Gastrointestinal Tract (GIT) drugs

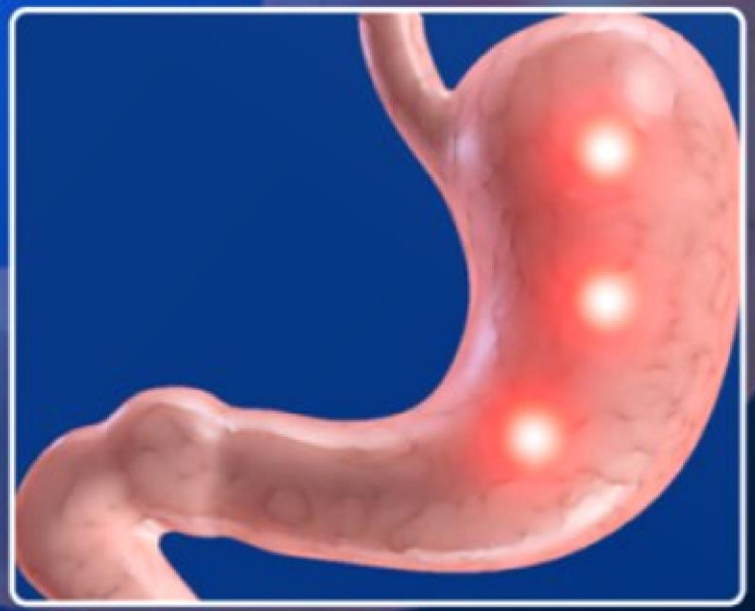
Today's lecture will be on drugs that affect the GIT system

I. Drugs use in Peptic ulcer disease.

II. Anti-emetic drugs.

III. Drugs used for Diarrhea and Constipation.

Peptic ulcer

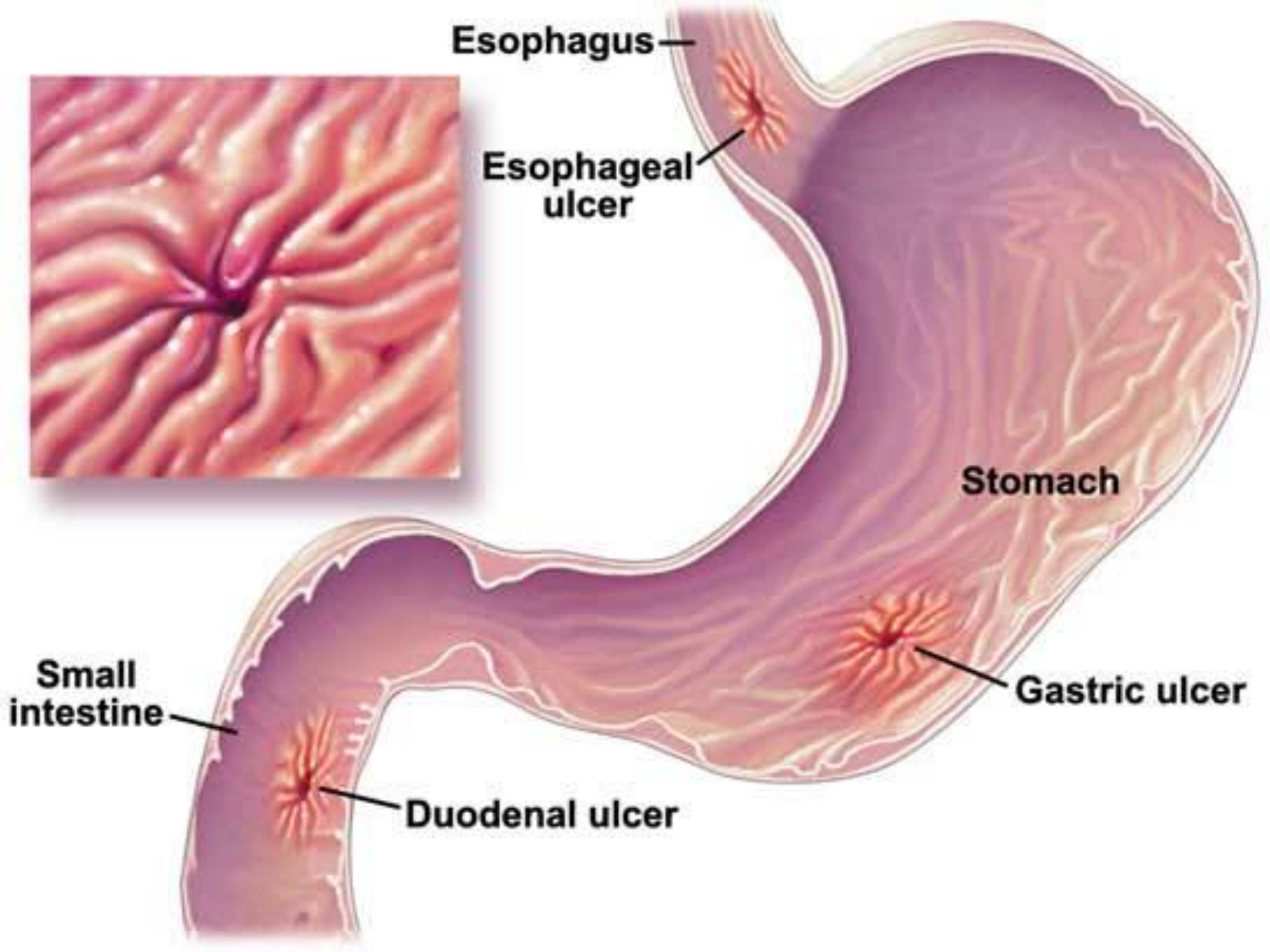


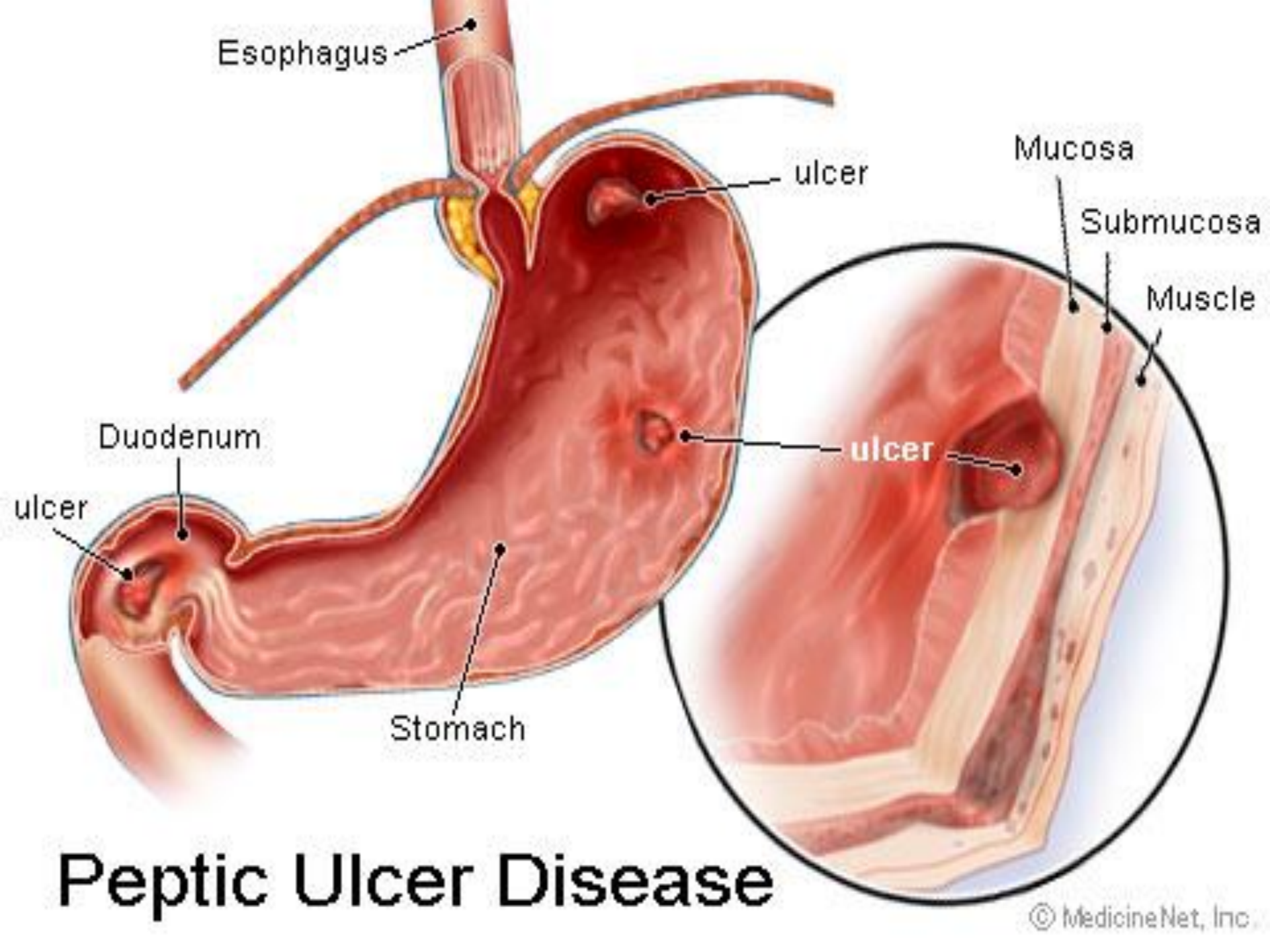
PEPTIC ULCER DISEASE

The term 'peptic ulcer' refers to an ulcer in the lower oesophagus, stomach or duodenum.

