Antiulcer Agents

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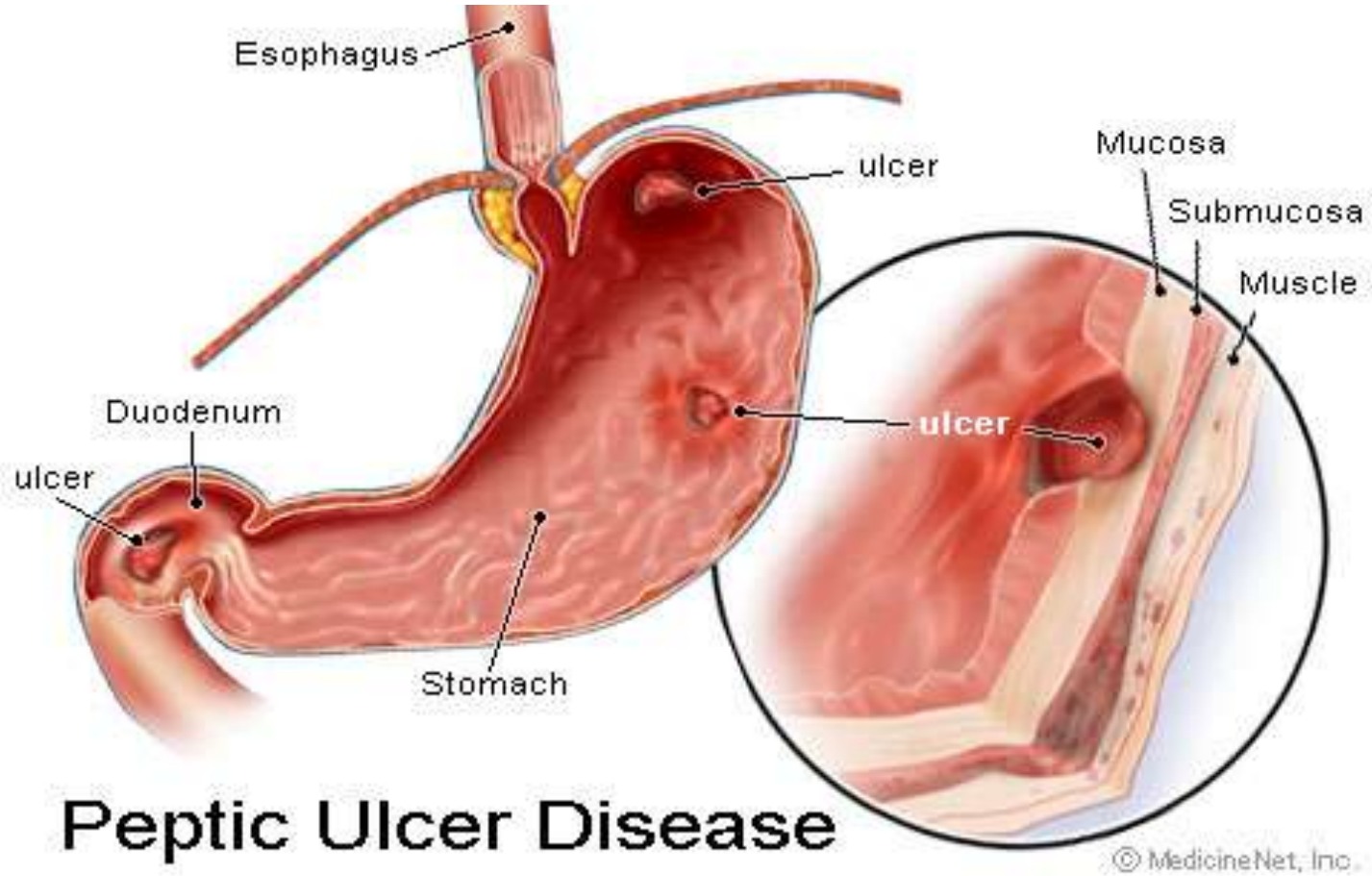
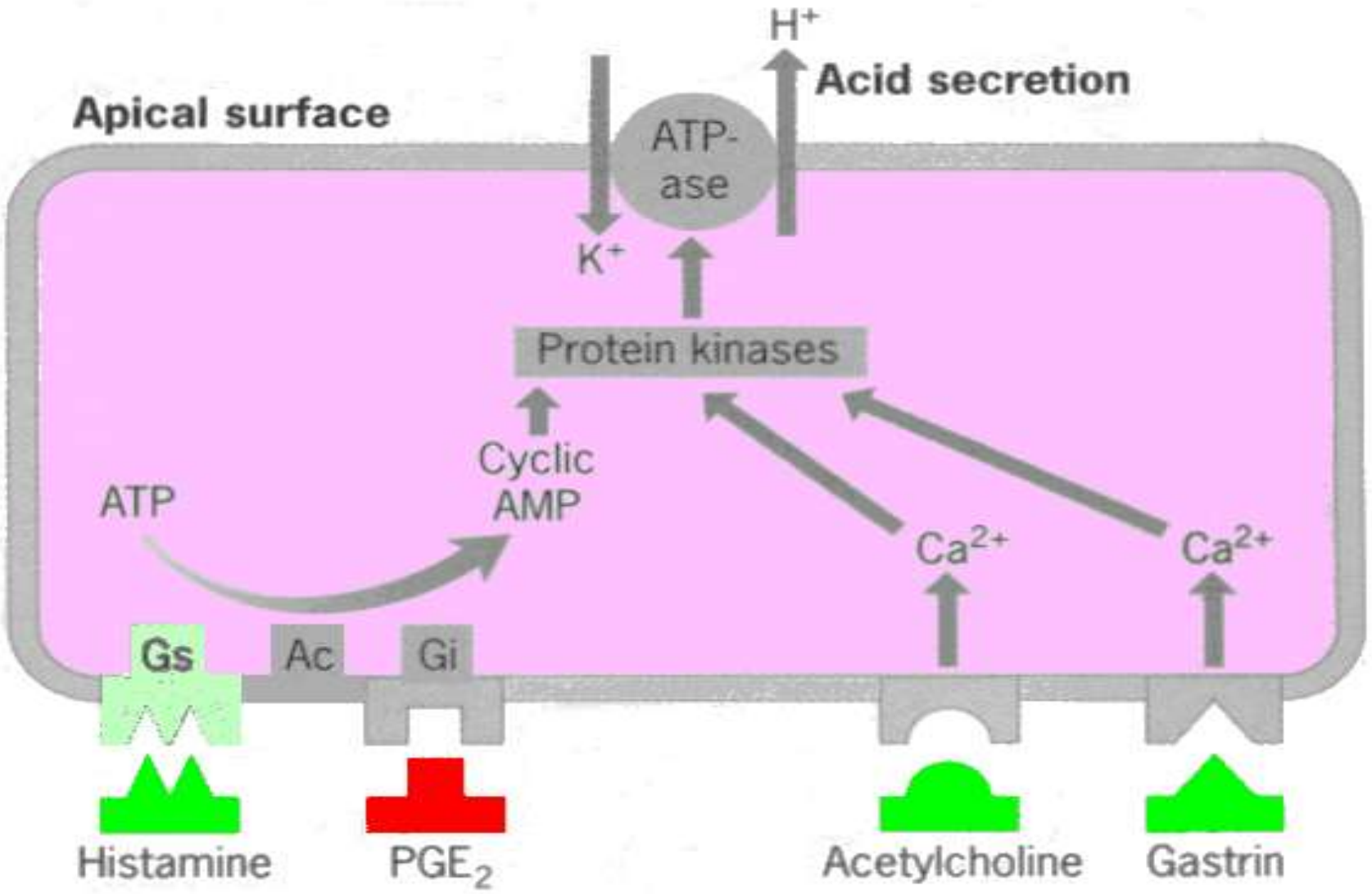
Peptic ulceration

