Anti Ulcer Drugs

B.Pharmacy : III Year II Semester

Prepared by

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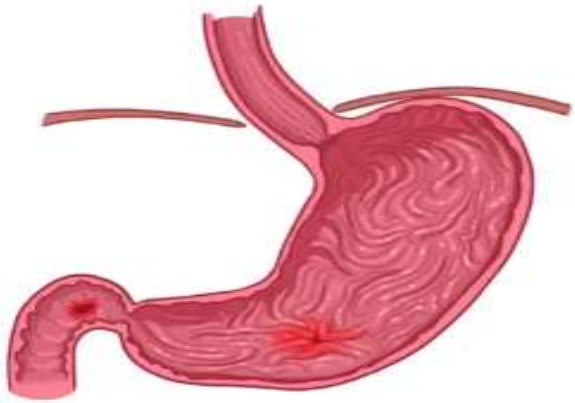


Anti Ulcer Drugs

- Anti-ulcer drugs, also known as anti-gastric ulcer agents or anti-peptic ulcer agents, are medications used to treat or prevent ulcers in the stomach, small intestine, or esophagus.
- Anti secretory agents are the drugs which decreases the secertion of gastric acid in the stomach.

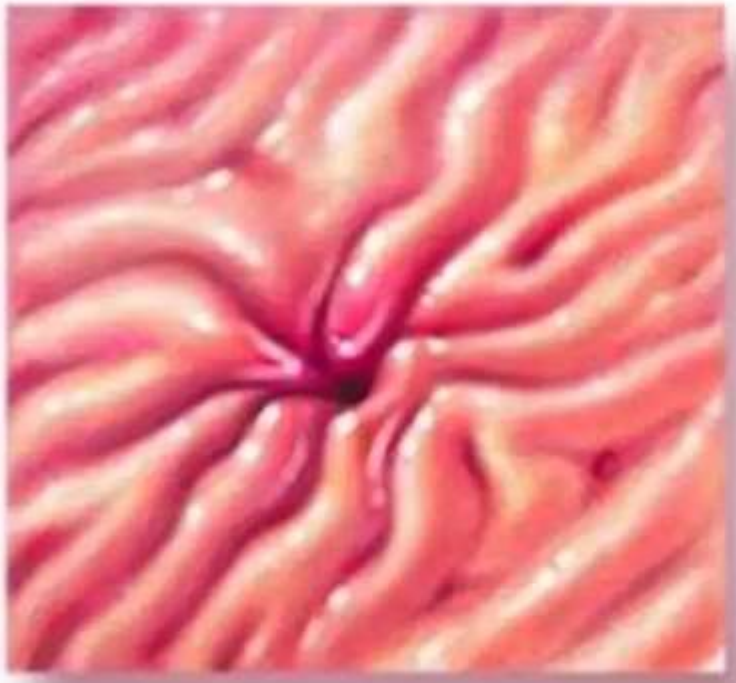
Ulcer:

- A peptic ulcer disease or PUD is an ulcer (defined as mucosal erosions ≥ 0.5 cm) of an area of the gastrointestinal tract exposed to the acid and pepsin secretion

TYPES

There are three types of peptic ulcers:

- **Gastric ulcers:** ulcers that develop inside the stomach
- **Esophageal ulcers:** ulcers that develop inside the esophagus
- **Duodenal ulcers:** ulcers that develop in the upper section of the small intestines, called the duodenum