Ulcers in the stomach or duodenum may be acute or chronic; both penetrate the muscularis mucosae but the acute ulcer shows no evidence of fibrosis.

Erosions do not penetrate the muscularis mucosae.


Esophagus
Esophageal ulcer
Stomach
Small intestine
Gastric ulcer
Duodenal ulcer


Esophagus
ulcer
Mucosa
Submucosa
Muscle
Duodenum
ulcer
ulcer
Stomach
Peptic Ulcer Disease
© MedicineNet, Inc.

How to Differentiate between

Gastric ulcer	Duodenal ulcer
Pts complain from wt loss.	• Pts complain from wt gain. • because the pain that occur relieve by food.

Pathogenesis of ulcers

Peptic ulcer occurs when there is an **imbalance** between the damaging (aggressive) effects of gastric acid and pepsin, and defense (protective) mechanisms, which protect the gastric and duodenal mucosa from these substance.

Protective	Aggressive
PG, Mucus ,bicarbonate ,mucosal blood flow	Acid ,pepsin, NSAIDs, H.Pylori

- Mucus layer covers the mucosa, so acid cannot directly reach the mucosa.

- Bicarbonate neutralize acid secretion.

- Blood flow→ is needed by cell .whenever there is damage ,good blood flow will make cell turnover quick, therefore damaged cell can be replaced by newer cell ,maintain healthy mucosa.

- PG:

responsible for good blood supply ,bicarbonate secretion and mucus secretion.

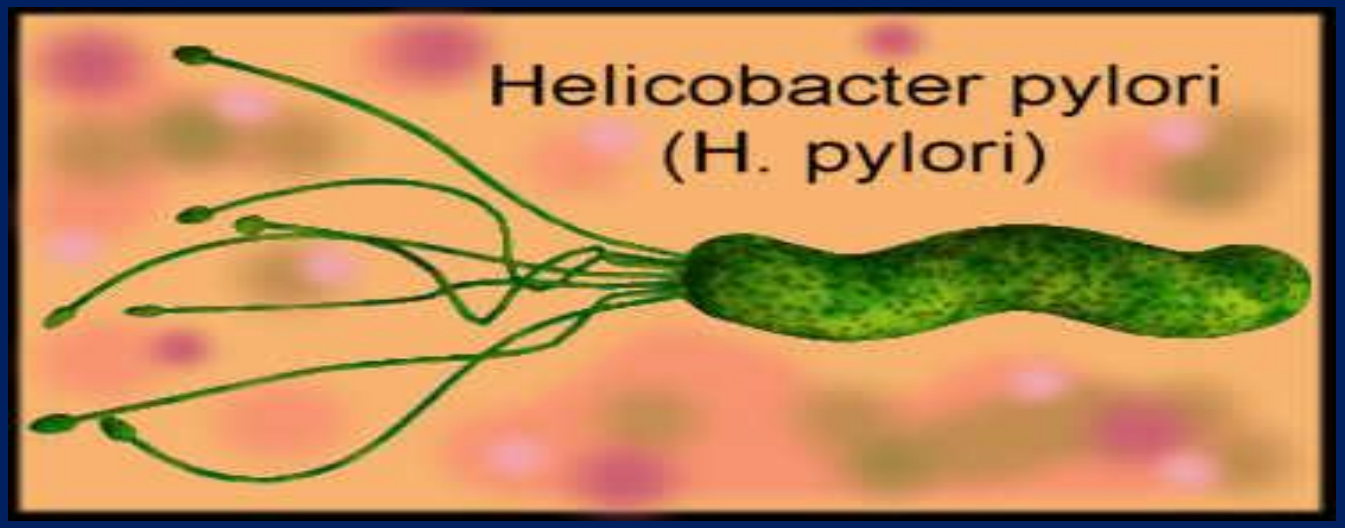
- That’s why pt. who take NSAID →basically inhibit PG secretion, reduction blood supply, mucus secretion and bicarbonate secretion → developing ulcer.

Pathophysiology

1-Infection by A microorganism called **Helicobacter pylori** (H.pylori).

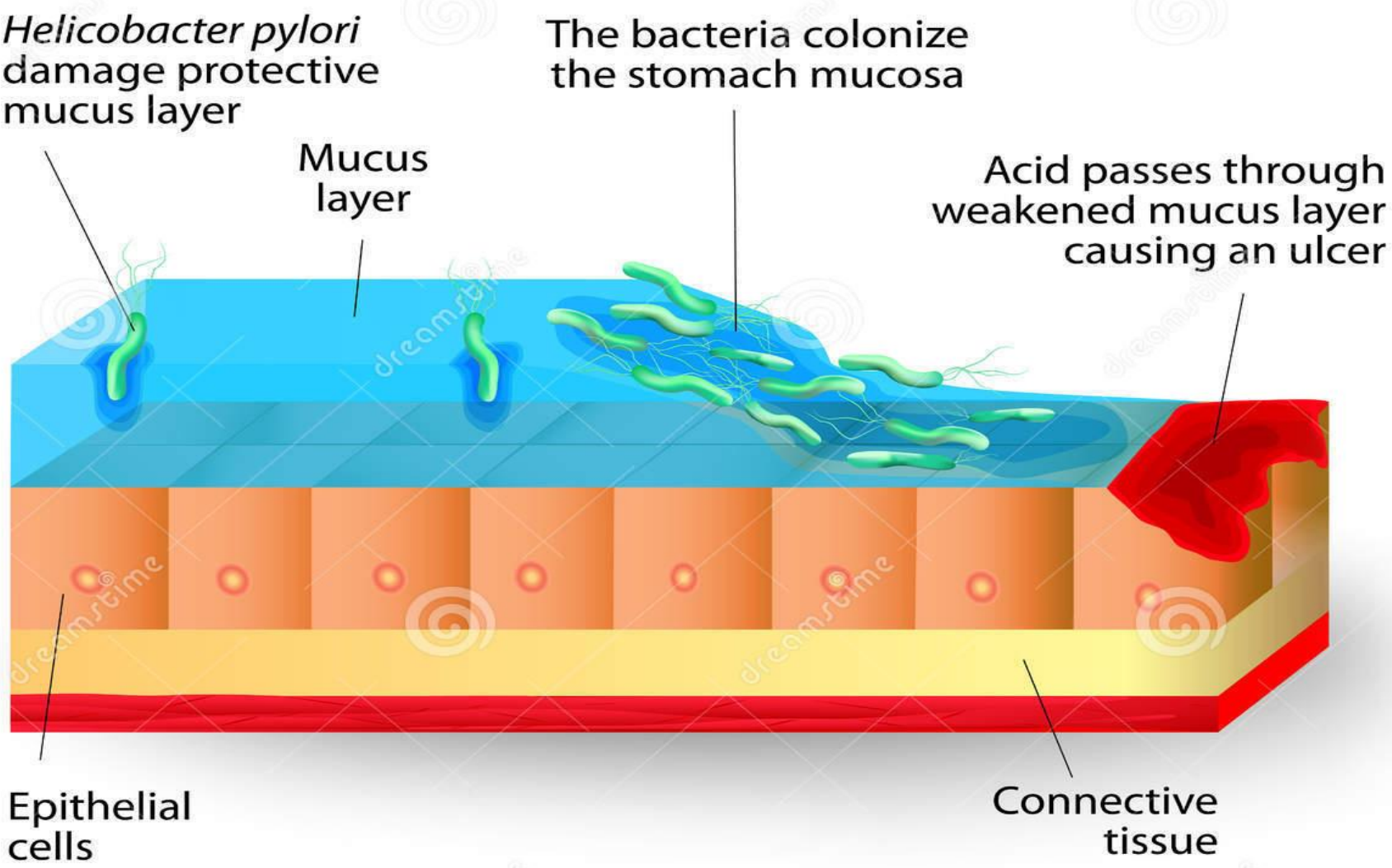
2- Excessive secretion of hydrochloric acid (HCL) & pepsin.

3- Reduced in mucosal defensive mechanism of the mucosa.



