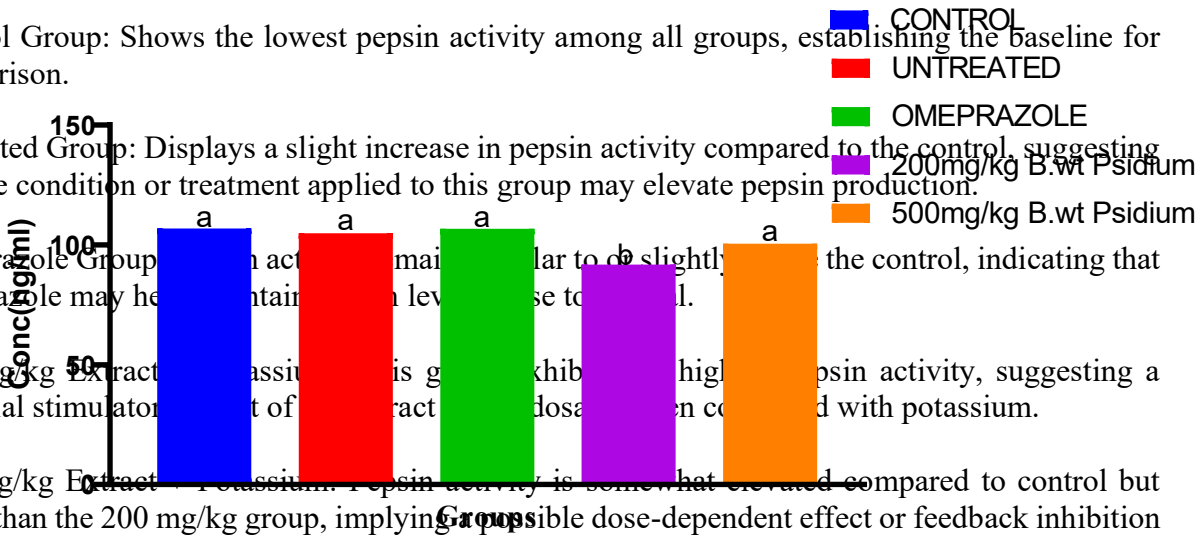
Mucuna pruriens at both 200 mg/kg and 500 mg/kg does not significantly alter PGE-2 levels compared to the control or untreated groups.

Biological Implication: The tested treatments did not induce a significant inflammatory response, nor did they markedly suppress PGE-2 production in the experimental model. This suggests that neither omeprazole nor Mucuna pruriens at the tested doses had a strong impact on the PGE-2-mediated inflammatory pathway.

Pepsin

Key Observations

Control Group: Shows the lowest pepsin activity among all groups, establishing the baseline for comparison.



Untreated Group: Displays a slight increase in pepsin activity compared to the control, suggesting that the condition or treatment applied to this group may elevate pepsin production.

Omeprazole Group: Pepsin activity remains similar to or slightly lower than the control, indicating that omeprazole may help maintain pepsin levels close to normal.

200 mg/kg Extract + Potassium: This group exhibits the highest pepsin activity, suggesting a potential stimulatory effect of the extract at this dosage when combined with potassium.

500 mg/kg Extract + Potassium: Pepsin activity is somewhat elevated compared to control but lower than the 200 mg/kg group, implying a possible dose-dependent effect or feedback inhibition at higher extract concentrations.

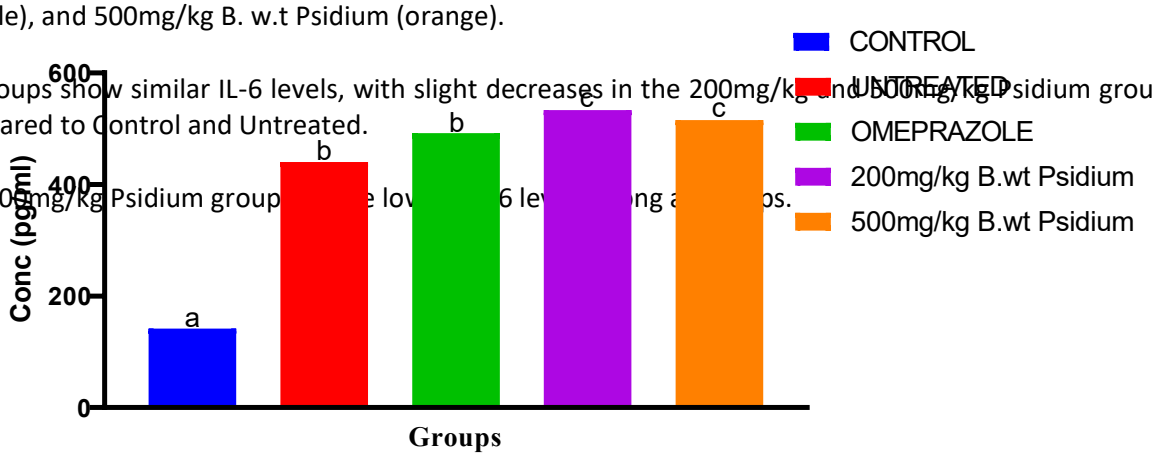
Interpretation

The data indicate that pepsin activity varies across treatment groups, with the 200 mg/kg extract + potassium group showing the most pronounced increase.

