ANTACIDS

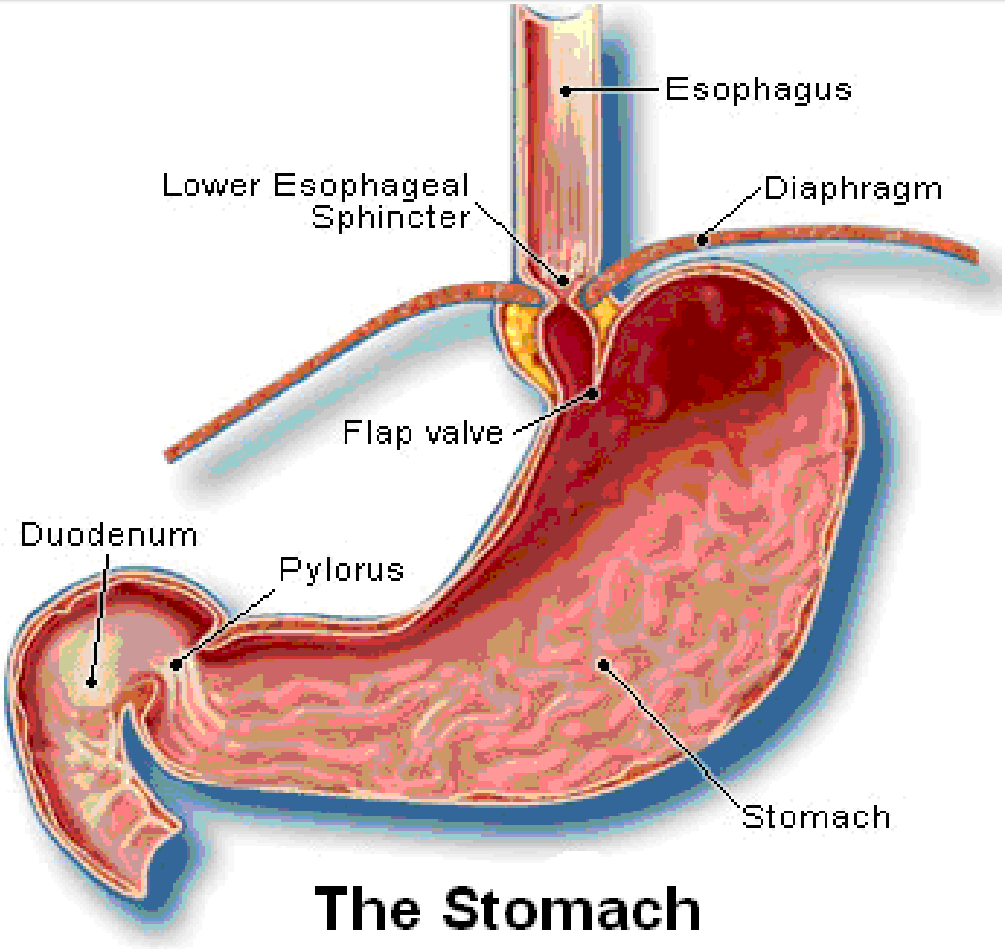
PHARMACEUTICAL CHEMISTRY 1
UNIT II (SECTION -A)

Digestion

- Digestion involves the break down of foods, particularly carbohydrates, lipids, and proteins into forms that can be metabolized in the cells.
- Amylase found in saliva begins the breakdown of starches.
- The breakdown of proteins occurs primarily in the stomach Hydrochloric acid through the action of the enzyme pepsin