- The most important etiological factor nowadays.
- They are gram negative organisms.
- H.pylori ~ Damaging the mucus coating that protects the stomach and duodenum.

PEPTIC ULCER



Download from
Dreamstime.com
This watermarked comp image is for previewing purposes only.
ID 35554627
Designua | Dreamstime.com

NSAIDs

- Inhibition prostaglandin(PG)
- **PGE2:**

formed in stomach ,reduces acidity and helps in the secretion of a layer of mucus which coat and protects the gastric lining and Bicarbonate...

So, inhibition PG → the protection is lost and ulcers are liable to develop.

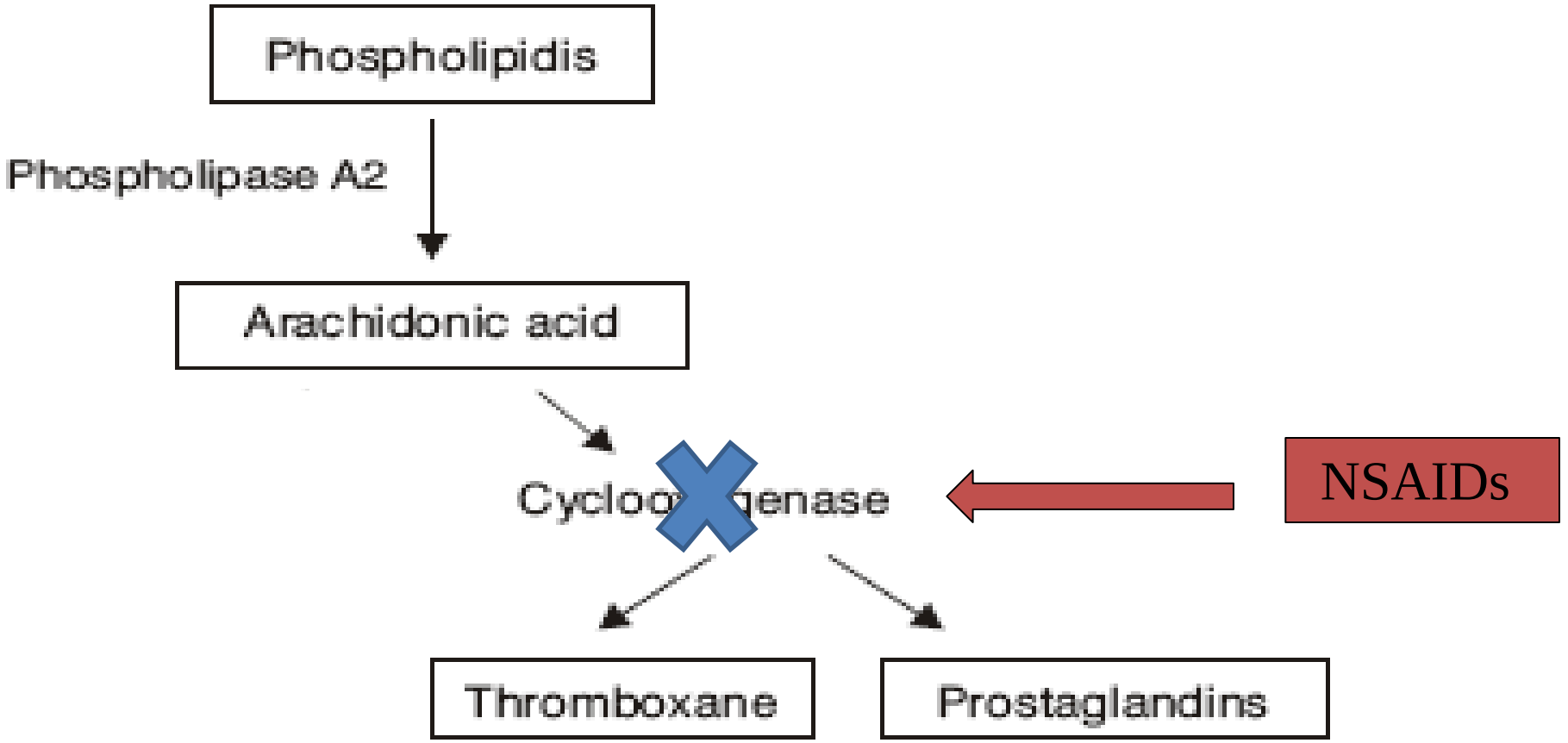
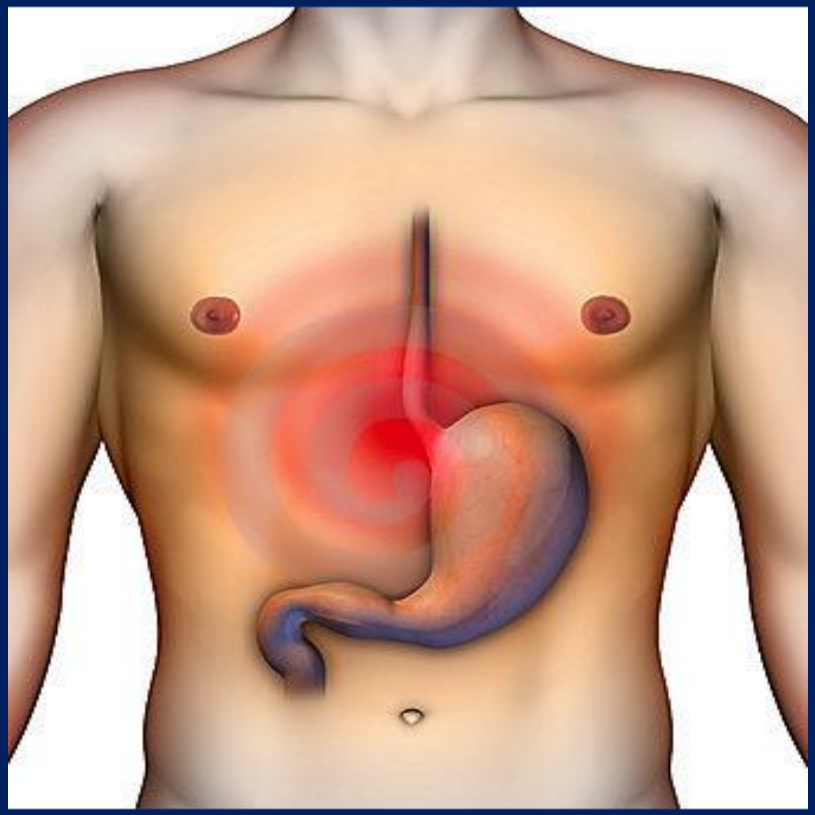
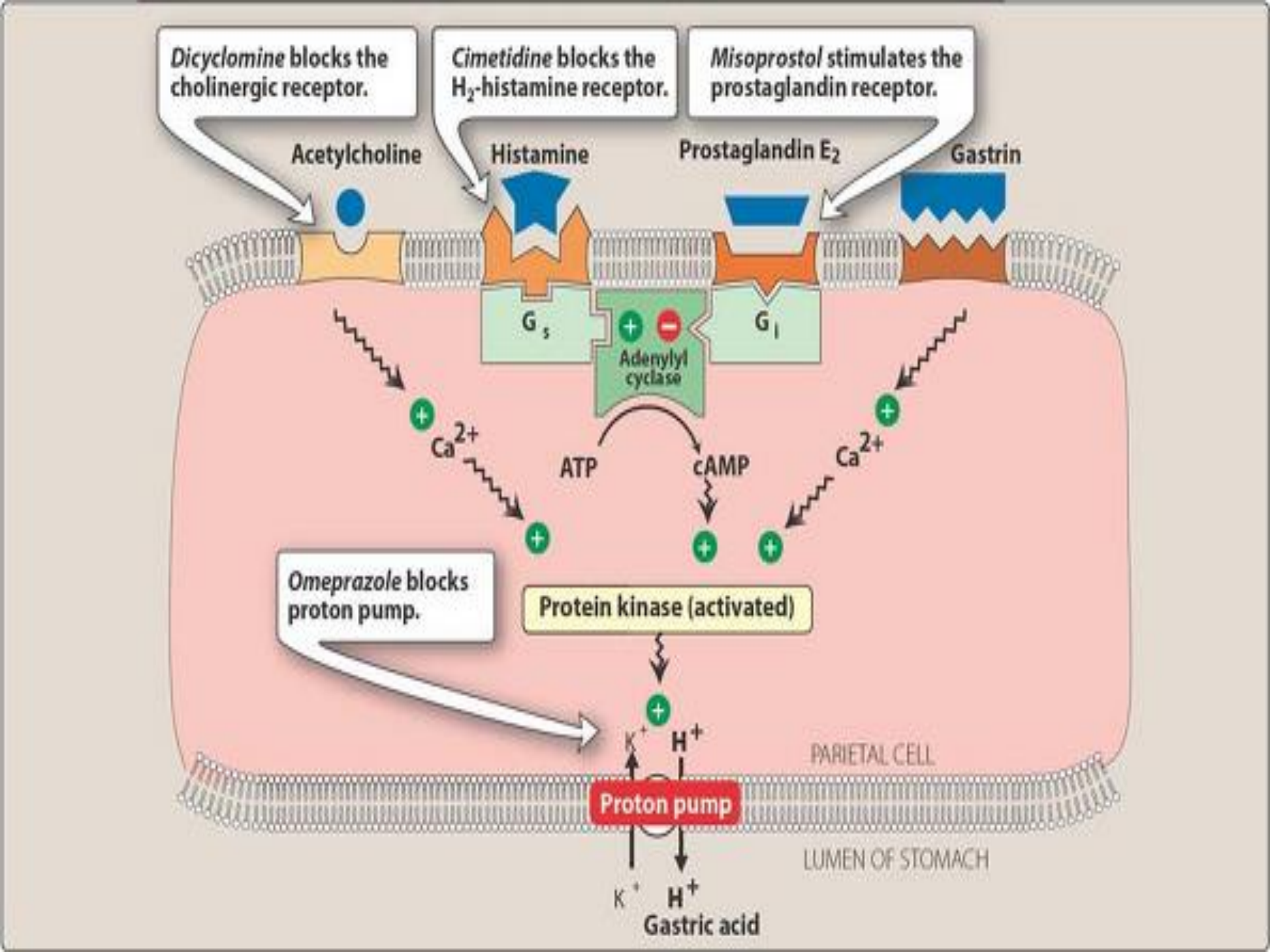


