Digestive System Drugs

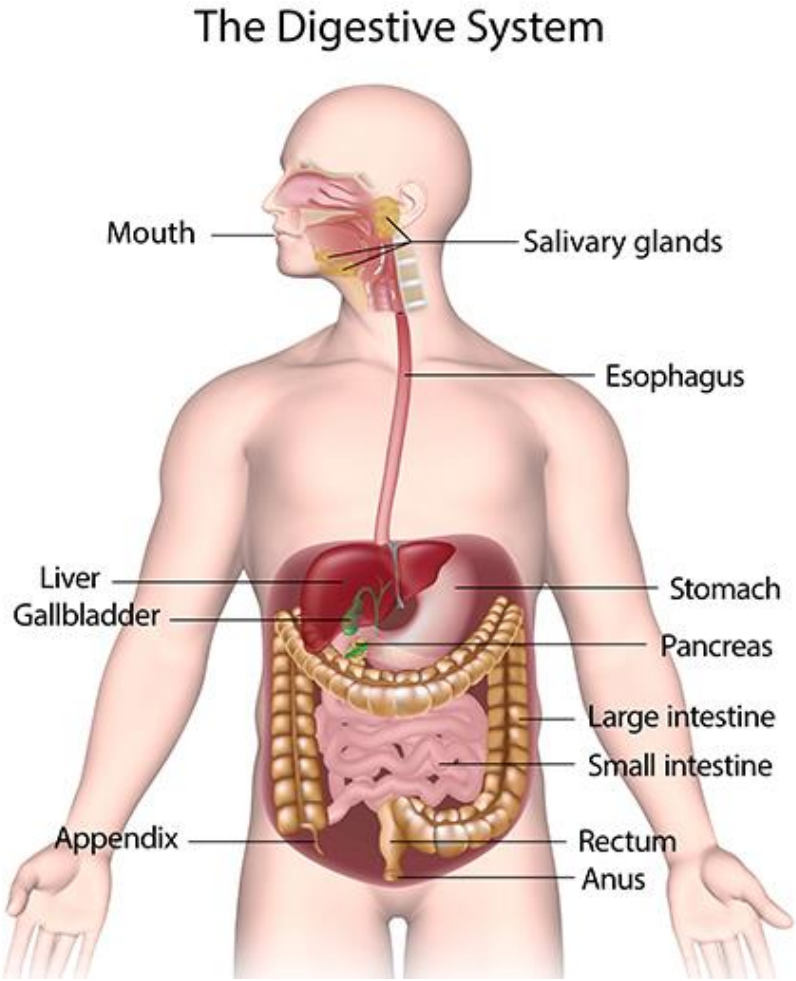
Pharmaceutical Chemistry IV

PHA 482

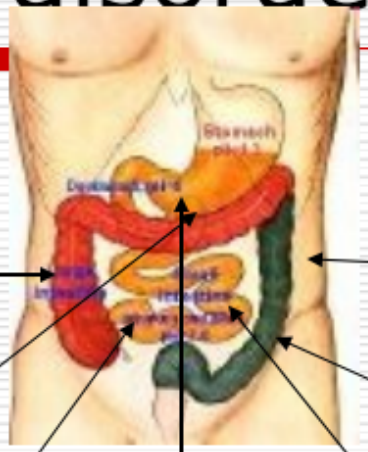
INTRODUCTION

- The digestive system is a group of organs consisting of the central gastrointestinal (GI) tract and its associated accessory organs that break down food into smaller components so that nutrients can be absorbed and assimilated, providing energy and sustaining the body.

- Also known as the gastrointestinal (GI) tract, it is a long tube of varying diameter beginning at the mouth and ending in the anus.



GIT related disorders



In appetence

Appetite stimulants

Other disorders

Different drugs

Acids

Antiacids

Diarrhoea

Antidiarhoeal

Indigestion

Digestants

Constipation

Laxatives and cathartics

Vomiting/Emesis

Emetics/antiemetics

DIGESTANTS AND ENZYMES

Digestants are a group of drugs used to promote the process of digestion in the gastrointestinal tract.