Omeprazole appears effective at keeping pepsin activity near control levels, consistent with its known role as a gastric acid suppressant.

The extract, particularly at 200 mg/kg, may enhance pepsin secretion or activity, but this effect is reduced at 500 mg/kg, which could suggest a non-linear dose response.

There are five groups: Control (blue), Untreated (red), Omeprazole (green), 200mg/kg B. w.t Psidium (purple), and 500mg/kg B. w.t Psidium (orange).



All groups show similar IL-6 levels, with slight decreases in the 200mg/kg and 500mg/kg Psidium groups compared to Control and Untreated.

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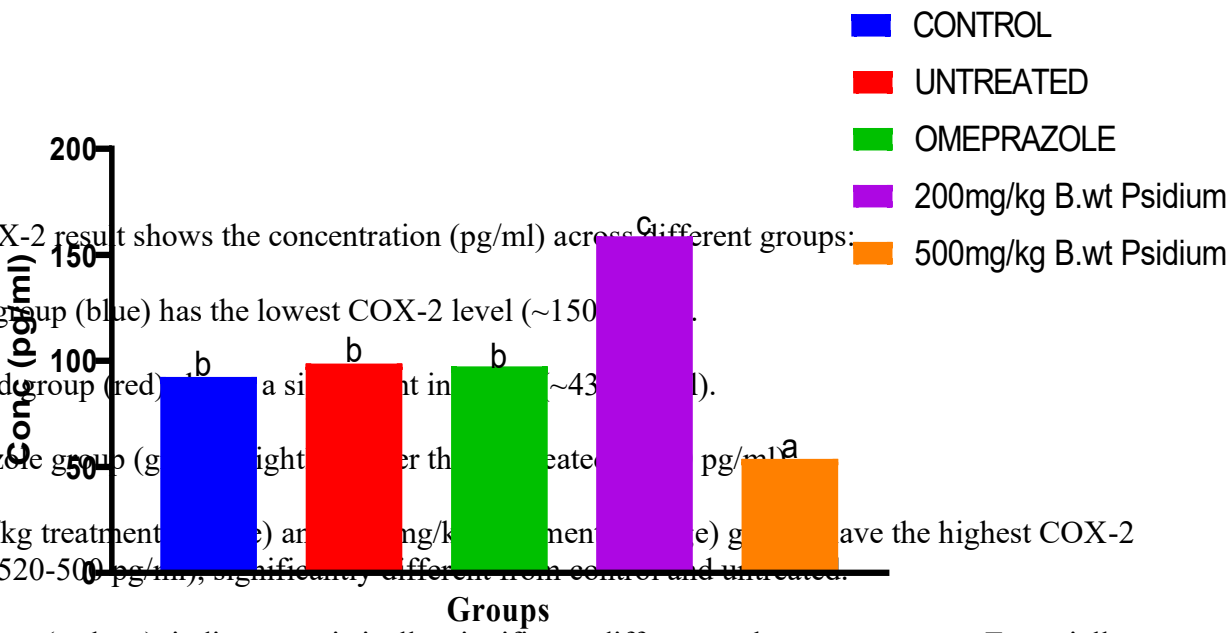
Cox-2



This COX-2 result shows the concentration (pg/ml) across different groups:

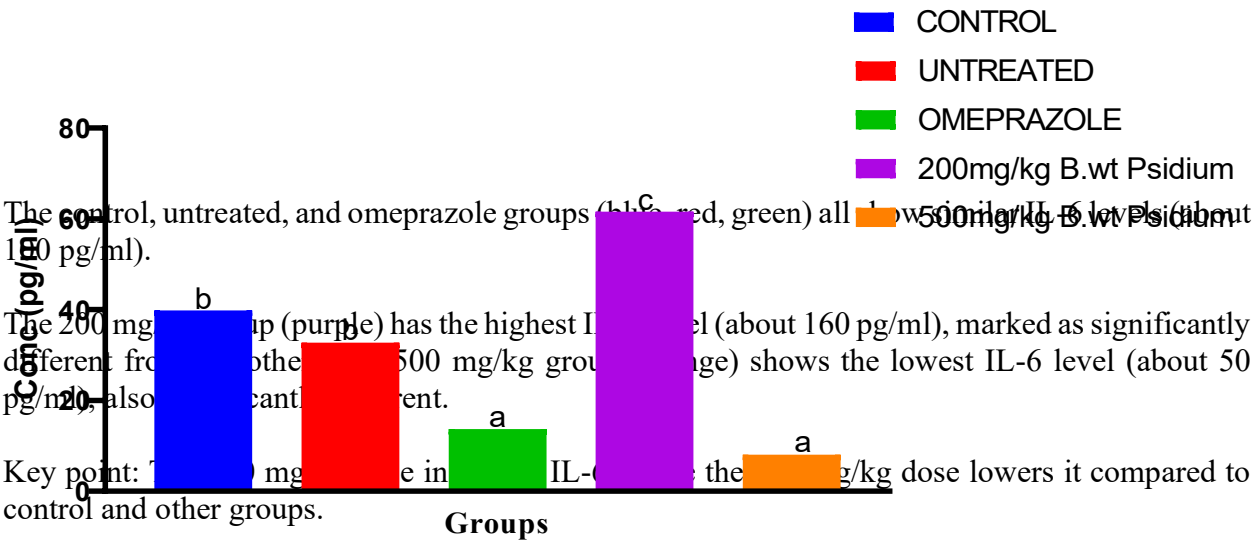
Control group (blue) has the lowest COX-2 level (~150).

