# Inorganic Pharmaceutical Chemistry

## 3rd Stage – 1st Semester

**Lecture 1**

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# Gastrointestinal Agents

- **Gastric gland** includes any of the branched tubules in the inner lining of the stomach that secrete gastric juice and protective mucus.
- **Important cells found in the gastric glands include:**

**1- mucous neck cells**:

- They produce mucus. Mucus is a glycoprotein that serves two purposes:
  - the lubrication of food masses in order to facilitate movement within the stomach
  - the formation of a protective layer over the lining epithelium of the stomach cavity.
- These cells also produce Bicarbonate to neutralize the acidity in the stomach.

**2- chief cells:**

- release pepsinogen, a precursor to pepsin.
- Pepsinogen is converted to pepsin (proteolytic) when activated by exposure to acid

**3- parietal cells (oxyntic cells):**

- secrete HCl. A low pH (1.5 to 2) activates pepsin.
- secrete intrinsic factor which is essential for the absorption of vitamin B12.
- Produce and release bicarbonate ions in response to histamine release from the nearby ECL, and so serve a crucial role in the pH buffering system.

**4- Enterochromaffin-like cells (ECL):**

- Store and release histamine when the pH of the stomach becomes too high.
- The release of histamine is stimulated by the secretion of gastrin from the G cells.
- Histamine promotes the production and release of HCl from the parietal cells.
- When the stomach pH decreases (becomes more acidic), the ECL stop releasing histamine.

**The stomach secretes:**

- Hydrochloric acid (HCl)
- Bicarbonate.
- Pepsinogen
- Intrinsic factor
- Mucus
- Histamine
- Prostaglandins: are found in high concentration in the gastric mucosa and gastric juice. Exogenous prostaglandins inhibit acid secretion, stimulate mucus and bicarbonate secretion, alter mucosal blood flow, and provide dramatic protection against a wide variety of agents which cause acute mucosal damage.

In general, Inorganic agents used to treat gastrointestinal disorders include:

1. Products for altering gastric pH
2. Protectives for intestinal inflammation
3. Adsorbents for intestinal toxins
4. Cathartic or laxative for constipation
5. Antidiarrheal drug

- **Hydrochloric Acid Related Diseases:**

I- **Achlorhydria** is the absence of hydrochloric acid in the gastric secretions. due to the failure of the parietal cells to produce gastric acid

- It is common for patients with achlorhydria to have pernicious anemia due to a lack of intrinsic factor the protein necessary to carry vitamin B 12 across the intestinal wall

- Patients with this condition fall into one of two groups:

(1) Patients remain lack gastric hydrochloric acid after stimulation with histamine

Patients with this type of achlorhydria include those with a subtotal gastrectomy, atrophic gastritis (chronic gastritis with atrophy of the mucous membrane and glands), carcinoma of the stomach or gastric polyps

(2) Patients are normally lack gastric hydrochloric acid but will secrete it upon histamine stimulation

It includes those with chronic alcoholism, tuberculosis, hyperthyroidism and parasitic infestations

**In general, the causes of achlorhydria include:**

**1- Drugs:**

Long term use or excessive use of the following drugs may result in achlorhydria:

a- Proton Pump Inhibitors (PPIs):

b- Histamine H2-Receptor Antagonist:

**2- Helicobacter pylori infection:**

a. causes of Low or No stomach acid:

b. The gastric Helicobacter pylori induces superficial gastritis and achlorhydria (or hypochlorhydria)

c. Untreated H. pylori infection may progress to atrophic gastritis and eventually gastric adenocarcinoma.

**3- Gastric cancer:**

**4- Surgery:**

**Treatment:**

Achlorhydria is treated by use 0.1N HCl. The doses depend on degree of lack of HCl secretion.

**II- Hyperacidity:**

- caused by imbalance of the cells of the gastric gland and their secretions
- Symptoms of overproduction of HCl by the parietal cells as indigestion, sour stomach, heartburn, acid stomach
- Helicobacter pylori (H. pylori) Bacterium found in GIT of 90% of patients with duodenal ulcers, and 70% of those with gastric ulcers.

**Gastric mucosal defense mechanisms include secretion of:**

a- Mucus: protective barrier against HCl
b- Bicarbonate: helps buffer acidic properties of HCl
c- Prostaglandins: prevent activation of proton pump which results in HCl production

**Treatment:**

A- includes types of Acid-Controlling Agents:

- Antacids
- H2 Receptor Antagonists
- Proton Pump Inhibitors (PPI)

B- Antiflatulents: used to relieve the painful symptoms associated with gas, such as activated charcoal and Simethicone.

C- Depending upon the extent of hyperacidity, an anticholinergic agent may be indicated

D- Depending on the degree of ulceration, surgery may also be required

**Antacids products:**

- ✓ Sodium containing antacids.
- ✓ Aluminum containing antacids.
- ✓ Calcium containing antacids.
- ✓ Magnesium containing antacids.

- **Mechanism of Action:**

- neutralize excess gastric hydrochloric acid which may be causing pain and ulceration.
- inhibit the activity of pepsin

- **Combination antacid preparations:**

- Most of these combination products are an attempt to balance the constipation effect of calcium and aluminum with the laxative effect of magnesium
- Some of these products are also mixture of an antacid with rapid onset of action and one with a longer duration of action

- **Antacids side effects:**

- Acid rebound:
- Sodium content of the antacid :
- Systemic alkalosis:
- The local effect in the GIT:

**H.W. Antacids-Drugs Interactions with examples**

**Proton-pump inhibitors (PPIs):**

inhibit the stomach's $H^+/K^+$ ATPase proton pump. They are the most potent inhibitors of acid secretion available.

PPIs include lansoprazole, omeprazole, pantoprazole, rabeprazole and esomeprazole.

**Side Effects:**

- In general, PPIs are believed to have few adverse effects, as they are generally well tolerated. Few minor side effects were reported such as headache, rash, dizziness, and gastrointestinal symptoms including nausea, abdominal pain, flatulence, constipation, and diarrhea
- Drug interactions with PPIs most commonly occur as a consequence of their effect on liver enzymes whereby they affect the metabolism and excretion of other medications. Drugs for which PPIs affect metabolism include: Antiepileptics: Phenytoin; Anticoagulants: Warfarin, clopidogrel.

**Histamine H2-receptor antagonists:**

also known as H2-blockers, are used to

- treat duodenal ulcers and prevent their return.
- treat gastric ulcers and for some conditions, such as Zollinger-Ellison disease, in which the stomach produces too much acid.

- Cimetidine, ranitidine, famotidine and nizatidine

- **Mechanism of Action:**

  H2-receptor antagonists decrease gastric acid secretion by reversibly binding to histamine H2 receptors located on gastric parietal cells, thereby inhibiting the binding and activity of the endogenous ligand histamine. H2 blockers thus function as competitive antagonists.

- **Side Effects:**

  Constipation, diarrhea, difficulty sleeping, dry mouth, dry skin, headaches, ringing in the ears, a runny nose, trouble urinating

**H.W. Drug-Drug Interactions?**