Figure 1 - Mechanism of action of nonsteroidal anti-inflammatories

Regulation of gastric acid secretion




Dicyclomine blocks the cholinergic receptor.
Cimetidine blocks the H_2-histamine receptor.
Misoprostol stimulates the prostaglandin receptor.
Acetylcholine
Histamine
Prostaglandin E_2
Gastrin
G_s
G_i
Adenylyl cyclase
Ca^{2+}
ATP
cAMP
Ca^{2+}
Omeprazole blocks proton pump.
Protein kinase (activated)
K^+
H^+
PARIETAL CELL
Proton pump
LUMEN OF STOMACH
K^+
H^+
Gastric acid

From this fig we can see the parietal cell and the luminal side where acid is secreted into the lumen (H+/K+ ATPase).

on the parietal cell have receptors:-

1- Muscarinic (cholinergic) receptors.
2- Histaminic receptors.
3- Prostaglandin receptors.
4- Gastrin receptors.

Gastric acid is secreted by the parietal cells in the gastric mucosa is stimulated by :-

1- Acetylcholine

2- Gastrin

3- Histamine

but stimulate acid secretion by different mechanisms, they will finally Results in activation of protein kinases , which in turn stimulates the proton pump **(which is the final common pathway for acid secretion)**then acid is secreted into the lumen or hydrogen ions in exchange for K into the lumen of the stomach.

In contrast , receptor binding of **prostaglandin E2 (PGE2)** decreased gastric acid production.

- Ach ,Gastrin ,Histamine receptors→ stimulant to gastric acid secretion

- PGE2 →

  -Inhibitory to acid secretion.

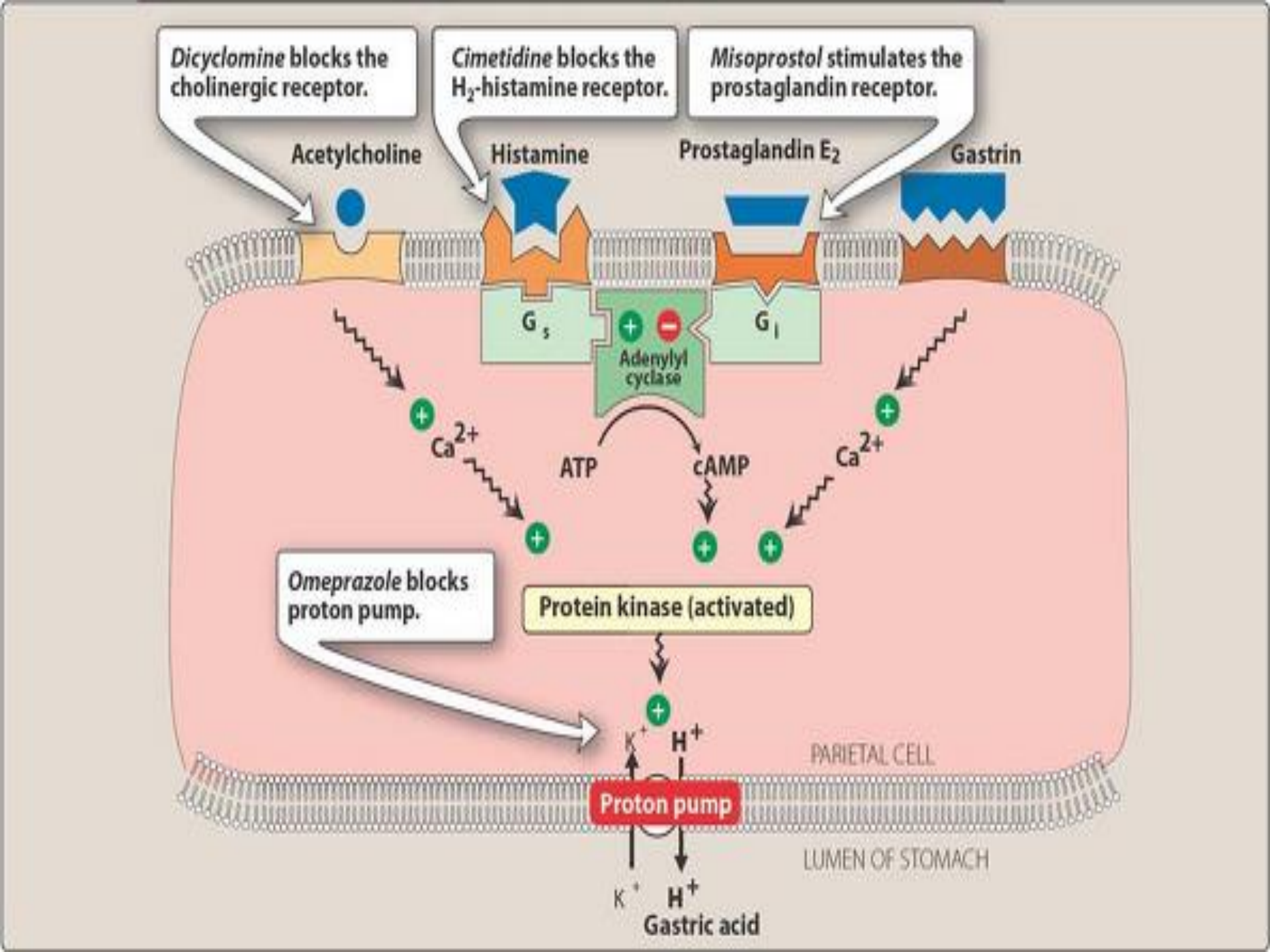
  -Stimulatory to mucus and sodium bicarbonate secretion.

What do u think the most effective drug reduce in acid secretion? Why?

- If we block gastrin receptor→

we still have histamine & Ach active → which stimulate acid secretion.

- If we block 2 of them the third will be active.
- If we prevent the final step (no matter what is the stimulant)
- We are blocking the final step irreversibly.