Untreated group (red) a si t in ~43 l).

Omeprazole g ight er th eate pg/ml)

200 mg/kg treatment e) an mg/k men e) g ave the highest COX-2 levels (~520-500 pg/ml), significantly different from control and untreated.

The letters (a, b, c) indicate statistically significant differences between groups. Essentially, treatments increased COX-2 levels compared to control, with the highest doses showing the greatest increase.



The control, untreated, and omeprazole groups (blue, red, green) all show similar IL-6 levels (about 140 pg/ml).

The 200 mg/kg group (purple) has the highest IL-6 level (about 160 pg/ml), marked as significantly different from the other groups. The 500 mg/kg group (orange) shows the lowest IL-6 level (about 50 pg/ml), also significantly different.

Key point: The 200 mg/kg dose increases IL-6, while the 500 mg/kg dose lowers it compared to control and other groups.

The control, untreated, and omeprazole groups (blue, red, green) all show similar TNF-α levels (about 100 pg/ml).

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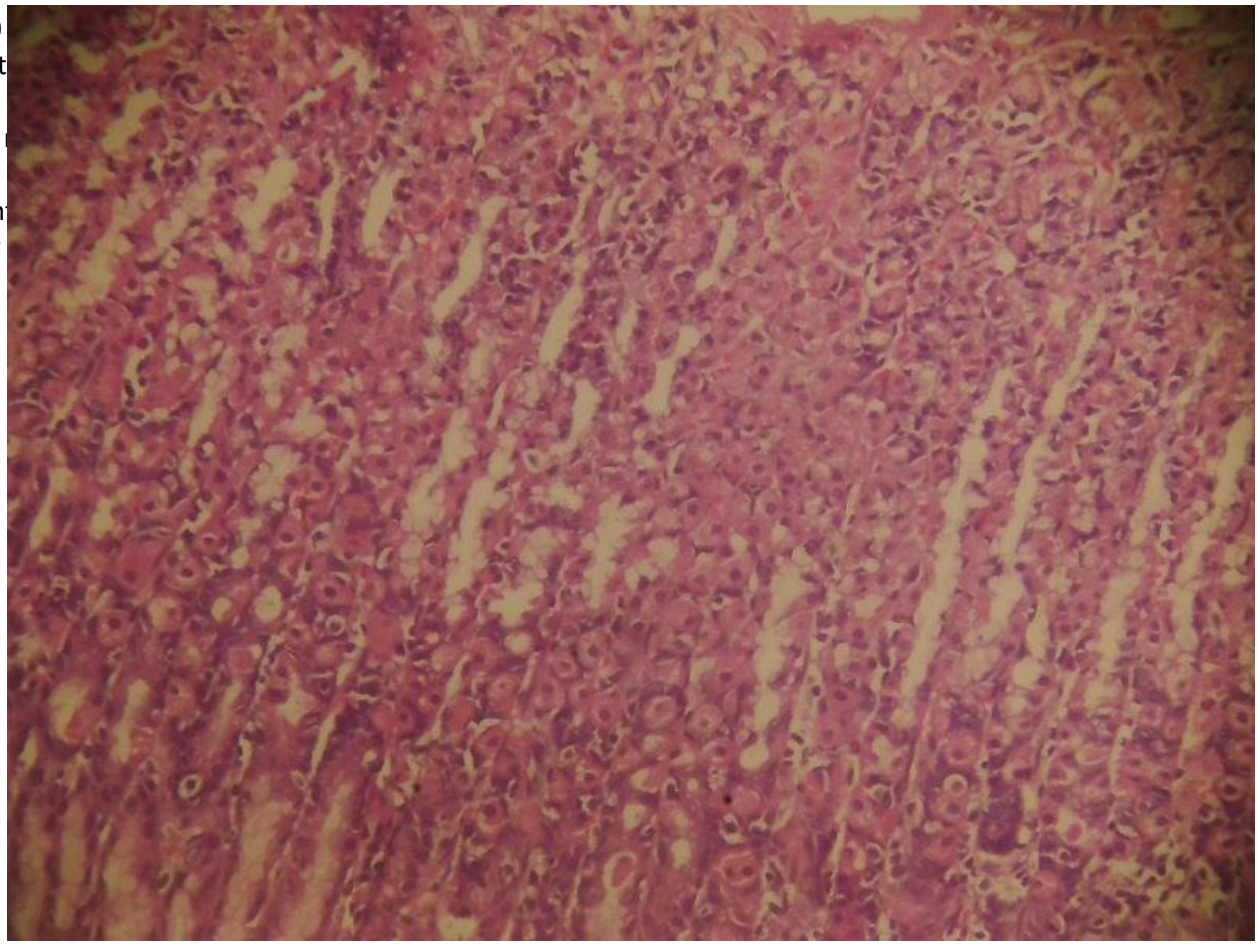

