

**Section V**  
**Digestive system**

**Chapter 5**  
**Drugs affecting**  
**digestive system**

**Prof. Chen Jiqiang**

# **Diseases of digestive system**

**Diseases of digestive system include the diseases of esophagus, stomach, intestine, liver, gallbladder, pancreas, *etc.***

**The types of these diseases include infection, inflammation, tumor, ulcer, and gastroenteric dysfunction, etc.**

# **Drugs affecting digestive system**

**Part 1. Drugs used for peptic  
ulcers**

**Part 2. Modulators of gastro-  
enteric functions**

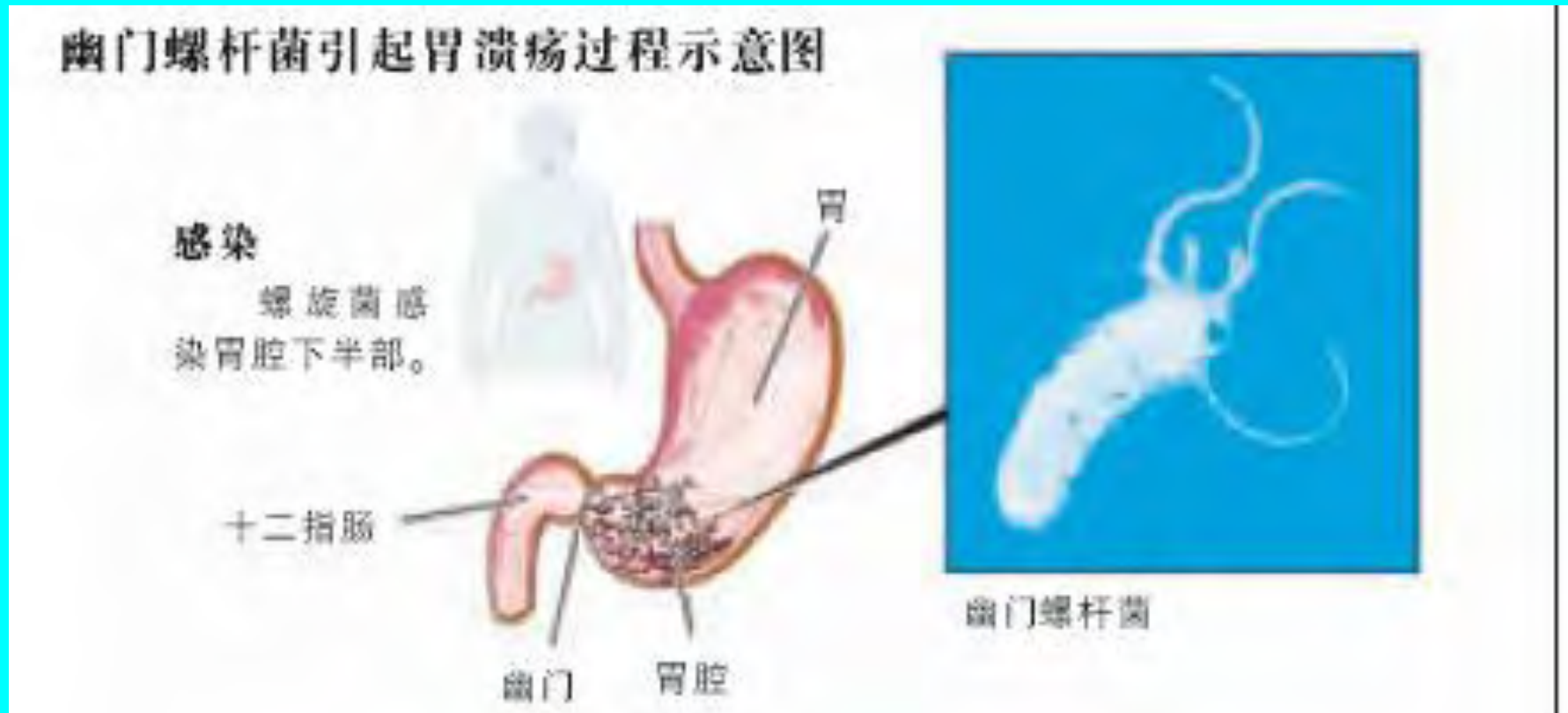
# Part 1. Drugs used for peptic ulcers

## The Pathogenesis of peptic ulcers:

1. Infection with *Helicobacter pylori* (*Hp*);
2. Increased gastric acid secretion;
3. Inadequate mucosal defense to gastric acid.

# Drugs used for peptic ulcers

## ▲ Infection with *Hp* and peptic ulcers:

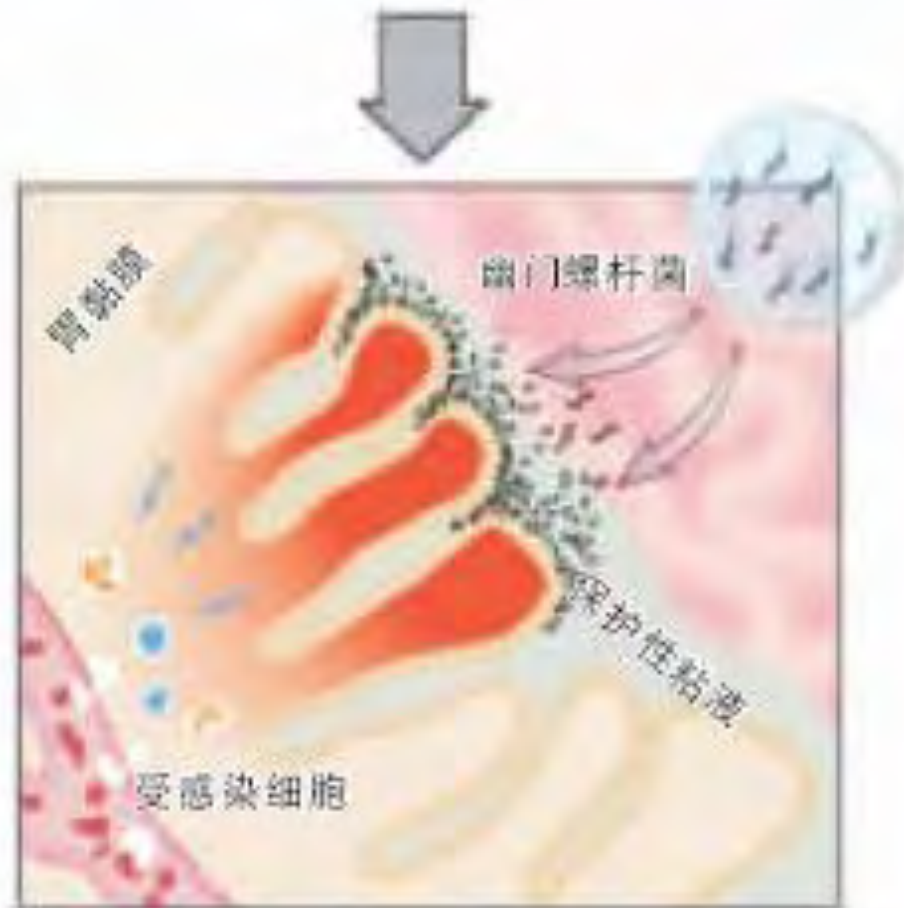


**Infection**

# Drugs used for peptic ulcers

## 发炎

幽门螺杆菌引起胃黏膜发炎。一般情况下没有任何症状。



# Inflammation

# Drugs used for peptic ulcers

## 溃疡

胃部发炎可能导致十二指肠溃疡或胃溃疡。严重的并发症包括出血溃疡和穿孔溃疡。



## 十二指肠溃疡

酸性分泌物增加



发炎



出血溃疡

## 胃溃疡



发炎

# Ulcers



幽门螺杆菌感染能引起消化性溃疡是由澳大利亚科学家**巴里·马歇尔(右)**与**罗宾·沃伦**共同发现的。这一研究成果获得了2005年诺贝尔生理学或医学奖。2005年10月3日正在工作聚会的两位澳大利亚科学家得知获得诺贝尔生理学或医学奖后举杯互相庆贺。