Esophagus

Stomach

Small intestine

Duodenal ulcer

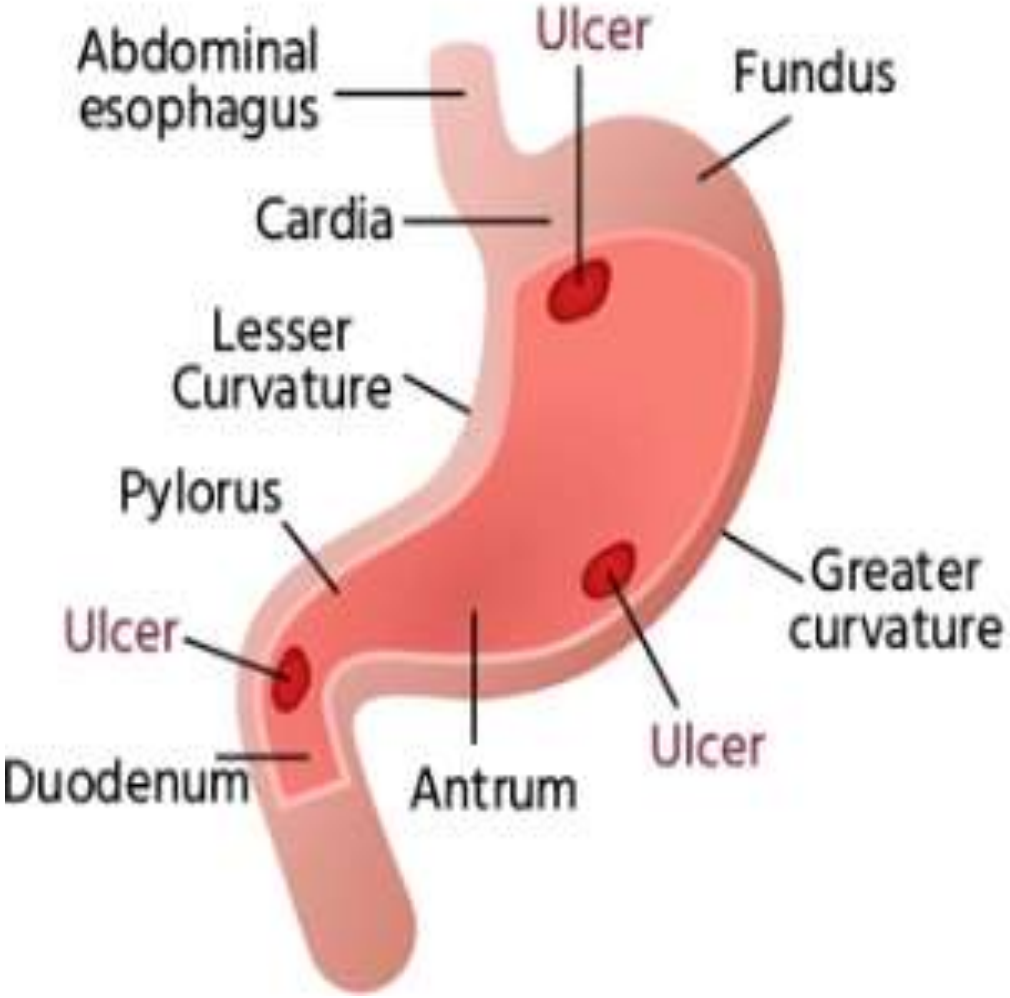
Gastric ulcer

Gastric Ulcer	Duodenal Ulcer
1. They occur in stomach.	1. They occur in duodenum.
2. They cause by injury like substances, alcohol, aspirin, NSAIDs, drugs.	2. But these are cause by HCl secretion by vagus nerve stimulation in fasting period.
3. Pain in left epigastric region in gastric ulcer.	3. Pain in right epigastric region.
4. Nausea is common.	4. Rarely.
5. Vomiting with blood occurs in this case.	5. Stool with blood.
6. Weight loss.	6. No weight loss.
7. Pain starts just after taking food.	7. Onset of pain after 2-4 hrs. of taking food.
8. Pain is present while hungry.	8. Absent.
9. Pain is regular.	9. Not regular.
10. Malignancy is not common.	10. Common.

Etiology:

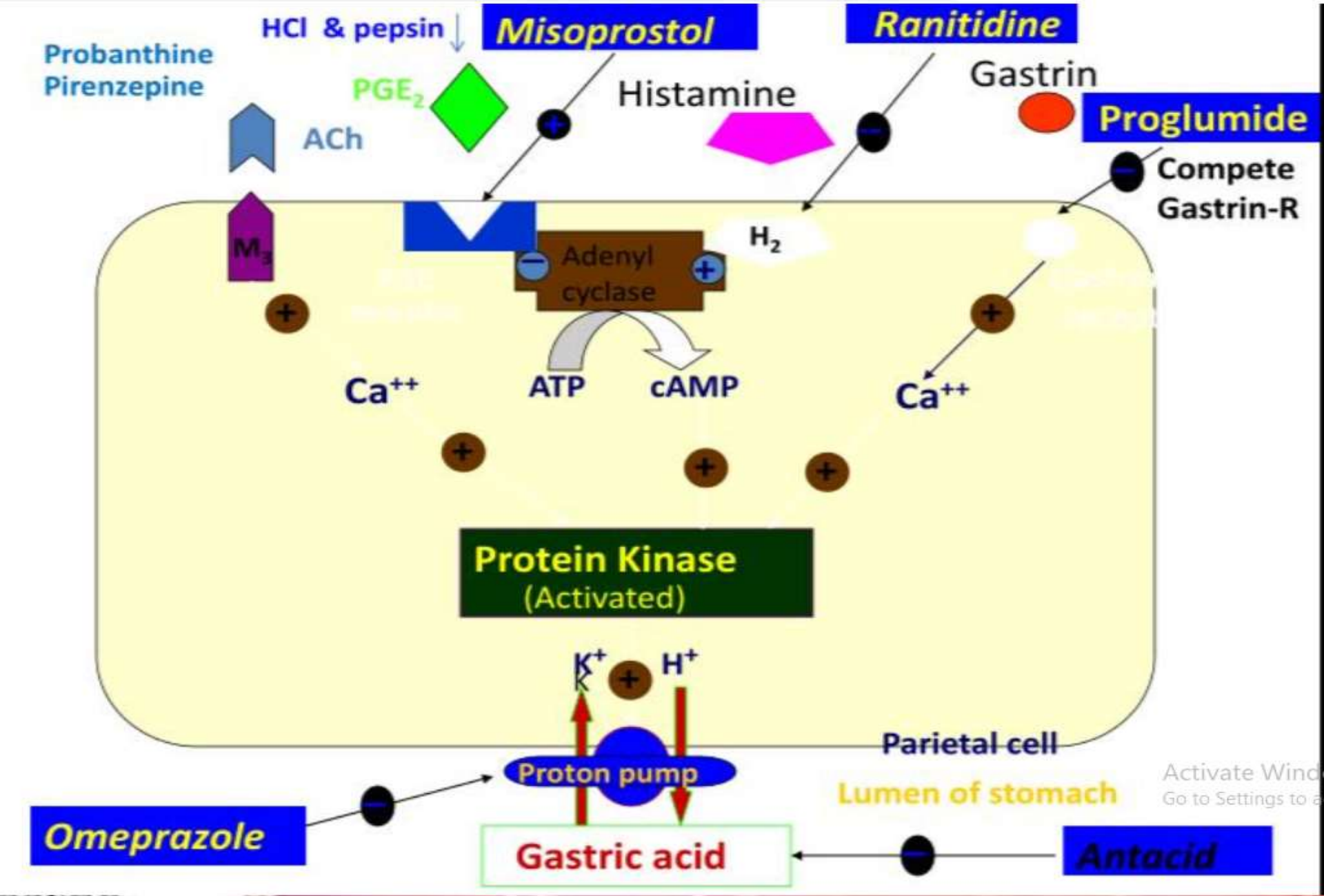
- Irregular food habit
- Increase intake of spicy foods
- Increase intake of tea and coffee
- Increase intake of alcohol and cigerate
- Stimulation of vagus nerve
- Excessive secretion of gastrin
- Release of Histamine
- Radiation therapy
- gm-ve bacteria H. Pylori infection
- Stress,ulcerogenic drugs (e.g. NSAIDs), male genders, age, & diet