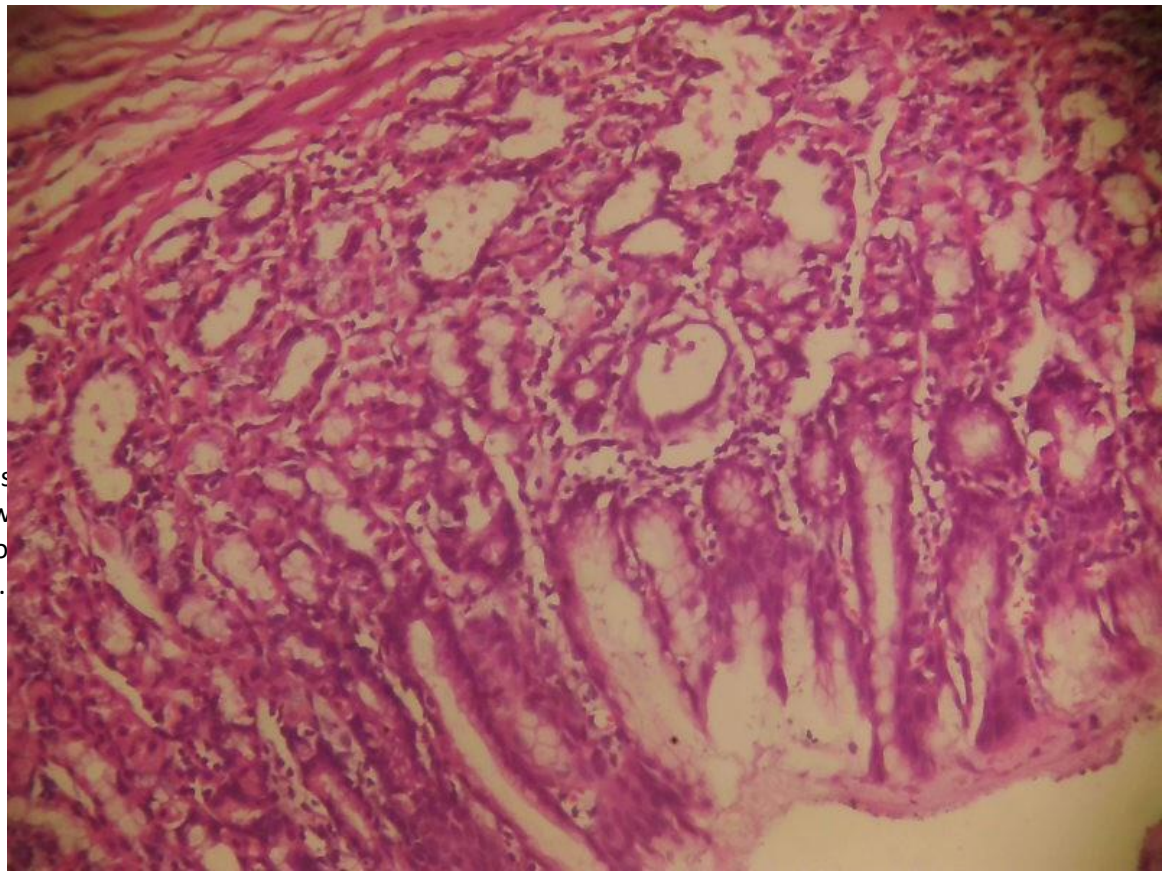

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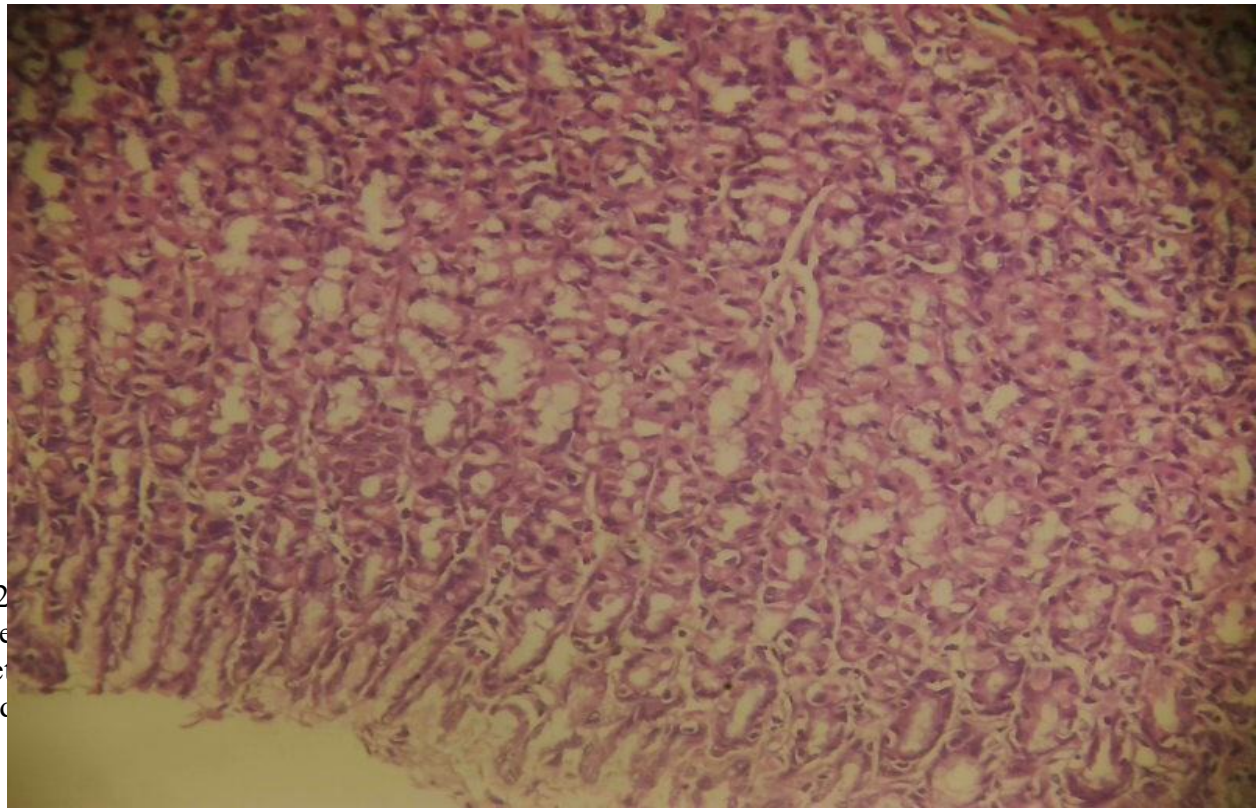

