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The Review on Peptic Ulcer Disease

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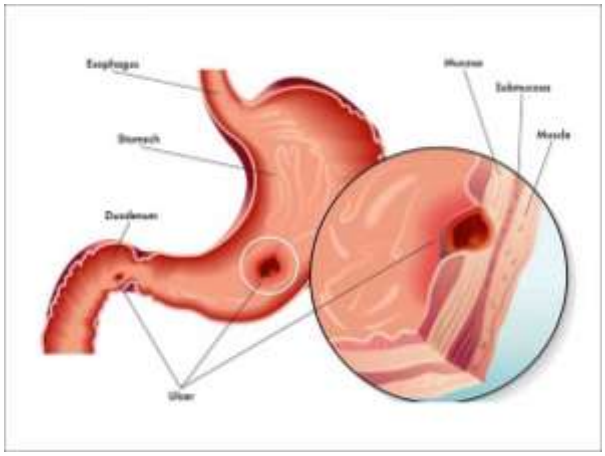
Abstract

Peptic ulcer is a chronic disease affecting up to 10% of the world's population. The formation of peptic ulcers depends on the presence of gastric juice pH and the decrease in mucosal defenses. Non-steroidal anti-inflammatory drugs (NSAIDs) and Helicobacter pylori (H. pylori) infection are the two major factors disrupting the mucosal resistance to injury.Conventional treatments of peptic ulcers, such as proton pump inhibitors (PPIs) and histamine-2 (H2) receptor antagonists, have demonstrated adverse effects, relapses, and various drug interactions.Peptic ulcer disease is characterized by discontinuation in the inner lining of the gastrointestinal (GI) tract because of gastric acid secretion or pepsin. It extends into the muscularispropria layer of the gastric epithelium. It usually occurs in the stomach and proximal duodenum. It may involve the lower esophagus, distal duodenum, or jejunum.Hence, this review presents common medicinal plants that may be used for the treatment or prevention of peptic ulcers.Peptic ulcer disease results from an imbalance between factors that protect the mucosa of the stomach and duodenum, and factors that cause damage to itPeptic ulcer disease presents with gastrointestinal symptoms similar to dyspepsia and can be difficult to distinguish clinically. It can have potentially serious complications such as bleeding or perforation, with a high risk of mortality.

Keywords:peptic ulcer disease, Helicobacter pylori infection, herbal treatment

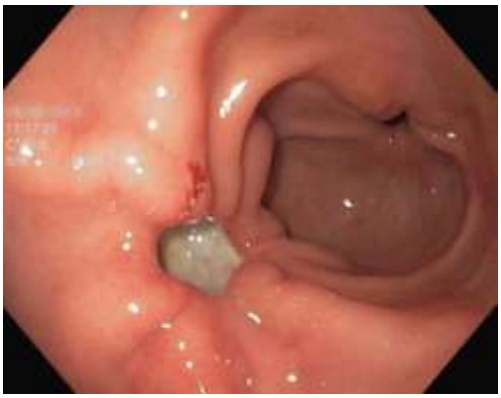
Introduction

Peptic ulcer is an acid-induced lesion of the digestive tract that is usually located in the stomach or proximal duodenum, and is characterized by denuded mucosa with the defect extending into the submucosa or muscularispropria.mucosal disruption in patients with the acid peptic disease is considered to be a result of a hypersecretory acidic environment together with dietary factors or stress. Risk factors for developing peptic ulcer include H. pylori infection, alcohol and tobacco consumption, non-steroidal anti-inflammatory drugs (NSAIDs) use, and Zollinger–Ellison syndrome.The main risk factors for both gastric and duodenal ulcers are H. pylori infection and NSAID use.However, only a small proportion of people affected with H. pylori or using NSAIDs develop peptic ulcer disease, meaning that individual susceptibility is important in the beginning of mucosal damage. Functional polymorphisms in different cytokine genes are associated with peptic ulcers. For example, polymorphisms of interleukin 1 beta (IL1B) affect mucosal interleukin 1β production, causing H. pylori-associated gastroduodenal diseases.Today, testing for Helicobacter pylori is recommended in all patients with peptic ulcer disease. Endoscopy may be required in some patients to confirm the diagnosis, especially in those patients with sinister symptoms. Today, most patients can be managed with a proton pump inhibitor (PPI) based triple-drug therapy.