# Drugs used for peptic ulcers

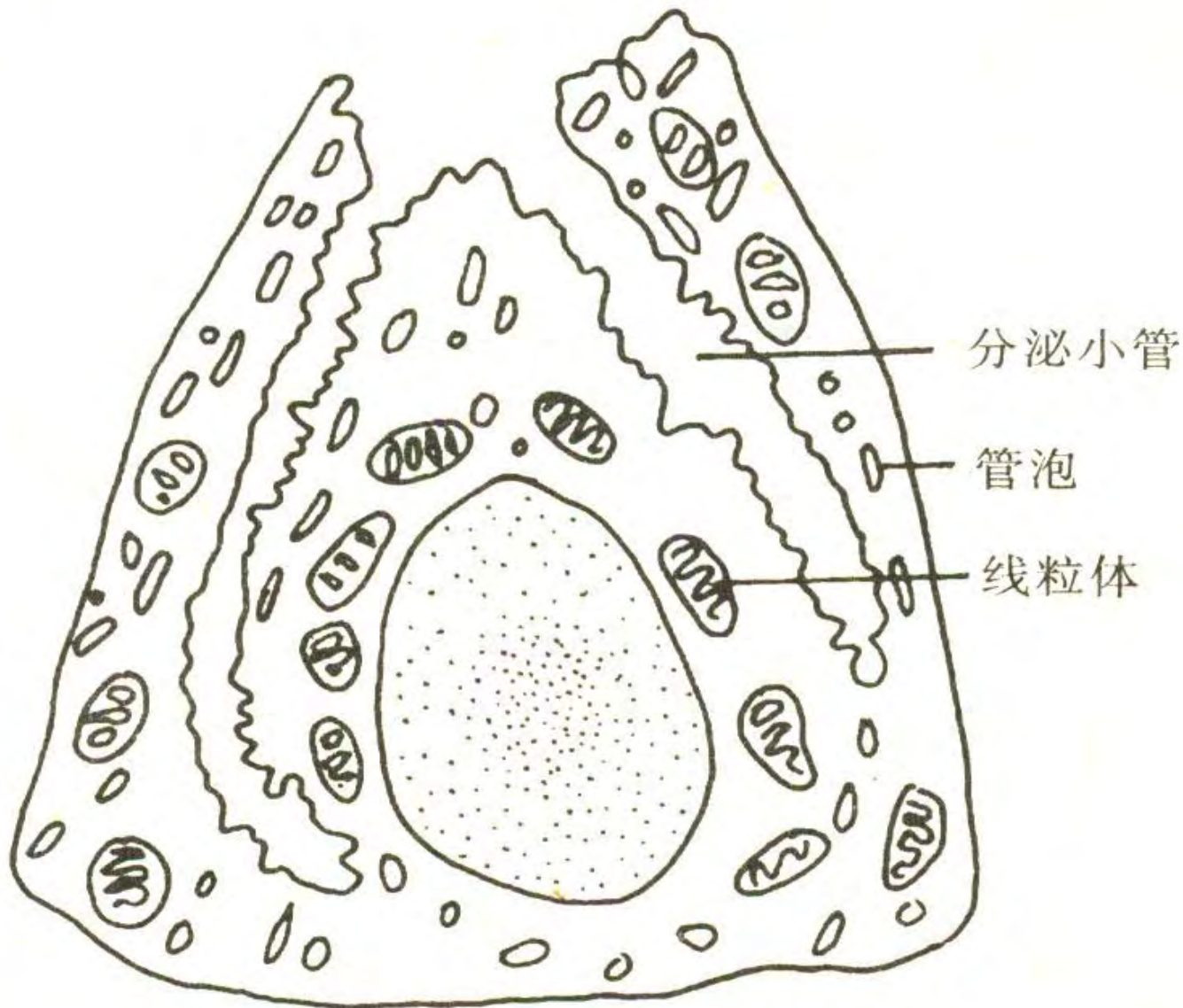
## Peptic ulcers and treatment

### Pathogenesis of peptic ulcers

- Infection with *Hp*;
- Increased gastric acid secretion;
- Inadequate mucosal defense to gastric acid.

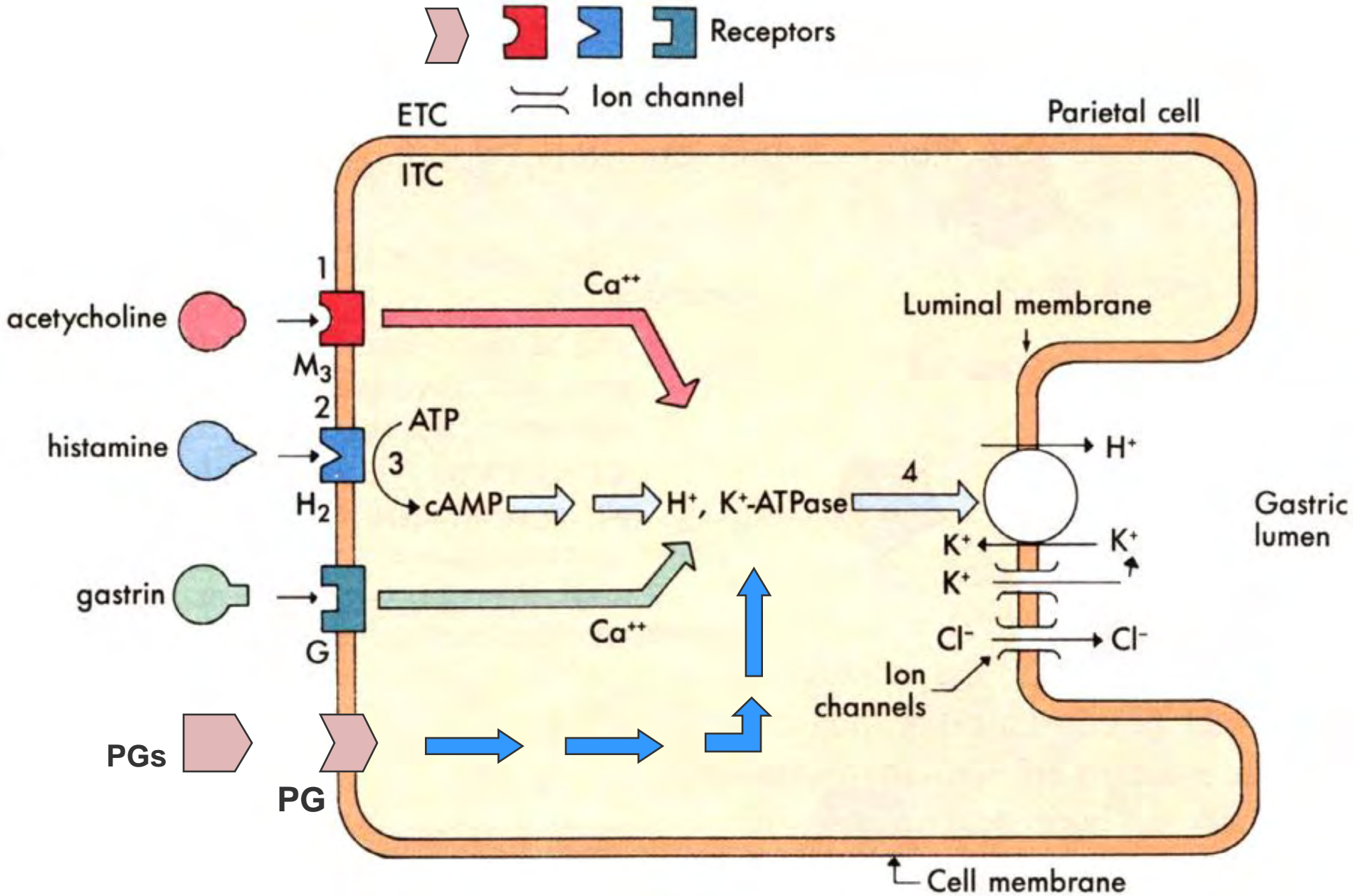
### Treatment approaches

- Eradicating *Hp*;
- Neutralizing gastric acid, or reducing secretion of the acid;
- Protecting the gastric mucosa from damage.



**Parietal cell(壁细胞)**

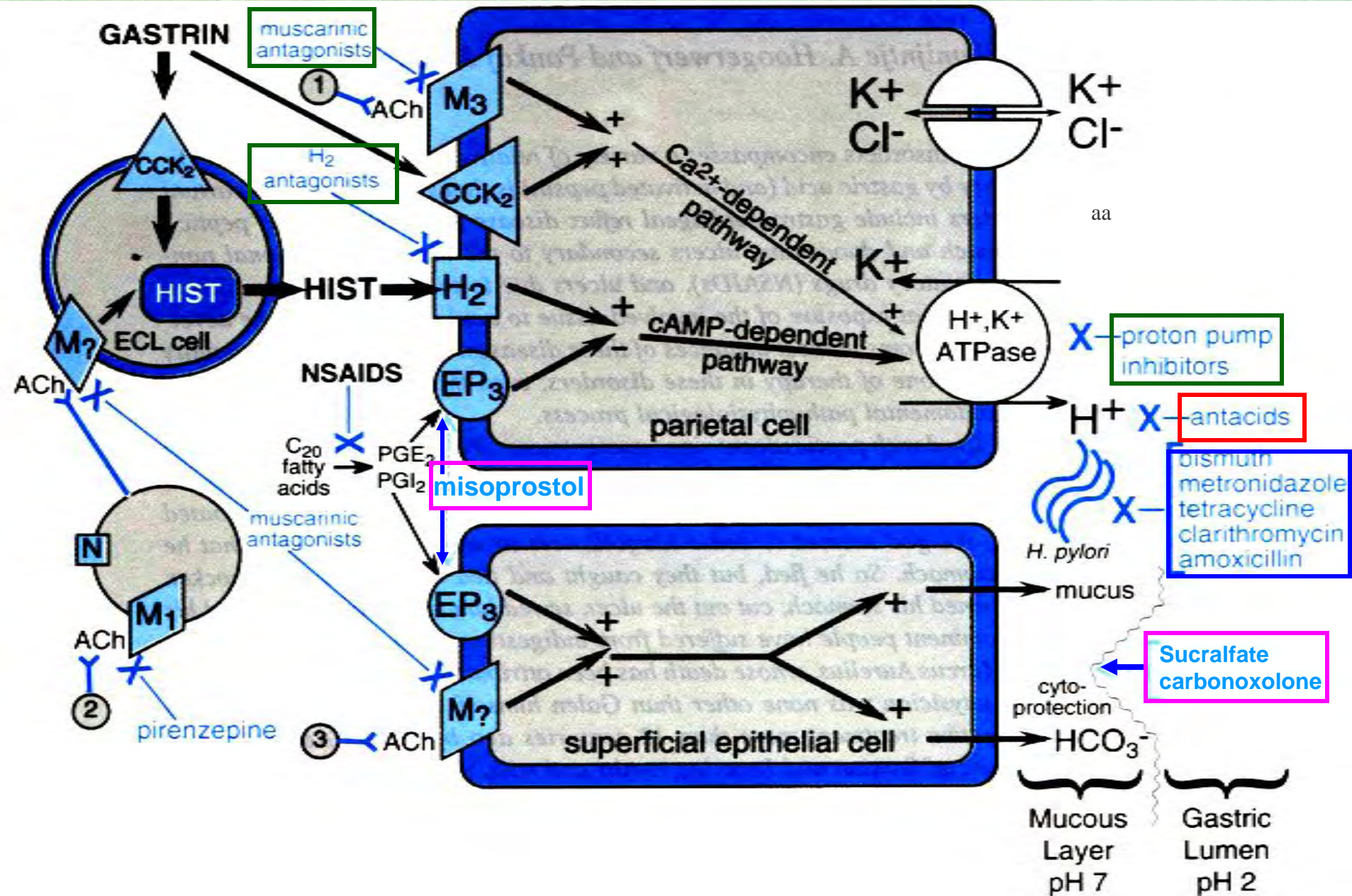
# Gastric acid secretion and regulation



# Drugs used for peptic ulcers

## Classification of anti-ulcer drugs

- I . Antacids;**
- II . Drugs inhibiting gastric acid secretion:**
  - A. Muscarinic receptor antagonists;**
  - B. H<sub>2</sub> receptor antagonists;**
  - C. H<sup>+</sup>-K<sup>+</sup>-ATPase inhibitors (proton pump inhibitors).**
- III. Mucosal protective drugs;**
- IV. Antimicrobial drugs (Anti-*Hp* drugs).**