- Mucose degradation



Mechanism of acid secretion



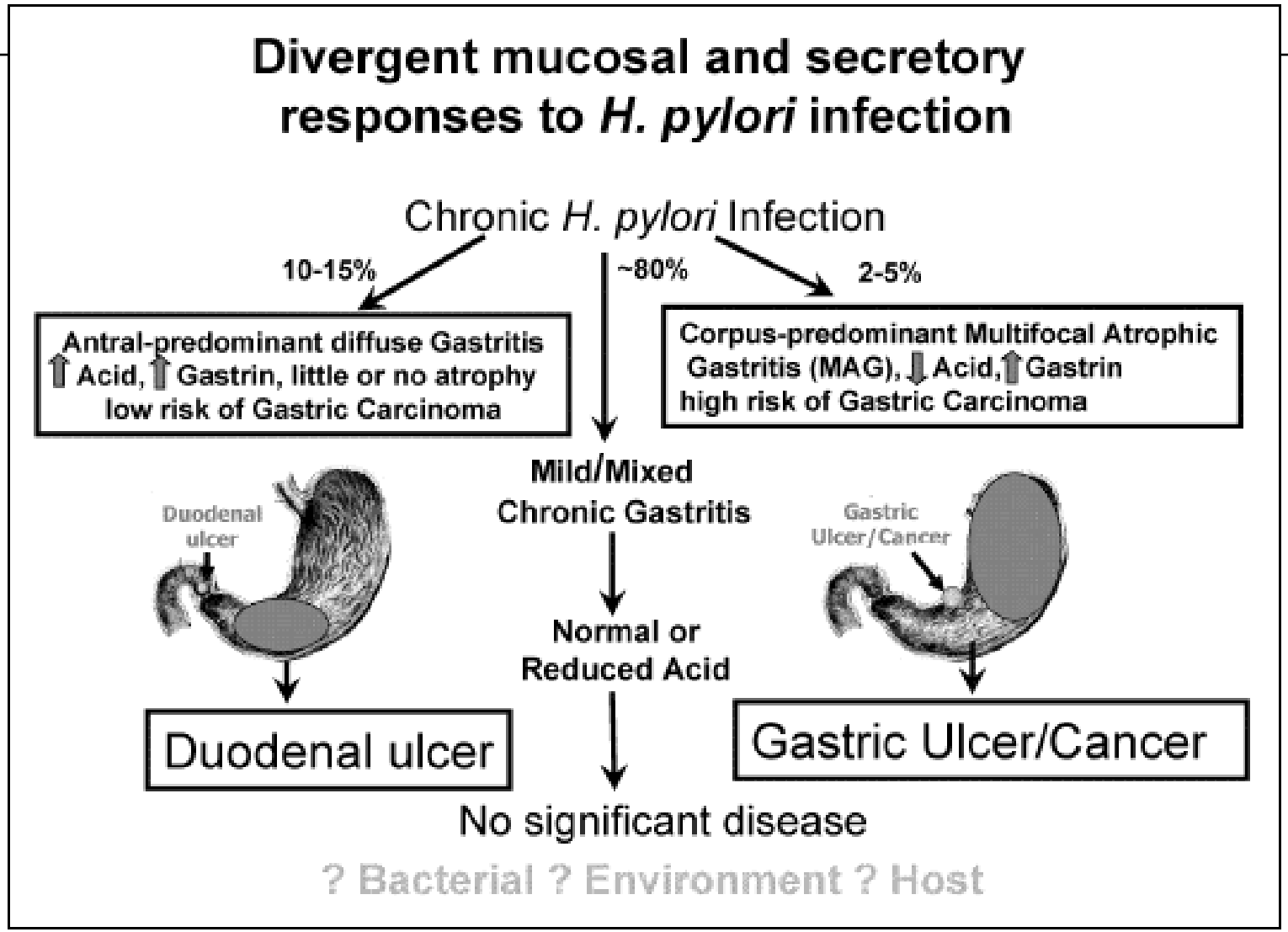
Peptic ulceration

- multifactorial disease:

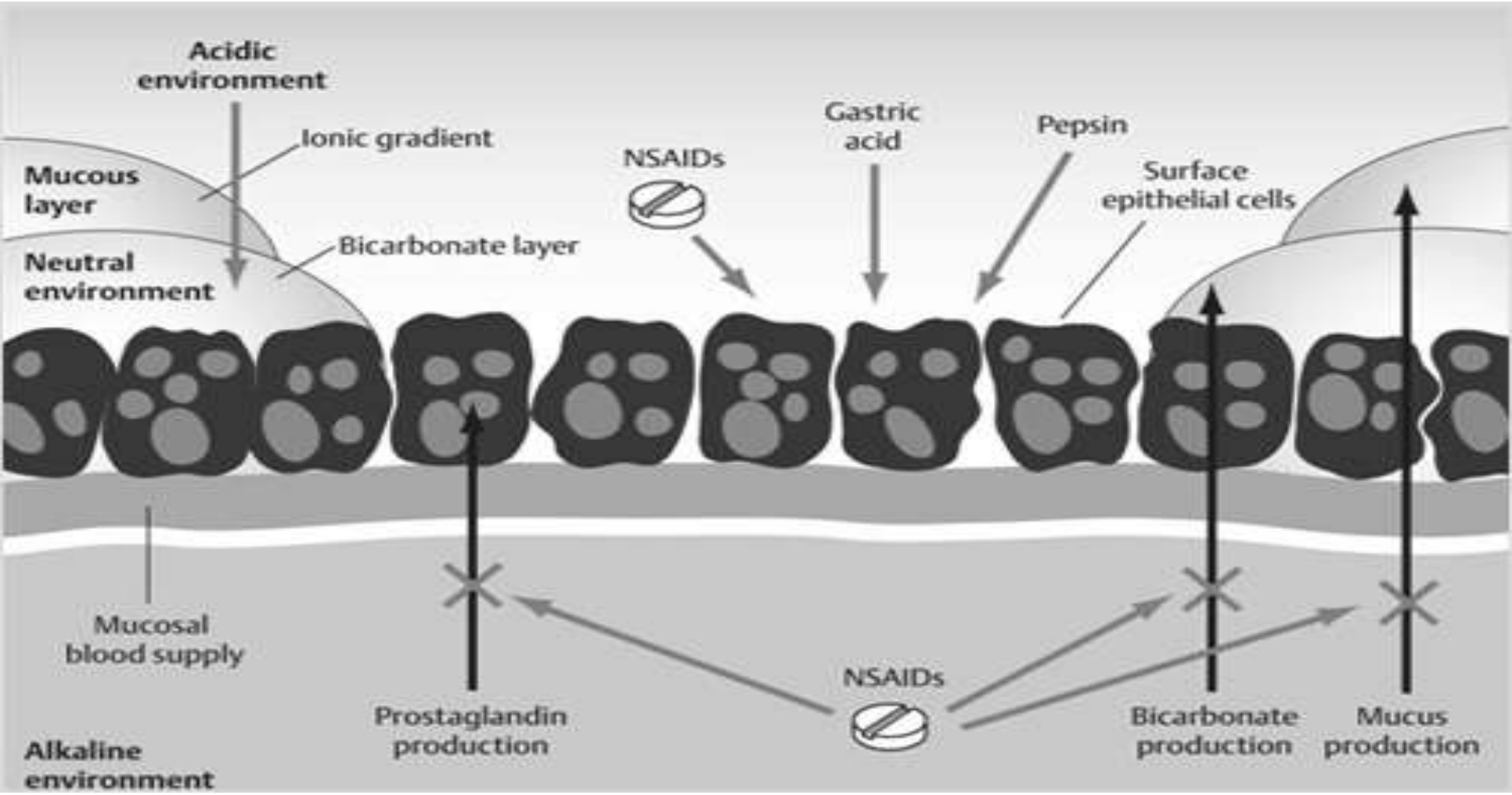
- increased acid production and enzyme activity
- decreased acid production and enzyme activity
- Helicobacter pylori infection
- long-term NSAID medication

