PEPTIC ULCER: AN OVERVIEW

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ABSTRACT

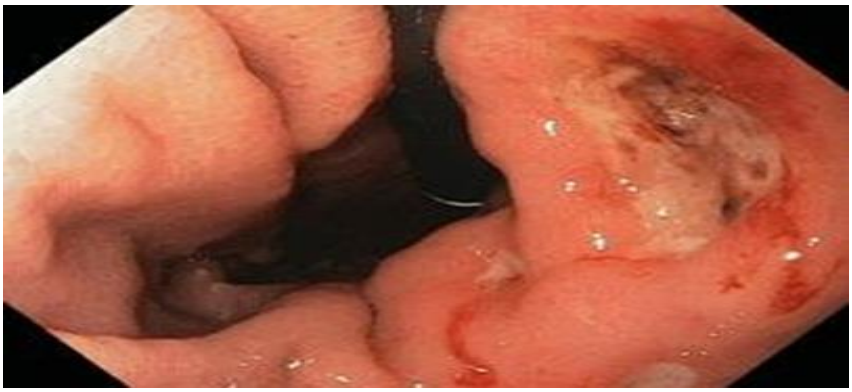
A persistent situation that affects up to 10% of people international is peptic ulcer sickness. The presence of gastric juice pH and the reducing of mucosal defenses are prerequisites for the improvement of peptic ulcers. the 2 primary factors which are disrupting the mucosal resistance to injury are Helicobacter pylori (H. pylori) infection and non-steroidal 07b031025f5f96dfa8443f843db463b6 capsules (NSAIDs). The hallmark of Peptic Ulcer disease (PUD) is the disruption of the GI tract's internal lining due to either pepsin or gastric acid secretion. It penetrates the gastric epithelium's muscularis propria layer. normally, it influences the proximal duodenum and belly. The jejunum, distal duodenum, or decrease esophagus can be affected. patients with gastric ulcers normally revel in epigastric pain 15–30 minutes after consuming, while duodenal ulcer sufferers typically enjoy ache 2–three hours later. Proton pump inhibitors (PPIs) and histamine-2 (H2) receptor antagonists, common remedies for peptic ulcers, had been
linked to facet effects, relapses, and a diffusion of drug interactions. Conversely, medicinal plant life and the chemical compounds they contain can be used to deal with and prevent a wide variety of ailments.

KEYWORDS: Peptic ulcer, Helicobacter pylori, Non-steroidal anti-inflammatory.

1. INTRODUCTION

The belly or proximal duodenum are the standard places of peptic ulcers, which can be acid-triggered lesions of the digestive tract characterised via denuded mucosa that extends into the submucosa or muscularis propria.[1] historically, an acidic surroundings that is hypersecretory in mixture with nutritional elements or strain is concept to be the purpose of mucosal disruption in patients affected by acid-peptic sickness. Alcohol and tobacco use, non-steroidal antidepressants, H. pylori infection, and different threat factors Use of nonsteroidal 07b031025f5f96dfa8443f843db463b6 tablets (NSAIDs) and Zollinger-Ellison syndrome.[2]

NSAID customers have a 4-fold elevated chance of peptic ulcer complications, even as aspirin users have a two-fold increased chance.[3] The risk of higher gastrointestinal bleeding increases when anticoagulants, corticosteroids, and selective serotonin reuptake inhibitors are used concurrently with NSAIDs or aspirin.[4] The role that NSAIDs and aspirin play in the pathophysiology of peptic ulcer ailment continues to be up for debate, even though many customers of these medicinal drugs also have concurrent H. pylori infections. Aspirin use, NSAID use, and H. pylori infection have been discovered to independently raise the hazard of peptic ulcer disorder in a meta-evaluation of observational research[5] Peptic ulcer circumstance can be visible inside the figure.1



discern 1: image of a peptic ulcer taken all through an upper endoscopy. This ulcer is a "gastric ulcer" because it is located within the stomach.

H. pylori-negative, NSAID-poor, and aspirin-bad peptic ulcer sickness, which is classified as an idiopathic ulcer, can be diagnosed in approximately one-5th of cases.[6] it's miles because of the imbalance among factors that make a contribution to mucosal integrity and aggressive insults, however the pathogenic mechanisms at the back of the development of idiopathic peptic ulcers are nonetheless unknown.[2]

1.1 ETIOLOGY

Although there are many causes of PUD, the majority of the disease etiology is related to Helicobacter pylori-associated PUD and NSAID-associated PUD.[7]

Common

1. H. pylori infection
2. NSAIDs
3. Medications.

Rare

- Zollinger-Ellison syndrome
- Malignancy (gastric/lung cancer, lymphomas)
- Stress (Acute illness, burns, head injury)
- Viral infection
- Vascular insufficiency
- Radiation therapy
- Crohn disease
- Chemotherapy.