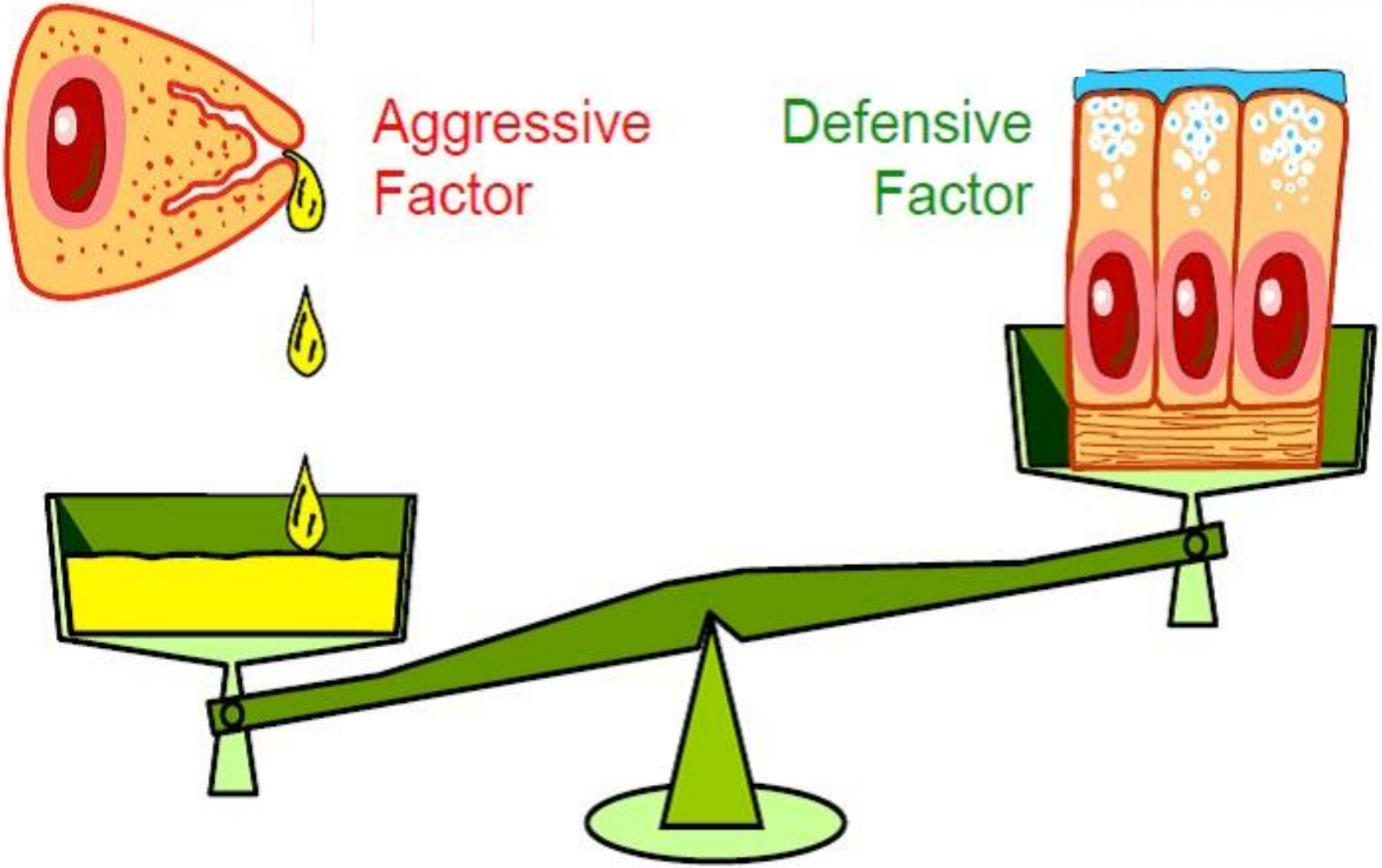

Dicyclomine blocks the cholinergic receptor.
Cimetidine blocks the H_2-histamine receptor.
Misoprostol stimulates the prostaglandin receptor.
Acetylcholine
Histamine
Prostaglandin E_2
Gastrin
G_s
G_i
Adenylyl cyclase
Ca^{2+}
ATP
cAMP
Ca^{2+}
Omeprazole blocks proton pump.
Protein kinase (activated)
K^+
H^+
PARIETAL CELL
Proton pump
LUMEN OF STOMACH
K^+
H^+
Gastric acid

Treatment……


© Original Artist
Reproduction rights obtainable from
www.CartoonStock.com
DR. GOODLIFE
"So Doc, if you write me a scrip for Relaxofy, is it okay if I'm still taking Stimulux, Enerjax and Krankmeup?"

Inhibition of Gastric Acid Secretion

Stimulation of Gastric Mucus Secretion and Synthesis



Aims of Treatment

1. **Eradication** of the **H.pylori infection.**
2. **Reducing secretion of gastric acid.**
3. Providing agents that **protect the gastric mucosa from damage.**
4. **Relieve symptoms and** prevent complication

Drugs for peptic ulcer ……

1- Eradication of H.pylori
(Combinations)

2- Reduction of acid secretion.
(PPI ,H2 blocker, Anti-Muscarinic agents)

3- Neutralization of secreted acid.
(Anti-acid)

4- Enhancement mucosal protective.
(sucrlfate , misoprostol)

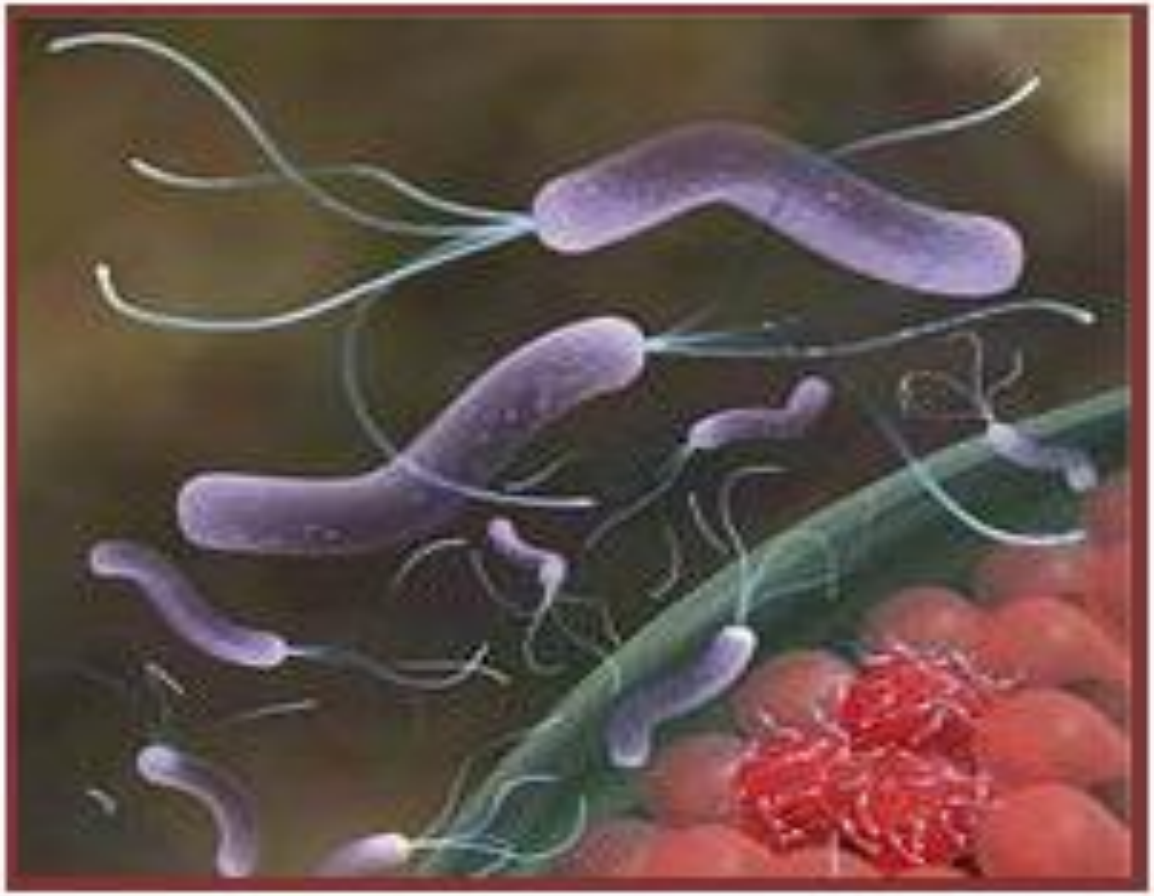
life style change

By reduce stress, smoking

& NSAIDs uses.

avoid certain food(coffee, chocolate, fatty food , piper,…),Avoid alcohol

Helicobacter pylori



With H. pylori infection doctors prescribe antibiotic and acid suppressing drugs.

Eradication of the H.Pylori

- Done by combination of antibiotics together with one of acid inhibitors.

TRIPLE THERAPY

PPI + amoxicillin (1 g twice daily) or metronidazole (500 twice daily) + clarithromycin (500mg twice daily) → 10 days

QUADRUPLE THERAPY

PPI or H2 receptor antagonist + Bismuth comp +Tetracycline + Metronidazole

1-PPIs (proton pump inhibitors)

(~ azol)

1-Omeprazol (prototype)

2-Lansoprazol

- PPIs **Irreversibly** inhibits the H/K ATPase (the proton pump)

- The most effective irreversibly inhibitor of acid secretion .
- Because it inhibits the H+/K+-ATPase pump (last step) .
- The activity remains blocked until a new enzyme is formed → so, the action is usually prolonged (24 hrs or even more 2-3 days)

Drug-Drug Interaction

Omeprazole

Enzyme inhibitor so, it will

Inhibits the metabolism of drugs such as

warfarin , phenytoin →

Resulting in increase the concentration of warfarin and phenytoin.