- leads to damage of mucose protective layer and ulcer formation

Helicobacter pylori infection



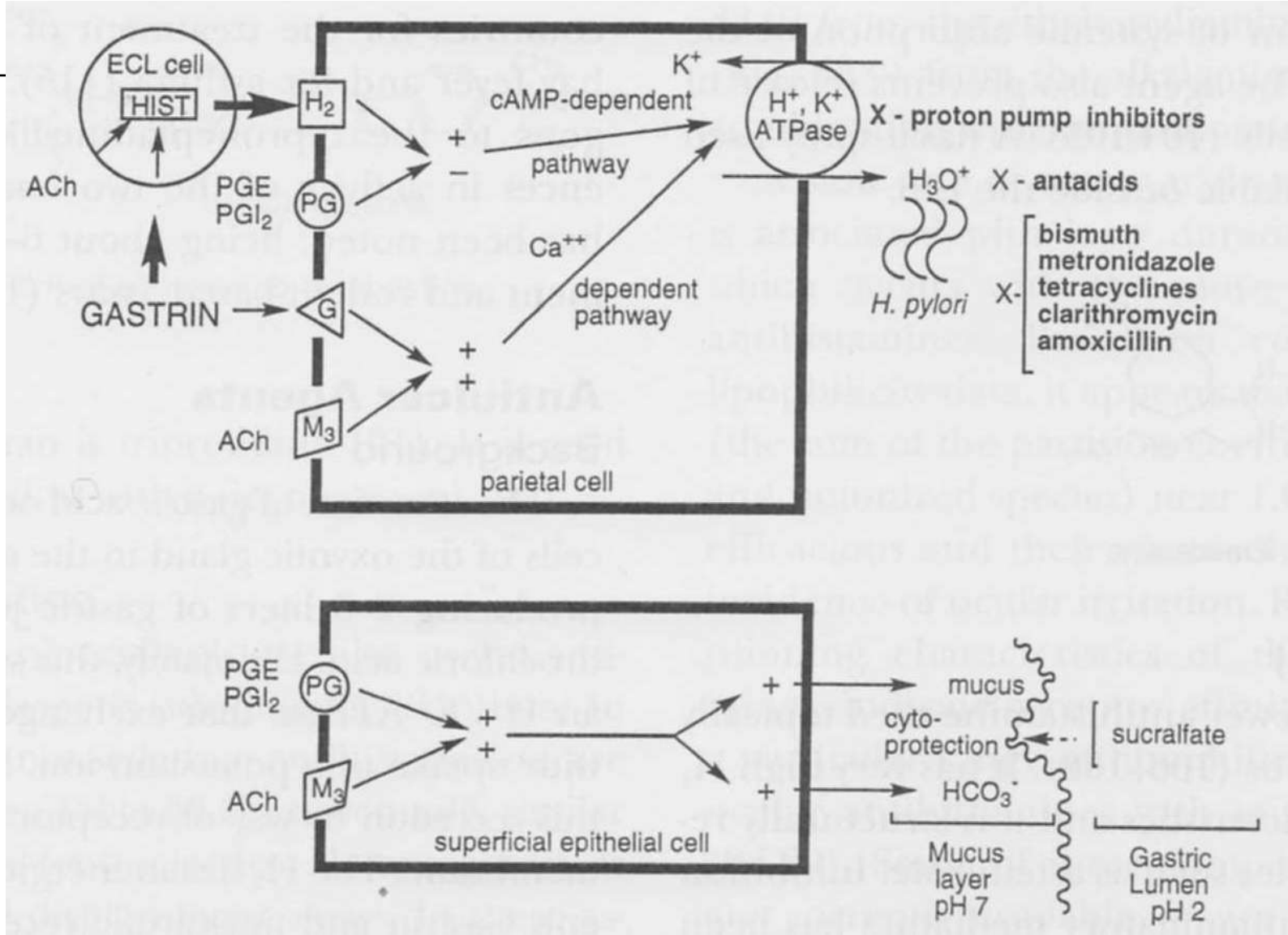
Long-term NSAID administration



Therapy

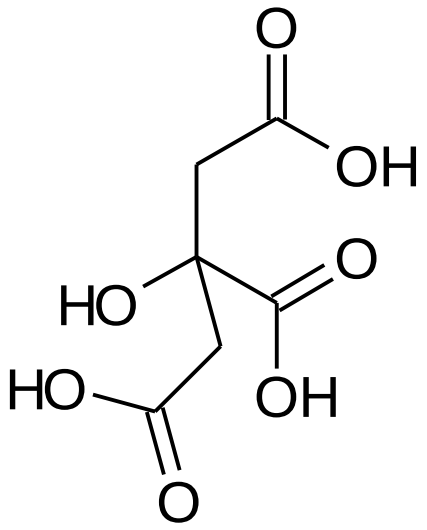
- acids and digestives
- direct antacids
- indirect antacids
- mucoprotective drugs
- drugs for Helicobacter pylori eradication

Mechanism of action

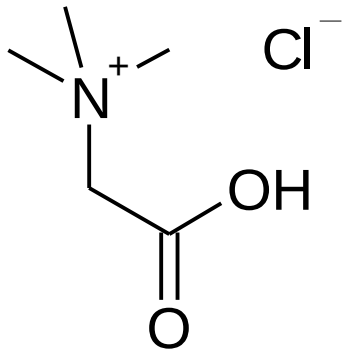


Acids

- achlorhydria – low or no HCl secretion
- increased pH damages mucosa
- citric acid, betaine hydrochloride



citric acid



betaine hydrochloride

Digestives

- insufficient digestion – longer pass through of food – gastritis, ulceration risk
- recombinant enzymes:

  pepsine, pancreatine, trypsine
  chymotripsine, amylase, lipase

Direct antacids

- Carbonates:

  $NaHCO_3$,

  $CaCO_3$,

  $MgCO_3$

- quick pH increase may lead to increased gastrine levels and excessive HCl secretion
- absorbtion of Mg^{2+}, Ca^{2+} and Na^{+} leads to ion dysballance

Direct antacids

Magnesium oxides and hydroxides:

MgO,

MgO_2,

$Mg(OH)_2$

- forming $MgCl_2$ has laxative effect

Direct antacids

Aluminium compounds:

$AlPO_4$,

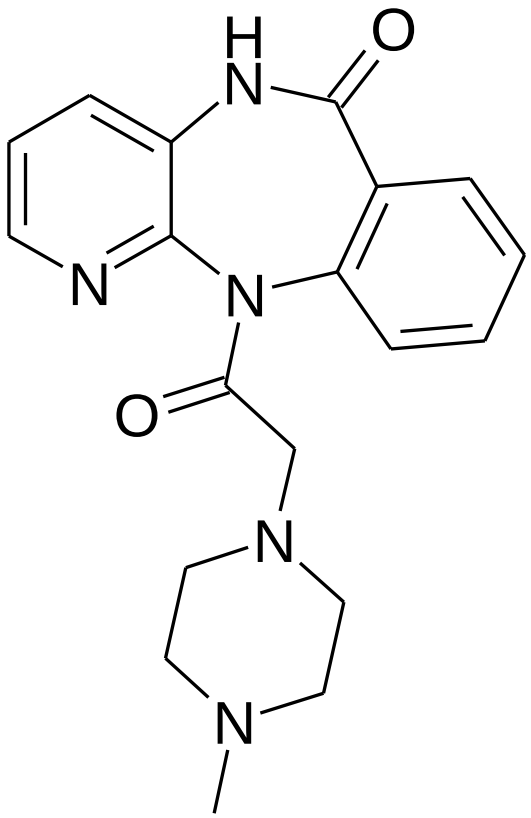
$Al(OH)_3$ (algeldrate),

$Al_5Mg_{10}(OH)_{31}(SO_4)_2.H_2O$ (magaldrate)