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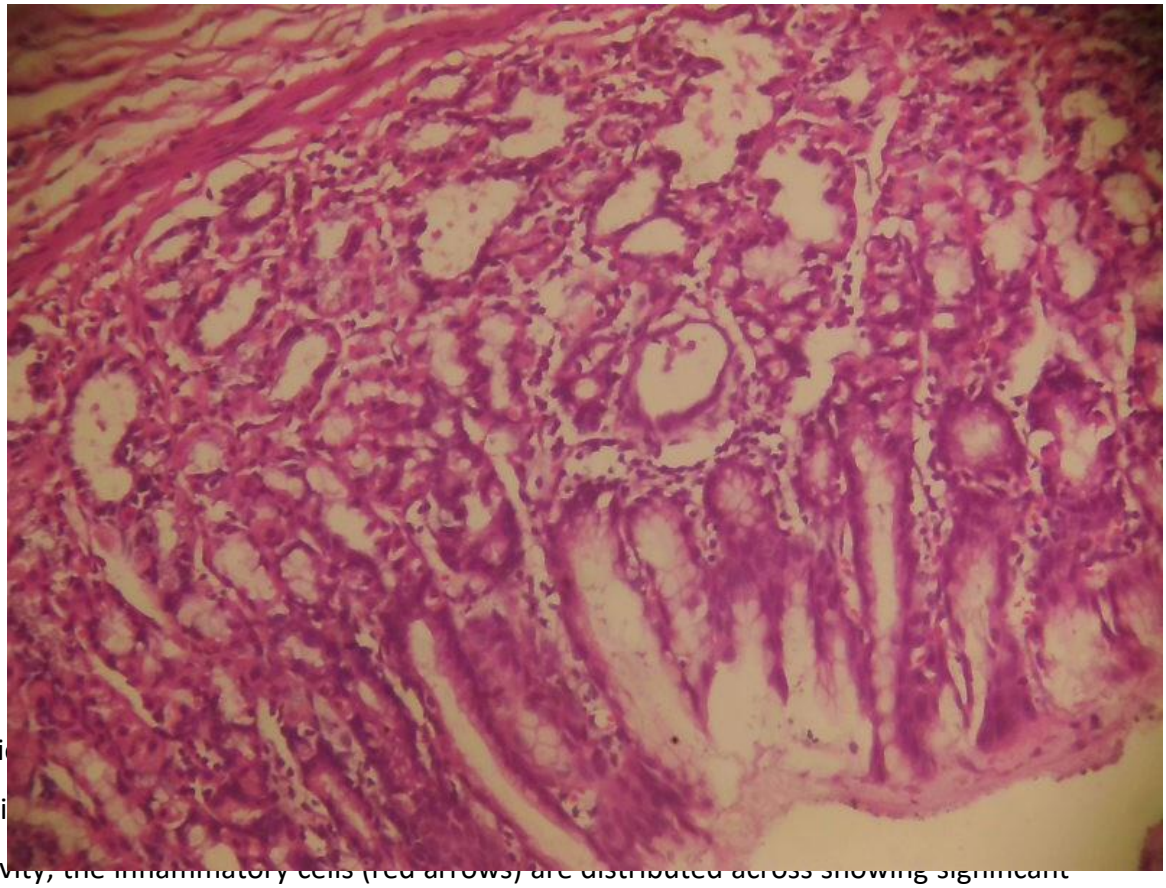