# Gastric structure related to peptic ulcer

# Drugs used for peptic ulcers

## I . Antacids(抗酸药)

# Drugs used for peptic ulcers

## I . Antacids(抗酸药)

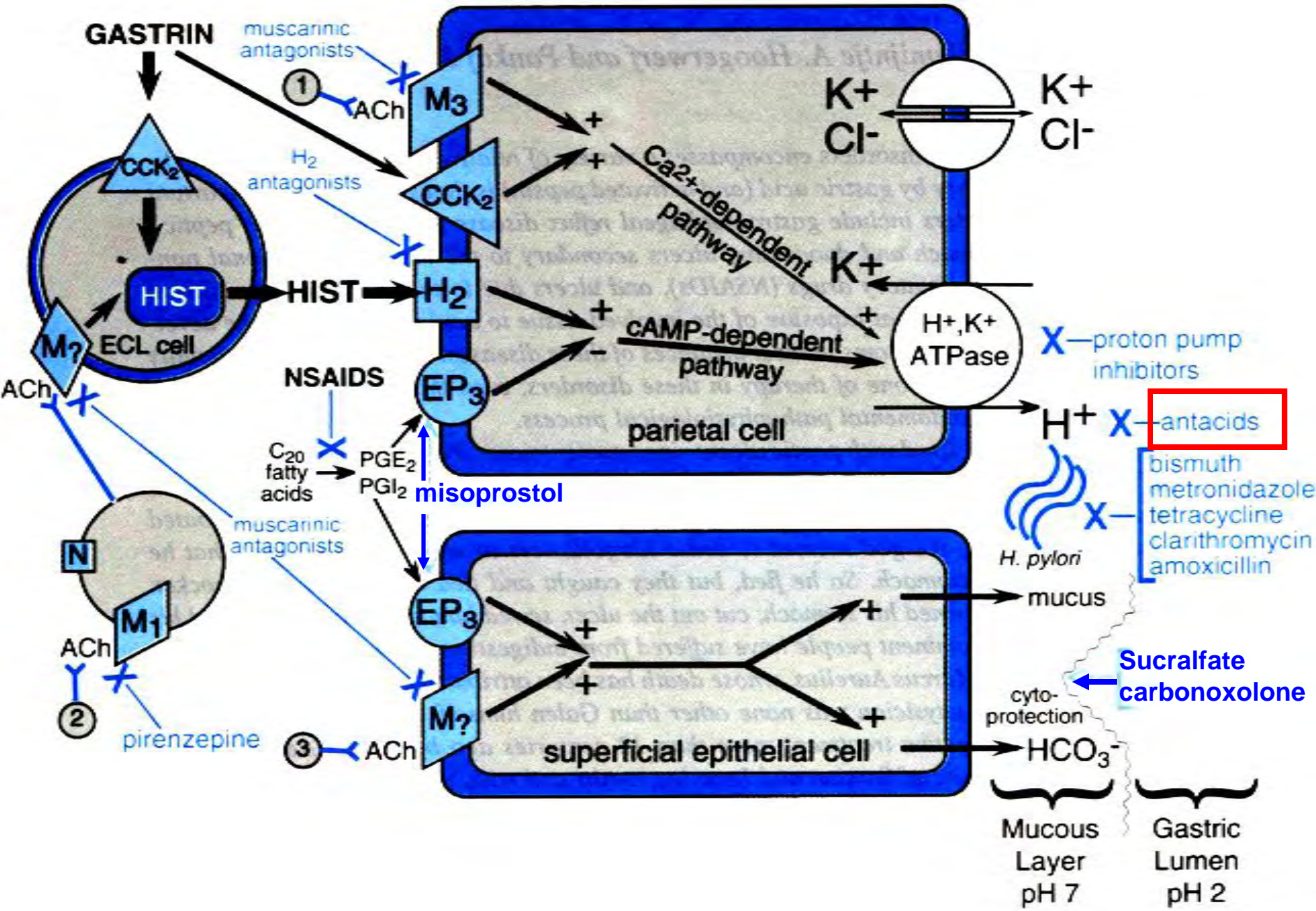
**1. Basic substances that can reduce gastric acidity by neutralizing HCl;**

**2. Drugs most in use:**

**Aluminium hydroxide(氢氧化铝),  
Magnesium hydroxide(氢氧化镁),  
Magnesium trisilicate(三硅酸镁),  
Magnesium oxide(氧化镁), *etc.***

**Composition resparation, *such as:***

**Tab aluminium hydroxide compound(复  
方氢氧化铝片, 胃舒平), *etc.***





# Drugs used for peptic ulcers

## II. Drugs inhibiting gastric acid secretion

- A. Muscarinic receptor antagonists;
- B. H<sub>2</sub> receptor antagonists;
- C. H<sup>+</sup>-K<sup>+</sup>-ATPase inhibitors (proton pump inhibitors).

# Drugs used for peptic ulcers

## II. Drugs inhibiting gastric acid secretion

### A. Muscarinic receptor antagonists (M receptor blocker):

#### Drugs most in use:

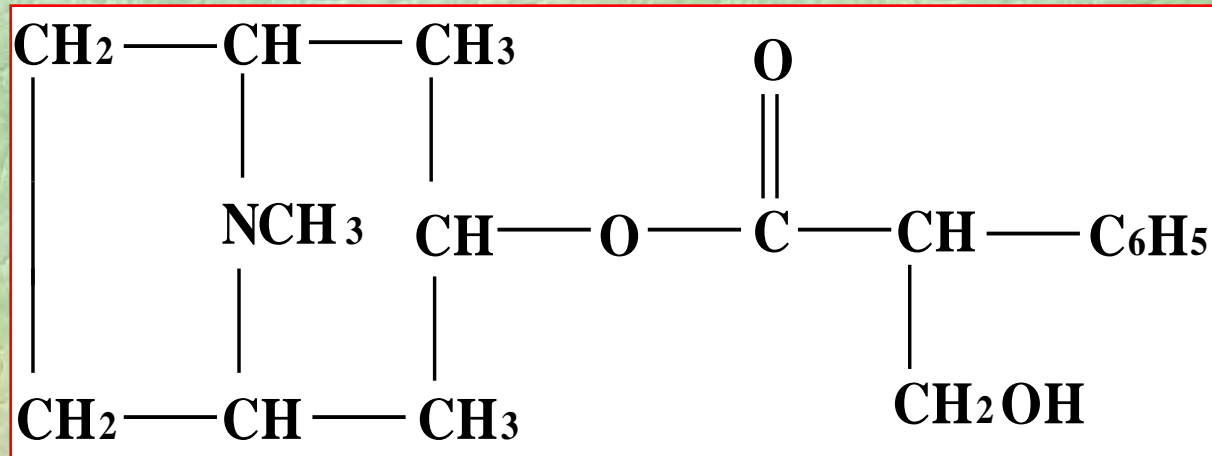
Atropine(阿托品)

Propantheline bromide(溴丙胺太林)

Pirenzepine(哌仑西平), and  
Telenzepine(替仑西平)