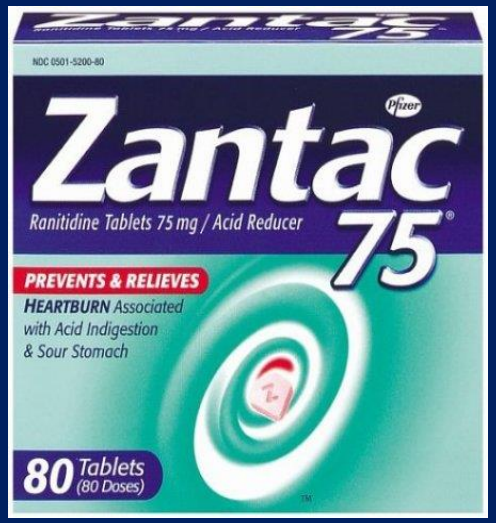
2- H2-receptors blockers

(~ tidine)

1-Cimetidine (prototype) (2x1).

2-Famotidine (1x1).

3- Ranitidine (oral ,IV).



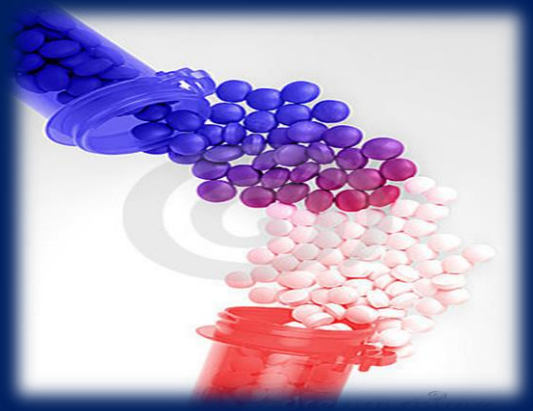
- Compete with histamine at the H2 receptors at the parietal cells of the stomach.

So, the effect is dose related.

- **H2- receptor blockers ≈ Effective against nocturnal acid secretion.**

- ***it's recommended to give these drugs only before bed time ,because research has shown the most causes of the ulcer is the acid secretion during the night.***

Drug-drug interaction



The most drug that has interaction and associated with adverse rxn is **cimetidine** (enzyme inhibitor)

→

phenytoin, morphine, warfarin ??

Adverse effects:-

Rare **(cimetidine)**

1- **CNS** (elderly)

(confusion, hallucination, agitation)

2- Anti-androgenic activity **:-**

gynecomastia , galactorrhea, impotence

All of them (H2 blockers) make some sorts of headache ,diarrhea ,constipation , abdominal discomfort.

That’s why (cimetidine) it has been replaced by other preparations.

Ranitidine (IV) in ER :

Cause hypotension…

Must diluted with fluid.

PPI & H2 blockers

- They reduce the stomach acidity → effect the rate of absorption of certain drugs which require acid to be absorbed :-

1. **Sucralfate** (mucosal protective).
2. **ketoconazole** (anti-fungal).
3. Reduced **vitamin B12** absorption.

3- Anti-Muscarinic agents

- **Pirenzepine** → more selective act on M1 receptors..
- **We need high dose ???**

acid secretion is one of the most resistant to the action of anticholinergic agents.

- Side effect :-

Anti-cholinergic effect..

Dryness of mouth, tachycardia ,urinary retention ,constipation ,decrease the sweating and salivation.

PPI ,H2 blockers AND anti cholinergic.

They all reduce the amount of acid secretion.

On the other hand ,antacids don't reduce the quantity or the volume, they only neutralize the acid available in the stomach, therefor;they are supposed to be very good drug for symptomatic therapy ,to relief the symptoms.

Antacid

Preparation :-

1- Magnesium salts (hydroxide,...)

2- Aluminum salts (hydroxide,...)

3- Na bicarbonate.

4- Ca bicarbonate.

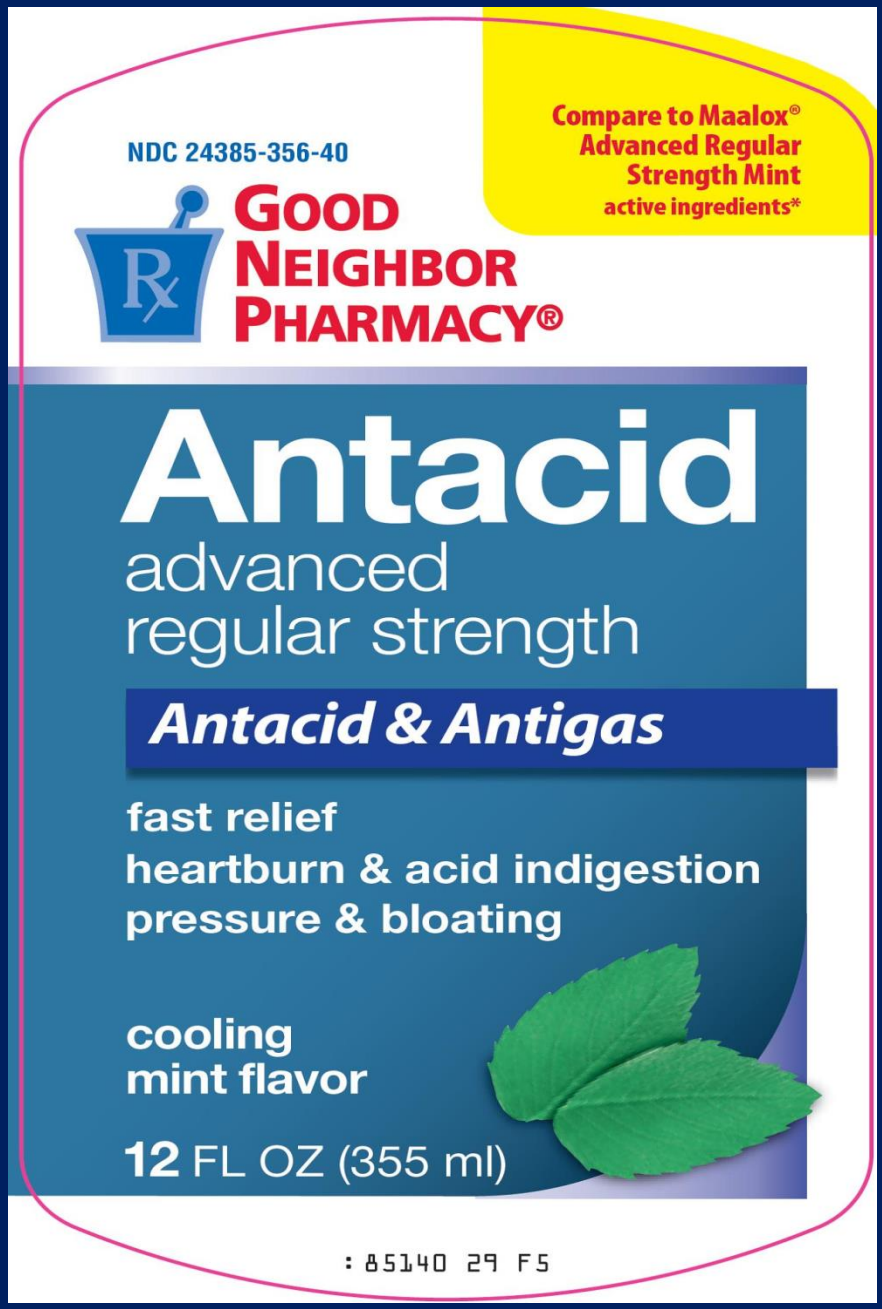
- Weak bases Quickly acting or reacts with gastric acid to form water and a salts.

- Just to reduce gastric acid by neutralizing the HCL in stomach (no effect on acid secretion)