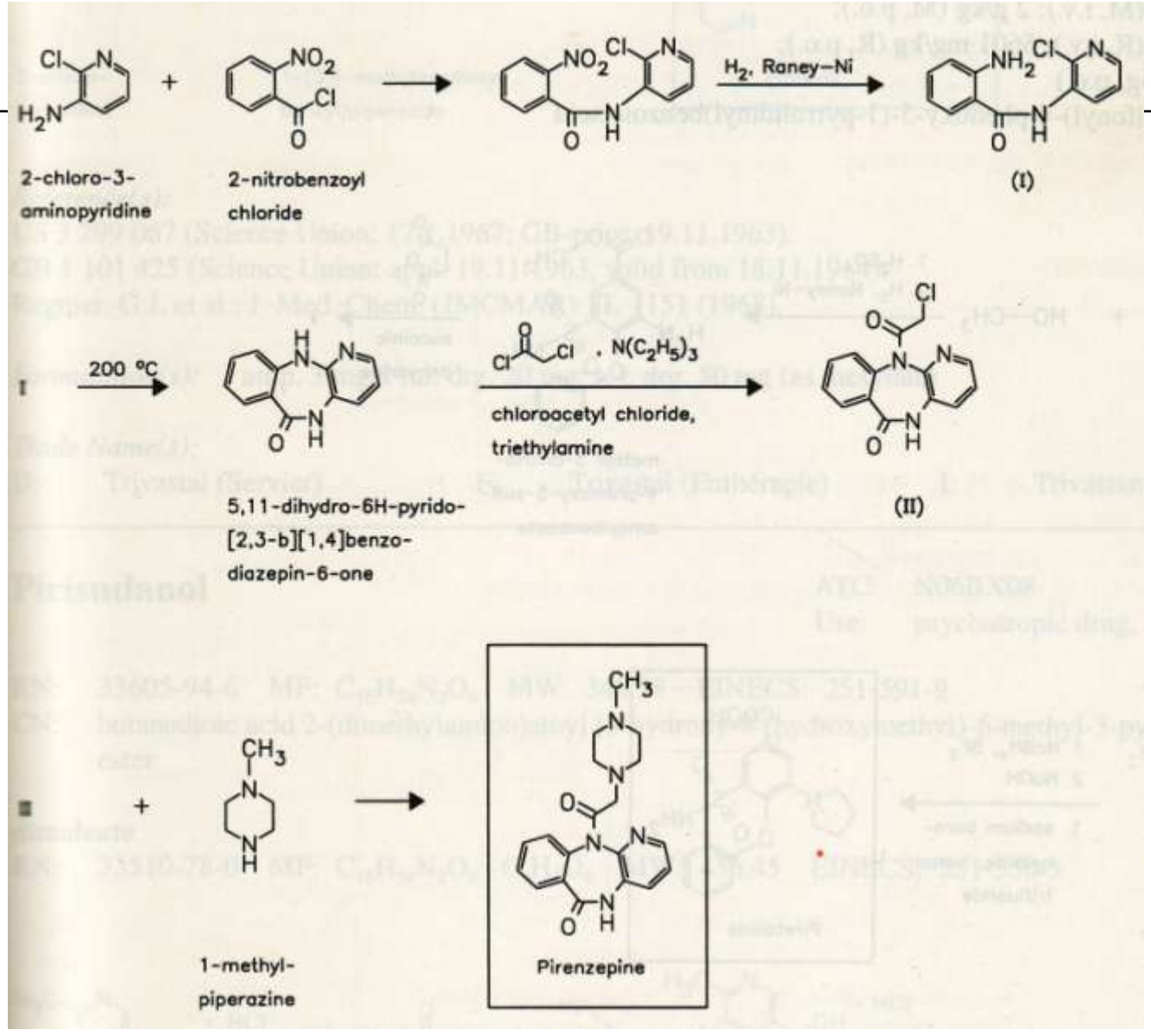
- both antacide and protective effect
- long-term administration of aluminium salts may cause obstipation

Antimuscarinic agents

- Pirenzepine

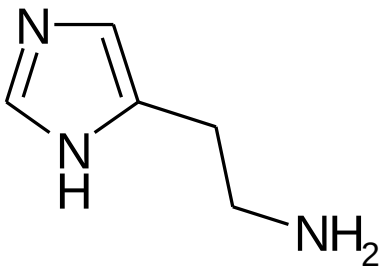


Pirenzepine synthesis

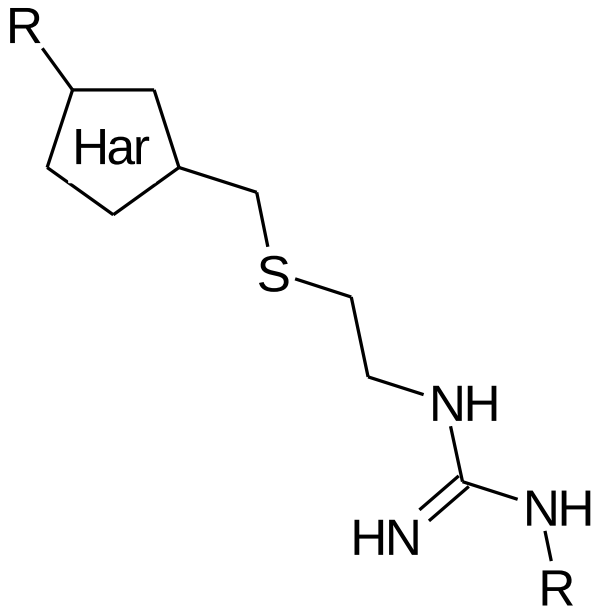


Selective H2 histamine receptor antagonists

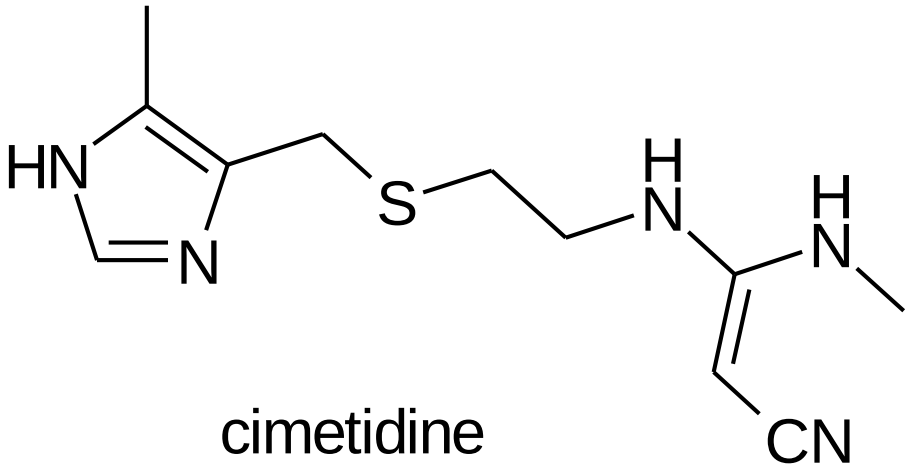
SAR of H2 antagonists:



histamine

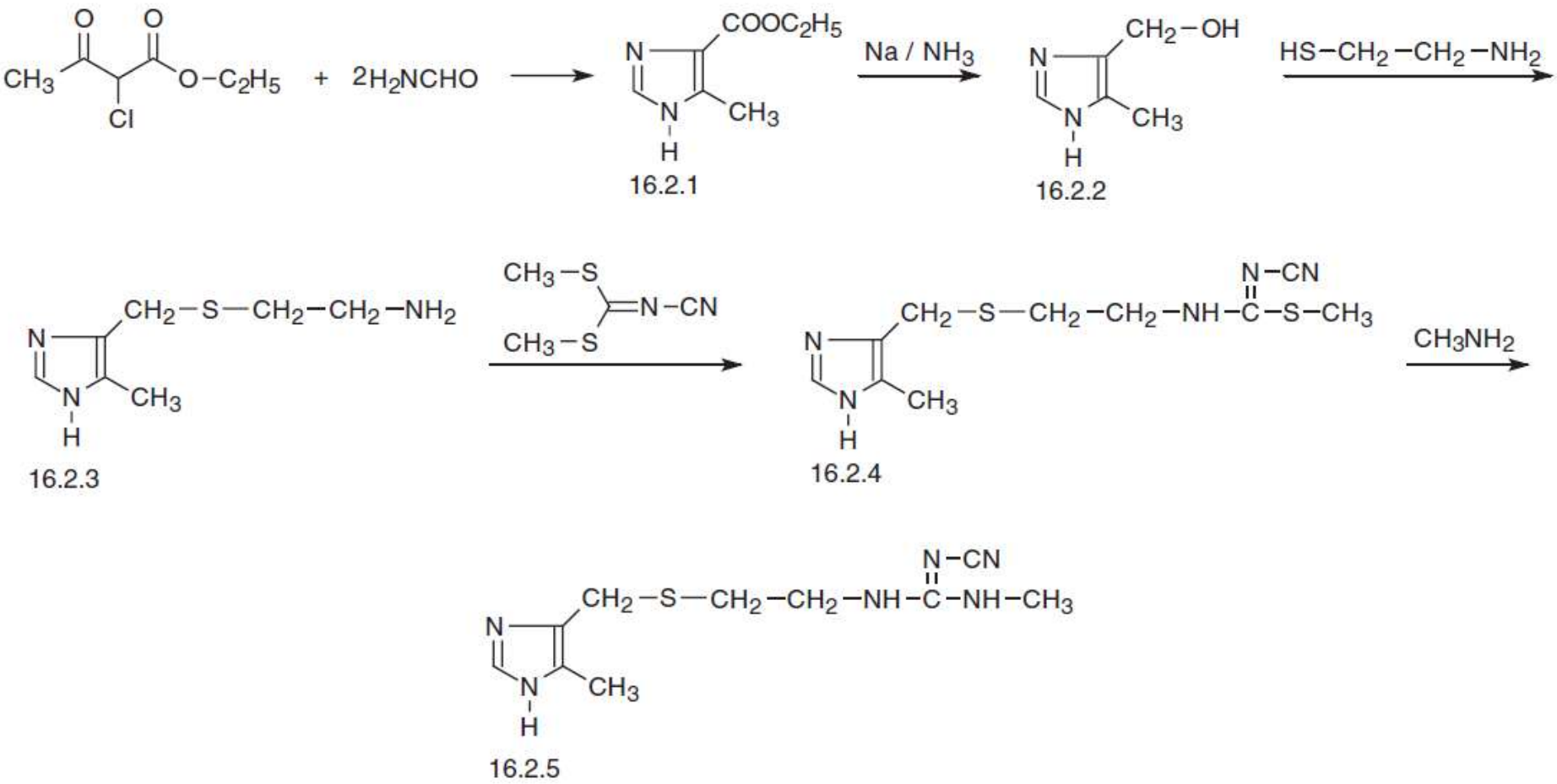


Cimetidine

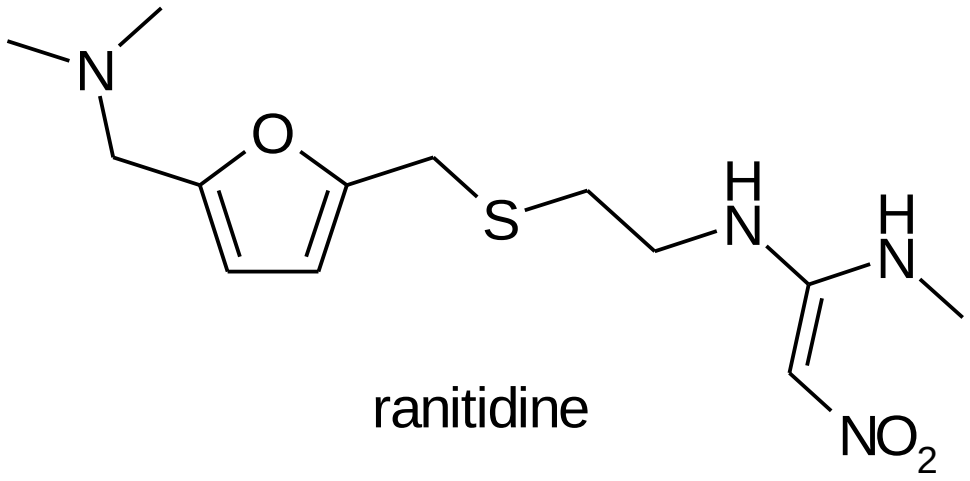


cimetidine

Cimetidine synthesis

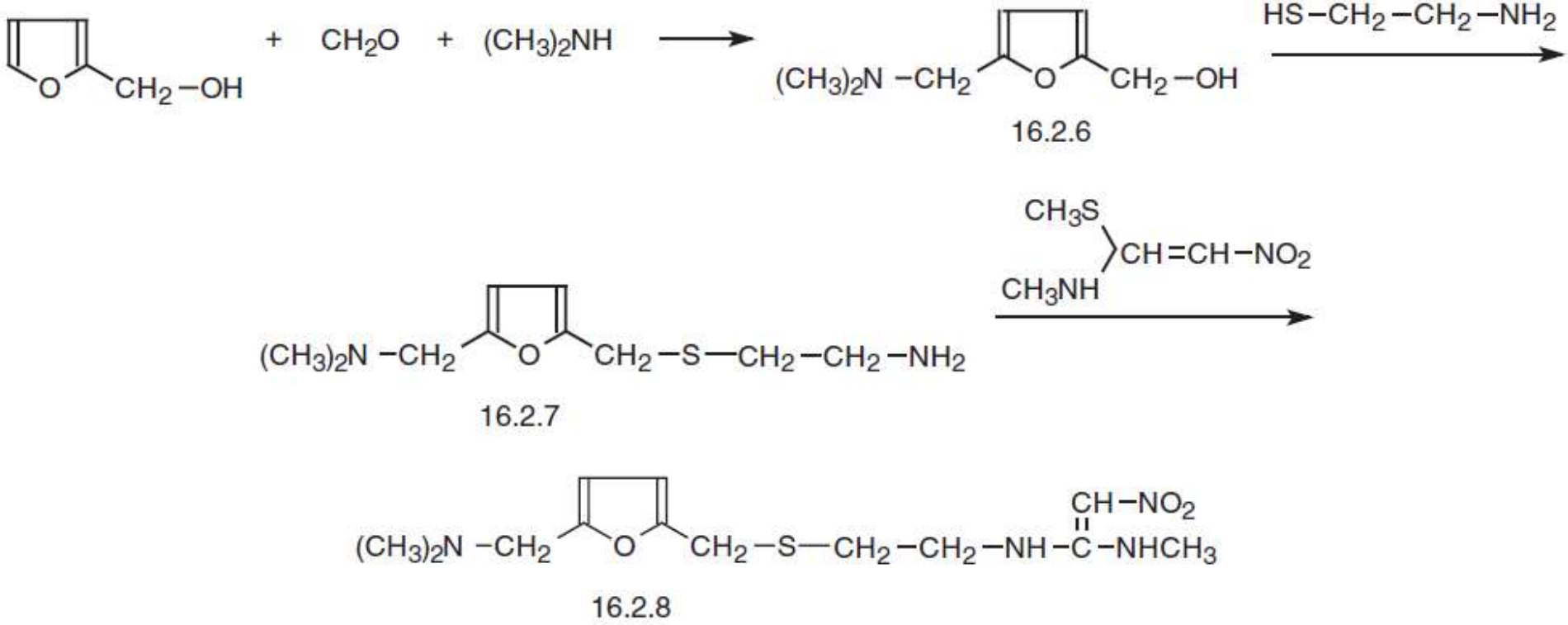


Ranitidine

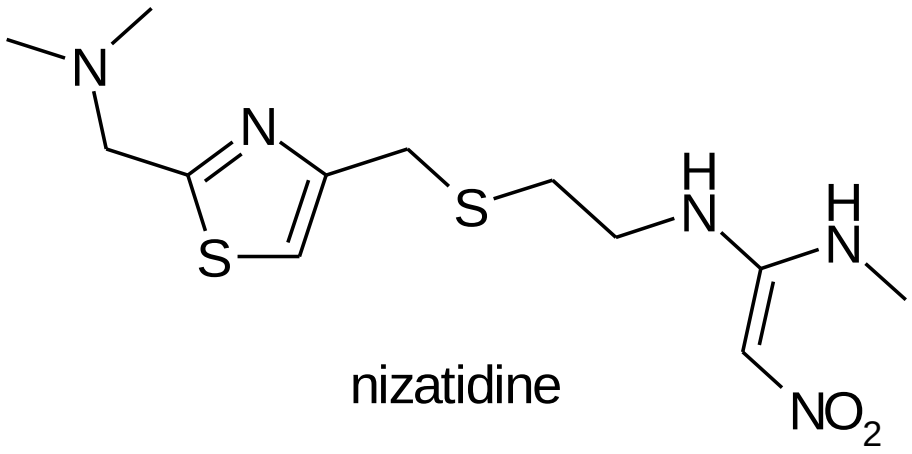


ranitidine

Ranitidine synthesis

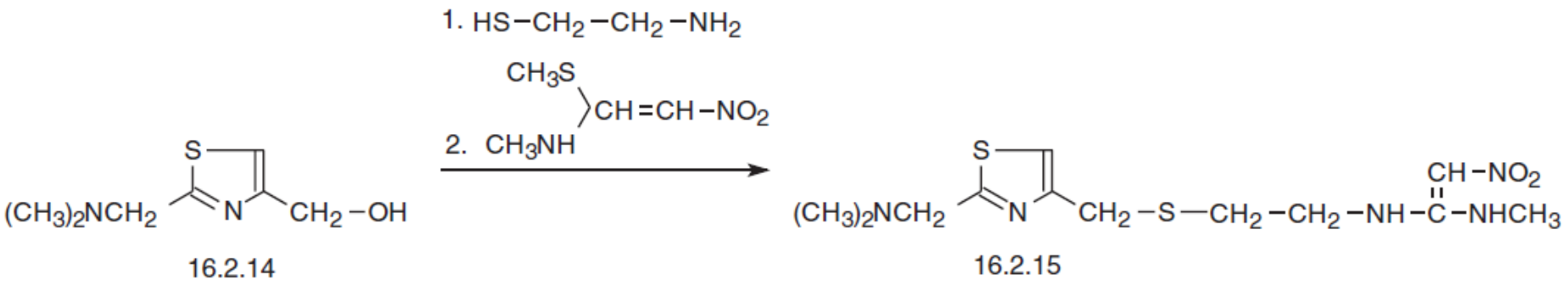


Nizatidine