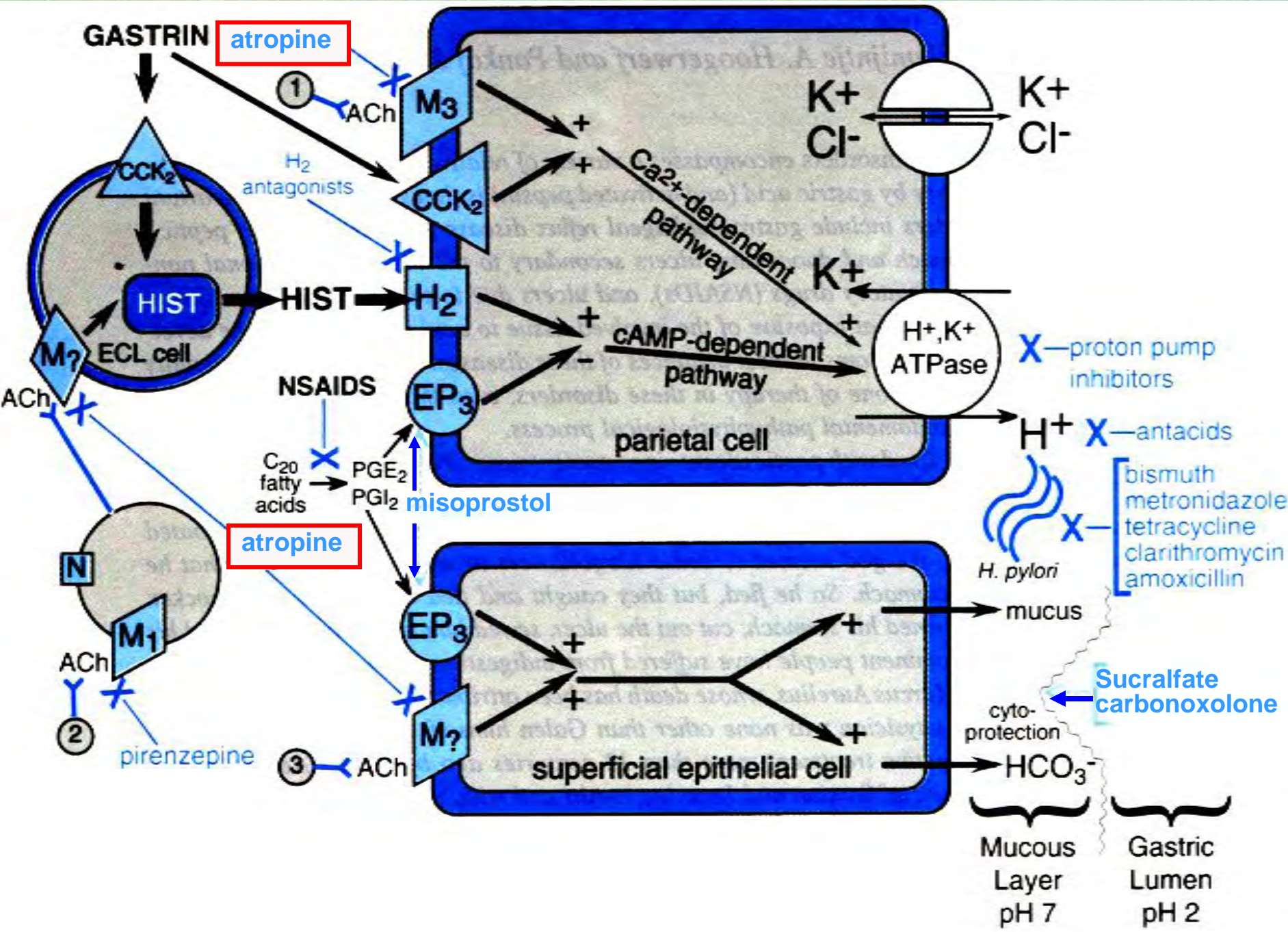
# Drugs used for peptic ulcers

## Atropine(阿托品)



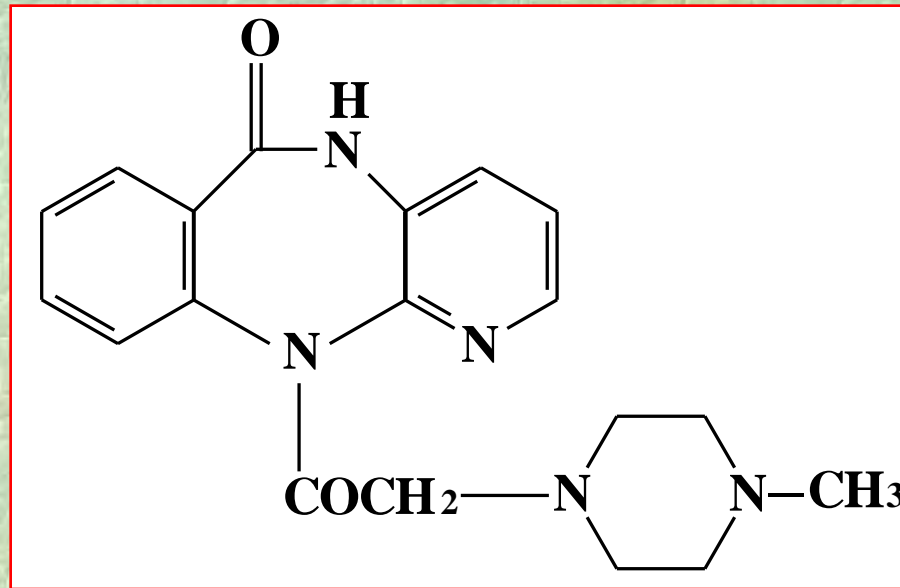
**Non-selective M receptor blocker:**  
**Can block M<sub>1</sub>, M<sub>2</sub>, M<sub>3</sub>, M<sub>4</sub>, and M<sub>5</sub> receptors.**

**Propantheline bromide**  
**(溴丙胺太林, 普鲁本辛)**

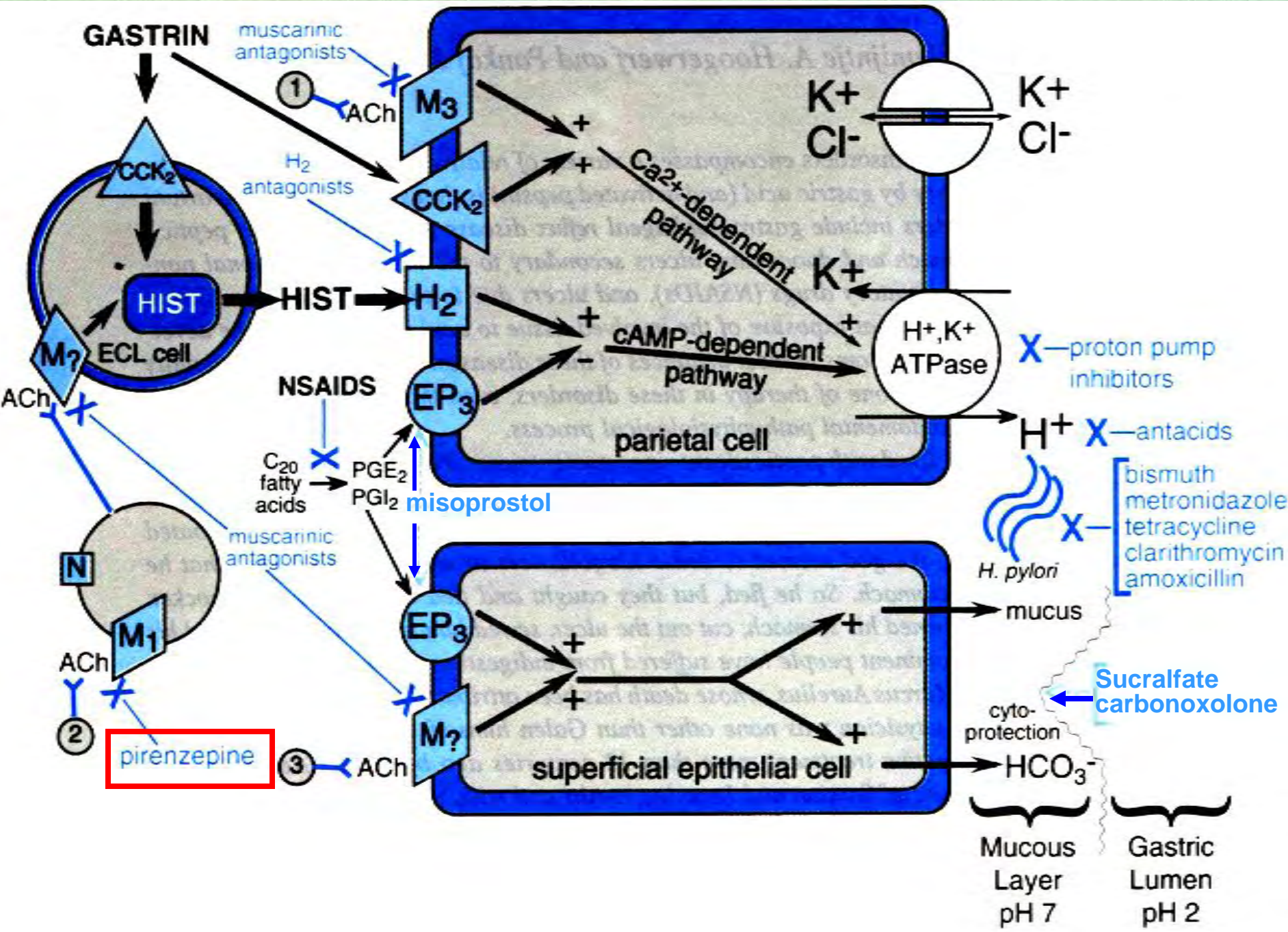


# Drugs used for peptic ulcers

## Pirenzepine(哌仑西平)



**Selective M receptor blocker:**  
**Only block M<sub>1</sub> and M<sub>3</sub>-receptors.**



# Drugs used for peptic ulcers

## 1. Pharmacological effects

high affinity for  $M_1$ - and low affinity for  $M_2$ -receptors of the smooth muscle of the ileum and urinary bladder.

blocking of  $M_1$ -muscarinic receptors in autonomic ganglia, inhibiting the secretion of HCl.

## 2. Clinical uses: peptic ulcers

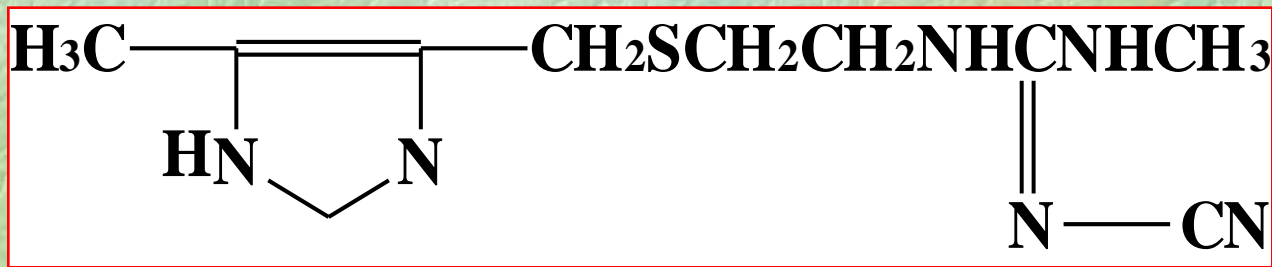
## 3. Adverse effects

Atropine-like effects, at larger doses.