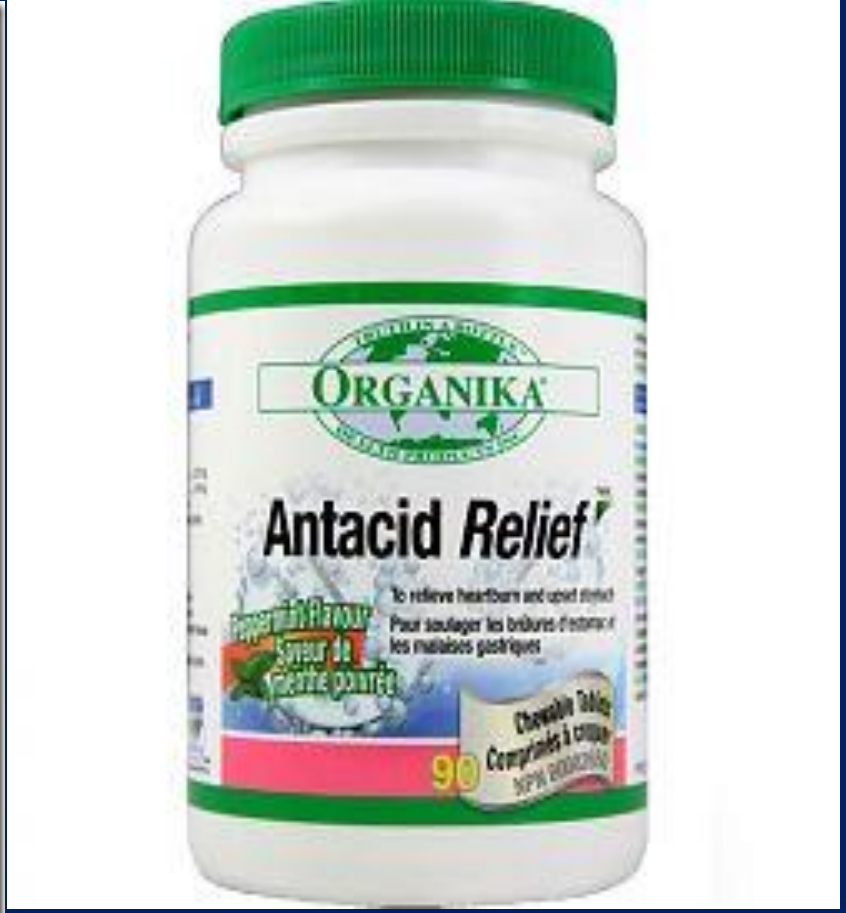
- So, anti-acid Not used for treatment of peptic ulcer, but ***used for symptomatic treatment.***

AlOH	MgOH
cause constipation	cause diarrhea.
AL and Mg → Mix to aid in normalizing bowel function.. Counteract the adverse rxn of the other **Novagel ® ,maalox ®**	

Na bicarbonate	Ca bicarbonate
both causing belching and flatulence	




Kroger
QUALITY GUARANTEED
NDC 30142-468-80
Calcium
Antacid
Tablets
EXTRA STRENGTH
Antacid/Calcium Supplement
Calcium Carbonate 750 mg
Assorted
Tropical Fruit
Naturally and Artificially Flavored
Our Pharmacists
Recommend
96 CHEWABLE TABLETS


ORGANIKA
Antacid Relief
90

Cytoprotective drugs

Or Enhancing the protective mechanism

EX:-

1- Sucralfate.

2- Bismuth chelate.

3-Misoprostol.

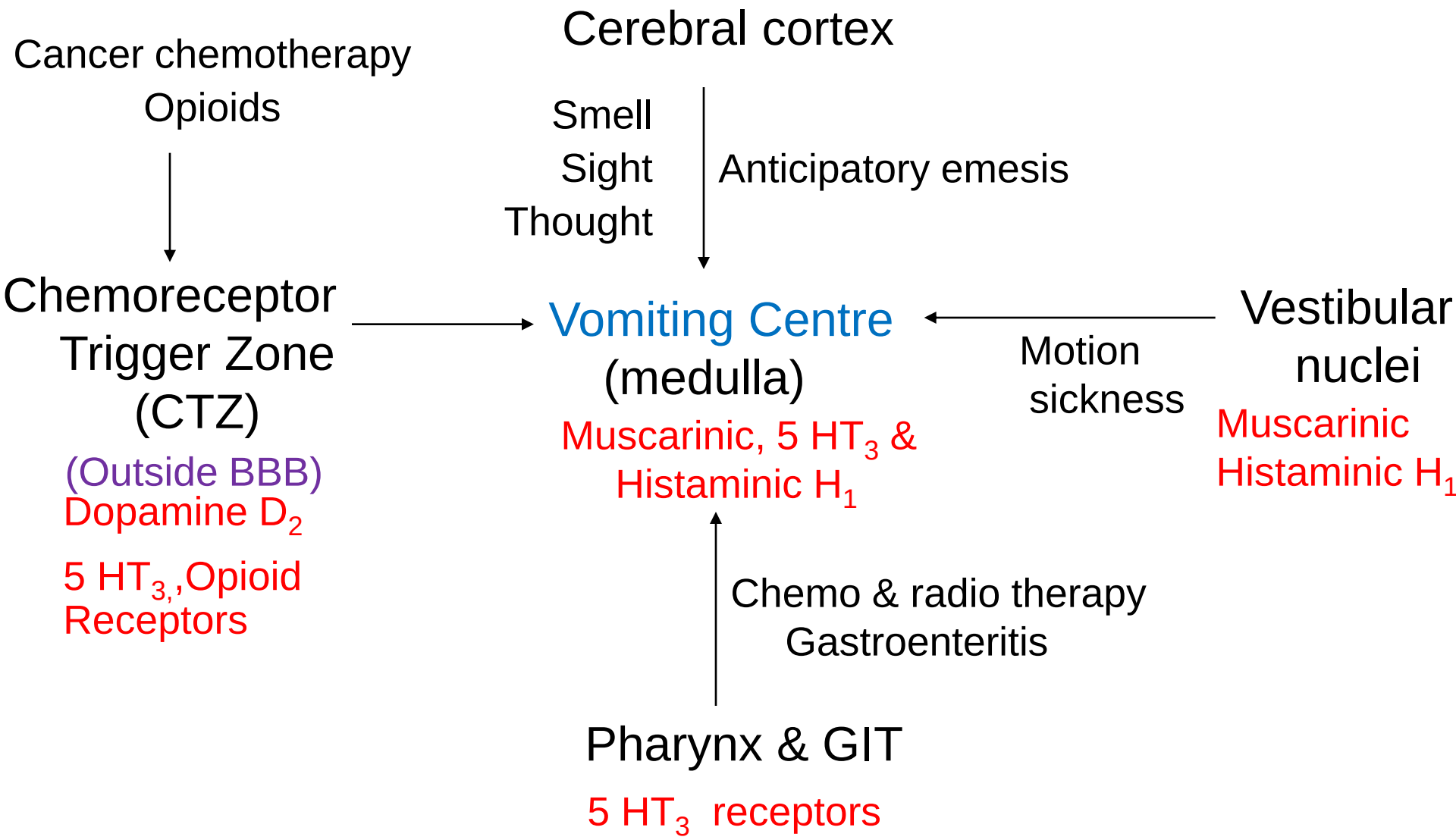
Drugs	Adverse effect
Sucralfate (complex salt of sucrose sulfate & ALOH) In the presence of acid in the stomach→ its converted to a jelly material.	**constipation**
Misoprostol (cytotec ®) Synthetic analogue of PG	**Stimulation of smooth muscle in the uterus,result in Uterine bleeding & Contraction -- Abortion**

- Now days any pts suffering from arthritis and he should use NSAIDs its always recommended to use one of the acid suppressants .

- Usually preferred PPI ,to prevent any recurrence.

Anti- -Emetic Drugs

Pathophysiology of Emesis



vomiting

Vomiting controlled by vomiting center (medulla)

The stimulating comes from the body :-

1- cerebral cortex

2-CTZ chemoreceptor trigger zone (opioid , cancer chemotherapy)

3-vestibular nuclei

4- GIT ,pharynx

Anti-emetics agents

1. Muscarinic receptor antagonists
2. Anti-histamine (H1)
3. Dopamine receptor antagonist (D2)
4. Serotonin 5 HT_3 Antagonists
5. Steroids

1- Muscarinic receptor antagonist	**Scopolamine ≈ hyoscine**	used as transdermal patch (applied behind the ear) for motion sickness(The drug of choice)
2-Anti histamine (H1)	**Promethazine.** →	has been used by NASA for people who went to the space to prevent motion sickness.
	Meclozine. →	Sever morning sickness of pregnancy.
3- Serotonin 5 HT_3 Antagonist	**Ondansetron** **(Zofran ®)** **IV ,Orally**	→used to prevent vomiting in pts receiving highly emetic cytotoxic drugs (cisplatin). given 30 min. before chemotherapy.