- **Hydrochloric acid**

Use- gastric achlorhydria

- **Pepsin**

Use- gastric achlorhydria

- **Bile acids and salts** (e.g. cholic acid, chenodeoxycholic acid)

Use- stimulate choleresis (bile flow)

- **Pancreatic enzymes (Pancreatin / Pancrealipase**

Contain- amylase, trypsin and lipase

Use- chronic pancreatitis, exocrine pancreatic deficiency

- **Diastase and Takadiastase**

CARMINATIVES

"Promotes expulsion of gases from the Gastro intestinal tract and give a feeling of warmth and comfort in the epigastrium"

Carminatives are specifically antispasmodic to the bowel, easing cramping, griping, and the discomfort caused by flatulence.

Drugs used as carminatives

- Sodium bicarbonate : 0.6-1.5 g
- Peppermint oil : 0.06-0.1 ml
- Tincture cardamom : 1-2 ml
- Oil of Dill : 0.06- 0.2 ml
- Tincture Ginger : 0.6-1 ml

USES;

Flatulent dyspepsia

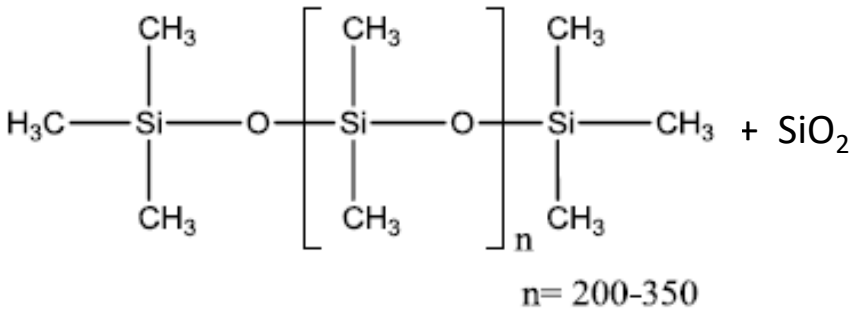
To prevent regurgitation of milk in infants.

*Sodium bicarbonate reacts with acid and form Carbon dioxide which distends stomach relaxes LES (lower esophageal sphincter) followed by eructation (reflex that expels gas noisily from the stomach through the mouth)

*Other contains volatile oils which give irritant action with motility and relaxation of lower esophageal sphincter which ends with warmth feeling and comfort

Simeticone is a synthetic anti-foaming compound used to reduce discomfort or pain caused by excessive gas. It does not reduce or prevent the formation of gas. It is not absorbed from g.i.t. and is pharmacologically inert. (METSİL, ANTİFLAT, FLATON, METEOSPAZMYL, ASİDOPAN)

(Dimethicone + 4-7% SiO_2 (% w/w)



Dimethicone (Polydimethylsiloxane), mixture with silicon dioxide

Drugs for Hypochlorhydria

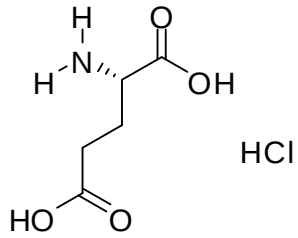
- In hypochlorhydria and achlorhydria , there is low or no gastric acid in the stomach, potentially leading to problems as the disinfectant properties of the gastric lumen are decreased. In such conditions, there is greater risk of infections of the digestive tract.
- The gastric chief cells of the stomach secrete enzymes for protein breakdown (inactive pepsinogen, and in infancy rennin). **Hydrochloric acid** activates **pepsinogen** into the enzyme **pepsin**, which then helps digestion by breaking the bonds linking amino acids, a process known as proteolysis.