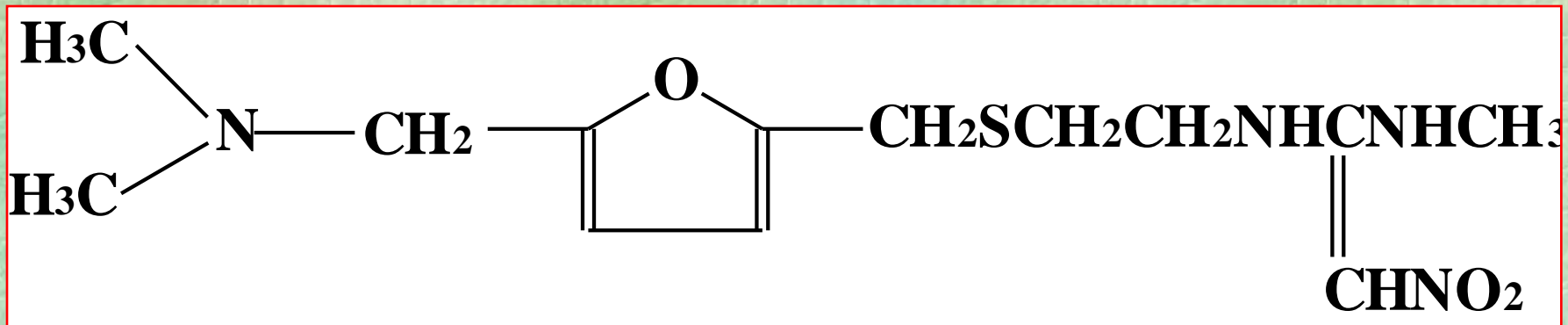
**Telenzepine(替仑西平)**

# Drugs used for peptic ulcers

## B. H<sub>2</sub> receptor antagonists:

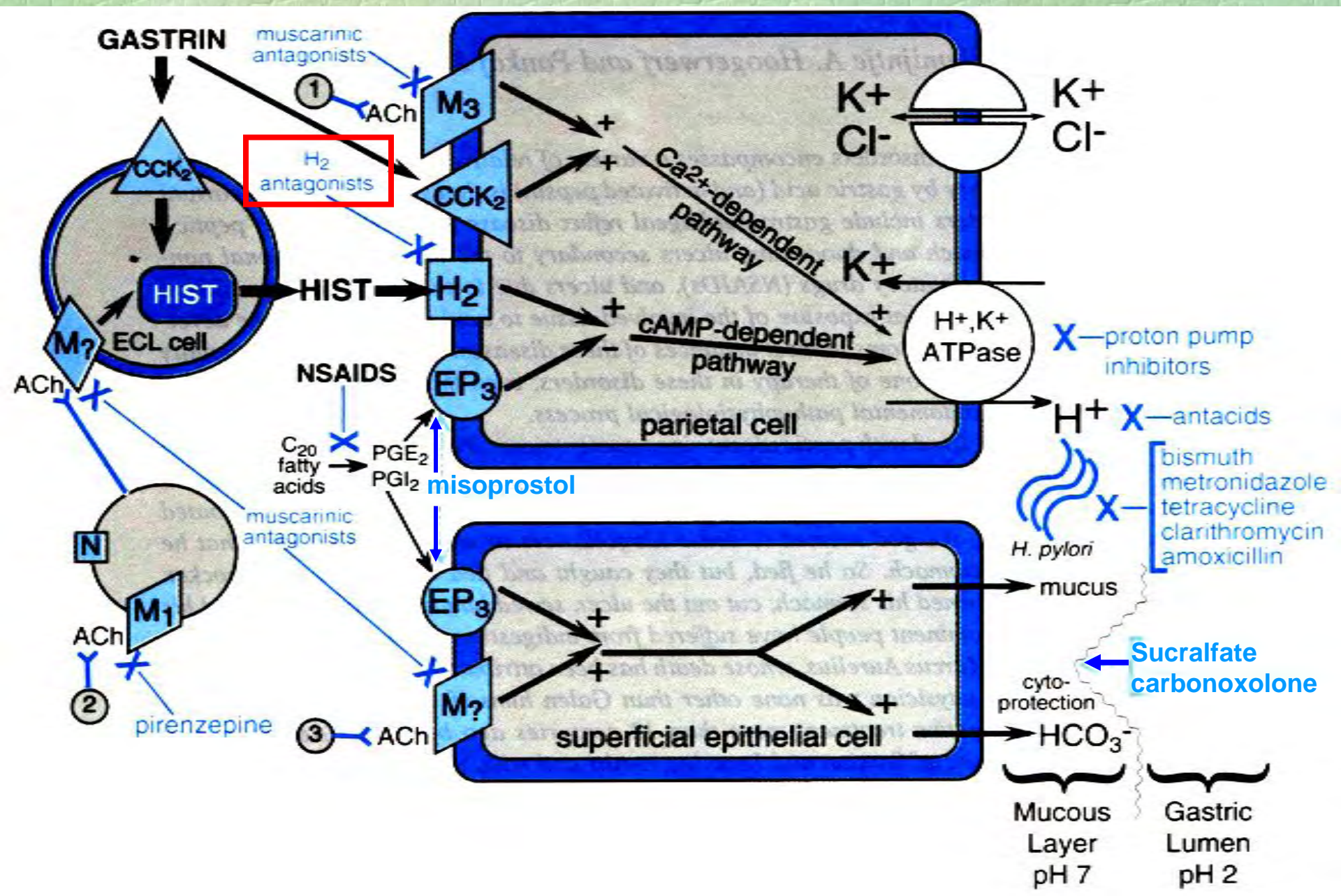


**Cimetidine**  
(西咪替丁)



**Ranitidine(雷尼替丁)**





# Drugs used for peptic ulcers

## Cimetidine(西咪替丁)

### 1. Pharmacological effects

Blocking  $H_2$  receptors, decreasing  $H^+$  secretion

### 2. Clinical uses

(1) Duodenal and gastric ulcer:  
— relieving symptoms, promoting healing of ulcers, and preventing ulcers.

(2) Reflux esophagitis;

(3) Acute stress ulcers, etc.

# Drugs used for peptic ulcers

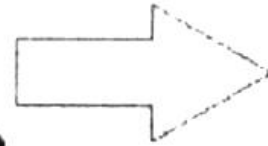
## 3. Adverse effects

- (1) Side effects: constipation, diarrhoea, tiredness, muscular pain, etc.
- (2) CNS effects: headache, dizziness, hallucination, etc. (elderly, long-term uses)
- (3) Endocrine effects: antiandrogen, gynecomastia(男性乳房发育), galactorrhea(溢乳), reduced sperm count, and male sexual dysfunction

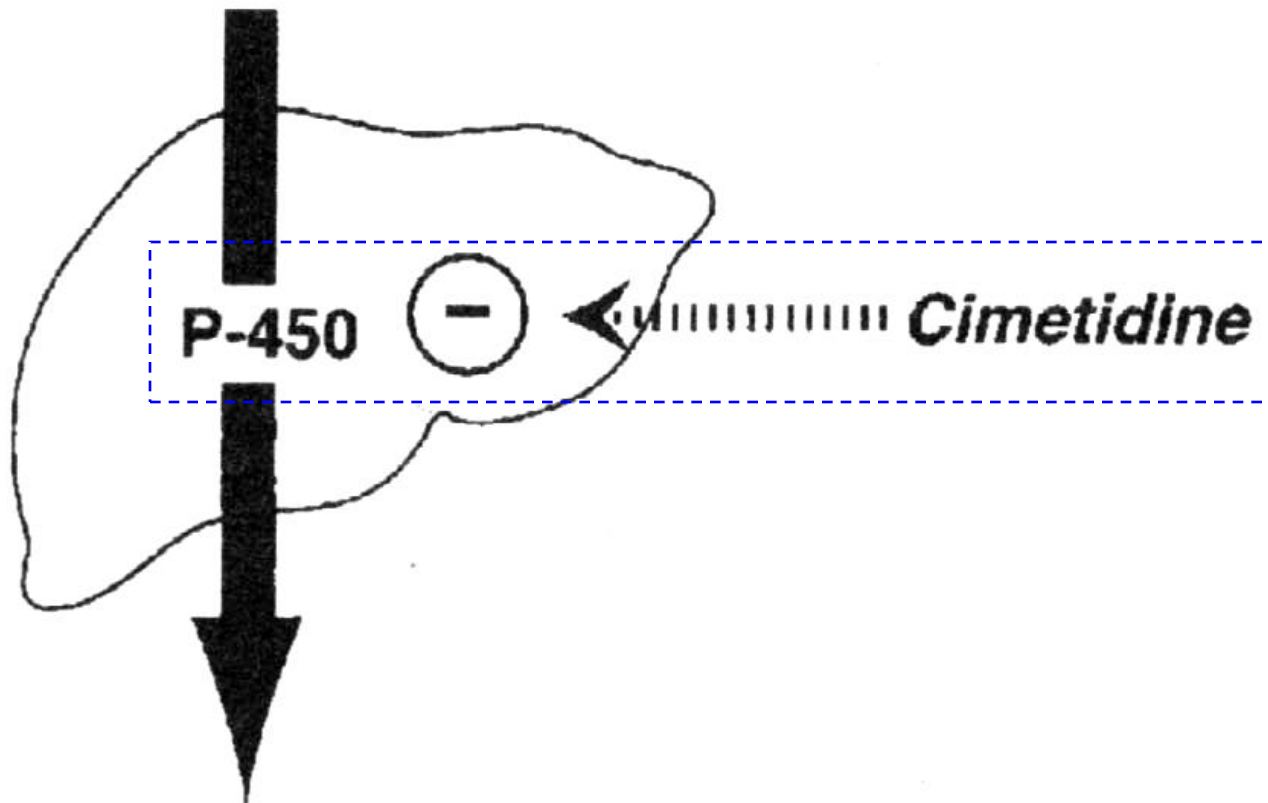
## 4. Drug interactions

**Inhibiting hepatic P<sub>450</sub>**: raising plasma concentrations of warfarin, phenytoin, diazepam, propranolol, quinidine and theophylline, etc.

**Warfarin**  
**Diazepam**  
**Phenytoin**  
**Quinidine**  
**Carbamazepine**  
**Theophylline**  
**Imipramine**



**Serum  
concentration  
increases**



**Metabolites**

# Drugs used for peptic ulcers

## Other H<sub>2</sub> receptor antagonists:

### Ranitidine(雷尼替丁)

Similar to cimetidine, but 5~10 times more potent, longer acting;

Minimal side effects, no antiandrogenic and prolactin-stimulating effects, less inhibiting P<sub>450</sub>.

### Famotidine(法莫替丁)

Similar to ranitidine, but 4~8 times more potent.

### Nizatidine(尼扎替丁)

The potent is similar to ranitidine.