Manufactured for:
AGP (Private) Limited
Under Licence from:
UCB Pharma S.A.
Belgium.
100 Tablets
Navidoxine®
(Meclozine, B6)
ucb
نیوی ڈاکسن
نیبیٹس

4-Dopamine D2 antagonist

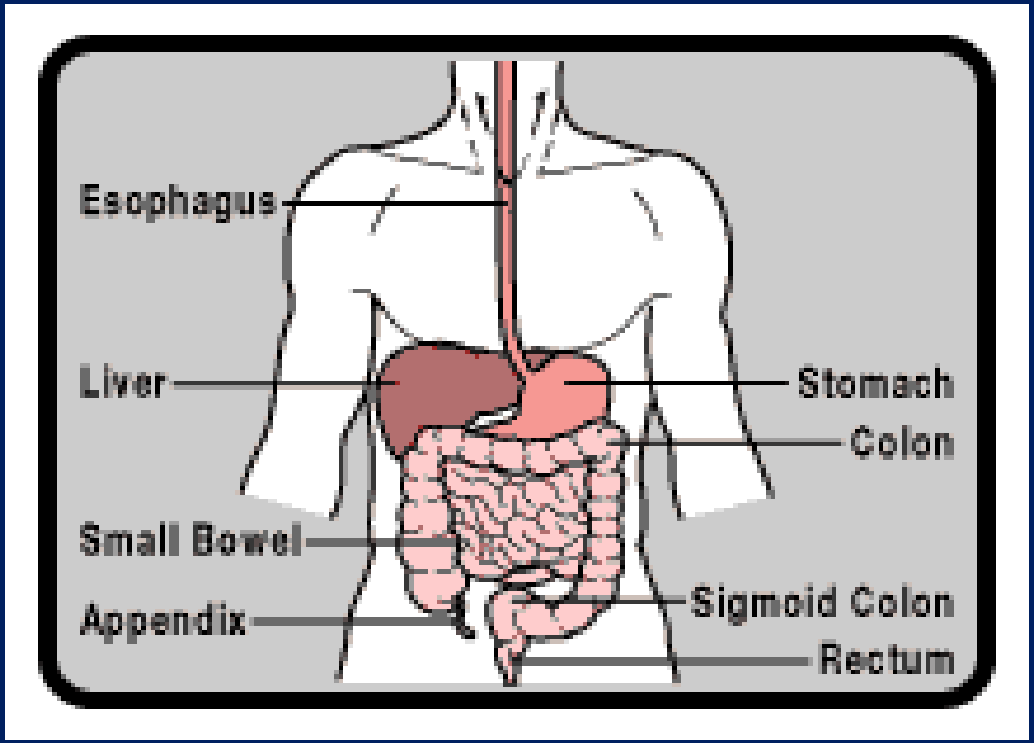
Antagonize D_2 receptors in CTZ (centrally)

Domperidone (Motilium ®, Costi ®) – Oral

Metoclopramide (Reglan®) – Oral & IV

Metoclopramide crosses BBB but Domperidone cannot.

Drugs affecting gastric motility



These drugs either

1- **Increase the motility** →

for constipation treatment.

2- **Decreased the motility** →

for diarrhea treatment.

Anti-Diarrheal Drugs

Pathophysiology of Diarrhea

I. Increase motility of the GIT……..
II. Increase in the secretion of fluids to the lumen…….
III. Decrease fluid absorption of intestine…..

→ Diarrhea and loss of electrolytes (sodium)and water → **Dehydration.**

Treatment Of Diarrhea

1- Fluid & electrolyte treatment

Specially in infant & elderly people.

EX:-

Oral **R**ehydration **S**olution (**ORS**)

(isotonic solution of NaCl + Glucose)

2- Anti-Diarrhoeal drugs:-

1- Anti -Motility drugs (loperamide)

2- Adsorbents (Kaolin, pectin,)

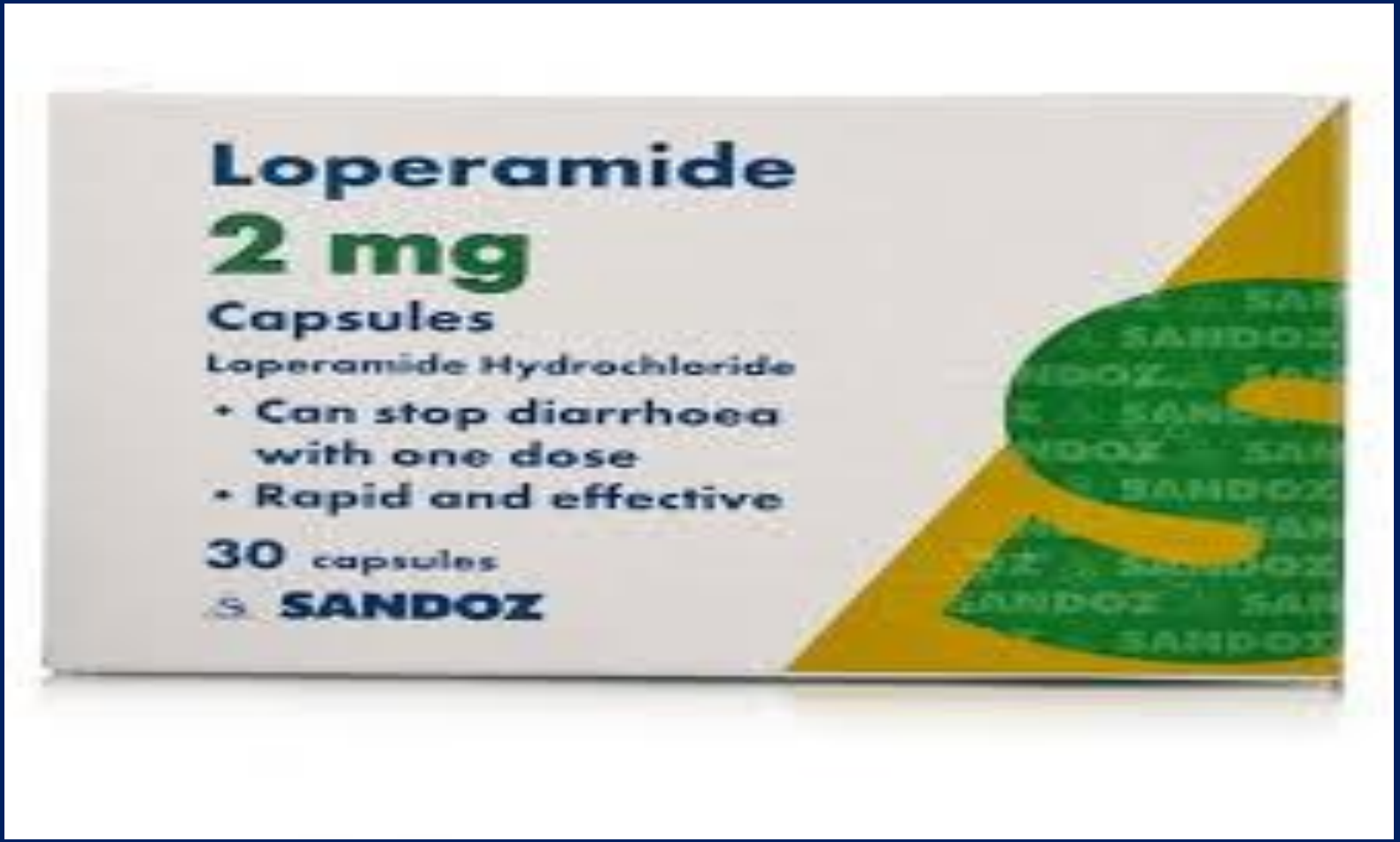
3- Decrease the fluid secretion in the bowel (bismuth subsalicylate)

loperamide (loperium ®)

opioid like actions on the GUT

Activates opioid receptors in GI smooth muscle ,causing segmental contraction → decrease peristalsis..

All morphine derivatives cause constipation



Take 2 tablet at once (maybe enough) ,then one tablet following each bowel movement.

Constipation

Treatment


Laxatives
Senna
Fleet
Carter's
LAXATIVE
CASTOR
OIL
Dulcolax
SWISS
KRISS

Also called cathartics or purgatives

- Defined as drugs that loosen the bowel ..
- Accelerate the movement of food through the GIT…to increase the motility.

Laxatives

1- Stimulants laxatives

(Bisacodyl ,castor oil,)

2- Bulk-forming laxatives

(Bran)

3- Osmotic laxatives

(Mg sulfate , lactulose)

4- Stool surfactants or softeners or lubricant.

(glycerin)


OVERNIGHT
RELIEF
Dulcolax
LAXATIVE TABLETS
(bisacodyl USP 5mg)
Gentle, predictable
overnight relief
#1
10
TABLETS


Fleet.
#1
Suppositories
laxative
bisacodyl
• Works in minutes!
• Foil-wrapped convenience
4 Suppositories


GENESIS
4Fiber
A Dietary Fiber
Supplement
Net Weight 9.8 oz


Pfizer
Original
GLYCERIN
SUPPOSITORIES
FOR INFANTS & CHILDREN
Gentle, fast-acting relief of occasional
constipation in 15 to 30 minutes.
12 Suppositories

Question

Q- PPI Inhibit gastric acid secretion more powerfully than do the H2 blockers ,**why** ???

PPI the most effective because it’s inhibit the final step in the acid secretion **(irreversibly)**

Q- A physician prescribed a tablet of **Ondansetron for prophylaxis of motion sickness** . even though Ondansetron is a potent and effective antiemetic , it did not produce any effect in this pt …

Can u explain

Because **we don’t have 5HT3 receptors** in the **vestibular nuclei , instead we have muscarinic and histaminic receptors**, so no matter how strong the antiemetic drug is, as long as it has no effect on muscarinic or histaminic receptors, they will not abolish the motion sickness..


Thank You!