INTRODUCTION
Ulcers are sore means open and painful wounds and the peptic ulcers are erosion of lining of stomach (The lining is a wrinkly bag that holds acids to help digest food) or the duodenum. Still, the etiology of peptic ulcer is not clearly known, but it has been well established that peptic ulcer occurrence takes place due to an imbalance between aggressive factors (like acid, pepsin, bile & \textit{H. pylori} infection) and defensive factors (like gastric mucosa, bicarbonate secretion, prostaglandins, nitric oxide and innate resistance of the mucosal cell). In gastric ulcer, acid secretion may be normal or low, while in duodenal ulcer, volume of acid secretion is high in half of patients and may be normal in rest. Mucosal cell death results from increase in H+ concentration in its immediate environment (decrease pH).  

Regulation of Gastric acid Secretion
The terminal enzyme H’K ATPase secretes H+ ions in the apical canaliculi of parietal cells, and can be activated by histamine, acetylcholine and gastrin acting via their own receptors located on the basolateral membrane of these cells. Histamine directly act through H₂ receptors followed by generation of cAMP formation, along with Ca++ mobilization, while acetylcholine & gastrin acts either may act directly through muscarinic & gastrin receptor respectively or may act indirectly by releasing histamine from “histaminocytes”. The muscarinic receptors & gastrin receptors (cholciyokinin receptors) function through IP₃-DAG pathway that mobilizes intracellular Ca++. Gastrin is secreted from the antrum in response of antral pH, food constituents & vegal mediated reflexes. Vagus releases acetylcholine which release histamine & gastrin through the acting on histaminocytes & gastrin secreting cells. Prostaglandins produced by gastric mucosa, inhibits acid secretion by opposing cAMP generation & gastrin release. The mechanism of NO is not yet clearly established.  

Common Causes of Peptic Ulcerations \textit{H. pylori}
The gram negative bacterium Helicobacter pylori (initially named as Campylobacter pyloridis), remains present between the mucous layer and the gastric epithelium, and is strategically designed to live within the aggressive environment of the stomach. Initially, \textit{H. pylori} resides in the antrum but over time, migrates toward the more proximal segments of the stomach. The genome of \textit{H. pylori} has been sequenced and encodes 1500 proteins. Amongst this multitude of proteins there are factors that are essential determinants of \textit{H. pylori}–mediated pathogenesis and colonization such as the outer membrane protein (Hop proteins), urease, and the vaculating cytotoxin (Vac A). The first step in infection by \textit{H. pylori} is dependent on the bacteria’s motility and its ability to produce urease. Urease produces ammonia & carbondioxide from urea which is secreted from the stomach. This CO₂ interact with environmental water & produce H₂CO₃ in presence of carbonic anhydrase, an essential step in alkalinizing the surrounding pH. This H₂CO₃ converts into the H³ & HCO⁻ and resulting H³⁺ ion react with NH₂⁻ to form NH₃ which can damage epithelial cells.  

Use of Non-steroidal Anti-inflammatory Drugs (NSAIDs)
Prostaglandins are chemicals promoting inflammation i.e. have protective role. The use of NSAIDs is common for the treatment of inflammatory responses; however, they may also inhibit certain prostaglandins causing protection of stomach lining from the corrosive effects of stomach acid. These protective prostaglandins are produced by an enzyme called Cox-1. By blocking the Cox-1 enzyme and disrupting the production of prostaglandins in the stomach, NSAIDs can cause ulcers and bleeding.  

Alcohol Consumption
Fermented and nondistilled alcoholic beverages increase gastrin levels and acid secretion. Alcoholic drinks containing sucinnic and maleic acid also stimulate gastric acid secretion. Low alcohol doses accelerate gastric emptying, whereas high doses delay emptying and slow bowel motility.  

Smoking & Tobacco
The relationship between the secretion of pepisin 1 (the most electronegative of the pepsinins), and the smoking habits of patients has been investigated. Significantly more cigarette smokers with peptic ulceration secreted pepsin 1 in greater than trace amounts after pentagastrin or histamine than non-smokers with ulceration.  

Stress
Studies have well established that susceptibility to gastric as well as duodenal ulceration increases under stress conditions. A no. of preclinical screening methods also based on this approach.

Fasting Condition
Fasting condition causes gastric empty which in some cases cause ulcers.  