STOMACH ULCER SYMPTOMS



- Pain
- Retching
- Vomiting
- Appetite changes
- Nausea
- Weight loss
- Bloating
- Dark blood in stools

Physiology of ulcer



Classification of Anti-ulcer Drugs

1. Reduction in Gastric acid secretion:
   - H_2 antihistamines: **Cimetidine, Ranitidine, Famotidine, Nizatidine and Roxatidine**
   - Proton pump inhibitors: **Omeprazole, Lansoprazole Pantoprazole, Rabeprazole and Esomeprazole**
   - Anticholinergics: **Pirenzepine, Propantheline and Oxyphenonium**
   - Prostaglandin analogue: **Misoprostol**

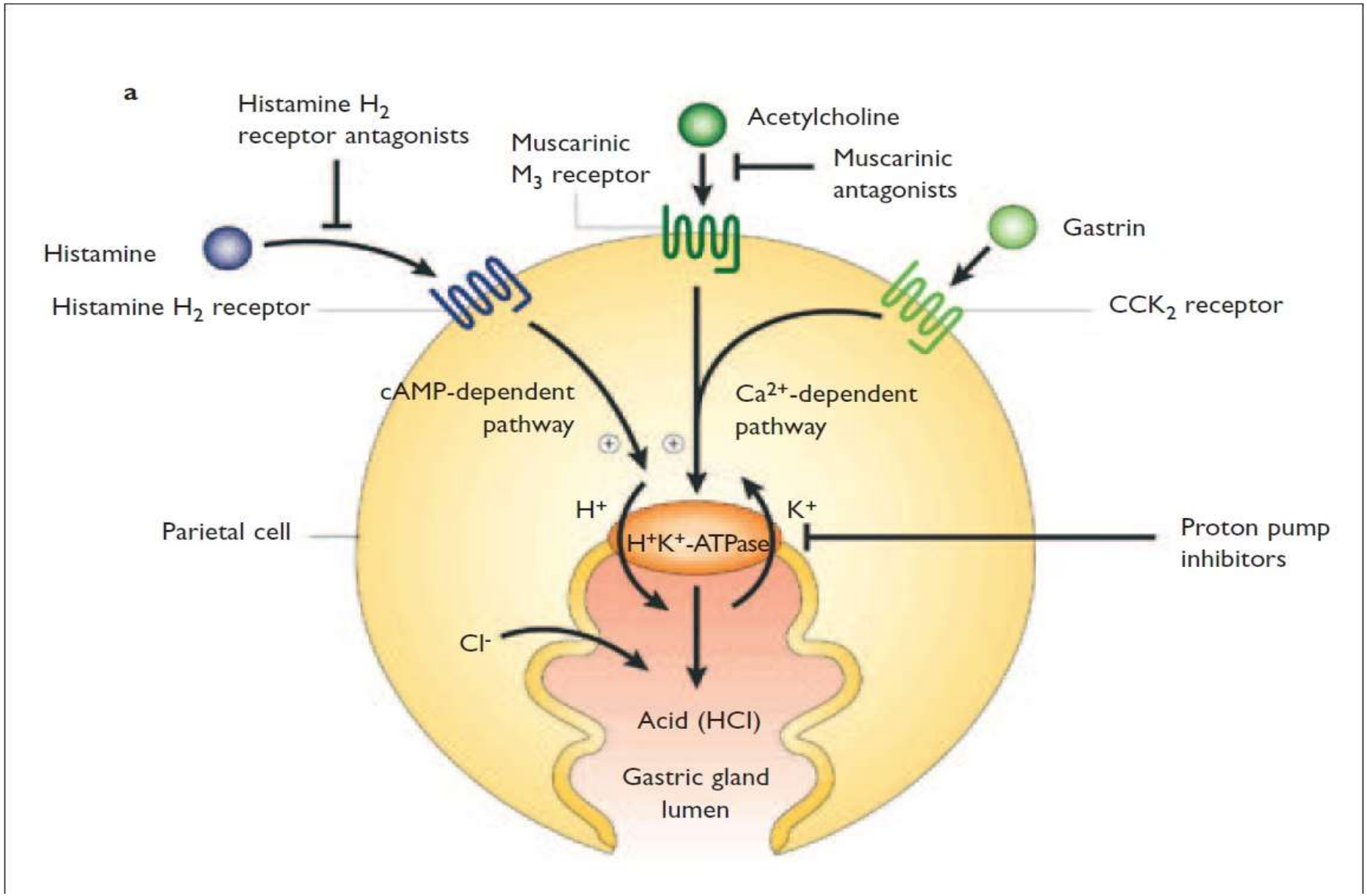
2. Acid Neutralizing agents: (ANTACIDS)
   - Systemic: Sodium Bicarbonate and Sod. Citrate
   - Nonsystemic: Magnesium hydroxide, Mag. Treisilicate, Aluminium hydroxide gel, Magaldrate and calcium carbonate