Pathogenesis of Peptic Ulcer

Almost half of the world's population is colonized by H. pylori, which remains one of the mostcommon causes of peptic ulcer disease . The prevalence of H. pylori is higher in developingcountries, especially in Africa, Central America, Central Asia, and Eastern Europe. Theorganism is usually acquired in childhood in an environment of unsanitary conditions and crowding,mostly in countries with lower socioeconomic status. H. pylori causes epithelial cell degeneration andinjury, which is usually more severe in the antrum, by the inflammatory response with neutrophils,lymphocytes, plasma cells, and macrophages.



Helicobacter pylori Eradication

Although successful H. pylori eradication alone is paramount for healing associated peptic ulcersand preventing relapses, the growing prevalence of antibiotic resistance made it a global challenge.The first effective therapy was introduced in the 1980s, and consisted of a combination of bismuth,tetracycline, and metronidazole that was given for two weeks [14]. The standard first-line therapy is atriple therapy consisting of a proton pump inhibitor (PPI) and two antibiotics, such as clarithromycinplus amoxicillin or metronidazole given for seven to 14 days [32]. However, with an increasingprevalence of antibiotic resistance, especially for clarithromycin, there has been a marked declinein the success of triple therapy over the last 10–15 years

Alternative Therapy for Peptic Ulcer

The usage of medicinal plants in healing numerous diseases is as old as human beings, andwell-known as phytotherapy. Moreover, in the past few years, there has been a rising interestin alternative therapies

and the usage of herbal products, in particular, those produced frommedicinal plants. Also, due to appearance of various side effects by usage of conventionaldrugs for numerous diseases, medicinal plants are considered the major reservoir of potentiallynew drugs. Plant extracts and their crude are the most significant sources of new drugs, andhave been shown to cause promising results in the treatment of gastric ulcer as well [61]. It isknown that numerous pharmaceutical agents such as proton pump inhibitors, anticholinergics,antacids, antimicrobial agents, H2-receptor antagonists, sucralfate, and bismuth are not fully effective,and produce numerous adverse effects such as impotence, arrhythmia, hematopoietic alterations,hypersensitivity, and gynecomastia [62,63]. Due to that, investigations of the new pharmacologicallyactive agents through the screening of different plant extracts led to the discovery of effective andsafe drugs with gastroprotective activity. Especially, plants with antioxidant capability as the mainmechanism are used as the herbal reservoir for the treatment of ulcer disease [63].Medicinal plants have achieved their therapeutic properties from their capability to producerenewable and various secondary metabolites, which are known as phytochemical constituents. Hence,numerous plants have used these phytochemicals as a protection mechanism against pathogens [64].On the other hand, the appearance of resistant pathogens has had a significant influence on thepharmaceutical companies to change their strategy in the development of conventional antibioticsand design new antimicrobial drugs derived from medicinal plants.

The Effect on H. pylori

Eradication

Several factors influence the conventional therapy failure. These include: the poor bioavailabilityof antibiotics, as the gastric mucus layer plays a barrier to antibiotic delivery, and therefore the drugsare unable to obtain the underlying gastric epithelium the stomach containing a pH from acidicto neutral, and only a few antibiotics are active in a wide pH range bacterial antagonism toantibiotics, where co-infection with multiple strains is quite an important feature deficiency ofpatient permissiveness to the therapy; patients lifestyle, and diet.

Korean Red Ginseng

Korean red ginseng extract plays a significant role in inhibiting H. pylori-induced 5-LOXactivity, such as inactivating c-jun, repressing NF-κB-DNA binding, inhibiting H. pylori-induced5(S)-hydroxyeicosatetraenoic acid biosynthesis, and preventing pro-inflammatory interleukin (IL)-8 or5-LOX mRNA. Consequently, these mechanisms decrease gastric carcinogenesis.

