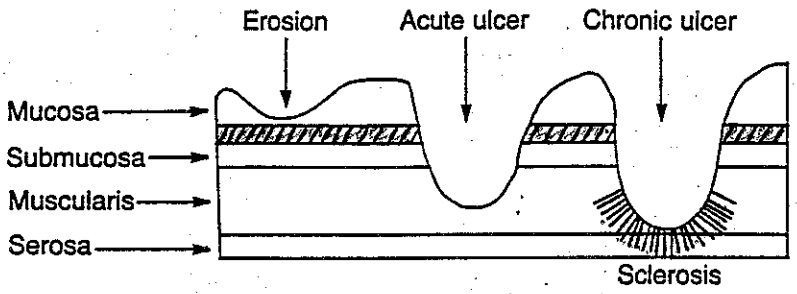


Figure 26.1 Morphologic distinction between erosions and acute and chronic ulcers. *(From Brook FP: Dig Dis Sci 1985;30(suppl): 15S–29S, with permission.)*

igure 26.2 Stimulants of acid secretion and sites of action of antiulcer drugs. H, histamine; ACh, cetylcholine; Antichol, anticholinergic; Gas, gastrin; Som, somatostatin; Gas-ant, gastrin antagonist. *(From Bertaccini G, Coruzzi G: Dig Dis Sci 1985;30(suppl):43S–51S, with permission.)*

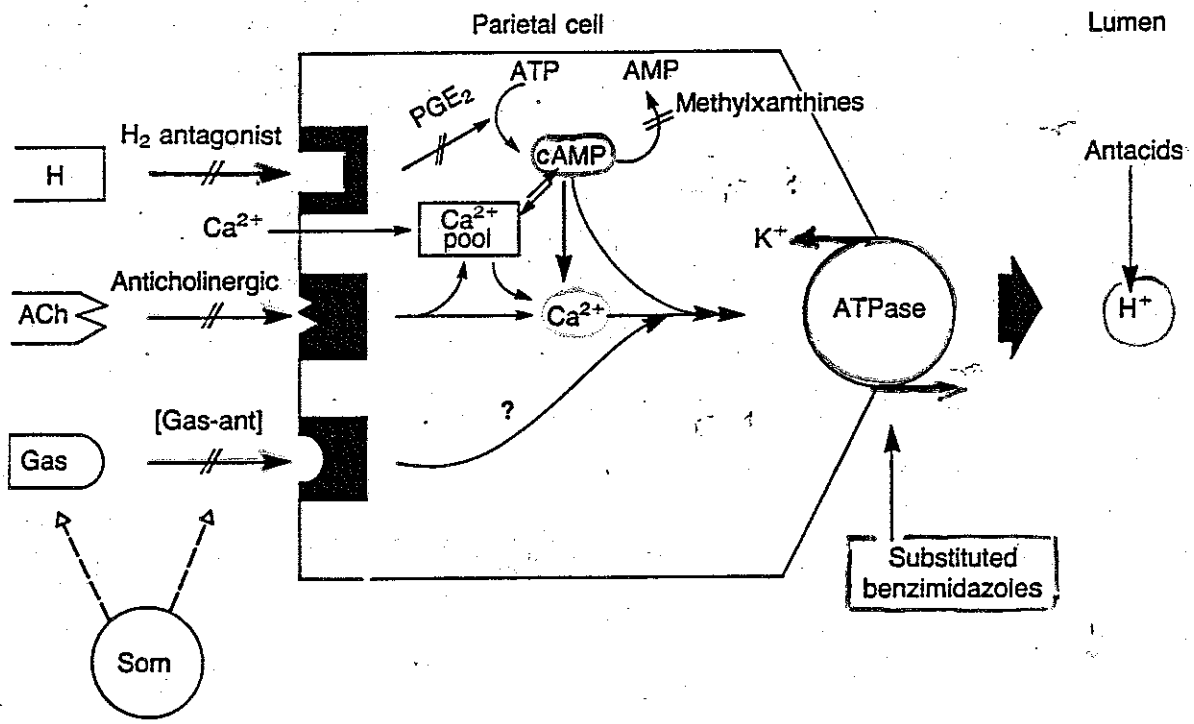


Table 26.2 Phases of Acid Secretion

Phase	*Stimulus*	*Total stimulation (%)*
Basal	Endogenous	15
Cephalic	Sight, smell, and taste of food, mediated by vagus nerve	30
Gastric	Food in stomach causes distension and stimulation of gastrin by amino acids	50
Intestinal	Digested food in jejunum	5

