Drugs acting on Gastro Intestinal Tract (Drugs for Peptic Ulcer)

Peptic ulcer:

Peptic ulcer is an ulceration of the mucous membrane of the oesophagus, stomach or duodenum caused by the action of the gastric juice or caused by acid pepsin digestion.

Aetiology:

- H. pyroli (Helicobacter pylori, previously Campylobacter pylori, is a gram-negative, microaerophilic bacterium found usually in the stomach)
- NSAID
- Acid hypersecretory states

Classification of antiulcerants:

1. **Acid neutralizing agents (Antacids):**
    - Aluminium hydroxide ($Al(OH)_3$
    - Sodium bicarbonate ($NaHCO_3$)
    - Magnesium hydroxide ($Mg(OH)_2$
2. **H_2-receptor blocker:**
    - Ranitidine
    - Cimetidine
    - Famotidine
3. **Proton pump inhibitor (PPI):**
    - Omeprazole
    - Lansoprazole
    - Pantoprazole
4. **Mucosal protecting agent:**
    - Colloidal bismuth
    - Sucralfate
5. **Antibiotics:**
    - Amoxycillin
    - Ciprofloxacin

Antacid

An antacid is a substance which neutralizes stomach acidity, which in turn relieves heartburn, indigestion or stomach upset.

Antacids are available over the counter and are taken by mouth to quickly relieve occasional heartburn, the major symptom of gastroesophageal reflux disease and also indigestion.

Properties of an ideal antacid:

- Action should be quick, efficient and prolonged

- Should be palatable, cheap and available
- Should not interfere with gastric digestion
- Should not impair absorption of food, vitamin and mineral
- Should not produce systemic alkalosis, acid-base imbalance, constipation and diarrhoea
- Should be nontoxic and non-irritant

Types:

There are 2 types of antacid preparation.

1. Systemic antacid
2. Non-systemic antacid

Systemic antacids:

The antacid which are completely absorbed in the systemic circulation are called systemic antacids.

Example:

- $NaHCO_3$
- $KHCO_3$
- Na-citrate
- Na-acetate

Non-systemic antacids:

The antacids which are not absorbed in the systemic circulation and do not produce systemic alkalosis are called non systemic antacids.

Example:

- $Al(OH)_3$
- $Ca(OH)_2$
- $Mg(OH)_2$
- $MgCO_3$

Q. Why $NaHCO_3$ is not used as systemic antacid?

$NaCO_3$ is not used as systemic antacid because-

- $NaCO_3$ releases enough CO_2 in the stomach which causes discomfort and belching.
- $NaCO_3$ is absorbed and causes systemic alkalosis which is dangerous in the patient with renal insufficiency.
- Excess Na intake may cause edema and heart failure.

Q. Why antacids are used in peptic ulcer?

Antacids are used in peptic ulcer to relieve pain caused by severe irritation and tissue destruction in ulcer by HCl. It is used because of the following reasons-

- Antacids reduce or neutralize gastric acidity.
- More than P^H of gastric content inactivates the pepsin
- Al and Mg directly inactivate pepsin

Q. Why stomach is not digested itself?

Stomach does not digest itself because-

- Gastric mucosal glands of the stomach secret mucous which form a protective gastric mucosal barrier. For this barrier HCl and pepsin does not come in contact with the mucous membrane of the stomach.
- Greater HCO_3^- ion concentration of blood flowing through gastric mucosa to counteract the effect of HCl.
- Presence of antipepsin to counteract pepsin digestion.

Physiolocal and pharmacological regulation of gastric acid secretions:

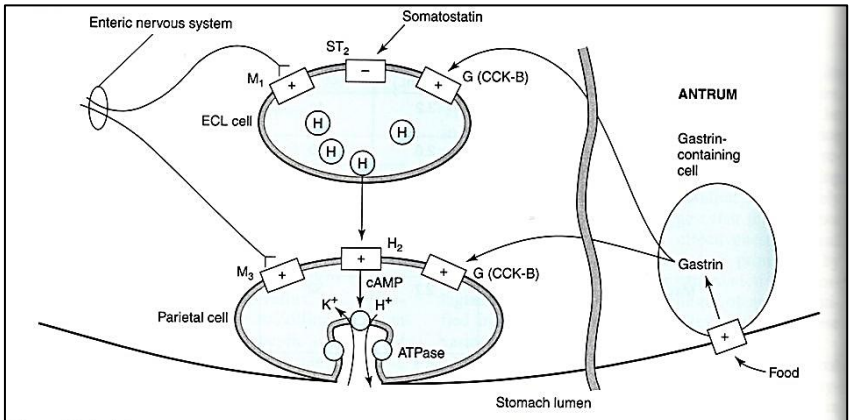


Figure 63–1. Schematic diagram of one model of the physiologic control of hydrogen ion secretion by the gastric parietal cell. ECL cell, enterochromaffin-like cell; G(CCK-B), gastrin-cholecystokinin-B receptor; H, histamine; H_2, histamine H_2 receptor; M_1, M_3, muscarinic receptors; ST_2, somatostatin$_2$ receptor; ATPase, K^+/H^+ ATPase proton pump. Some investigators place histamine receptors—and possibly cholinoceptors—on nearby tissue cells rather than on the parietal cell itself. (Modified and redrawn from Sachs G, Prinz C: Gastric enterochromaffin-like cells and the regulation of acid secretion. News Physiol Sci 1996;11:57, and other sources.)

Enterochromaffin like cell (ECL)

Ach / gastrin binds with ECL cell receptor

⬇

Release histamine

⬇

Histamine binds with H_2 receptor on parietal cell

⬇

Activates adenylyl cyclase (AC)

⬇

Increased cAMP

⬇

Activates protein kinase

⬇

Stimulates acid secretion by proton pump

Parietal cell

Ach / gastrin binds with parietal cell receptor

⬇

Increased cytosolic Ca^{2+}

⬇

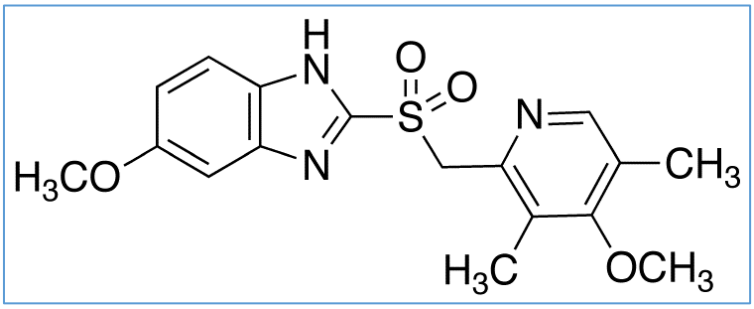
Activates protein kinase

⬇

Stimulates acid secretion from H+ / K+ ATPase pump (Proton pump) on the canalicular surface

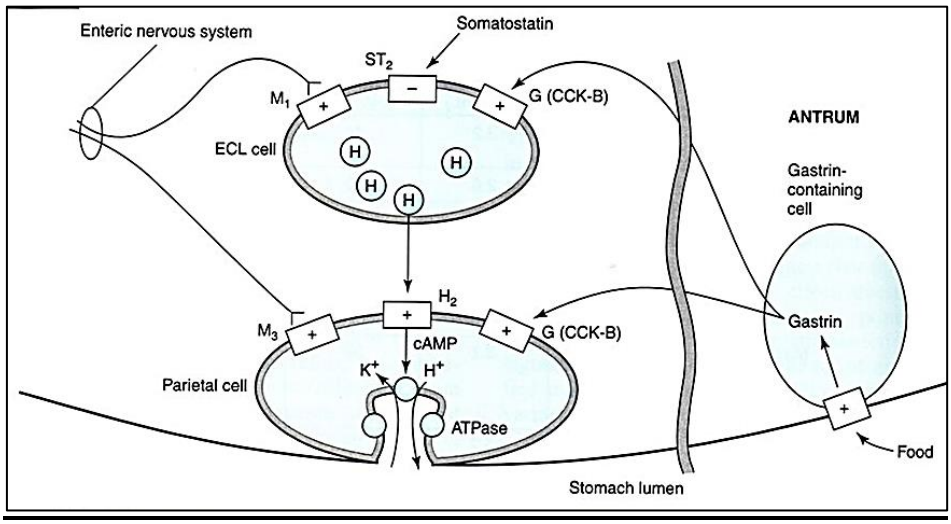
Proton Pump Inhibitor (PPI)

Proton pump inhibitors (PPIs) are a group of drugs whose main action is a pronounced and long-lasting reduction of gastric acid production.