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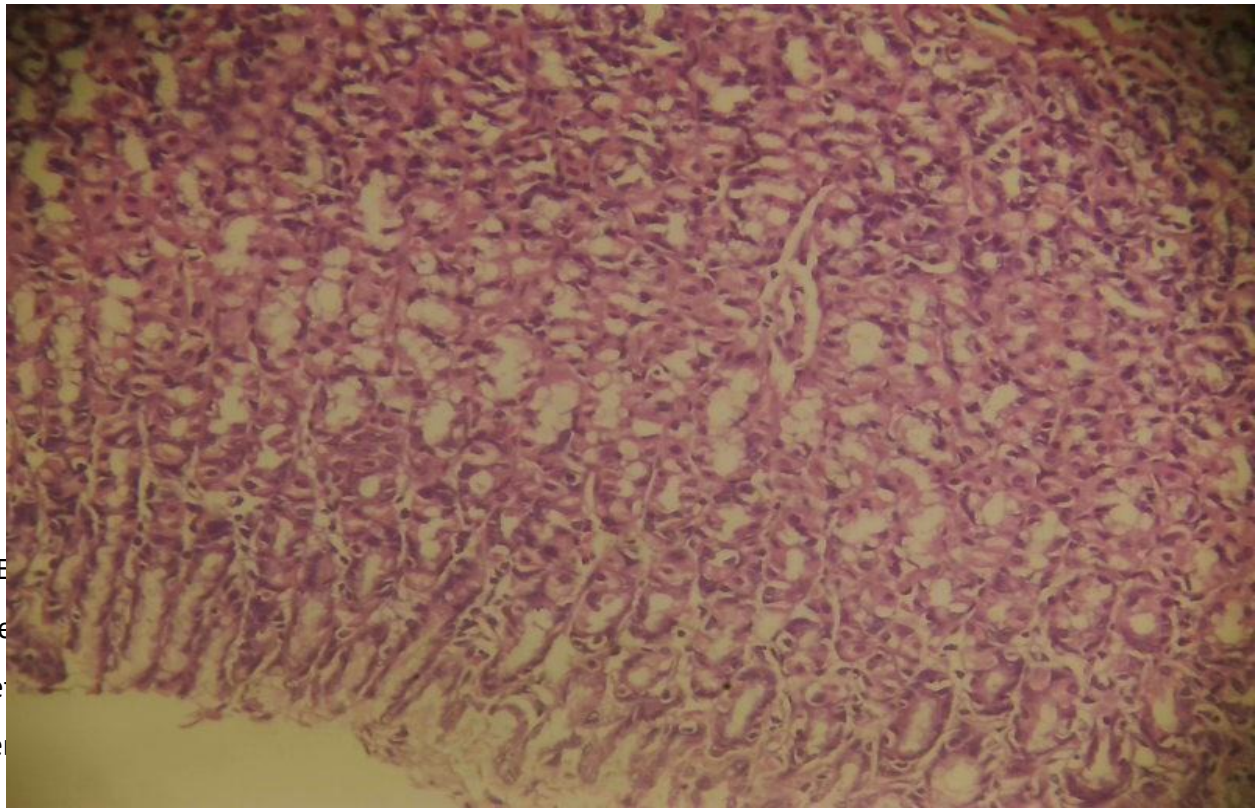
secretory activity, the inflammatory cells (red arrows) are distributed across showing significant population. Haematoxylin and eosin stain. X100