In acute conditions;

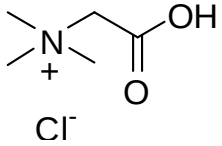
- Injection of histamine or pentagastrin (a synthetic pentapeptide that has effects like gastrin) can stimulate the production of acid component of the gastric juice.

In chronic conditions;

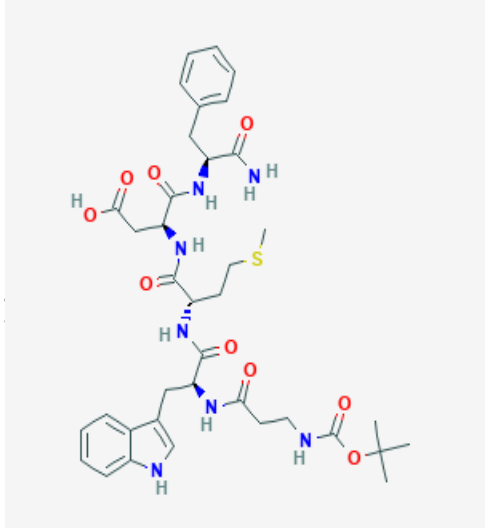
- Diluted HCl
- Glutamic Acid hydrochloride
- Betaine hydrochloride



(carboxymethyl(trimethyl)azanium;chloride/ trimethylmethanaminium chloride),



are used as a gastric acidifier supplement.



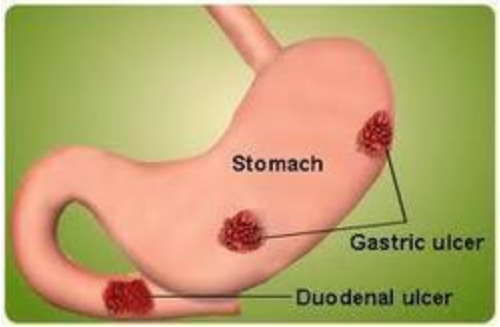
pentagastrine

Anti-ulcer Drugs

1) Neutralization of gastric acid (Antacids)
   - Systemic: Sodium bicarbonate, Sodium citrate
   - Non-systemic (Local): MgOH, Al(OH)3, CaCO3
2) Reduction of gastric acid secretion
   - H_2 antihistamine: Cimetidine, ranitidine, famotidine,roxantidine
   - Proton Pump Inhibitors (PPTs): Omeprazole, pantoprazole, rabeprazole, esmoprazole
   - Anticholinergics: Pirenzepine,propantheline,oxyphenonium
   - Prostaglandin analogues: Misoprostol, enprostil, rioprostil
3) Ulcer protectives: Sucralfate, CBS (Colloidal Bismuth Subcitrate)
4) Ulcer healing Drugs: Carbenoxolone sodium
5) Anti-H. pyloric drugs: Amoxicillin, clarithromycin, metronidazole, tinidazole, tetracycline

Ulcer

An **ulcer** is a kind of **open wound** accompanied by **inflammation**. It can occur both on outer skin and internal epithelium such as surface of the stomach or inside the mouth.



• Ulcers start when the top layer (surface) of **skin** or mucous membrane is hurt. This top layer dies. When it **dies,** the skin or mucous membrane opens. This leaves an open sore called an ulcer.

• Ulcers can be from

– infection with H.pylori (responsible 90% of petide ulcers)
– substances that will burn skin or mucous membranes, such as stomach acid
– from pressure on a part of the skin.
– from cancer to diseases of blood vessels.