Radiation
Ulcers are wounds caused by the acute or chronic effects of ionizing radiation. The most common cause of radiation injury is an adverse effect of therapeutic radiation therapy. Other causes are occupational or environmental exposures.
Types and Symptoms of Peptic Ulcers

The two most common types of peptic ulcer are called “gastric ulcers” and “duodenal ulcers”. The name refers to the site of ulceration. A person may have both gastric and duodenal ulcers at the same time.

- **Gastric ulcers (GU)** are located in the stomach, characterized by pain (especially higher in the abdomen) and common in older age group (especially in female). Eating may increase pain rather than relieve pain. Other symptoms may include nausea, vomiting and weight loss. Although patients with gastric ulcers have normal or diminished acid production, yet ulcers may occur even in complete absence of acid.11

- **Duodenal ulcers (DU)** are found at the beginning of small intestine (duodenum) and are characterised by severe pain (in lower abdomen or chest area) with burning sensation in upper abdomen that awakens patients from sleep. Generally, pain occurs when the stomach is empty (about two hours after meal or during the night), and relieve after eating. DU are more common in younger individuals and predominantly affects males. In the duodenum, ulcers may appear on both the anterior and posterior walls i.e. Kissing Ulcers.12

In some cases, peptic ulcer can be life threatening with symptoms like; bloody stool (blood may be red, black or tarry in texture), severe abdominal pain and cramps along with Vomiting blood (resembling coffee grounds).13

**Diagnosis** Peptic ulcerations can be diagnosed by:

- **Barium containing X-ray**
  A whitish liquid containing barium contents is administered orally, and X-ray film is collected. The ulcer outline can be observed on X-ray film.14

- **Endoscopy**
  A lighted tube with a special camera on its end is inserted into the stomach or upto initial part of small intestines. The inner lining of organs is observed on monitor. Tissues can be removed during an endoscopy and also used for detection of H. pylori presence.15

**Test for presence of H. pylori**

Serological tests, breath analysis and stool analysis can be made for the detection of H.pylori, which is a dominant reason for the development of peptic ulcerations.16

**MANAGEMENT OF PEPTIC ULCER**

A number of approaches have been made for the management of peptic ulcers using chemically synthesized drug or product containing herbal ingredients. Some of them are discussed below;

**Chemically synthesized antiulcer drugs**

1. **For reduction volume of gastric acid**
   a. Antihistamines such as; cimetidine, ranitidine, famotidine, roxatidine and JB932227
   b. Proton pump inhibitors such as; omeprazole, lansoprazole, pantoprazole, rabeprazole, esomeprazole, dexlansoprazole
   c. Anticholinergics such as; pirenzepine, propantheline, oxyphenonium
   d. Prostaglandin analogue such as; misoprostol

2. **For neutralization of gastric acid**
   a. Systemic such as; sodium bicarbonate, sodium citrate
   b. Nonsystemic such as; hydroxide/ carbonate/ trisilicates containing magnesium, aluminum or calcium

3. **For protection of gastric mucosa**
   a. such as; sucralfate, colloidal bismuth subcitrate
   b. Use of antifungal agents for treatment of H. pylori infection: such as; amoxicillin, clarithromycin, metronidazole, tinidazole, tetracycline

**Reported Plants from Cucurbitaceae Family with Ulcer Healing Property**

- **Wilbrandia ebracteata**
  The antiulcer potential of *Wilbrandia ebracteata* leaves was investigated using hydro-methanol extract against ethanol induced ulceration and indomethacin induced gastric damage in mice. The results indicate significant ulcer protective potential in ethanol induced ulceration as the total area of lesions were very less with respect to control group , but was ineffective in indomethacin-induced gastric damage model.19

- **Gynostemma pentaphyllum**
  Rujjanawate et al (2003) evaluated butanol fraction (GBP) of *Gynostemma pentaphyllum* for antiulcer activity using indomethacin, ethanol and stress induced ulcer in rat, and the result revealed that the butanol fraction of Gynostemma pentaphyllum possess significant gastroprotective potential as the mucous protective effect along with reduction in gastric acid volume was observed.19

- **Cucurbita pepo**
  Sarkar et al (2008) evaluated aqueous extract of *Cucurbita pepo* fruit pulp for ulcer healing potential against the drug (Aspirin) induced ulcer in albino rats. The result shows that pretreatment of Cucurbita pepo fruit pulp extract significantly reduced ulcerative index in animals, and established its antiulcer activity.20

- **Cucumis sativum**
  Gill et al (2009) evaluated the antiulcer activity of methanolic extract of *Cucumis sativum* seeds against the pyloric ligation and water immersion stress induced ulcer model in rats. The reduction of gastric acid volume, free acidity and total acidity was observed. The antiulcer activity was supposed due to its antioxidant property.21