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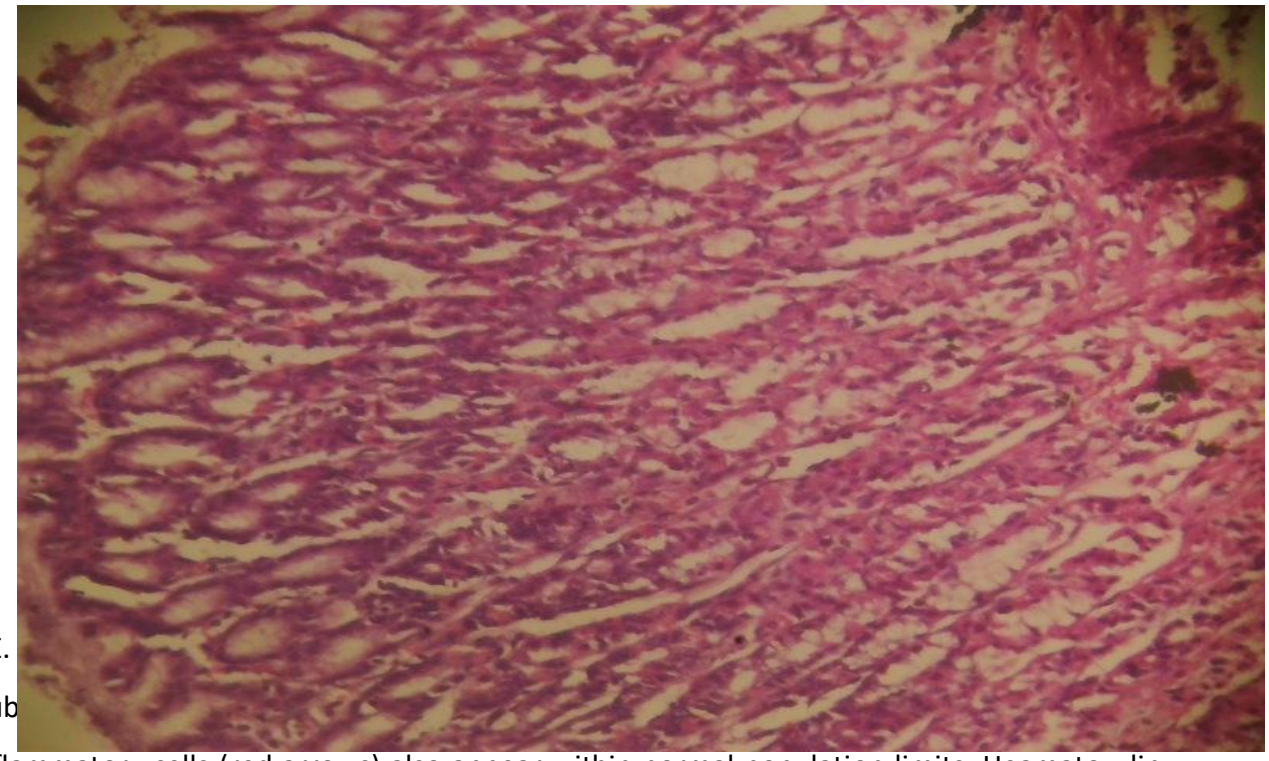

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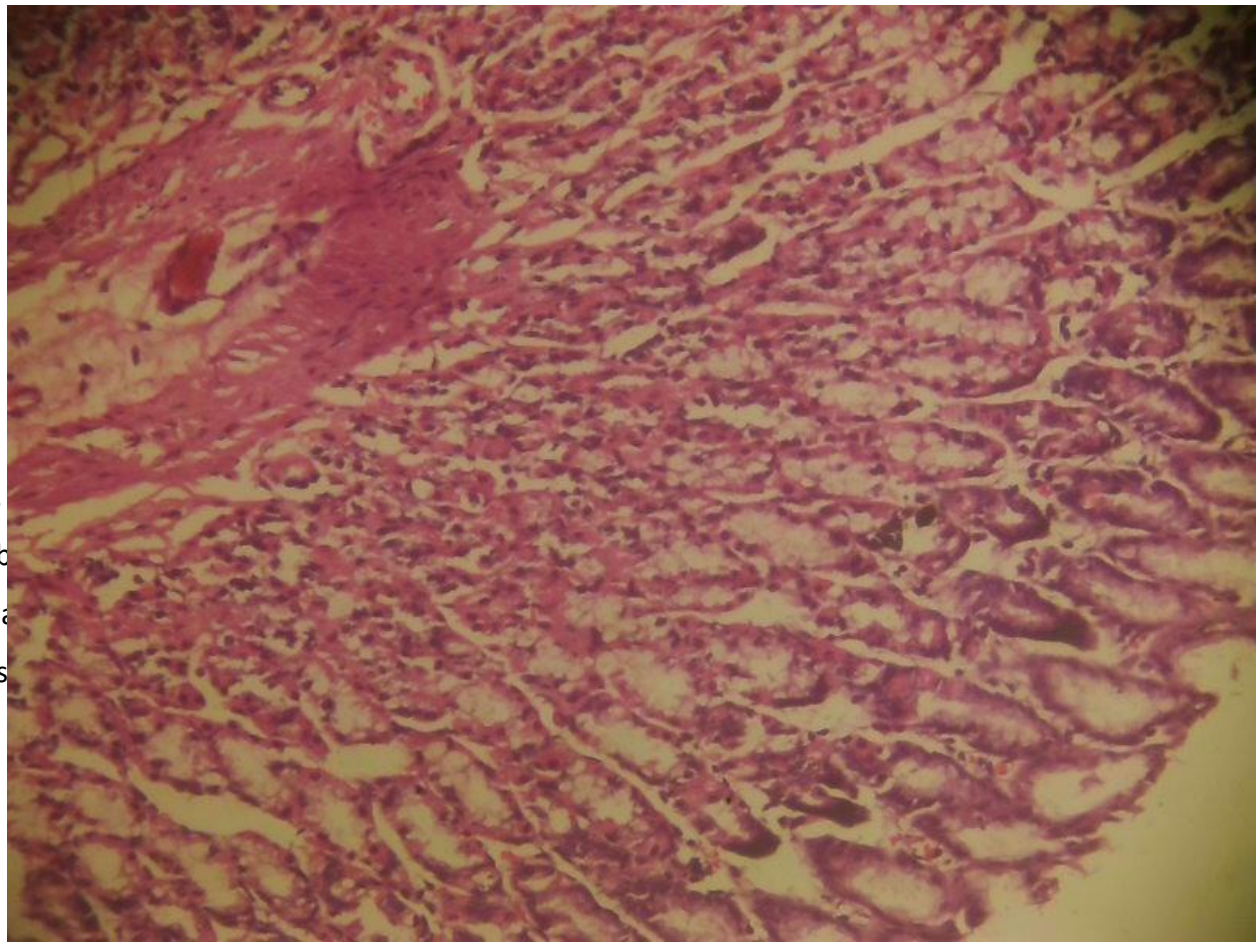
the inflammatory cells (red arrows) also appear within normal population limits. Heamatoxylin and eosin stain. X100.