3. Ulcer protectives: Sucralfate, Colloidal Bismuth sudcitrate
4. Anti-H. pylori Drugs: Amoxicillin, Clarithromycin, metronidazole, tinidazole and tetracycline

5. Ulcer healing agents: Carbinoxalone sodium

H_2 blockers

Mechanism of action :



Pharmacokinetics

- Route : oral, I.V
- Absorption : 60%
- B.A : 60-70%
- Onset of action: 30 minutes
- Duration of action:4 to 8 hours.
- Plasma half life: 2Hrs
- Cross : BBB and PB
- Peak plasma con: 1 to 3 hours
- PPB : 15 – 20%
- Metabolism : Liver
- Excretion : urine: 48-75% & Feces:2-3%

Adverse effects

- Headache
- Dizziness
- Bowel upset
- Dry mouth
- Rashes
- Confusion
- Gynacomasthia
- Sexual dysfunction
- Nausea & vomiting
- Diarrhea
- Muscle pain

Drug interaction

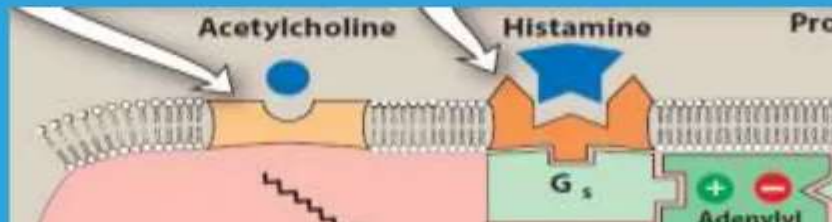
Drug	Interaction
Atazanavir	Decreased absorption of Atazanavir (Require acid for absorption) Note – Other H_2 Blocker and proton pump inhibitors would be expected to have the same effect.
Benzodiazepine	Decreased metabolism of alprazolam, Chlordiazepoxide, diazepam, halazepam, prazepam, but not oxazepam, Lorazepam or temazepam
Carmustine	Increase bone marrow suppression
Indinavir	Decreased absorption of Indinavir (Require acid for absorption) Note – Other H_2 Blocker and proton pump inhibitors would be expected to have the same effect.
Lidocaine	Decreased metabolism of Lidocaine, Increased serum Lidocaine concentration
Phenytoin	Decreased Phenytoin metabolism, increased serum phenytoin concentration
Procainamide	Decreased renal excretion of procainamide, increased serum procainamide concentration
Quinidine	Decreased metabolism of quinidine, increase serum quinidine concentration

Uses

- Gastric ulcer
- Duodenal ulcers
- GERD
- Zollinger – Ellision syndrome
- Heartburn
- Acid indigesion
- Sour stomach