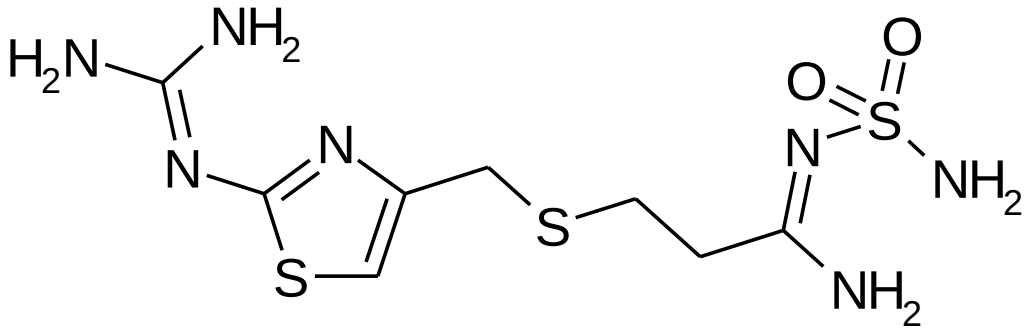


nizatidine

Nizatidine synthesis

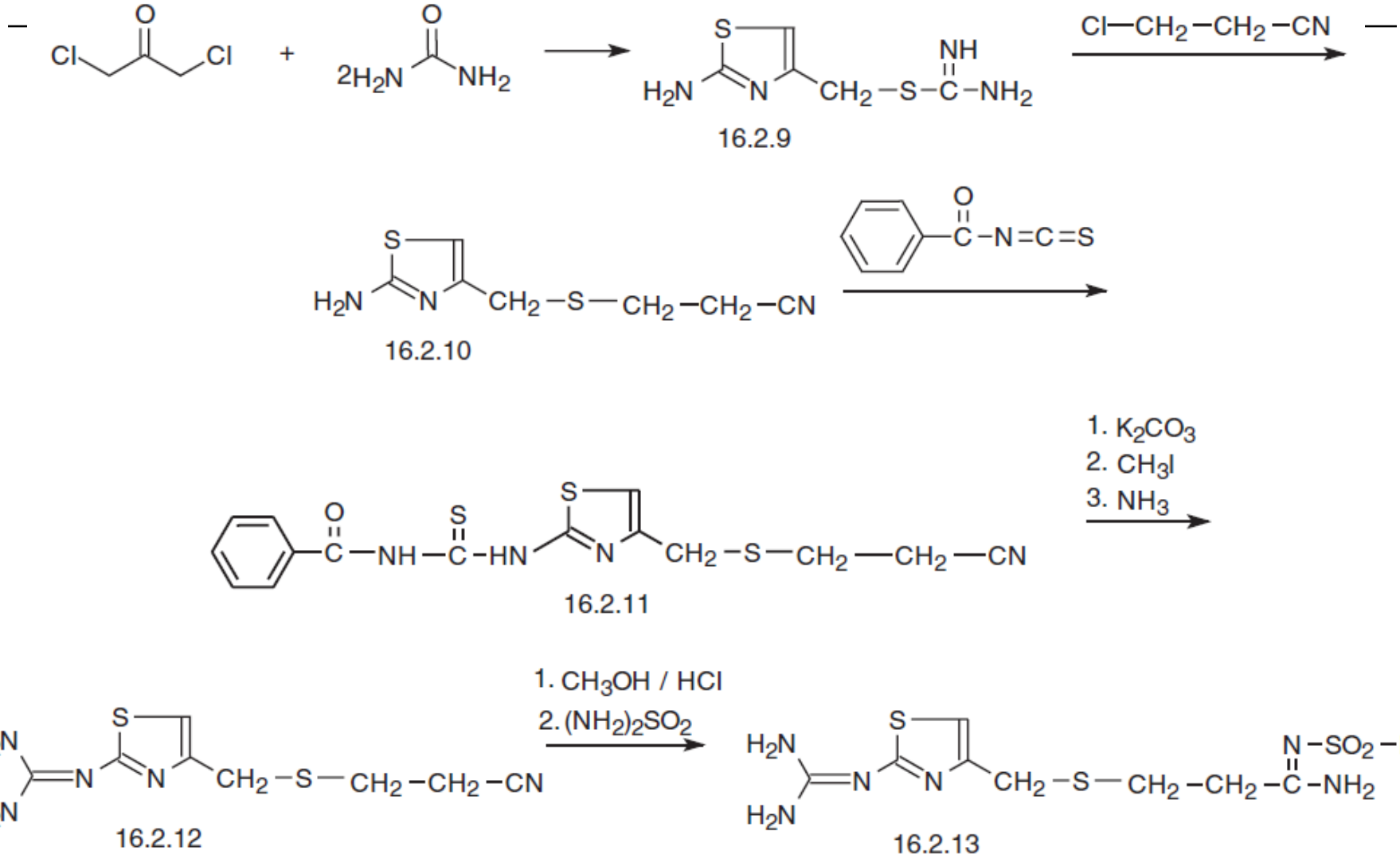


Famotidine



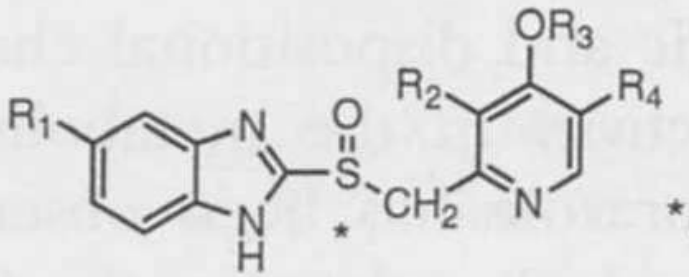
famotidine

Famotidine synthesis



Proton pump inhibitors

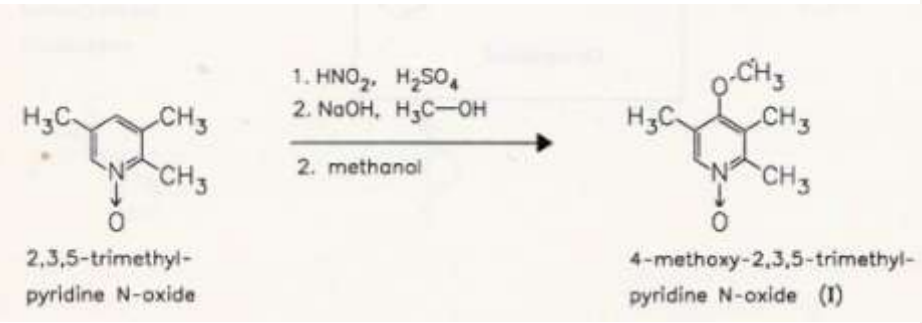
Table 33.10. H^+/K^+-ATPase Proton Pump Inhibitors