ACID SECRETION

Parietal cells secrete acid into the stomach lumen. This is achieved by a unique H^+/K^+ ATPase (proton pump) which catalyzes the exchange of intracellular H^+ for extracellular K^+. The secretion of HCl is stimulated by *acetylcholine* (ACh) released from vagal postganglionic fibres (right of figure) and *gastrin*, released into the bloodstream from G-cells in the antral mucosa when they detect amino acids and peptides (from food) in the stomach, and by gastric distension via local and long reflexes.

Although the parietal cells possess muscarinic (M_1) and gastrin receptors (G), both acetylcholine and gastrin mainly stimulate acid secretion indirectly, by releasing *histamine* from paracrine cells (right, □) located close to the parietal cells. Histamine then acts locally (⇦) on the parietal cells, where activation of histamine H_2-receptors (H_2) results in an increase in intracellular cAMP and the secretion of acid. Because acetylcholine and gastrin act indirectly by releasing histamine, the effects on acid secretion of both vagal stimulation and gastrin are reduced by H_2-receptor antagonists.

Cholinergic agonists can powerfully stimulate acid secretion in the presence of H_2-antagonists, indicating that ACh released from the vagus must have limited access to the parietal cell muscarinic receptors. Gastrin acting directly on the parietal cells has a weak effect on acid secretion, but this is greatly potentiated when the histamine receptors are activated.

TABLE 2. Association of Helicobacter pylori with Common Pathologic Lesions of the Upper Gastrointestinal Tract

Lesion	*Association with H. pylori*
Peptic esophagitis	No association[4]
Barrett's esophagus	May colonize distal-most gastric epithelium in patients with gastric colonization[5]
	No association[70]
Chronic diffuse superficial gastritis	Nearly always associated[5,22]
Type A (pernicious anemia) gastritis	Negative association[71]
NSAID gastropathy	Negative or no association[72]
Acute erosive gastritis (alcohol, aspirin, etc.)	No association[5]
Gastric ulceration	Nearly universally observed in patients who are not ingesting NSAIDs or aspirin[70]
Duodenal ulceration	Nearly universally associated with "idiopathic" lesions (non-drug-induced, non-Zollinger-Ellison syndrome)[70,73,74]
Gastric adenocarcinoma	Associated with cancers of the body and antrum but not of the cardia[75–77]
Gastric lymphoma	Strongly associated with MALT-type B-cell lymphomas[78,79]

Abbreviations: NSAID, nonsteroidal anti-inflammatory drug; MALT, mucosal-associated lymphoid tumors.