Mechanism of action

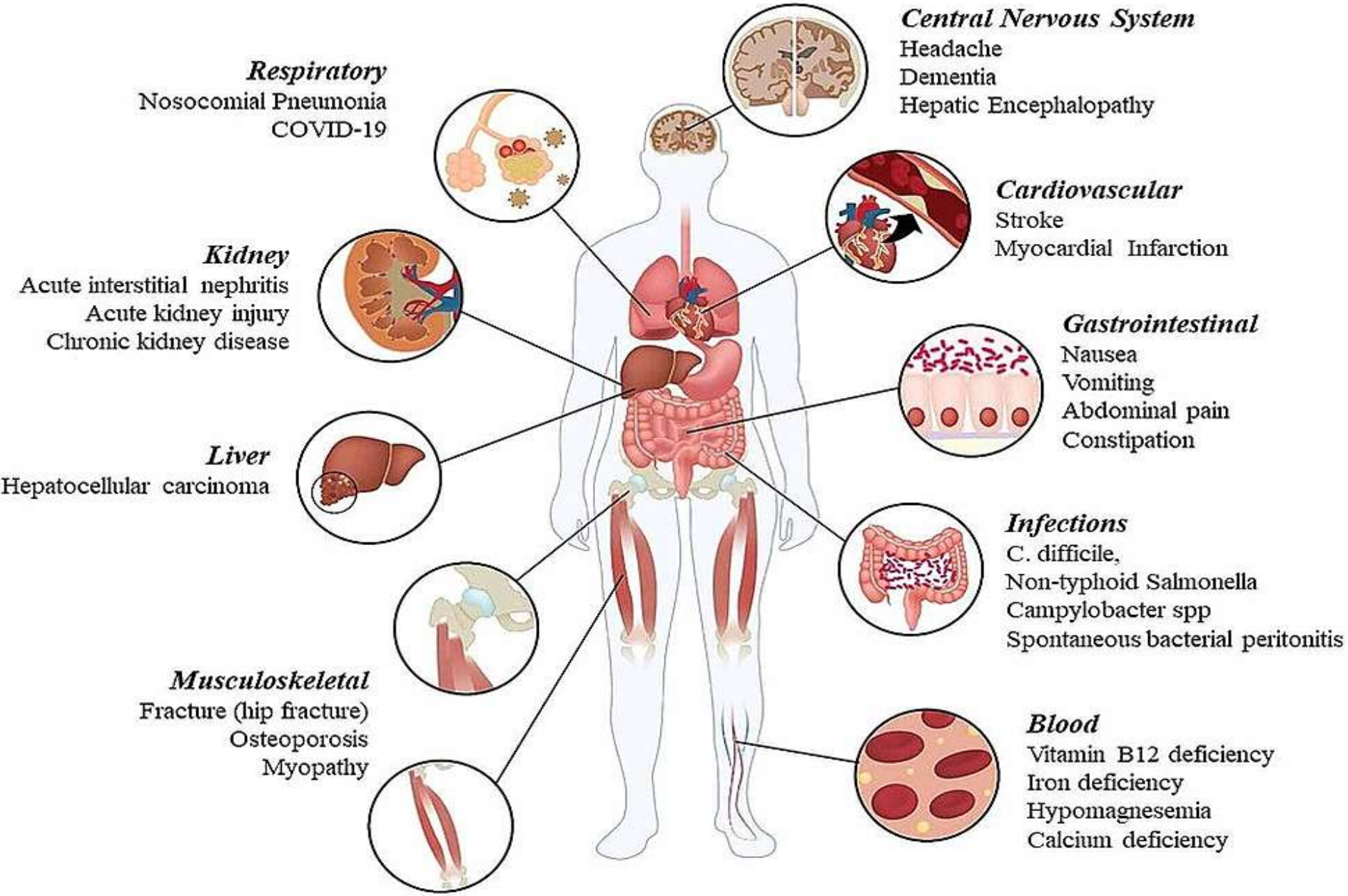
- **Omeprazole** inhibits secretion of gastric acid by irreversibly blocking the enzyme system of hydrogen/potassium adenosine triphosphatase, the “proton pump” of the gastric parietal cell.
- resulting in suppression of gastric acid secretion



Pharmacokinetics

- Route : oral
- Absorption : 60%
- B.A : 35%
- Onset of action : 1Hrs
- Duration of action: 72hours.
- Plasma half life : 1Hrs
- Cross : BBB and PB
- Peak plasma con: 0.5 to 3.5hour
- PPB : 95 - 98%
- Metabolism : Liver
- Excretion : urine: 80%

Adverse effects



Drug interaction

- Omeprazole +warfarin -----→ inhibit metabolism
- Omeprazole +phenytoin----→ inhibit metabolism
- Omeprazole +diazepam-----→ inhibit metabolism
- Omeprazole +cyclosporin---→ inhibit metabolism

uses

1. Peptic ulcer
2. GERD
3. H pylori infection
4. NSAID induced ulcer
5. Reflux esophagitis
6. Zollinger-Ellison syndrome
7. Prophylaxis for ulcers