Bioavailability is near 100%, principally eliminated by kidney

# Drugs used for peptic ulcers

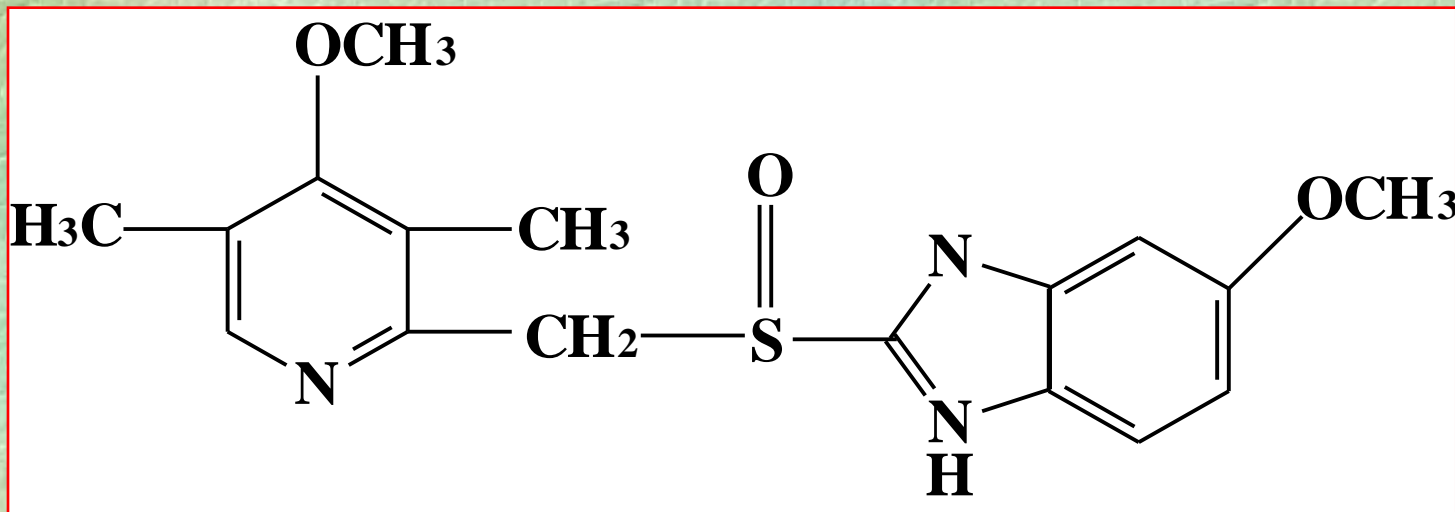
## 4 种H<sub>2</sub>-受体阻断药的比较

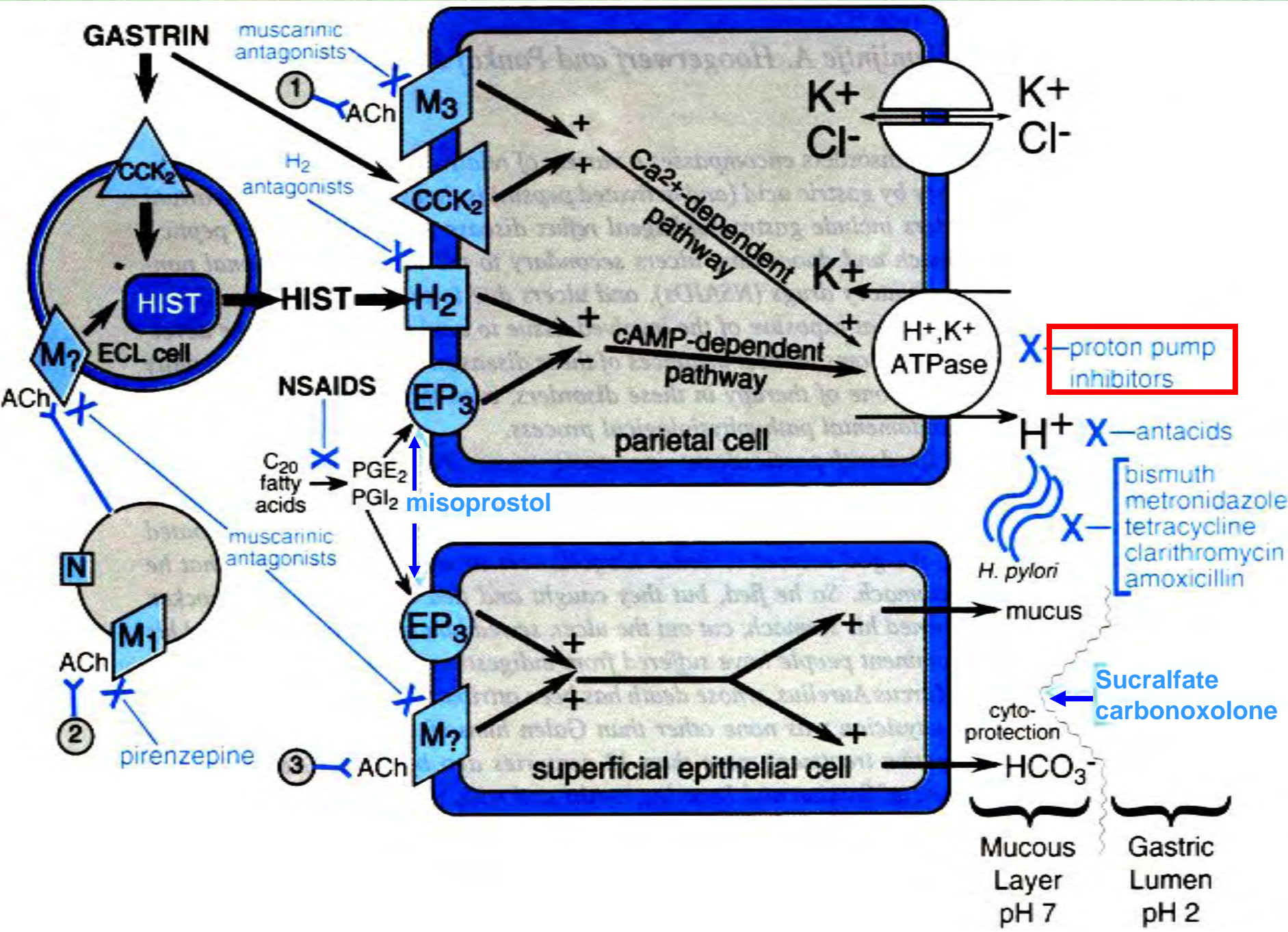
药名	t <sub>1/2</sub> (h)	相对抑酸活力	剂量	对肝药酶抑制
西咪替丁	2	1	400mg, bid	1
雷尼替丁	2-3	5-10	150mg, bid	0.1
法莫替丁	2.5-4	40	20mg, bid	0
尼扎替丁	2	5-10	150mg, bid	0

# Drugs used for peptic ulcers

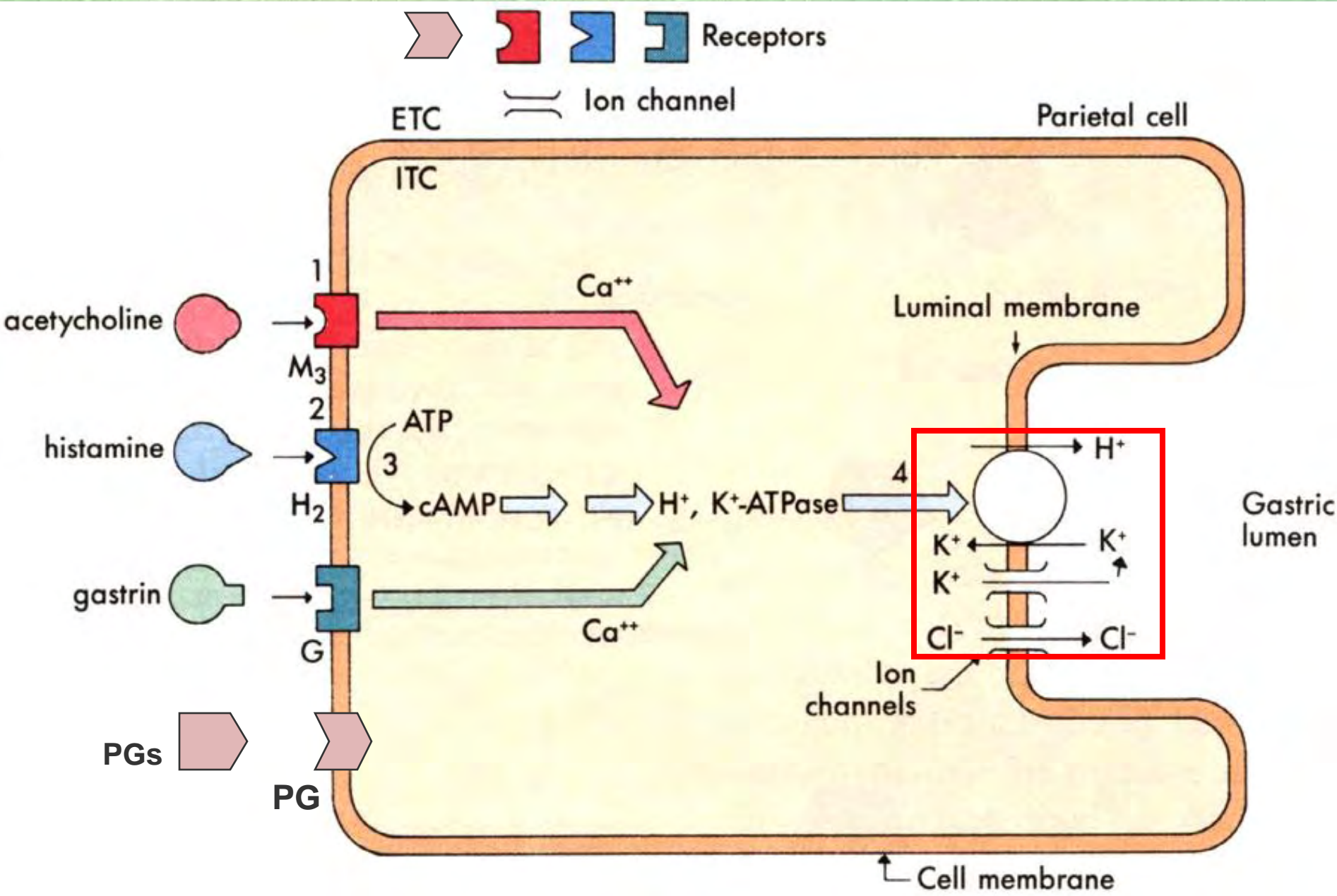
## C. $H^+$ - $K^+$ -ATPase inhibitors (proton pump inhibitors)