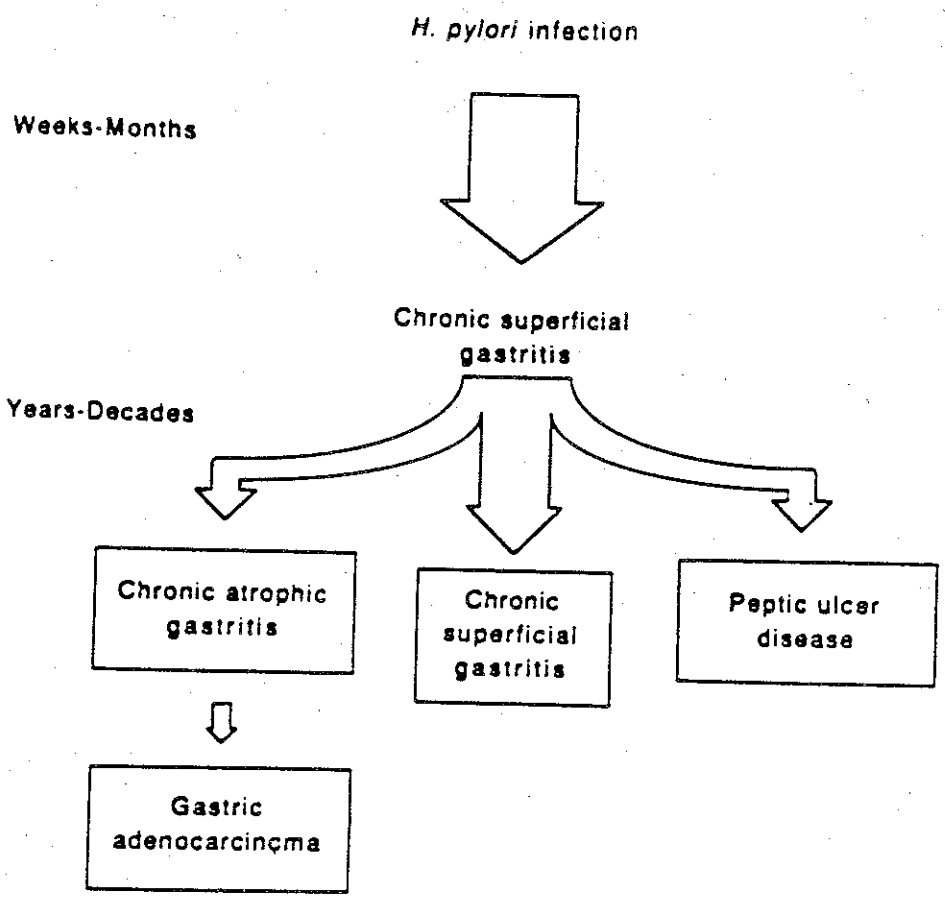


FIG. 2. Natural history of *H. pylori* infection. Virtually all infected persons develop persistent infection.