1.2 SIGN AND SYMPTOMS

A peptic ulcer may present with one or more of the following signs and symptoms:

- Traditionally, epigastric abdominal pain is closely associated with mealtimes.
- When a person has a duodenal ulcer, the pain usually wakes them up three hours after they eat.
- Bloating and fullness in the abdomen.
- Waterbrash, a surge of saliva following a regurgitation episode that lessens the acid in the esophagus, though it is more commonly linked to gastroesophageal reflux disease.
- Nausea and frequent vomiting.
- Appetite loss and weight loss in cases of gastric ulcers.
- Weight gain in cases of duodenal ulcers because eating relieves pain.
- Hematemesis, or blood vomiting, can be brought on by bleeding directly from a stomach ulcer or by prolonged, severe vomiting that damages the esophagus.
- Melena: a foul-smelling, tarry stool caused by oxidized iron from hemoglobin.
- In rare cases, an ulcer can result in a gastric or duodenal perforation, causing severe, stabbing pain and acute peritonitis[8], which calls for immediate medical attention.

1.3 PATHOGENESIS OF PEPTIC ULCER

The mechanism by way of which H. pylori induces the improvement of different forms of lesions in the gastroduodenal mucosa is not completely defined. H. pylori infection can bring about both hypochlorhydria or hyperchlorhydria, therefore figuring out the form of peptic ulcer. despite the fact that cytokines that block parietal cellular secretion are the number one mediators of H. pylori contamination, the micro organism can also immediately effect the H+/ok+ ATPase subunit, set off sensory neurons connected to somatostatin that are related to calcitonin gene-associated peptide (CGRP), or save you the gastrin from being produced. at the same time as hyposecretion is linked to the development of gastric ulcers, 10-15% of sufferers inflamed with H. pylori have hypergastrinemia, which ends up in elevated gastric secretion, and decreased antral somatostatin content material. This causes the parietal and stomach cells to secrete greater histamine, which in turn reasons them to secrete greater acid or pepsin. furthermore, somatostatin mRNA expression rises and gastrin mRNA expression decreases when H. pylori is eradicated. Hypochlorhydria is connected to gastric ulcers in most people of patients who stay.

The systemic inhibition of constitutively expressed cyclooxygenase-1 (COX-1), that's in rate of prostaglandin synthesis and is linked to reduced mucosal blood waft, low mucus, and other unfavourable outcomes, is the primary mechanism of NSAID-related harm to the gastroduodenal mucosa. secretion of bicarbonate and the suppression of cell division. NSAIDs reversibly and concentration-dependently inhibit the enzyme. Mucosal harm and the chance of ulcers are decreased while exogenous prostaglandins and COX-2-selective NSAIDs are used collectively.[10] NSAIDs reason the uncoupling of mitochondrial oxidative phosphorylation and disturb the phospholipids in mucus, which starts offevolved the harm to the mucosa.

NSAIDs emerge as protonated in acidic gastric juice (pH 2) and penetrate lipid membranes to enter epithelial cells (pH 7.four) unencumber and ionize H+. In that form, NSAIDs emerge as trapped in epithelial cells because of their lack of ability to go the lipid membrane, which causes oxidative phosphorylation to uncouple and mitochondrial J. Clin. Med. 2019, eight, 179 3 of 19 mobile integrity, accelerated permeability, and energy manufacturing. individuals who take excessive doses or combinations of NSAIDs, are over 65, have a records of peptic ulcers or hemorrhage, and also use steroids or anticoagulants are maximum prone to developing NSAID-brought about ulcers.[1]

The main pathophysiological mechanisms and the sites of action of antiulcer treatment are shown in the Figure 1.