Allium sativum

Throughout history, the health benefits of garlic have been well documented, and the main useof Allium sativum was for its medicinal properties. The organosulfur components of Allium sativum,including S-allyl-L-cysteine (SAC) sulfoxidesandδ-glutamyl S-allyl-L-cysteine, are known as maincompounds of its bioactivity. Raw Allium sativum is easy to convert in bioinactive form. Accordingly,numerous types of its extract with different compositions of bioactive components have beendeveloped, and their efficacy has been observed and evaluated in numerous studies . The major roleof Allium sativum extract has been observed in antioxidant effect by scavenging reactive oxygen species

Curcuma Longa and Artemisia Asiatica

Medicinal plants with antioxidant and anti-inflammatory activity have had a demonstratedeffect on gastroesophageal reflux disease (GERD). The medicinal plants and herbal preparationswith antioxidant and anti-inflammatory mechanisms include Curcuma longa,Panaxquinquefolium,Artemisiaasiatica, and Lonicera japonica. Moreover, other mechanisms include: the down-regulationof the genes encoding proteins that have key role in acute inflammation, including 1 intercellularadhesion molecule-1 (ICAM-1) and cytokine-induced neutrophil chemoattractant-2-beta (CINC-2-2beta) (Panaxquinquefolium); ameliorating the function and gastric mucus (Morus alba, Curcuma longa);reducing gastric acid, such as for instance Curcuma longa,Morus alba, and acidinol syrup, increasingtonic contractions of the lower esophageal sphincter (LES) (Salvia miltiorrhiza, STW 5), and preventingthe pro-inflammatory cytokines IL-1 b and TNF-a.

Herb–Drug Interactions

Together with increasing use of herbal supplements worldwide, the number of adverse eventsand drug interactions is rising. Interactions between an herbal supplement and a drug can manifestas a pharmacokinetic or pharmacodynamic interaction. Pharmacokinetic interaction is a result ofusing the

same mechanism of absorption, distribution, metabolism, or excretion between anherbalsupplement and a co-administered drug, leading to the change of the drug's concentration in the bloodand pharmacologic action. Pharmacodynamic interactions involve a direct effect on the mechanism ofaction of a co-administered drug without changing the drug's concentration, only by antagonizing orexacerbating the drug's clinical effects.

Medical Treatment

Antisecretory drugs used for peptic ulcer disease (PUD) include H2-receptor antagonists and the proton pump inhibitor (PPIs). PPIs have largely replaced H2 receptor blockers due to their superior healing and efficacy. PPIs block acid production in the stomach, providing relief of symptoms and promote healing.

Peptic ulcer disease

It involves the full thickness of GIT mucosa & penetrate the muscle layer of the stomach or deodenum.They are caused by disruption of the normal balance between the corrosive effect of gastric juice & the protective effect of mucus on the gastric epithelial cells. They may be viewed as an extension of the gastric erosion found in acute gastritis. The most common sites for ulcers are the stomach & 1st few centimetres of the deodenum.More rarely, they occurs in the oesophagus& round the anastomosis of the stomach & small intestine, following gastrectomy.

H.pylori infection is very common, affecting 50-60% of adults worldwide. Most people remain healthy & asymptomatic with only a minority developing symptoms; it is thought that infection is acquired in childhood. H.pylori is strongly associated with peptic ulcer disease, being found in 90% of people with duodenal ulcer & 70% of those with gastric ulcers. Most other gastric ulcers are attributed to the use of nonsteroidal anti-inflammatory drugs (NSAIDs).

Smoking Predisposes to peptic ulceration & delays healing. The incidence of peptic ulcers is greater in men than in women & increase with age.If gastric mucosal protection is impaired, the epithelium can be exposed to gastric acid, causing the initial cell damage that leads to ulceration. The main protective mechanism are a good supply, adequate mucus secretion & efficient epithelial cell replacement.

Blood supply. Reduced blood flow & ischemia may be caused by cigarette smoking & severe stress, either physical or mental. In streesfull situations the accompanying sympathetic activity causes constricticti on of the blood vessels supplying the alimentary tract.

Secretion of mucus. The composition & the ammount of mucus may be altered, foe example:

1)By regular & prolonged use of aspirin & other anti-inflammatory drugs

2) By the reflux of bile acids & salts

3) In chronic gastritis.

Epithelial cell replacement. There is normally a rapid turnover of gastric & intestinal epithelial cells. This may be reduced:

•by raised levels of steroid harmones,eg.in response to stress or when they are used as drugs

•in chronic gastritis

• by radiotherapy & cytotoxic drugs.