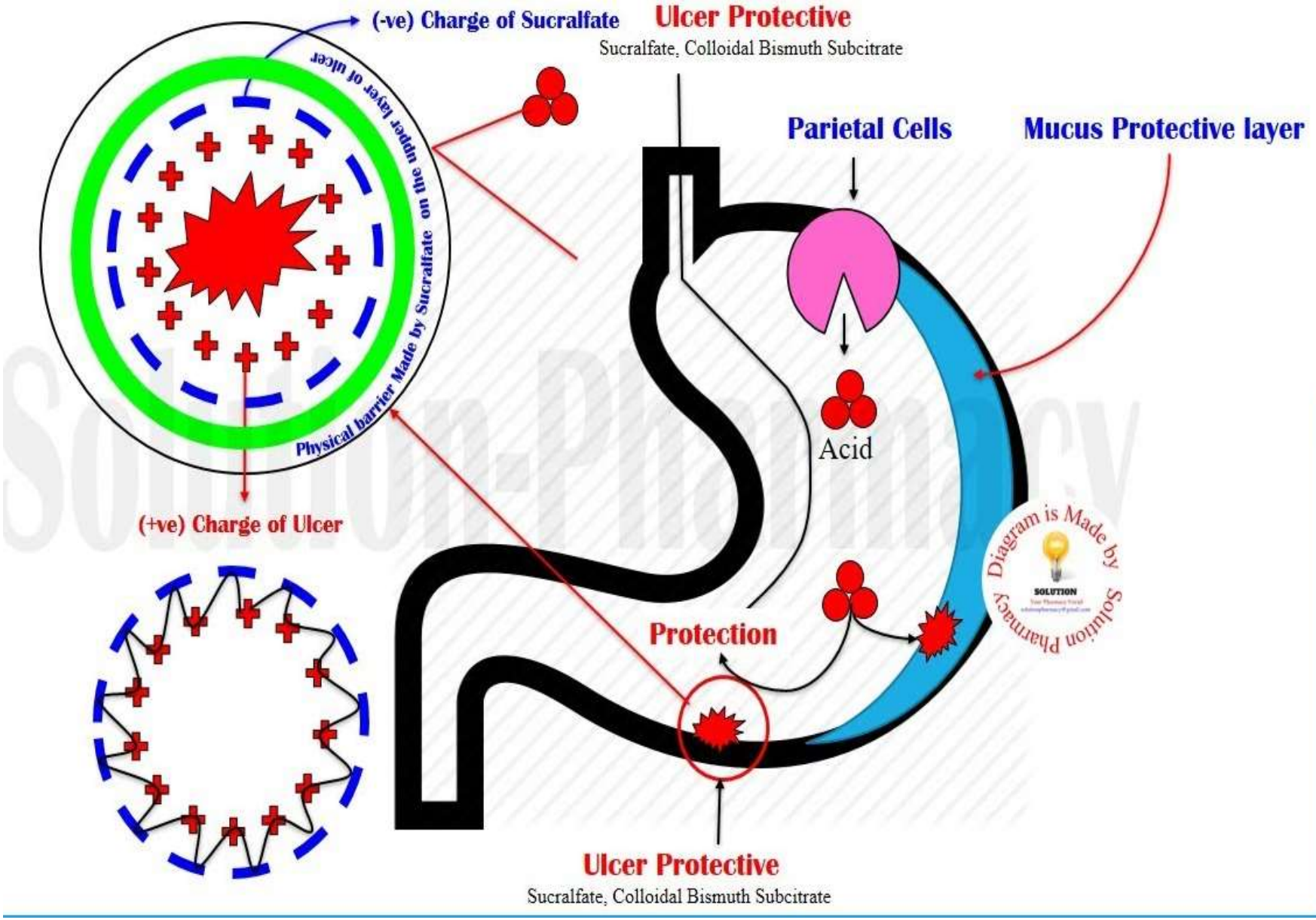
Ulcer protective

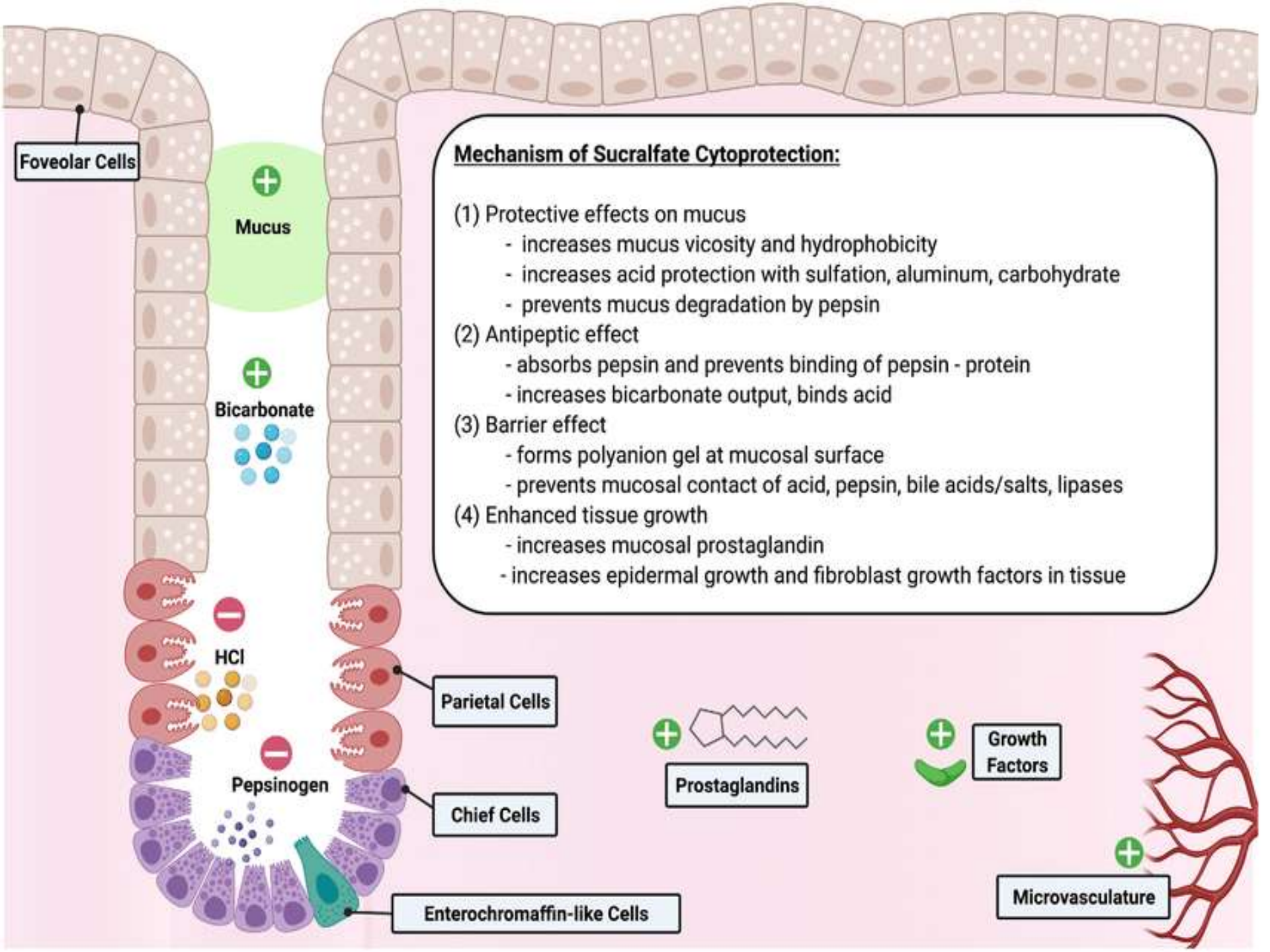
Sucralfate

- Basic aluminum salt of sulfated sucrose.
- Polymerizes at pH < 4 by cross linking of molecules
- Strongly adheres to ulcer base to remain there for ~ 6 hours

Mechanism of action:

- Acts as a physical barrier preventing acid, pepsin and bile from coming in contact with the ulcer base.
- Inhibiting hydrolysis of mucosal proteins by pepsin.
- Additional - Stimulation of local production of PGs and epidermal growth factor.


(-ve) Charge of Sucralfate
Ulcer Protective
Sucralfate, Colloidal Bismuth Subcitrate
Parietal Cells
Mucus Protective layer
upper layer of ulcer
Physical barrier Made by Sucralfate on the
Acid
(+ve) Charge of Ulcer
Diagram is Made by Solution Pharmacy
SOLUTION
Protection
Ulcer Protective
Sucralfate, Colloidal Bismuth Subcitrate


Foveolar Cells
Mucus
Bicarbonate
HCl
Pepsinogen
Parietal Cells
Chief Cells
Enterochromaffin-like Cells