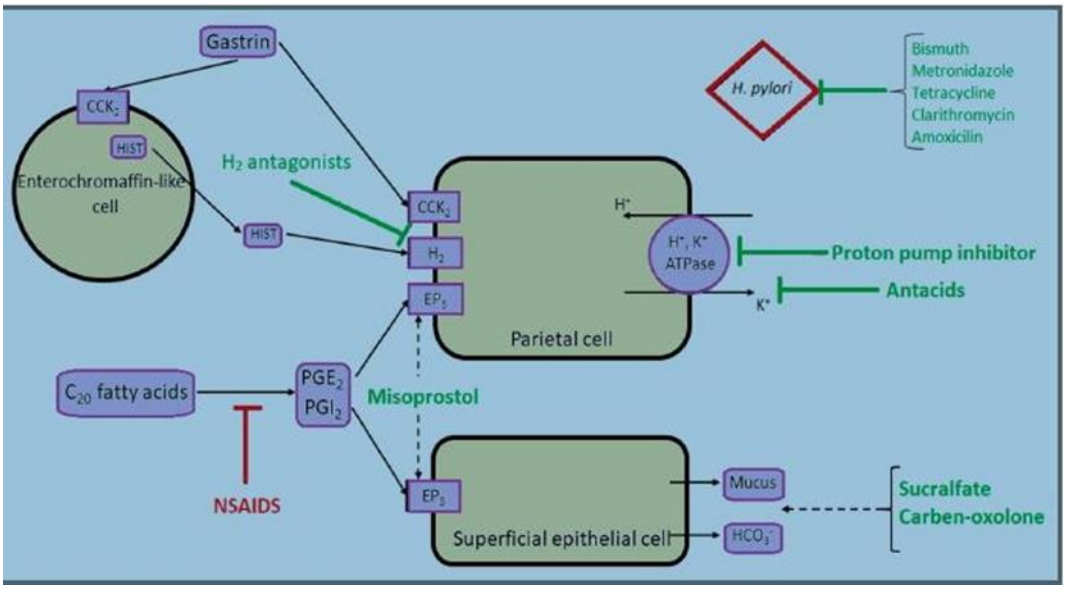


Figure 1: Schematic presentation of main pathophysiological mechanisms involved in the development of peptic ulcer disease, and the sites of action of the most commonly used pharmacological options in the treatment of peptic ulcer disease.

CCK2 = Cholecystokinin Receptor; PGE2 = Prostaglandin E2.

PGI2 = Prostaglandin I2; EP3 = Prostaglandin E receptor 3; HIST = Histamine.

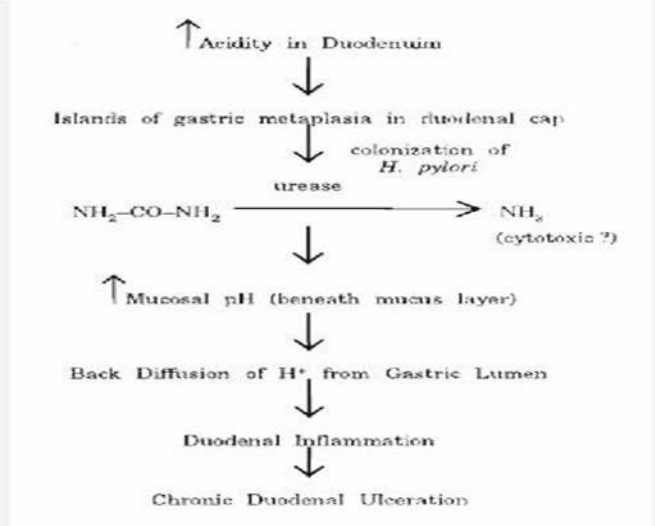
peptide (CGRP) sensory neurons linked to somatostatin, or inhibit the production of gastrin.[9]

1.4 DIAGNOSIS

All participants were asked if they had been diagnosed with a peptic ulcer within the 11-year observation period. Participants with a first-time diagnosed ulcer reported how and when the diagnosis was made. To ensure that all first-time diagnosed ulcers were recorded, information was also obtained from the National Danish Hospital Discharge Registry (NDHDR) in which all cases of hospital admissions in Denmark are registered with a discharge diagnosis. The search included the following PUD diagnoses (WHO ICD-8 codes: 531. X (gastric ulcer),

532. X (duodenal ulcer), and 533. X (gastro-duodenal ulcer)). Medical records from those who reported an ulcer or who were registered with a PUD diagnosis in the NDHDR were retrieved and reviewed. Only ulcers verified by upper endoscopy, barium meal examination, or surgery were regarded as true incident ulcers.[19]

Most peptic ulcers are treated medically after diagnosis is typically made by upper gastrointestinal tract endoscopic examination (esophagus-gastro-duodenoscopy, or OGD). Typically, surgery, interventional radiology, and therapeutic endoscopy Jaiswal along with others.designed to treat peptic ulcer disease complications like bleeding, perforation, and obstruction of the outflow. Single or multiple ulcers most often affect the lower curve of the stomach and the upper portion of the duodenum. The most popular technique for identifying H. pylori during endoscopy is the rapid urease test (CLO test), which is easily accessible. Its advantages include high sensitivity, speed, and affordability.