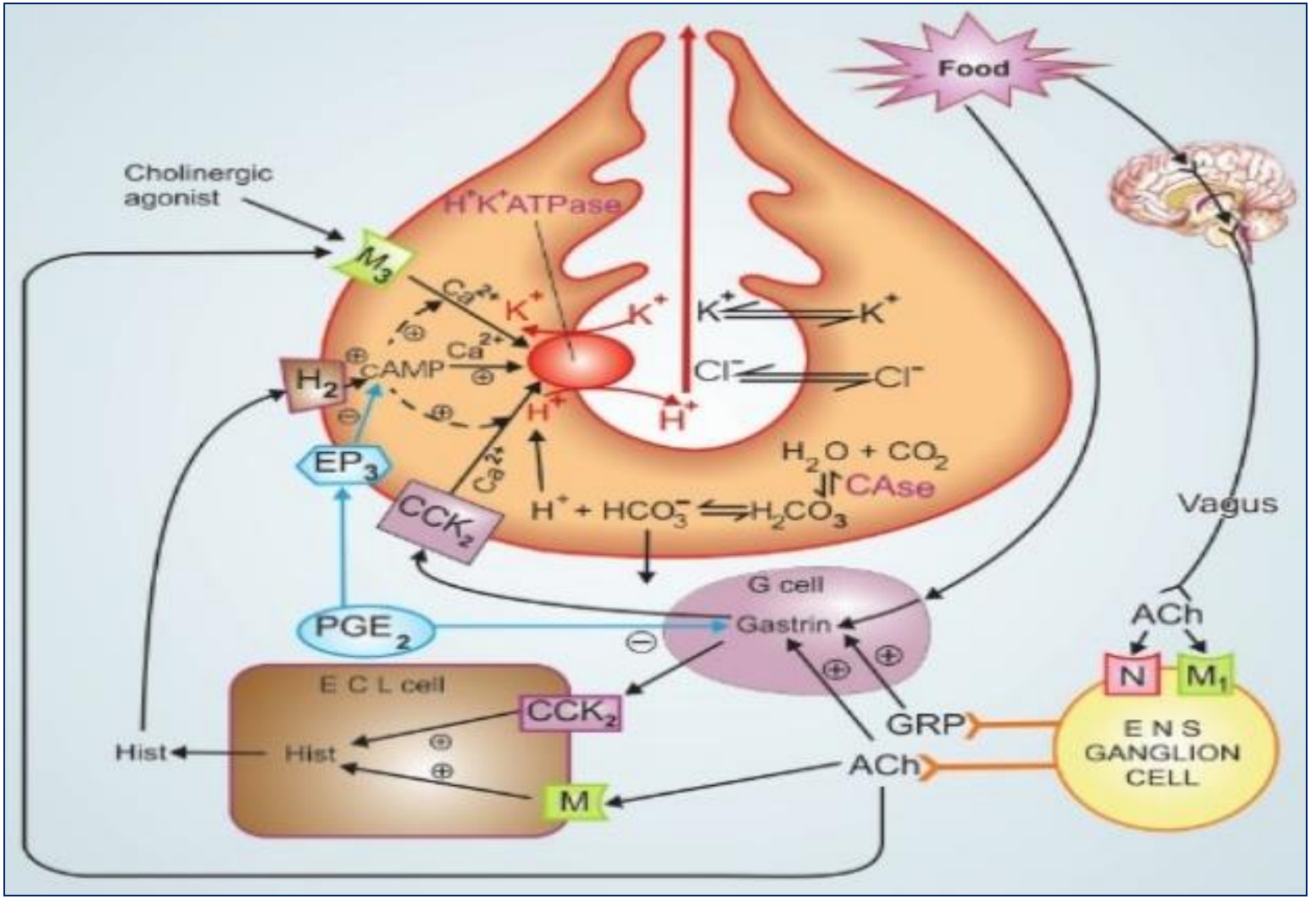
Acid secretion in stomach

- Within the gastric mucosa lies the **oxystic glands those parietal cells secrete about 2-3 litre of HCl of pH 1 into** the stomach
- **The cells don't store a reservoir of HCl acid. H^+ and Cl^- are secreted separately into the stomach;H+ by proton pumps and Cl- by chlorine ion channels**
- The working of proton pump is controlled by various regulators and drugs for ulcers have effect on them
  - Histamine at H2 receptors
  - Gastrin at G receptors
  - Acetylcholine at M2 receptors