### Omeprazole (奥美拉唑, Losec)

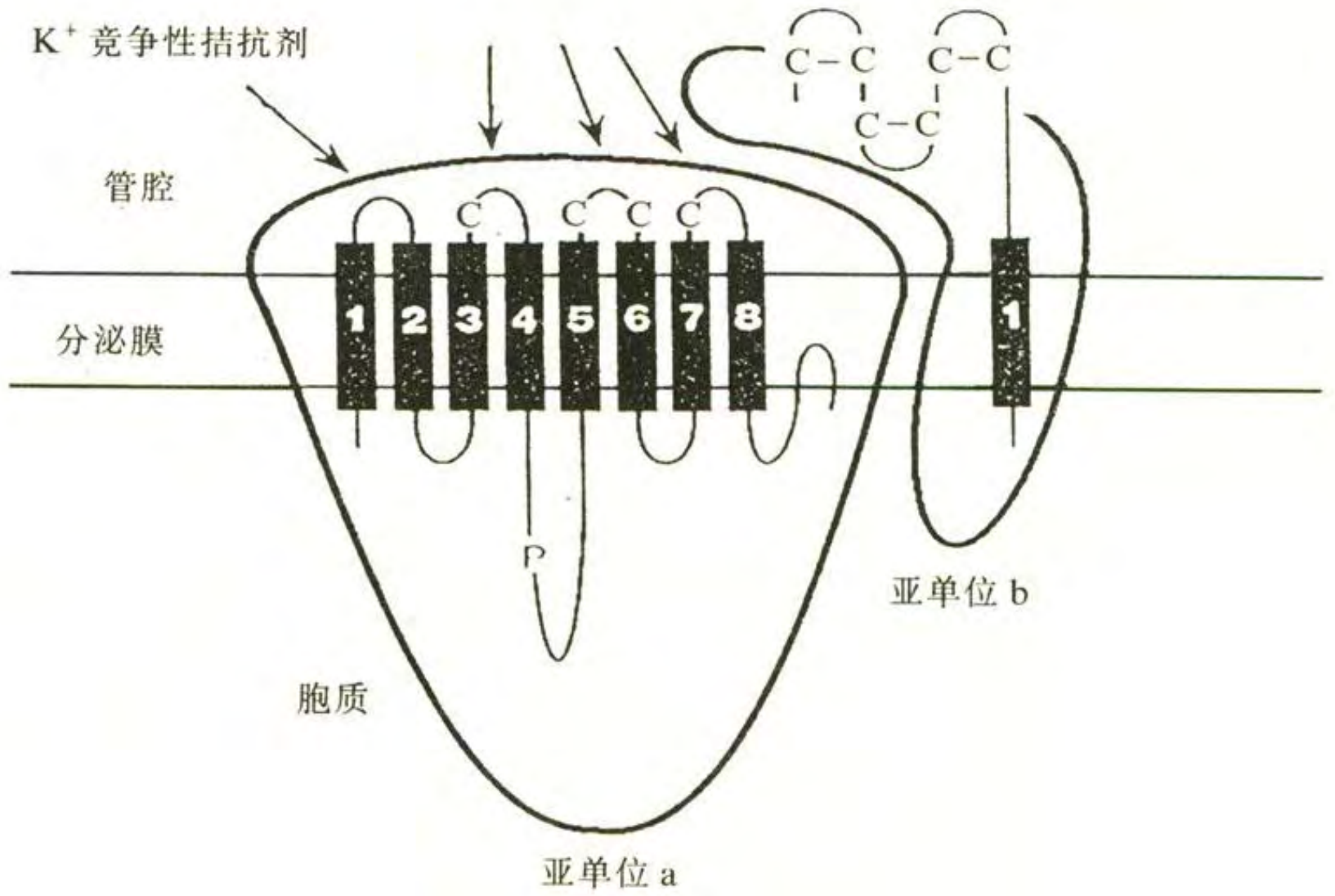








# 苯并咪唑化合物共价键拮抗剂



## 质子泵的分子构型

# Drugs used for peptic ulcers

## 1. Pharmacological effects:

- (1) Inhibiting gastric acid secretion by various stimuli (such as: histamine, gastrin, aspirin, ethanol, stress, etc.)
- (2) Inhibiting *Hp*.

## 2. Clinical uses:

- (1) Highly effective for duodenal and gastric ulcer: relieving symptoms, and promoting healing of ulcers  
Used with antimicrobial agents to eradicate *Hp*.
- (2) Reflux esophagitis;

# Drugs used for peptic ulcers

## 3. Adverse effects:

### (1) Side effects:

Less, such as: nausea, headache, diarrhoea, constipation and rash occur.

### (2) Increase of gastric carcinoid tumor

### (3) Others:

hypersensitivity, gynecomastia(男性乳房发育)

## 4. Drug interactions:

Inhibiting hepatic P450, raising plasma concentrations of warfarin, phenytoin, diazepam, etc.

# Drugs used for peptic ulcers

## Others

- **Lansoprazole(兰索拉唑)**
- **Pantoprazole(泮他拉唑)**
- **Rebeprazole(雷贝拉唑)**

## 几种质子泵抑制剂的比较

药名	$t_{1/2}$ (h)	有效抑酸 时间(h)	剂量 (mg/d)	对肝药 酶影响
奥美拉唑	1.0	12~24	20~40	+
兰索拉唑	1.5	24	30	±
潘托拉唑	1.3	24	20~40	-
雷贝拉唑	1.0	24	20	-

# **Drugs used for peptic ulcers**

## **III. Mucosal protective drugs**

# Drugs used for peptic ulcers

## III. Mucosal protective drugs

Misoprostol(米索前列醇)

Enprostil(恩前列素)

Sucralfate(硫糖铝)

Colloidal bismuth subcitrate(CBS, 胶体次枸橼酸铋)

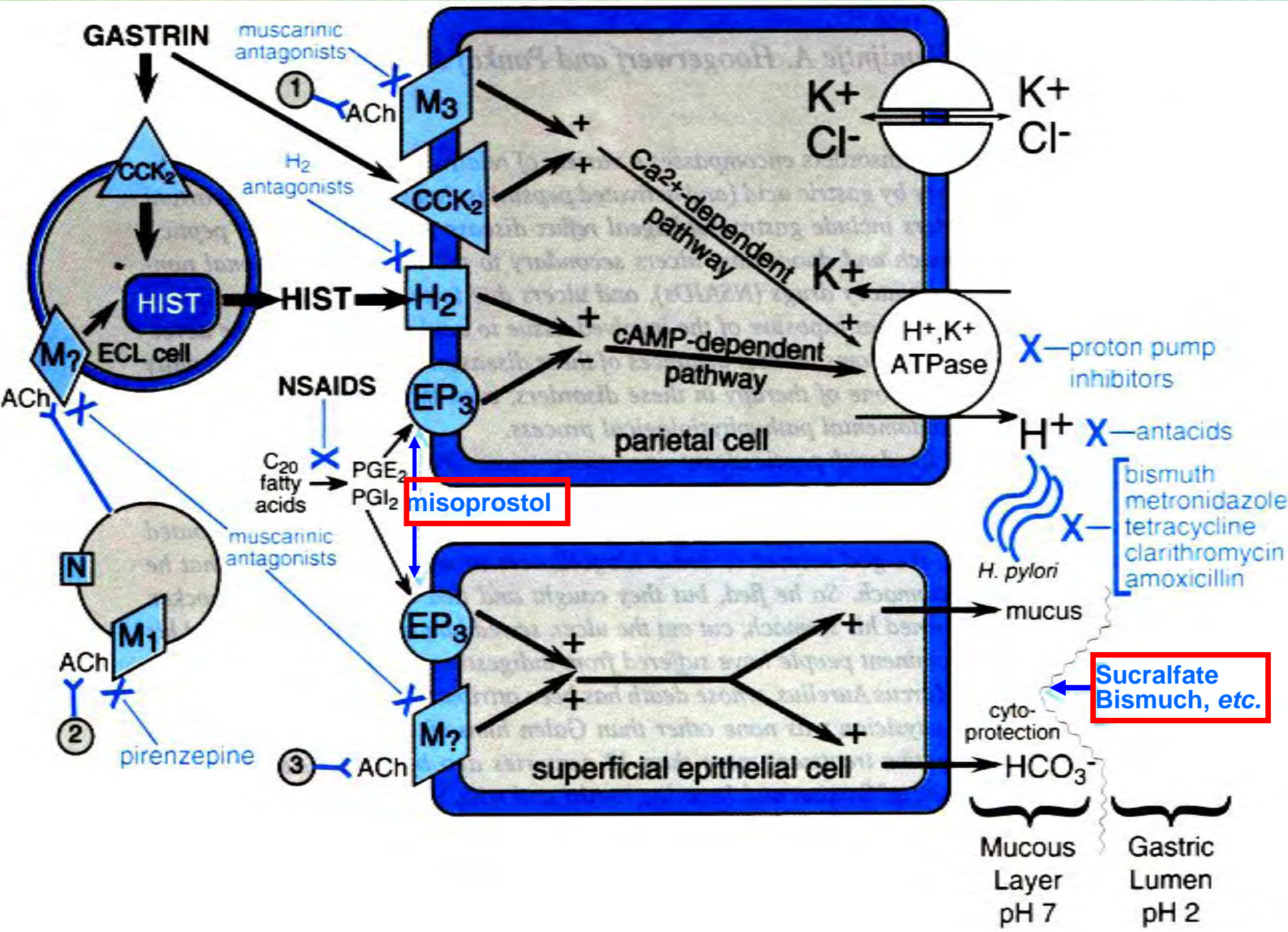
Proglumide(丙谷胺)

Teprenone(替普瑞酮)

Marzulene(麦滋林)

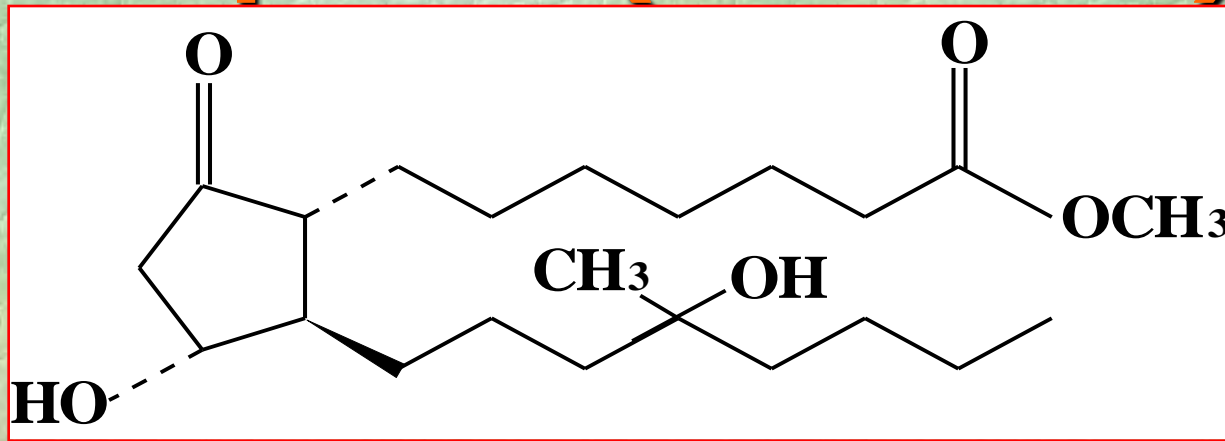
Smectite(思密达), *etc.*





# Drugs used for peptic ulcers

## Misoprostol(米索前列醇)



It is the derivative of prostaglandin  
(前列腺素).