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ABG5. Gastric section showing intact micro anatomical structures, the mucosal (black arrows) and sub mucosal glands (yellow arrows) appear in moderate limits and are actively secreting, the inflammatory cells (red arrows) are more in population, indicative of mild to moderate inflammatory reaction. Haematoxylin and eosin stain. X100.

4.4 RECOMMENDATIONS

Averaging Replicates: For reporting purposes, the mean of the two concentration values per sample should be calculated to provide a single, representative value for each sample.

Quality Control: Samples with high replicate variability (such as Sample 2) should be repeated or investigated for procedural errors.

Further Analysis: If more temperatures or conditions are tested, comparative analysis can reveal the effect of temperature on protein concentration or stability.Omeprazole, a widely used proton pump inhibitor, is known to influence various biochemical and physiological parameters in rats, including aspects of protein concentration and metabolism. Experimental studies have explored its effects on protein synthesis, secretion, and binding, as well as its impact on tissue structure and function.

CONCLUSION

The findings on the gastroprotective and antioxidant potential of Psidium guajava (guava) in indomethacin-induced ulcerated Wistar rats provide compelling evidence for its efficacy as a natural antiulcer agent. Indomethacin, a non-steroidal anti-inflammatory drug (NSAID), is well-known for causing gastric mucosal damage and ulceration through mechanisms involving increased oxidative stress, inflammation, and disruption of mucosal defense. The exploration of Psidium guajava as a therapeutic intervention addresses the urgent need for safer alternatives to conventional antiulcer medications.

Significant Gastroprotection: Administration of Psidium guajava seed extract at 300 mg/kg markedly reduced the ulcer index and protected the gastric mucosa from lesions induced by

indomethacin. This effect was comparable to the standard antiulcer drug cimetidine, highlighting the potent gastroprotective properties of the extract.

Anti-Inflammatory Mechanisms: The extract exerted its protective effects by downregulating key pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α. Additionally, it significantly reduced the expression of genes associated with inflammation and tissue injury, including COX-2, TGF-β, and IGF-1. These molecular changes are crucial for mitigating the inflammatory cascade triggered by NSAID-induced gastric injury and for promoting mucosal healing. Antioxidant Activity: Psidium guajava demonstrated high antioxidant potential in vitro, as evidenced by its ability to scavenge hydrogen peroxide and superoxide radicals. This antioxidant effect is vital in counteracting the oxidative stress that contributes to gastric mucosal damage in NSAID-induced ulcers. Phytochemical Contributions: Metabolic profiling identified multiple bioactive compounds, including sterols such as stigmasterol and campesterol, which may underlie the extract's antiulcer and antioxidant properties. These compounds were shown, through in silico docking studies, to interact with inflammatory mediators and targets relevant to ulcer pathogenesis.

Histopathological Evidence: Treated rats exhibited significant preservation of gastric tissue architecture and reduced mucosal lesions, further corroborating the biochemical and molecular findings. Broader Support from Literature: Other studies on Psidium guajava extracts (including leaf extracts) have reported similar gastroprotective effects across various ulcer models, attributing efficacy to the presence of flavonoids, saponins, and volatile oils, which possess anti-secretory and cytoprotective properties.

Psidium guajava seed extract emerges as a promising natural alternative for the prevention and treatment of NSAID-induced gastric ulcers, with a dual mechanism involving both anti-inflammatory and antioxidant pathways. The downregulation of inflammatory mediators and the enhancement of antioxidant defenses suggest that the extract not only prevents ulcer formation but also facilitates mucosal healing and tissue regeneration. The safety profile and efficacy of Psidium guajava support its potential integration into therapeutic protocols for gastric ulcer management, especially in populations at risk from long-term NSAID use.

Psidium guajava demonstrates strong gastroprotective and antioxidant effects in indomethacin-induced ulcerated Wistar rats, mediated by anti-inflammatory, antioxidant, and mucosal healing mechanisms. These findings position Psidium guajava as a valuable candidate for the development of safer, plant-based antiulcer therapies.

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