Acute peptic ulcers

These lesions may be single or multiple. They are found in many sites in the stomach & in the 1st few centimetres of the deodenum. Their development is often associated with acute gastritis, severe stress,eg.severe illness, shock, burns, severe emotional disturbance & following major surgery. Healing without the formation of fibrous tissue usually occurs when the stressor is removed, although haemorrhage, which may be life-threatening, can be a complication.

Chronic peptic ulcers

There ulcers are 2-3 times more common in the duodenum than in the stomach. They usually occur singly in the pylorus of the stomach or in the duodenum. Healing occurs with the formation of fibrous tissue. It's subsequent shrinkage may cause:

• Structure of the lumen of the stomach

•Gastric outflow obstruction or stenosis of the pyloric sphincter

•adhesions to adjacent structures, eg. Pancreas, liver or transverse colon.

Complications of peptic ulcers

Performation. When an ulcer erodes through the full thickness of the wall of the stomach or duodenum, the contents of these structures enter the peritoneal cavity, causing acute peritonitis.

Infected inflammatory material may collect under the diaphragm, forming a subphrenic abscess, & the infection may spered through the diaphragm to the pleural cavity.

Haemorrhage

When a major artery is eroded, a serious & possibly life-threatening haemorrhage may occur, causing shock, haematemesis&/or malaena.

Anaemia

Chronic, persistent, low-level bledding from an ulcer may lead to development of iron deficiency anaemia

Gastric outflow obstruction

Also known as pyloric stenosis, fibrosis tissue formed as an ulcer in the pyloric region heals, causes narrowing of the pylorus that obstructs outflow from the stomach, & results in persistent vomiting.

Conclusions

The combination of herbal products and standard anti-gastric ulcer drugs might present asynergistic effect against H. pylori and gastric ulcer disease and improve the outcome for patients with gastric ulcer. With only a few human studies, it is suggested to conduct further clinical studies with larger sample sizes on the efficacy and safety of medicinal plants with antiulcer activity. Also, it would be beneficial to

design studies to investigate and further elucidate the mechanisms of action ofmedicinal plants used for the treatment or prevention of peptic ulcer. Finally, herbal products used for medicinal purposes require licensing in order to ameliorate their safety and quality, and ensure that randomized controlled investigations validate demands of its possible efficacy. With increased reports of herb–drug interactions, there is still a problem of deficient research in this field, with no measures taken to address this problem. Hence, pharmacists and doctors should be aware especially of the risks associated with the usage of herbal preparations, whether on their own or in combination with other herbal or standard conventional therapy.

Abbreviations:

1. IL1B = Interleukin 1 beta
2. COX-1 = Cyclooxygenase 1
3. COX-2 = Cyclooxygenase 2
4.CYP = Cytochrome
5.FDA = Food and drug Administration
6. H. Pylori = Helicobacter Pylori
7. CCK2 = Cholecystokinin receptor
8. PGE2 = Prostaglandin E2
9. PGI2 = Prostaglandin I2
10. EP3 = Prostaglandin E receptor 3
11. HIST = Histamine
12. H2 receptor agonists = Histamine - 2 receptor agonists
13. NSAIDS = Non - steroidal anti - inflammatory drug
14. PPIs = Proton Pump Inhibitor.
15. 5 - LOX = 5 - Lypoxigenase
16. iNOS = Inducible nitric oxide synthase
17. SAC = S-allyl-L-cystiene
18. EGCG = Epigallocatechingallate
19. vacA = Vacuolatingcytotoxin A
20. CRS = Cold Restraint stress
21. PL = Pylorus ligation
22. GERD = Gastroesophageal reflux spihincter
23. LES = Lower esophageal spinchter
24. IL = Interleukin
25. ROS = Reactive Oxygen Species
26. TNF-alpha = Tumor necrosis factor - alpha
27. ICAM 1 = Intercellular adhesion molecule 1
28. CINC 2- beta = Cytokine - induced Neutrophil chemoattractant - 2 - beta
29. OATP1A1 = Organic anion Transporting protein 1 a 1
30. OATP1A2 = Organic anion transporting 1 a 2
31. STW 5 = A complex herbal combination preparation composed of 9 different herbal extracts
32. CYP3A4 = Cytochrome P450 3A4

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