## Enprostil(恩前列素)

# Drugs used for peptic ulcers

## Misoprostol, Enprostil

### 1. Pharmacological effects:

Inhibiting gastric acid secretion  
Promoting mucus and  $\text{HCO}_3^-$  secretion,  
and mucosal repair.

### 2. Clinical uses:

Ulcers, especially for NSAIDs-induced.

### 3. Adverse effects:

Side effects(13%): nausea, abdominal pain, diarrhea, headache, *etc.*

**Contraindicated in pregnancy women.**

# Drugs used for peptic ulcers

## IV. Antimicrobial drugs (anti-*Hp* drugs)

# Drugs used for peptic ulcers

## IV. Antimicrobial(anti-*Hp*) drugs

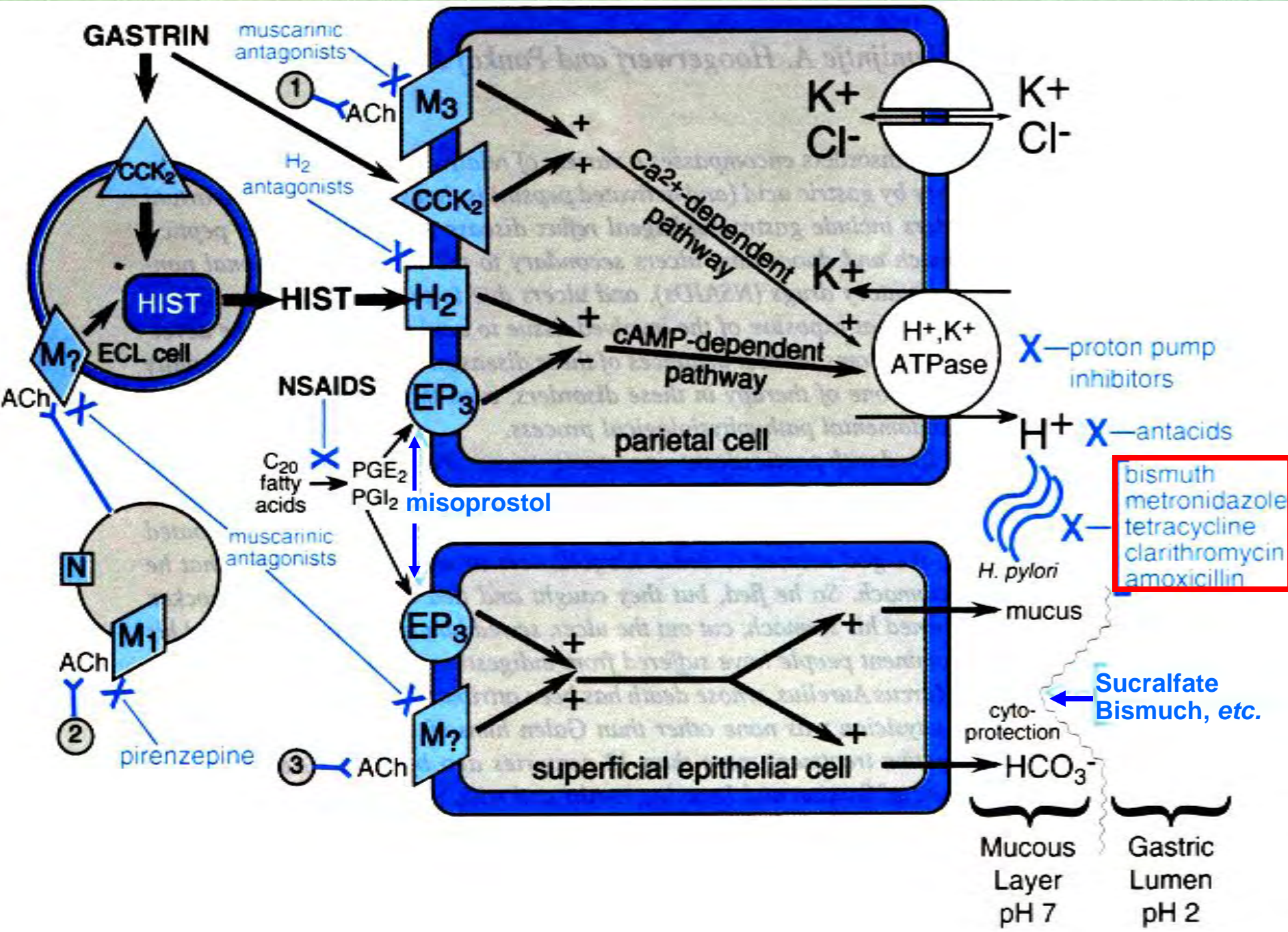
### 1. Antimicrobial drugs:

Amoxicillin(阿莫西林), Tetracycline(四环素), Gentamicin (庆大霉素), Clarithromycin (克拉霉素), Metronidazole(甲硝唑), *etc.*

### 2. Anti-ulcer drugs:

H<sup>+</sup>-K<sup>+</sup>-ATPase inhibitors; bismuch(铋剂); sulralfate(硫糖铝), *etc.*

**Weaker, combined with antimicrobial drugs.**



# Drugs used for peptic ulcers

## The Classification of anti-ulcer drugs and the representative drugs

### I . Antacids:

Aluminium hydroxide, Magnesium trisilicate.

### II . Drugs inhibiting gastric acid secretion:

#### A. Muscarinic receptor antagonists:

Pirenzepine, Telenzepine.

#### B. H<sub>2</sub> receptor antagonists:

Cimetidine, Ranitidine, *etc.*

#### C. H<sup>+</sup>-K<sup>+</sup>-ATPase inhibitors (proton pump inhibitors):

Omeprazole, Lansoprazole, *etc.*

### III. Mucosal protective drugs:

Misoprostol, Enprostil, Sucralfate, *etc.*

### IV. Anti-*Hp* drugs:

Amoxicillin, Metronidazole, *etc.*

# **Part 2. Modulators of gastro- enteric functions**



# Contents

**I . Promoting digestive drug;**

**II . Antiemetic and prokinetic drugs:**

**1. antiemetic drugs(止吐药);**

**2. prokinetic drugs(胃动力药).**

**III. Drugs for treatment of diarrhea:**

**1. antimotility drugs(抗蠕动药);**

**2. astringents(收敛药);**

**3. absorbants(吸附药).**

**IV. Laxatives:**

**1. contact(stimulant) laxatives;**

**2. osmotic laxatives;**

**3. faecal softners(emollients).**

# Modulators of gastrointestinal functions

## I . Promoting digestive drug:

**Pepsin(胃蛋白酶);**

**Pancreatin(胰酶);**

**Lactasin(乳酶生, Biofermin, 表飞鸣),  
*etc.***

# Modulators of gastrointestinal functions

## II. Antiemetic and prokinetic drugs:

### 1. Antiemetic drugs(止吐药):

**H<sub>1</sub> receptor antagonists(H<sub>1</sub>受体阻断药):**

Diphenhydramine(苯海拉明);

Dimenhydrinate(茶苯海明);

Meclozine(美克洛嗪), *etc.*

**M receptor antagonists:**

Scopolamine(东莨菪碱)

**D<sub>2</sub> receptor antagonists:**

Chlorpromazine(氯丙嗪)

**5-HT<sub>3</sub> receptor antagonists:**

Ondansetron(昂丹司琼);

Grasetron(格拉司琼);

Tropisetron(托烷司琼), *etc.*

# Modulators of gastrointestinal functions

## 2. Prokinetic drugs(胃动力药):

### Metoclopramide(甲氧氯普胺, 胃复安, 灭吐灵)

D<sub>2</sub> receptor block: antiemetic effects(CTZ), and promoting GI motility.

Adverse effects: CNS reactions, extrapyramidal effects, *etc.*

### Domperidone(多潘立酮, 吗丁啉)

D<sub>2</sub> receptor block: promoting GI motility.

Adverse effects: headache, prolactin ↑, gastric acid ↑

### Cisapride(西沙必利)

ACh release ↑: promoting intestinal and colon motility.

# Modulators of gastrointestinal functions

## III. Drugs for treatment of diarrhea: (止泻药)

### 1. Antimotility drugs(抗蠕动药):

agonists for  $\mu$  receptors in GI tract,

Opium preparations(阿片制剂);

Diphenoxylate(地芬诺酯):

CNS effects at larger doses.

### 2. Astringents(收敛药):

Tannalbin(鞣酸蛋白);

Bismuch subsalicylate(次硅酸铋);

Bismuch subcarbonate(次碳酸铋).

### 3. Absorbants(吸附药):

Medical charchol(药用炭, 活性炭);

Agysical(矽炭银).

# Modulators of gastrointestinal functions

## IV. Laxatives(泻药):

### 1. Stimulant laxatives(刺激性泻药):

Phenolphthalein(酚酞);

Bisacodyl(必沙可啶);

Rhubarb(大黄)、Senna(番泻叶), *etc.*

### 2. Osmotic laxatives(渗透性泻药):

Magnesium sulfate(硫酸镁);

Sodium sulfate(硫酸钠);

Lactulose(乳果糖);

Sorbitol(山梨醇);

Glycerol(甘油);

Celluloses(纤维素类).

### 3. Faecal softeners(粪便软化药, emollients):

Liquid paraffin(液体石蜡).

**The class is over !**