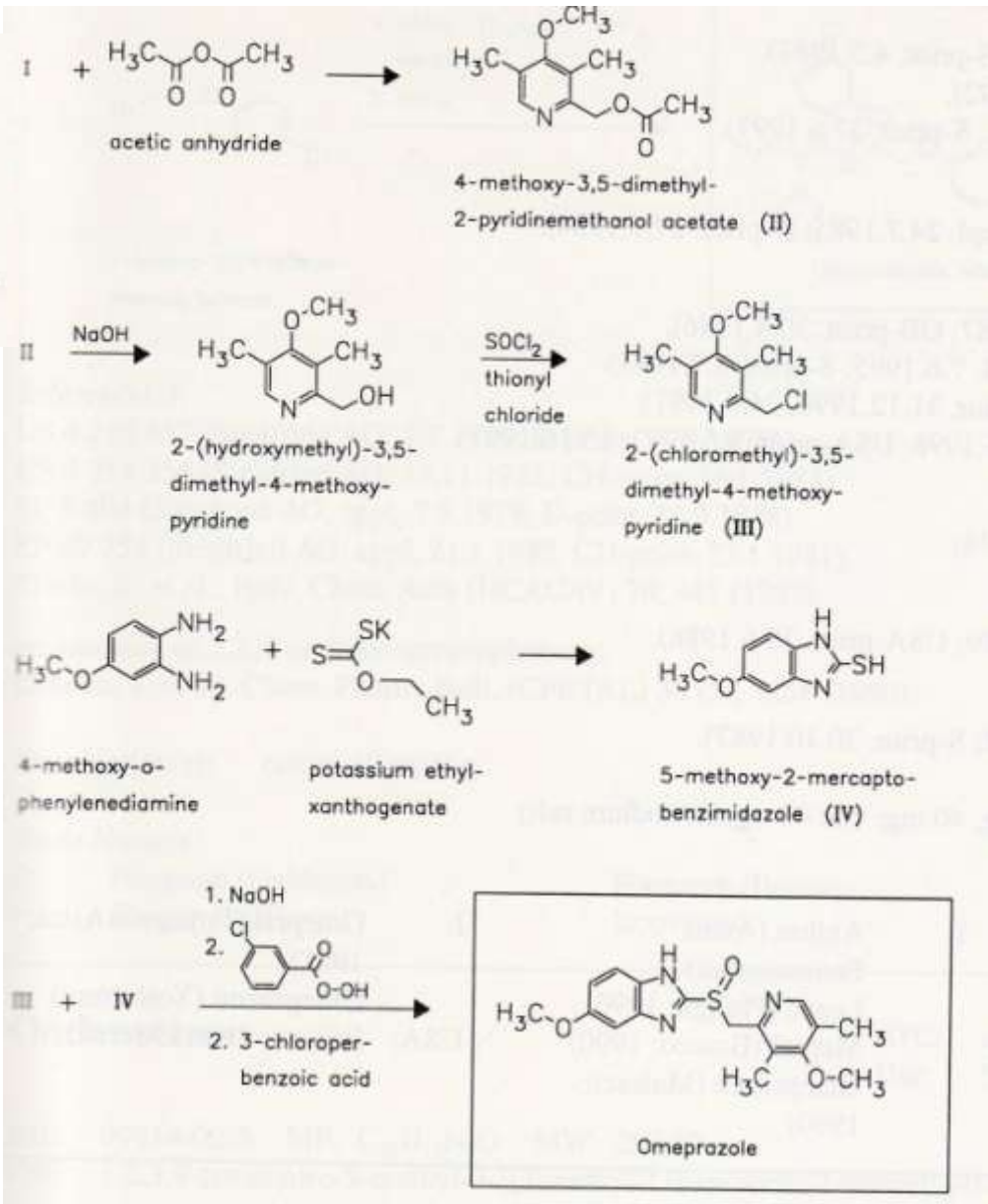


*chiral center

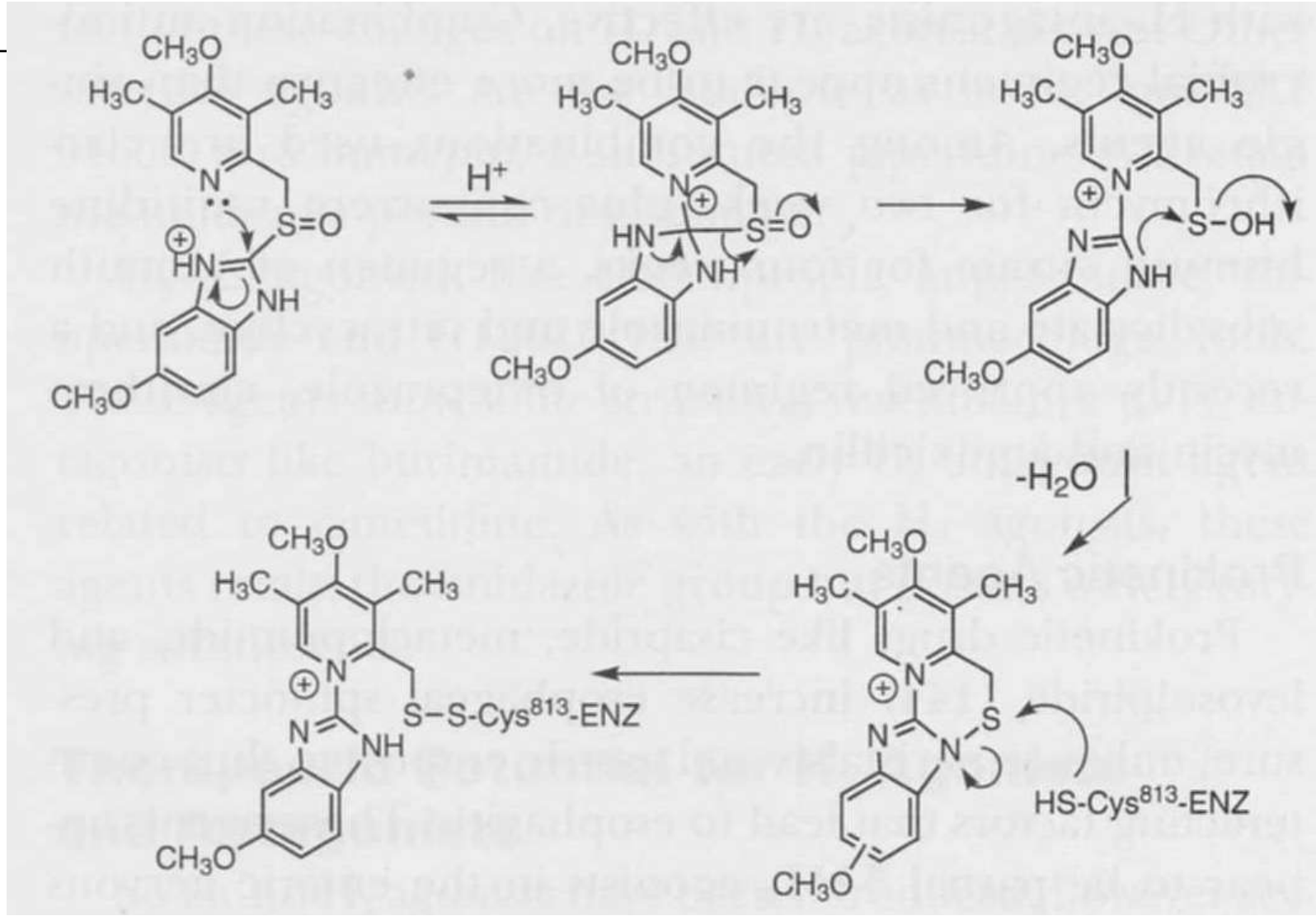
Drugs	Trade Name	R_1	R_2	R_3	R_4
Omeprazole	Prilosec	OCH_3	CH_3	CH_3	CH_3
Esomeprozole (S-enantiomer)	Nexium	OCH_3	CH_3	CH_3	CH_3
Lansoprazole	Prevacid	H	CH_3	CH_2CF_3	H
Rabeprazole	Aciphex	H	CH_3	$(CH_2)_3OCH_3$	H
Pantoprazole	Protonix	$OCHF_2$	OCH_3	CH_3	H