For individuals who choose not to have an endoscopy, there are also less invasive diagnostic tests available for H. pylori. One of these is a urea breath test (specificity 100%, sensitivity 95%), which depends on H. pylori's capacity to convert carbon radiolabelled urea taken orally into carbon dioxide, which the patient exhales and leaves behind, and which can be found on their breath. The sensitivity and specificity of the increasingly popular H. pylori stool antigen test, which is a non-invasive alternative, have been shown in recent studies to be around 95%. It is generally not advised to perform H. pylori antigen serology because it may result in false positive results in people who have previously had an infection but are not currently infected.[20]

1.4 TREATMENT

The objectives of peptic ulcer disease treatment are to reduce symptoms, close craters, stop complications, and avoid recurrences. Drug therapy should be a part of medical therapy, and the following goals should be pursued:

1) Diminish the acidity of the stomach through methods that prevent or balance acid production,
2) Apply coating to ulcer craters to stop acid and pepsin from reaching the base of the ulcer, offer a prostaglandin analog,
4) eliminate environmental contaminants like smoking and NSAIDs, and
5) lessen psychological stress (in certain patients).

Table No. 1: Provides a summary of the traditional antiulcer treatment options.

MEDICINE	MECHANISM OF ACTION	ADVERSE REACTION	REFRENSES
PROTON PUMP INHIBITOR Omeprazole Lansoprazole Rabeprazole Esomeprazole Pantoprazole	Inhibition of the gastric H+/K+- ATPase (proton pump)	Headache Abdominal pain Diarrhea Nausea Vomiting Constipation Flatulence Vitamin B12 deficiency Osteoporosis	[11,12]
H2 ANTAGONIST Cimetidine Famotidine Nizatidine Ranitidine	Blocking the action of histamine at the histamine H2 receptors of parietal cells	Headache Anxiety Depression Dizziness Cardiovascular events Thrombocytopenia	[13]
ANTACID Aluminum hydroxide Magnesium hydroxide	Increases gastric pH to greater than four, and inhibits the proteolytic activity of pepsin Frequency not defined:	Vomiting Hypophosphatemia Chalky taste Constipation Abdominal cramping Diarrhea Electrolyte imbalance	[14]
Potassium-Competitive Acid Blocker Vonoprazan	Inhibits H+, K+-ATPase in gastric parietal cells at the final stage of the acid secretory pathway	Nasopharyngitis Fall Contusion Diarrhea Upper respiratory tract inflammation Eczema Constipation Back pain	[15,16]

Table 1: Mechanisms of action and adverse effects of the most commonly used antiulcer treatment options.

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[15,16] Cytoprotective Agents
Misoprostol SucralfateStimulate mucus production and enhance blood flow throughout the lining of the gastrointestinal
tract Diarrhea Abdominal pain Headache Constipation[17,18]

1.5 MEDICINAL PLANT IN PEPTIC ULCER TREATMENT

Phytotherapy, or the use of medicinal plants to treat a variety of illnesses, is as old as humanity. Additionally, there has been an increase in interest in complementary therapies and the use of herbal products in recent years, particularly those made from herbal remedies.[21,22] Additionally, medicinal plants are thought to be the main source of potentially novel drugs due to the emergence of different side effects from the use of conventional drugs for a wide range of diseases. Crude plant extracts are the primary source of novel pharmaceuticals, and have demostrated encouraging outcomes when used to treat stomach ulcers.[23] It is well known that many medications, including sucralfate, bismuth, anticholinergics, antimicrobial agents, proton pump inhibitors, and antacids, are not entirely effective and can have a variety of negative side effects, including gynecomastia, hypersensitivity, impotence, and hematopoietic changes.[24,25] The ability of medicinal plants to generate diverse and renewable secondary metabolites, also referred to as phytochemical constituents, is what gives them their medicinal qualities. As a result, many plants have employed these phytochemicals as a defense mechanism against infections.[26] However, the emergence of resistant pathogens has forced pharmaceutical companies to rethink how they develop traditional antibiotics and instead create novel antimicrobial medications made from medicinal plants.[27] However, as antimicrobial medications, synthetic antibiostics continue to rule the market.