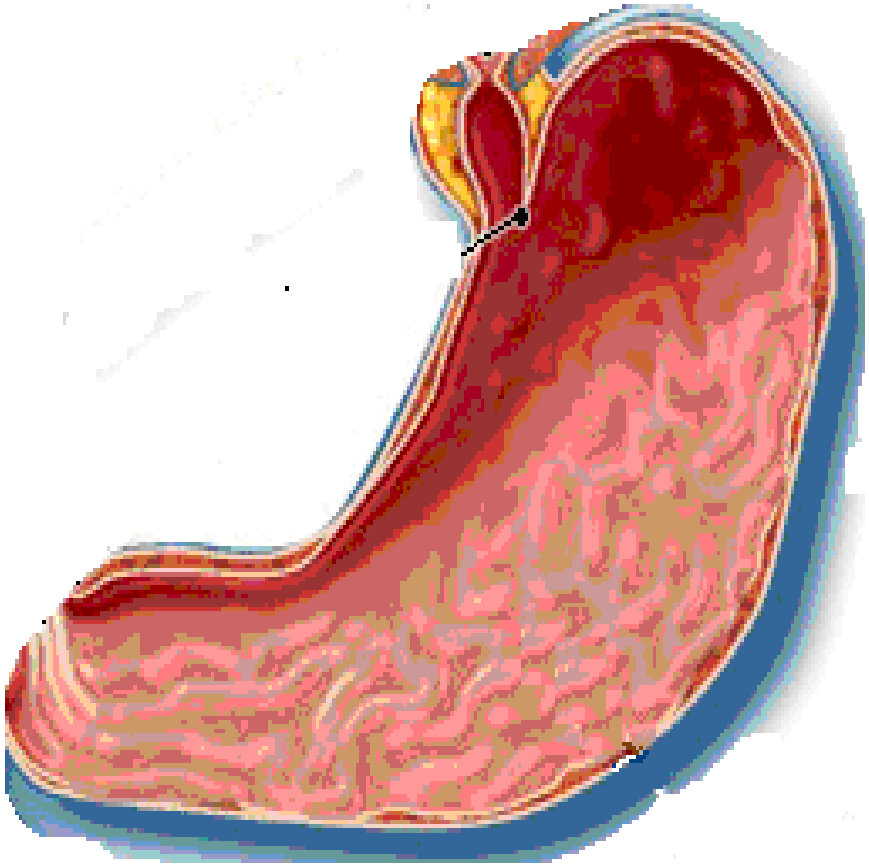
The Stomach

- The walls of the stomach are lined with cells that secrete mucus, pepsinogen and hydrochloric acid.