Prostaglandins
Growth Factors
Microvasculature
Mechanism of Sucralfate Cytoprotection:
(1) Protective effects on mucus
- increases mucus vicosity and hydrophobicity
- increases acid protection with sulfation, aluminum, carbohydrate
- prevents mucus degradation by pepsin
(2) Antipeptic effect
- absorbs pepsin and prevents binding of pepsin - protein
- increases bicarbonate output, binds acid
(3) Barrier effect
- forms polyanion gel at mucosal surface
- prevents mucosal contact of acid, pepsin, bile acids/salts, lipases
(4) Enhanced tissue growth
- increases mucosal prostaglandin
- increases epidermal growth and fibroblast growth factors in tissue

Pharmacokinetics

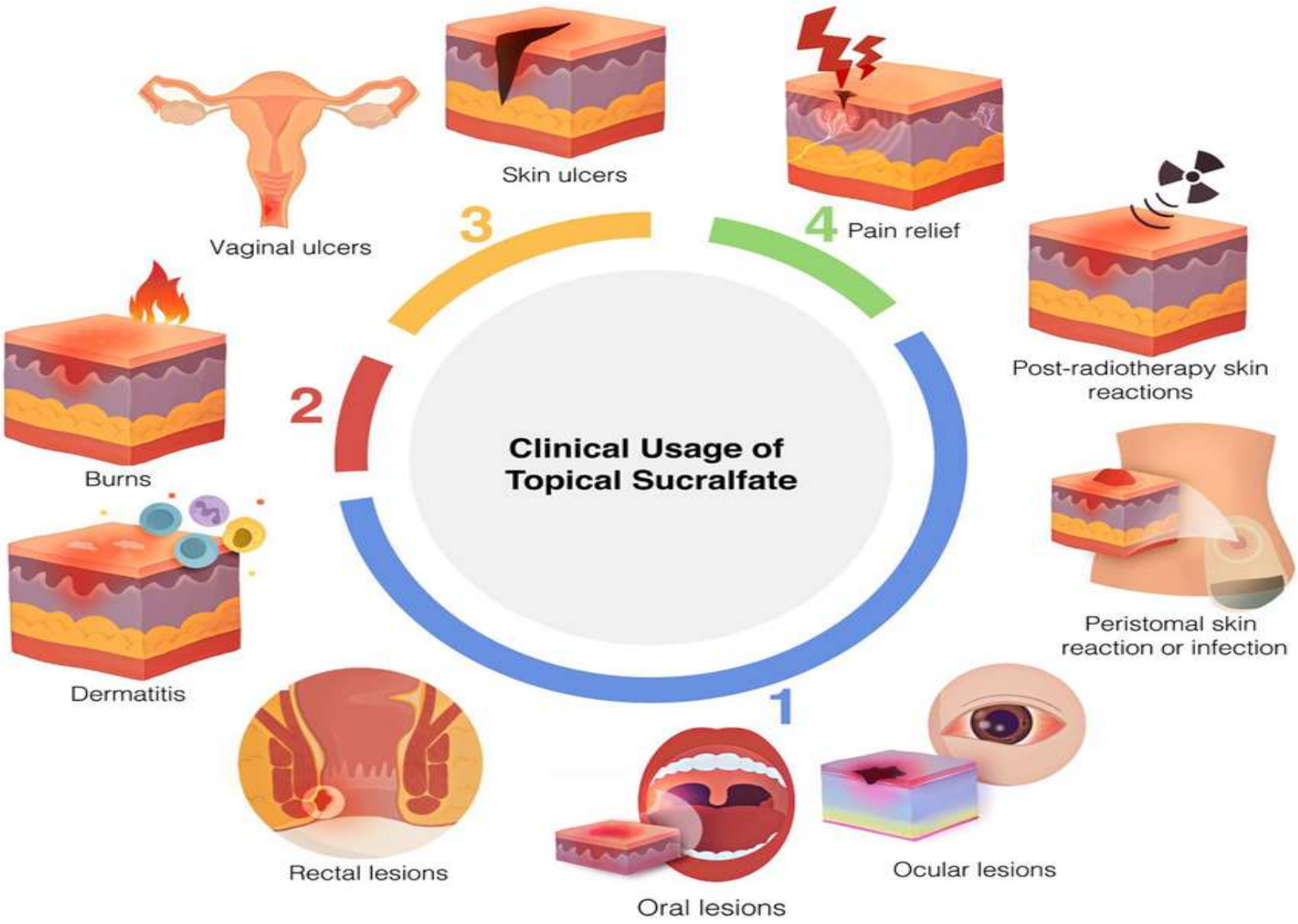
- Route : oral, rectal and topical
- Absorption : 5%
- B.A : 5%
- Onset of action : 1- 2Hrs
- Duration of action: 6hours.
- Plasma half life : 6 - 20Hrs
- Cross : BBB and PB
- Peak plasma con: 0.5 to 3.5hour
- Metabolism : Liver
- Excretion : urine: 48%