  Promote acid secretion
  - Prostaglandin (PgE2)
  - Somatostatin (SST)

  Inhibit acid secretion

Proton pump stimulated by His, Ach and Gastrin and inhibited by PgE2



Antacids

- This medication is used to treat the symptoms of too much stomach acid such as stomach upset, heartburn, and acid indigestion. It is also used to relieve symptoms of extra gas such as belching, bloating, and feelings of pressure/discomfort in the stomach/gut. Also it is used to relief of peptic ulcer pain associated with hyperchlorhydria.
- Hyperacidity, Peptic ulcer diseases, Gastritis, Esophageal Reflux

Classification of Antacids:

Systemic	Non-systemic	
$NaHCO_3$	MgO	Magnesium oxide
$CaCO_3$	$Mg(OH)_2$	Magnesium hydroxide
	$MgSO_4$	Magnesium sulfate
	$Mg_2O_8Si_3$	Magnesium trisilicate
	$AlPO_4$	Aluminum phosphate
	$MgAl_2(SiO_4)_2$	Magnesium aluminum silicate
	$NH_2CH_2COOAl(OH)_2$	Dihydroxyaluminum aminoacetate
	$Al(OH)_3$	Aluminum hydroxide
	$Al_5Mg_{10}(OH)_{31}(SO_4)_2 \cdot nH_2O$	Aluminum magnesium hydroxide (magaldrate)

-Aluminum and magnesium antacids work quickly to lower the acid in the stomach. Liquid antacids usually work faster/better than tablets or capsules.
-This medication works only on existing acid in the stomach. It does not prevent acid production. It may be used alone or with other medications that lower acid production (e.g., H_2 blockers and proton pump inhibitors).
-If you are taking the chewable tablets, chew thoroughly before swallowing, then drink a full glass of water (8 ounces or 240 milliliters).

Some common antacid reactions:

$CaCO_3 + 2\ HCl \rightarrow CaCl_2 + H_2O + CO_2$

$NaHCO_3 + HCl \rightarrow NaCl + H_2O + CO_2$

$Al(OH)_3 + 3\ HCl \rightarrow AlCl_3 + 3\ H_2O$

$Mg(OH)_2 + 2\ HCl \rightarrow MgCl_2 + 2\ H_2O$

$MgO + 2\ HCl \rightarrow MgCl_2 + H_2O$

$Mg_2O_8Si_3.nH_2O + 4HCl \longrightarrow 2MgCl_2.H_2O + 3SiO_2.H_2O + H_2O$

$Al_5Mg_{10}(OH)_{31}(SO_4)_2.nH_2O + 31H^+ \longrightarrow 5AlCl_3.nH_2O + 8MgCl_2.nH_2O + 2MgSO_4.nH_2O + nH_2O$

Who Cannot Take Antacid

Patient with kidney failure or heart disease: Sodium bicarbonate has high sodium content and is not appropriate for people who are on salt restricted diets or have congestive heart failure, high blood pressure, or kidney problems.

In pregnancy: If you are pregnant, antacids are safe to use for heartburn symptoms. But do not use antacids that have sodium bicarbonate. They can cause fluid buildup. During pregnancy it is okay to use antacids that have calcium carbonate

Problem with liver and kidney : If you have a problem with the function of your kidneys or liver, you should be careful with using antacids. All drugs are broken down and removed from the body by the combined action of the liver and kidneys. If your kidneys are not working correctly, it is possible that too much of the drug will build up in your body.

Drug-Drug Interactions

- Whether antacids are taken with other medications such as digoxin, phenytoin, chlorpromazine, isoniazid, ciprofloxacin, iron they cause the absorption of these drugs to be decreased, which causes low blood concentrations of the drugs.

- Antacids that contain magnesium hydroxide reduce the absoption of tetracycline antibiotics.