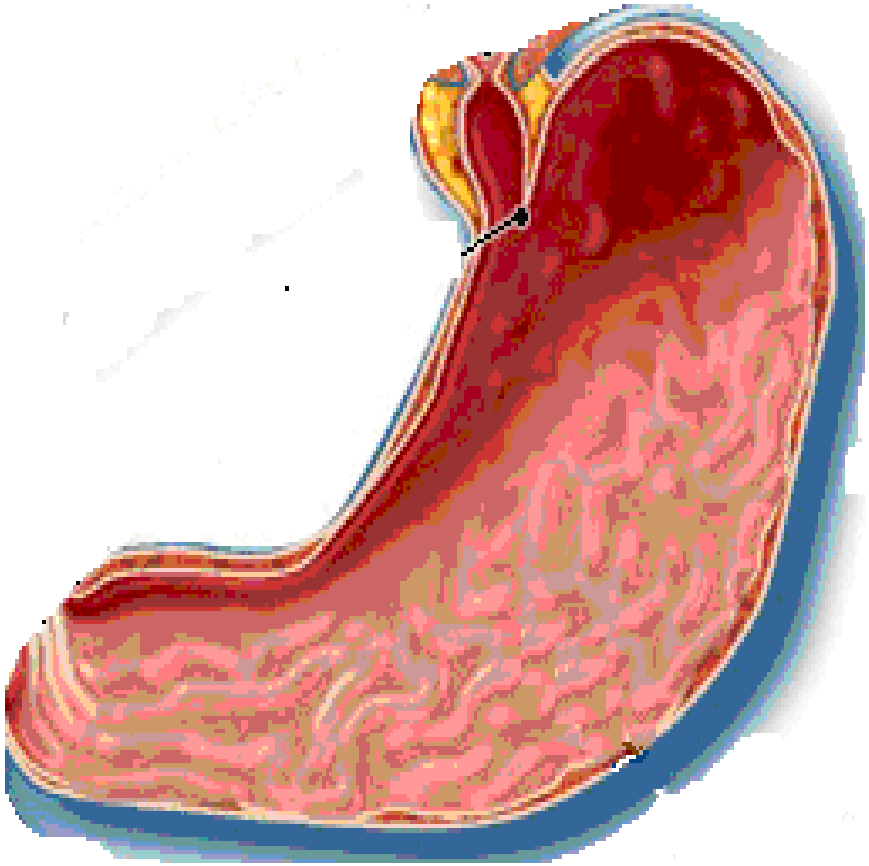
The Stomach

- The hydrochloric acid concentration of the stomach ranges from 0.03 M to 0.003 M which corresponds to a pH range of about 1.5 to 2.5



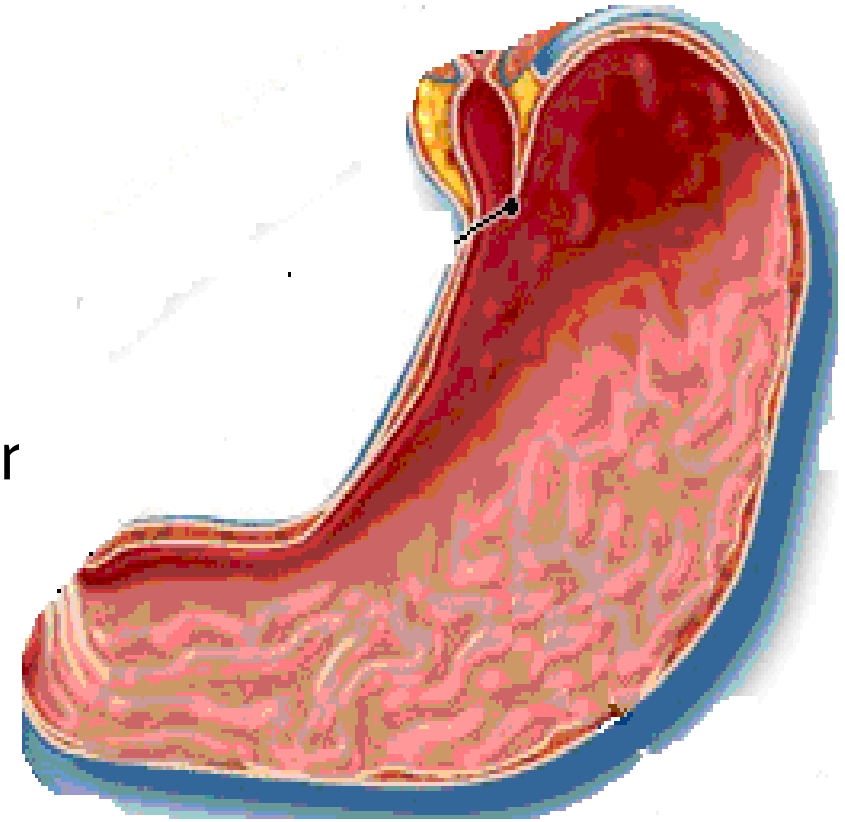
The Stomach

- The mucus lining of the stomach protects the stomach walls from the action of stomach acid



Acid Indigestion and (Heartburn)

- When excess acid is produced a condition known as acid indigestion results.
- If excess acid is forced into the esophagus acid reflux or "heart burn" results.
- High acid concentrations can damage the stomach lining resulting in ulcers.