Sucralfate: Adverse Effects

- Constipation
- Nausea
- Vomiting
- Aluminum intoxication
- Hypophosphatemia

Sucralfate: Drug Interactions

- Decreased absorption of
  - Ciprofloxacin, norfloxacin
  - Theophylline (conflicting data)
  - Tetracycline
  - Phenytoin
  - Digoxin
  - Amitriptyline


Clinical Usage of Topical Sucralfate
1
2
3
4
Vaginal ulcers
Skin ulcers
Pain relief
Post-radiotherapy skin reactions
Peristomal skin reaction or infection
Ocular lesions
Oral lesions
Rectal lesions
Dermatitis
Burns

Ulcer Healing agents(Cytoprotectie agent)

Carbenoxolone

- An anti-ulcer drug obtained from glycyrrhiza (obtained from licorice)
- Rapid absorption from stomach & intestine
- Structure similar to Steroid

Mechanism of action:

- ↑ release of endogenous prostaglandins
- ↑ gastric mucous secretion
- ↓ the exfoliation and increasing the half life of gastric mucosal cells

MOA

Carbenoxolone

↓

Act by

↓

+synthesis of protective mucous

↓

- conversion of pepsinogen to pepsin

↓

Heal ulcer without increase PH

Pharmacokinetics

- Route : oral
- Plasma half life : 43 and 41 min
- PPB : High
- Cross : BBB and PB
- Peak plasma con: 0.5 to 3.5hour
- Metabolism : Liver
- Excretion : urine: 48%

Adverse effects

- Mineralocorticoid action
- Carbonoxolone sodium induces salt and water retention, hypokalaemia leading to impaired neuromuscular function and muscle and renal damage with prolonged treatment

Drug interactions

it increases the risk of hypokalemia with acetazolamide, thiazides, and loop diuretics.

Amiloride and spironolactone may also inhibit the pharmacological response to carbenoxolone.

Uses

- Carbenoxolone is used for the treatment of peptic ulcers
- Carbenoxolone is used for the treatment of esophageal ulcers
- Carbenoxolone is used for the treatment of oral ulceration and inflammation.
- Carbenoxolone is used for the treatment of GERD
- Carbenoxolone is used for the treatment of dermatitis and eczema.

Anti H –Pylori agents

- H-Pylori is Gram –ve bacillus present in the stomach and duodenum
- H-Pylori infection spreads through faecal oral route
- H-Pylori secretes various enzymes like ureases, lipases, proteases and an endotoxin

Ureases catalyses Urea ↓ $Co_2 + NH_3$

The ammonia neutralizes gastric HCl and create neutral environment around the bacteria

The endotoxin and proteases and lipases degrade the protective mucous layer

They leads to inflammation and gastritis ultimately leads to ulcer

Combination therapy

- Omeprazole + Amoxicillin- 7 -10Days

  (40 mg +1000mg b.i.d)
- Ranitidine + clarithromycin - 7 -10Days

  (500 mg +500mg)
- Omeprazole +clarithromycin+amoxicillin -14days

  (20mg b.i.d+500mg b.i.d +500mg b.i.d)
- omeprazole + Bismuth salicylate+T.C +Metronidazole – 14Days
  - (20mg + 525mg q.i.d + 500mg q.i.d + 250mg q.i.d)


Thank you!