Omeprazole

Mechanism of action of PPI:



PPI (Omeprazole)

⬇

Binds with H^+/K^+ ATPase in the parietal cell

⬇

Blocks irreversibly H^+/K^+ ATPase (Proton pump)

⬇

Inhibits exchange of H^+/K^+ pump

⬇

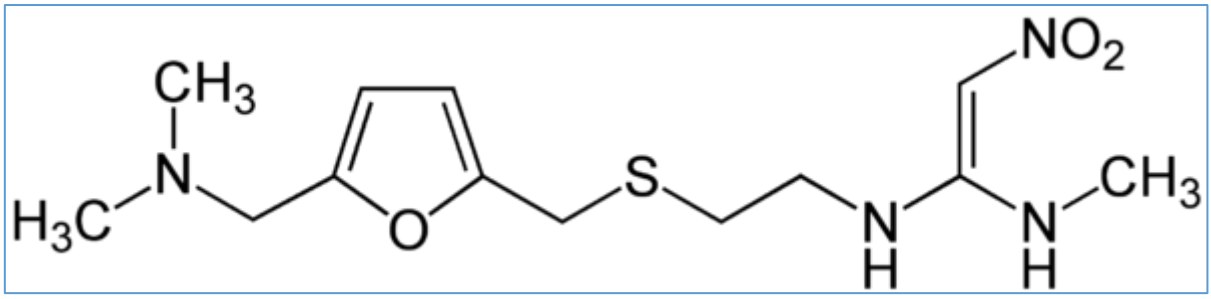
No secretion of gastric HCL

The proton pump is the terminal stage in gastric acid secretion, being directly responsible for secreting H^+ ions into the gastric lumen, making it an ideal target for inhibiting acid secretion.

Targeting the terminal step in acid production, as well as the irreversible nature of the inhibition, results in a class of drugs that are significantly more effective than H_2 antagonists and reduce gastric acid secretion by up to 99%.

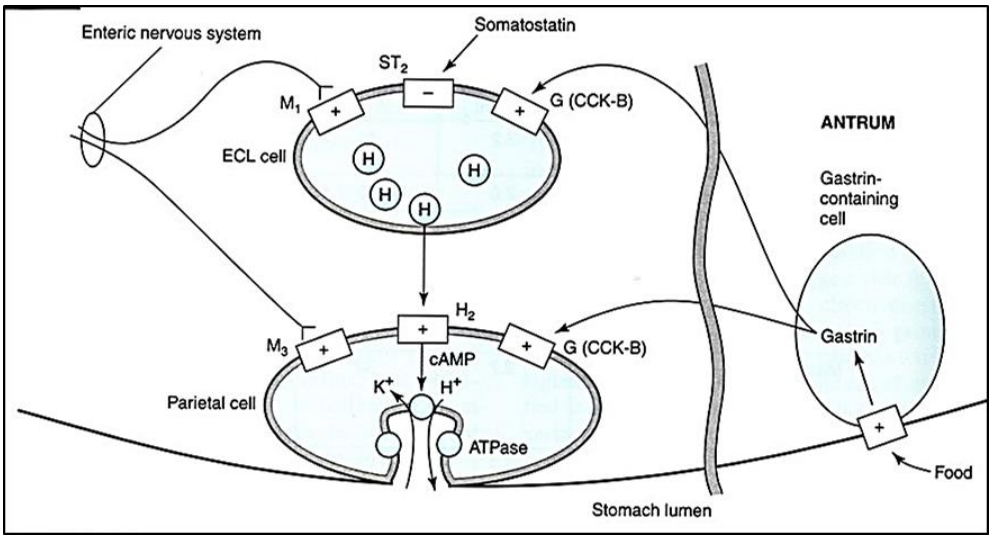
H_2 receptor blocker

H_2 antagonists, also called H_2 blockers, are a class of medications that block the action of histamine at the histamine H_2 receptors of the parietal cells in the stomach. This decreases the production of stomach acid.



Ranitidine

Mechanism of action:



H_2 blocker (Ranitidine, Famotidine)

⬇

Block H_2 receptor of parietal cell

⬇

Inhibit the release of histamine

⬇

Inhibit cAMP formation

⬇

No acid secretion

⬇

Healing of ulcer