Causes of Acid Indigestion

- Excess stomach acid results in a state of discomfort known as acid indigestion
- Acid indigestion may result form a variety of factors including:
  - Overeating
  - Alcohol consumption
  - Eating certain foods
  - Anxiety
  - Smoking
  - Certain Drugs, i.e. Aspirin

Antacid Compounds

- Antacids are weak bases that are used to neutralize excess stomach acid
- Most antacids are weak inorganic bases
- Common examples include
  - $CaCO_3$
  - $NaHCO_3$
  - $Al(OH)_3$
  - $Mg(OH)_2$
  - MgO and $Mg(OH)_2$ (Milk of Magnesia)

Commonly used Antacids

Calcium Carbonate	Magnesium Salts	Aluminium Salts (usually hydroxide)
• Alka-mints tablets • Childrens' Mylanta Tablet • Chooz Gum • Alcalak • Titralac	• Milk of Magnesia • Philips Tablets • Philips Oral Suspension	• Maalox • Mylanta • ALternaGEL
• Most potent antacid ingredient; acts rapidly with more prolonged action than sodium bicarbonate	• Less potent that Ca • Slow acting • Can use hydroxide, phosphate & trisilicate (common in Singapore)	• Mild and slow acting antacid, last longer • Most stable form of aluminium salts under normal conditions

Reactions of Antacids

- Antacids react with HCl in the stomach
- Some common antacid reactions include:

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

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

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

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

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

Reactions – Calcium containing antacids

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

- $CaCl_2 + CO_3^{2-} \rightarrow CaCO_3 + Cl^-$ (higher pH in intestine)
- Some unchanged calcium is absorbed by the gut, which can raise the pH of the blood causing alkalosis – can affect proteins
- Calcium is then removed through the renal system

Reactions – magnesium containing antacids

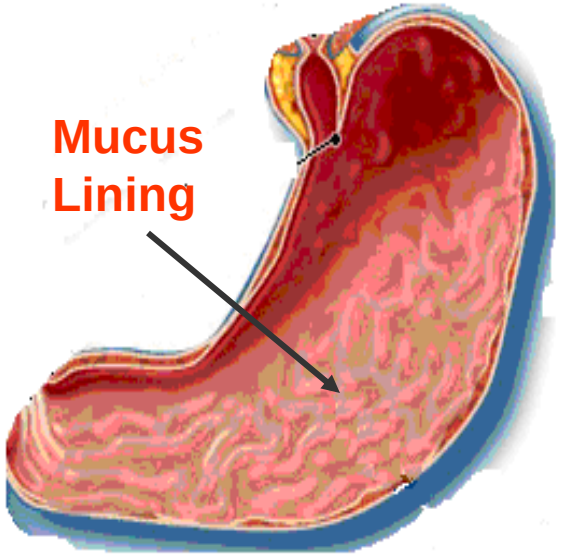
- Magnesium oxides, hydroxides and carbonates are poorly soluble, only Chloride are soluble.

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

- Although non-absorbable, 5% - 10% of Mg enter systemic circulation which is then rapidly removed by kidney

Effect of Antacids

- In addition to neutralizing excess gastric acid they may be helpful in preventing inflammation, relieving pain and discomfort, and allowing the mucus layer in the stomach lining to heal.
- They are often used to treat ulcers by preventing the stomach acids from attacking the stomach lining allowing it to heal.



Reactions – Aluminum containing antacids

- $Al(OH)_3 + 3HCl \rightarrow AlCl_3 + 3H_2O\ Al(H_2O)_6^{3+}$
- Solubility of Al increases as pH decrease, above ph>5 neutralizing effect will stop
- $Al^{3+} + PO_4^{3-} \rightarrow AlPO_4$ (insoluble)
- Inadequate amount of phosphate ions will cause Al^{3+} to be absorbed
- It will rebind back at soft tissue or bones where phosphates are found

Side Effects of Antacid

- **Antacids** are relatively harmless but they can have minor contraindications
- **Magnesium Compounds** may cause diarrhea
- **Aluminum Compounds** may cause constipation and they also may interfere with the adsorption of phosphates in the formation of bones. This is more likely to be true if these compounds are taken for an extended period of time.
- **Carbonates** may generate carbon dioxide leading to bloating and flatulence.

Alginates and Antifoaming Agents

- Antacids are often combined with alginates and anti-foaming agents
- Aliginates float on the stomach contents to form a neutralizing layer preventing reflux of stomach acids up into the esophagus. Hence they help to prevent acid reflux or heart burn
- Anti-foaming agents such as simethicone (dimethicone) prevent the formation of gases and reduce flatulence.