MEDICINAL PLANT	POSSIBLE MECHANISM	EFFECTS	ADVERSE EFFECT	REFRENCES
Korean red ginseng	Inhibition of H. pylori-induced 5-lipoxygenase (5-LOX) activity; preventing pro-inflammatory interleukin (IL)-8 or 5-LOX mRNA	Anti-inflammatory effect; increase eradication rates of H. pylori; reduction of gastric inflammation and oxidative DNA damage	Interaction with conventional drugs	[29,30]
Zingiber zerumbet	Gastroprotective mechanism of zerumbone (significant increased in the endogenous antioxidant GSH, reduction of lipid peroxidation level); other mechanism need to be investigated	Antioxidant, antiproliferative, anti-inflammatory, antisecretory effect; reduction of ulcer area formation	Nausea and vomiting in pregnant women; restless, heartburn; interaction with conventional drugs (anticoagulants, analgesics)	[35,36]
Allium sativum	Inhibition of lipoprotein oxidation and lower serum glucose induction of antioxidant enzymes; mechanisms need to be more investigated	Antioxidant; suppressive effect of H. pylori-induced gastric inflammation in vivo and in vitro	Interaction with conventional drugs	[31]
Camellia sinensis (Green tea polyphenols)	Suppression of tumor necrosis factor-alpha (TNF-_) gene expression; inhibition of urease	Antioxidant; improvement in the function of intestinal bacterial flora	Interaction with conventional drugs; dizziness, diarrhea, headaches, insomnia, heartbeat, may cause deficiency of iron	[37,38]
Zingiber officinalis	Inhibition of PGE2 and parietal cell H+, K+-ATPase	Anti-inflammatory effect; antioxidant	Nausea and vomiting in pregnant women; restless, heartburn; interaction with conventional	[33-35]

It is crucial to stress that herbal products could include a variety of bioactive ingredients with both harmful and advantageous effects. Therefore, laws to regulate the quality of herbal products as well as increased education for physicians and patients regarding herbal therapy are required.particularly for additional randomized studies to ascertain the efficacy and safety of numerous products in the treatment of gastrointestinal and other disorders.[28]Ultimately, the knowledge gained from Ayurveda combined with modern medicine may produce better antiulcer medications made from medicinal plants that have fewer adverse effects.[29] Table 3 lists many medicinal plants that are beneficial for treating gastric ulcer disease and have strong antibacterial activity against H. pylori.

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1.6 HERB-DRUG INTERACTION

Worldwide usage of herbal supplements is growing, and this is also leading to an increase in side effects and medication interactions. Pharmacokinetic or pharmacodynamic interactions can occur when a medication and a herbal supplement interact. The outcome of pharmacokinetic interaction is utilizing the same mechanism of absorption, distribution, metabolism, or excretion to alter the drug's pharmacologic action and blood concentration when given in combination with a herbal supplement. Pharmacodynamic interactions occur when a co-administered drug's mechanism of action is directly impacted, without affecting the drug's concentration; instead, the drug's clinical effects are exacerbated or neutralized.[37]

Drugs like digoxin, doxorubicin, rosuvastatin, and verapamil that are transported by P-gp have their concentrations reduced by allium sativum extract.[39] The most researched interaction between Allium sativum and warfarin has not yet been validated by randomized clinical trials. Furthermore, it restricts platelet aggregation, thus individuals receiving anticoagulant medication or those with clotting disorders should use it cautiously.[40] Zingiber officinalis inhibits thromboxane synthetase, which lengthens bleeding times; however, a clinical trial has not supported this.[41] Because ginkgo biloba inhibits platelet aggregation, it may raise the risk of bleeding, particularly when taken with anticoagulant medications. Although ginkgo biloba contains flavonoids that have antiplatelet activity, these compounds have no effect on human blood coagulation or platelet function.[40]

CONCLUSION

In our setting, peptic ulcer disease is still a common clinical issue that primarily affects individuals of all ages. It is anticipated that peptic ulcer disease will continue to have a major global impact on patient quality of life, health economics, and the delivery of healthcare as its prevalence rises with age. In our setting, peptic ulcer disease is still a common clinical issue that primarily affects individuals of all ages. Given how common peptic ulcers are UPI Journal of Pharmacy and Medical Science, 5(1), 2022: 19–26 Jaswanth et al.

The prevalence of this common disease rises with age, and it is anticipated that it will continue to have a major global influence on patient quality of life, health economics, and the delivery of healthcare.

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Herbal remedies and conventional anti-gastric ulcer medications may work in concert to combat H. pylori and gastric ulcer illness, as well as to help patients with the condition's prognosis. Considering the paucity of human research, more clinical trials involving increased sample sizes regarding the safety and effectiveness of therapeutic herbs having antiulcer properties. Designing studies to look into and clarify the mechanisms of action of medicinal plants used to treat or prevent peptic ulcers would also be beneficial.

Lastly, licensing is necessary for herbal products used for medicinal purposes in order to improve their quality and safety and guarantee that claims of potential efficacy are validated by randomized controlled trials.

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