- **Trichosanthes cucumerina**
  The antiulcer activity of hot water extract of *Trichosanthes cucumerina* have also been investigated and established. Arawawawala et al (2010) evaluated hot water extract of *Trichosanthes cucumerina* for antiulcer potential against indomethacin induced gastric ulcer and alcohol-induced gastric ulcer in wistar rats and observed that the extract possess significant ulcer healing property as compared to standard drug cimetidine. They observed protective effect on gastric mucosa along with acidity of gastric secretion and conclude the remark about its antiulcer property.22

- **Momordica cymbalaria**
  Dhasan et al (2010) evaluated different extracts of unripe fruits of *Momordica cymbalaria* for antiulcer activity in animal models, against aspirin, alcohol and pyloric induced ulcerations. The result showed that the methanolic extract of unripe fruits of *Momordica cymbalaria* significantly reduced the volume of gastric acid secretion, free acidity, total acidity and ulcer index, while pH of the gastric medium was found to be increased.23

- **Cholchin cheinomorbidia**
  Kim et al (2010) evaluated dried ripe seeds of *Cholchincheinomorbidia* for antiulcer effect in rats using acetic acid induced gastric ulceration model, and found ulcer healing property. The result suggested that the dried ripe seeds of *Cholchincheinomorbidia* accelerate the healing process by up-regulation of vascular endothelial growth factor (VEGF) and angiogenesis.24

- **Coccina grandis**
  The ethanolic and aqueous extract of *Coccina grandis* leaves were investigated for antiulcer potential against the pylorus ligated ulcer in rats & data revealed that ulcer healing capacity of ethanol extract were nearer to the standard drug omeprazole with respect to reduction in total acidity and mucosal defense.25

- **Benincasa hispida**
  The petroleum ether and methanol extract of *Benincasa hispida* fruits have been studied for ulcer protective effect in rats against
pylorus ligation induced ulcer and cold restraint stress induced ulceration and the result show significant reduction of ulcer in all models as compared to omeprazole treated group.26 The similar activity was further confirmed using methanolic extract of seed part.27

**Citrullus Colosynthis**

Methanolic extract of *Citrullus Colosynthis* seeds have also been investigated for antiulcerogenic property in animals against pylorus ligation induced ulcer. It was suggested that the ulcer protective effects may be due to free radical scavenging property within the plant.28

**Cucumis melo**

Gill et al (2011) investigated methanolic extract of *Cucumis melo* seeds for antiulcer property against pyloric ligation, stress & NSAID’s induced ulcers in various animal models. The result confirmed significant antiulcer activity of extract as inhibition of gastric volume; free acidity and total acidity were observed. The activity was supposed due to its high antioxidant activity.29

**Momordica Charantia**

Venu et al (2011) evaluated alcoholic & aqueous extract of *Momordica charantia* fruit at the dose of 200 mg/kg b.w. and 400 mg/kg b.w. separately, against pylorus ligation, aspirin and stress induced ulcer in rats.30

**Lagenaria siceraria**

In the same course of study antiulcer activity of methanolic extract of *Lagenaria siceraria* fruits was evaluated and established in animals against pylorus ligation, ethanol induced, NSAID’s induced and cold strain stress induced ulcers.31

**Lagenaria vulgaris**

Sathaye et al (2011) evaluated *Lagenaria vulgaris* fruit juice for antiulcer potential using NSAID’s induced ulcerations in albino rats. The result data illicit that the fruit juice of *Lagenaria vulgaris* exhibit better ulcer protective along with ulcer healing property as compared to β-carotene.32

**Lagenaria breviflora**

Ethanolic extract of *Lagenaria breviflora* fruit have also been studied for antiulcer activity in different animal models. The results revealed that the ulcer healing property of extract was dose dependent against cold restraint stress induced gastric ulcer. On the other hand the extract also exhibited significant ulcer protective effect in pyloric ligation induced ulcer, aspirin induced ulcer and alcohol induced ulcer models as compared to standard drug.33

**CONCLUSION**

Although the etiology of peptic ulceration is unknown but the various causative agents have been suggested and identified for that. The various approaches have also been established for their effect in pyloric ligation induced ulcer, aspirin induced ulcer and cold restraint stress & cold strain stress induced gastric ulcer. Its suggested that the ulcer protective activity was supposed due to its high antioxidant property as free radical scavenging property within the fruit.34

**REFERENCES**