H2 Blockers

- H2 blockers impede acid production in the stomach by blocking the actions of histamine, a substance produced by the body that encourages acid secretion in the stomach.
- These drugs cannot cure ulcers, but in certain cases they are useful in reducing inflamation allowing the stomach to heal
- H2 blockers are effective only for duodenal ulcers, however, and have little effect on stomach (gastric) ulcers.

H_2 - Blockers

- Four H2 blockers are currently available as over the counter drugs in the US:
  - Famotidine (Pepcid AC)
  - Cimetidine (Tagamet)
  - Ranitidine (Zantac)
  - Nizatidine (Axid).

Proton Pump Inhibitors

- Proton Pump Inhibitors reduce the production of acid by blocking the enzyme in the wall of the stomach that produces acid.
- Inhibitors do not neutralize excess acid but inhibit the initial production of hydrochloric acid
- The reduction of acid prevents ulcers and allows any ulcers that exist in the esophagus, stomach and duodenum to heal.

Proton Pump Inhibitors

- Proton Pump Inhibitors are generally available only by prescription but low doses of some products are now approved for over the counter use
- Commonly prescribed Proton Pump inhibitors include
  - Rabeprazole (Aciphex)
  - Lansoprazole (Prevacid)
  - Omeprazole (Prilosec)
  - Esomeprazole (Nexium)

commonly used antacid products

Examples of OTC Heartburn Products			
Drug Class	**Brand Name (Active Ingredients)**	**Onset of Relief**	**Duration of Relief**
Antacids	Maalox (per 5 mL aluminum hydroxide 200 mg, magnesium hydroxide 200 mg, simethicone 20 mg) Maalox Antacid Barrier (calcium carbonate USP 500 mg) Mylanta (per 5 mL aluminum hydroxide 200 mg, magnesium hydroxide 200 mg, simethicone 20 mg) Children's Mylanta Chewable Tablets (calcium carbonate 400 mg) Rolaids (per tablet, calcium carbonate 675 mg, magnesium hydroxide 135 mg, simethicone 60 mg) Tums (per tablet, calcium carbonate USP 750 mg) Tums Kids (calcium carbonate USP 750 mg) Tums Ultra 1000 (calcium carbonate USP 1000 mg) Gaviscon (per 5 mL, aluminum hydroxide 254 mg, magnesium carbonate 237.5 mg)	<5 min	20-30 min (food may prolong duration of relief)
H_2 receptor antagonists	Tagamet HB (cimetidine 200-mg tablets) Pepcid AC (famotidine 10-mg tablets) Pepcid AC Maximum Strength (famotidine 20 mg) Maximum Strength Pepcid AC EZ Chews (famotidine 20 mg) Axid AR (nizatidine 75-mg tablets) Zantac (ranitidine 75-mg tablets) Maximum Strength Zantac (150-mg tablets)	30-45 min	4-10 hr
H_2 receptor antagonists with antacid	Pepcid Complete (famotidine 10 mg, calcium carbonate 800 mg, magnesium hydroxide 165 mg)	<5 min	8-10 hr
Proton pump inhibitor	Prilosec OTC (omeprazole 20-mg tablets)	2-3 hr	12-24 hr
Combination products	Mylanta Ultimate Strength Liquid (aluminum hydroxide 500 mg, magnesium hydroxide 500 mg) Mylanta Supreme Liquid (calcium carbonate 400 mg, magnesium hydroxide 135 mg) Maalox Max (each 5 mL contains calcium carbonate 100 mg, simethicone 600 mg) Rolaids Multisymptom (calcium carbonate 675 mg, magnesium hydroxide 135 mg, simethicone 60 mg) Alka Seltzer Gold (sodium bicarbonate 969 mg, citric acid 832 mg, potassium bicarbonate 312 mg)	<5 min	20-30 min (food may prolong duration of relief)

H_2 = Histamine 2.
Adapted from references 1,5.