Omeprazole synthesis



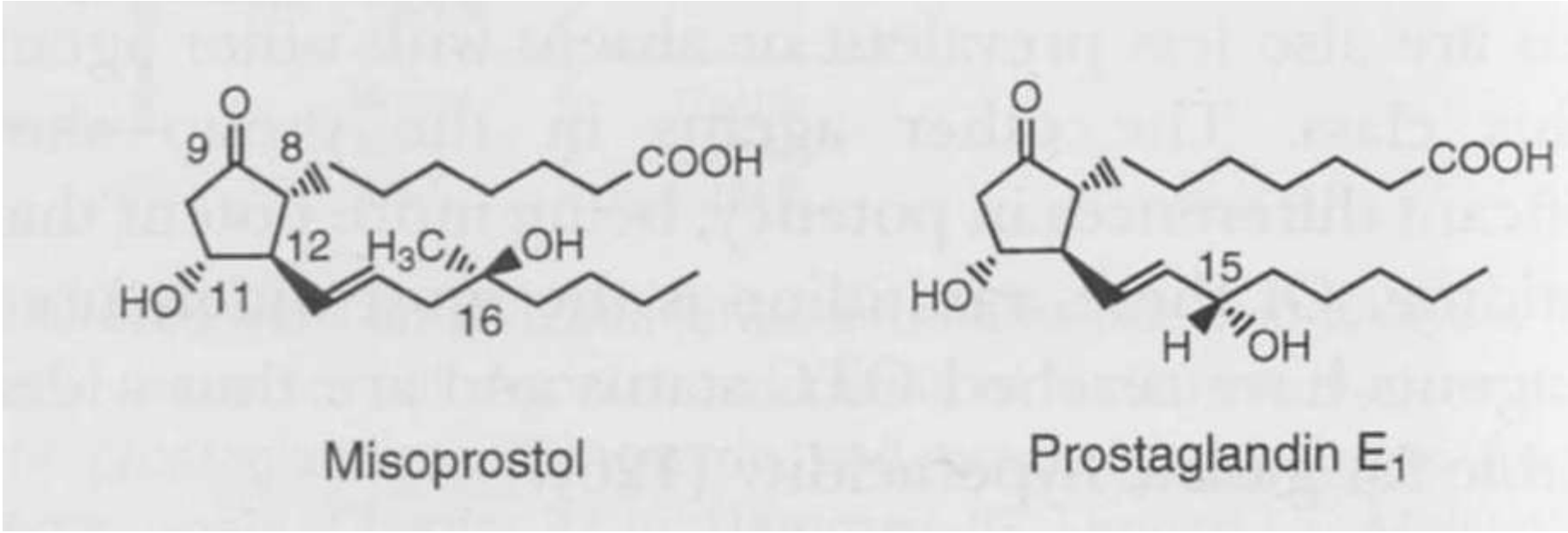


Mechanism of action



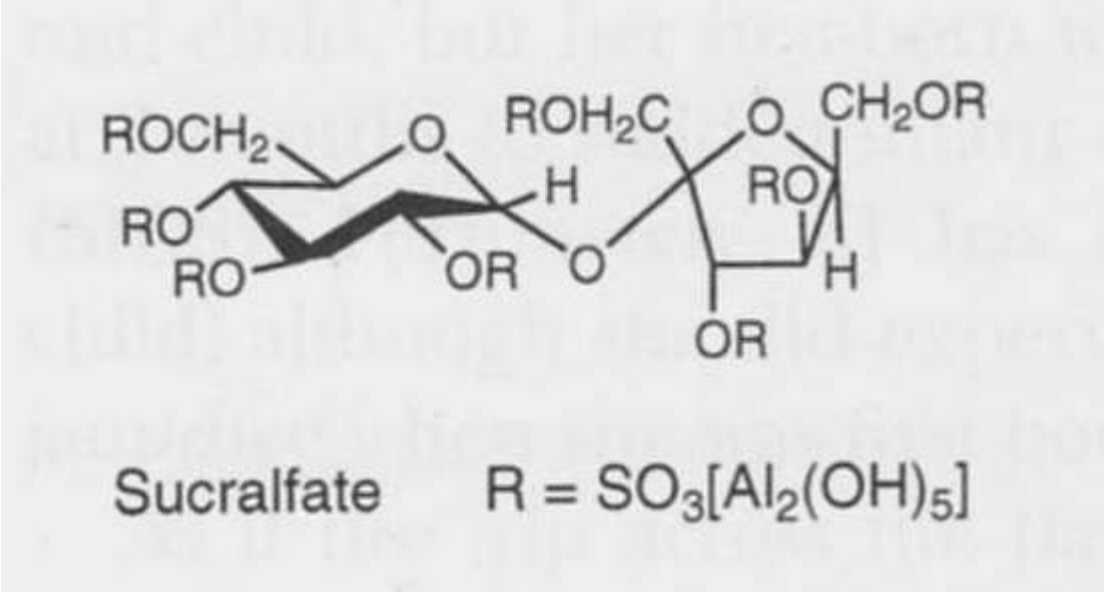
Mucoprotective agents

- misoprostol



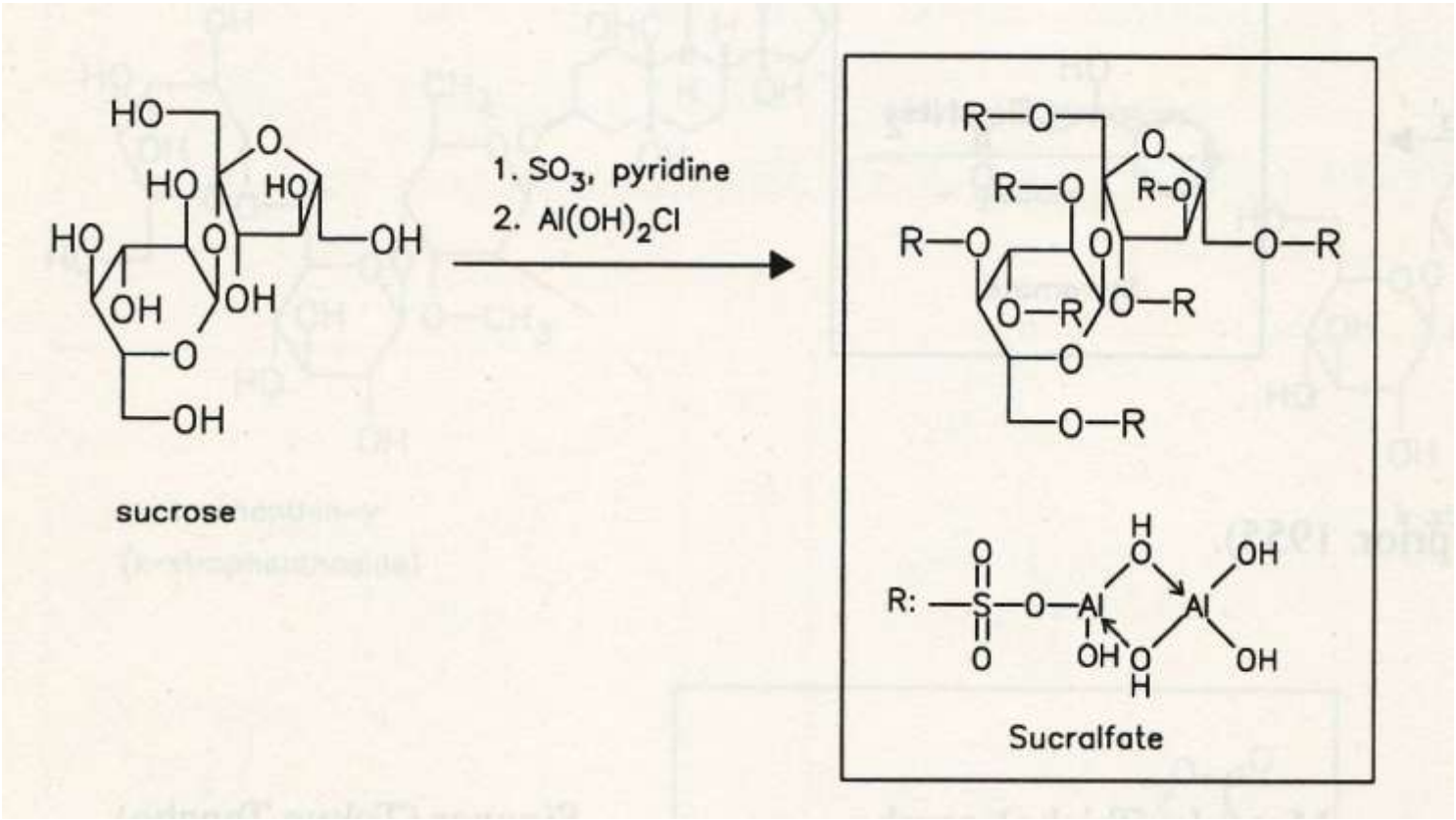
Mucoprotective agents

- alginic acid, pectines (natural drugs)
- sucralfate



Sucralfate R = $SO_3[Al_2(OH)_5]$

Sucralfate synthesis



Drugs for Helicobacter pylori eradication

- metronidazole
- azithromycine, clarithromycine
- amoxyciline
- tetracycline
- bismuth salts: subcitrate, subsalicylate