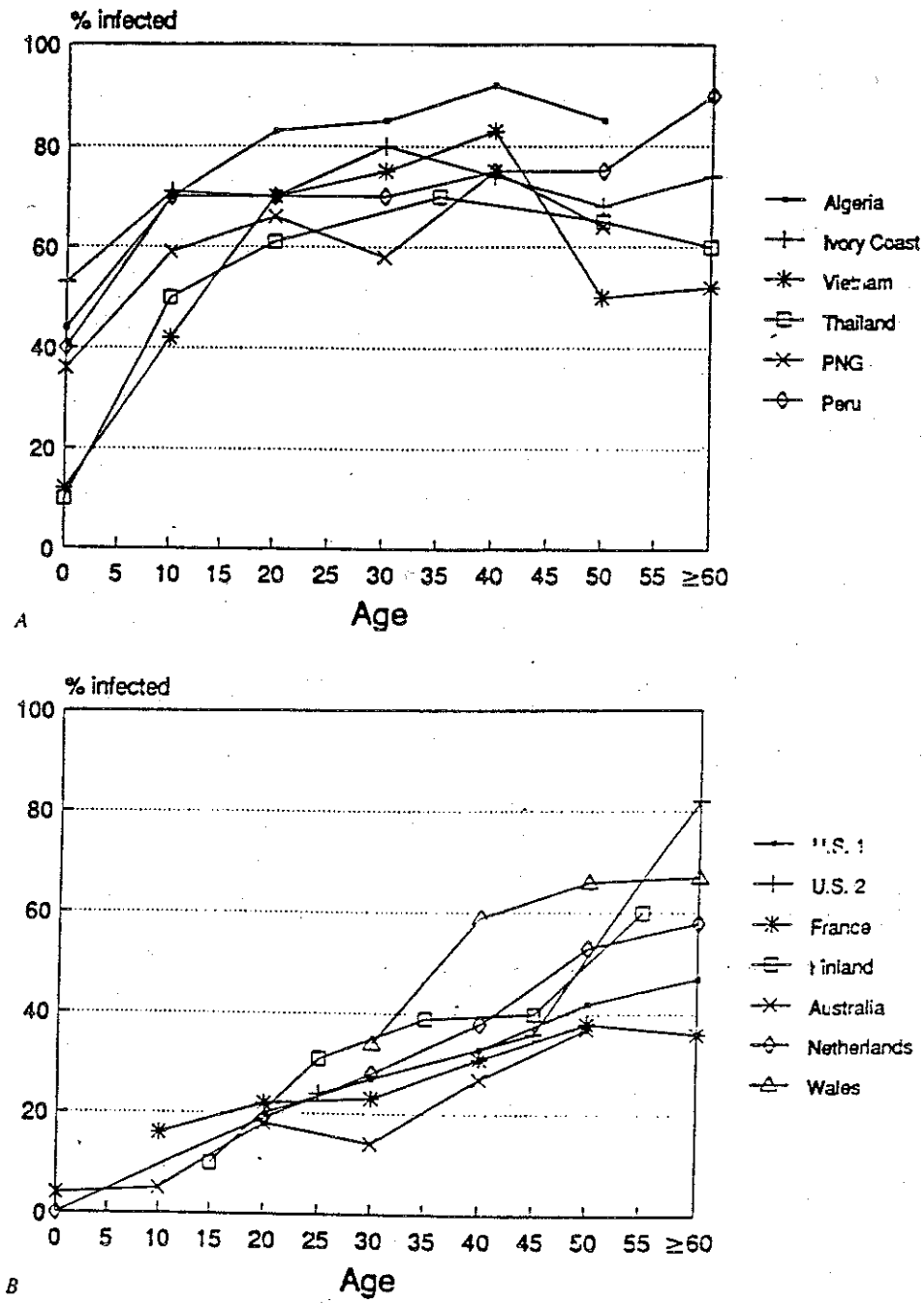


FIG. 1. Seroprevalence of *H. pylori* infection among healthy persons (**A**) in populations in developing countries and (**B**) in developed countries. *Helicobacter pylori* infection is acquired earlier and is more common at all ages in developing countries compared with developed countries. (From Taylor and Blaser,[16] with permission).

ANTIBACTERIAL TREATMENT OF GASTRIC ULCERS ASSOCIATED WITH *HELICOBACTER PYLORI*

JOSEPH J.Y. SUNG, M.D., S.C. SYDNEY CHUNG, M.D., THOMAS K.W. LING, PH.D., MAN YEE YUNG, B.N., VINCENT K.S. LEUNG, M.D., ENDERS K.W. NG, M.D., MICHAEL K.K. LI, M.D., AUGUSTINE F.B. CHENG, M.D., AND ARTHUR K.C. LI, M.D.

Abstract *Background.* There is a strong association between infection with *Helicobacter pylori* and gastric ulcers that are unrelated to the use of nonsteroidal antiinflammatory medications. We studied the efficacy of antibacterial therapy without medication to suppress gastric acid for the treatment of patients with *H. pylori* infection and gastric ulcers unrelated to the use of nonsteroidal agents.

Methods. Patients with gastric ulcers seen on endoscopy and with *H. pylori* infection confirmed by smear or culture were randomly assigned to receive either a one-week course of antibacterial agents (120 mg of bismuth subcitrate, 500 mg of tetracycline, and 400 mg of metronidazole, each given orally four times a day) or a four-week course of omeprazole (20 mg orally per day). Follow-up endoscopies were performed after five and nine weeks. The patients and their physicians were aware of the treatment assignments, but the endoscopists were not.

Results. A total of 100 patients were randomly assigned to treatment, and 85 completed the trial. At five weeks, *H. pylori* had been eradicated in 41 of the 45 patients in the antibacterial-treatment group (91.1 percent; 95 percent confidence interval, 82.9 to 99.3) and in 5 of the 40 in the omeprazole group (12.5 percent; 95 percent confidence interval, 2.3 to 22.7; P<0.001). The gastric ulcers were healed in 38 of the patients treated with antibacterial drugs (84.4 percent; 95 percent confidence interval, 73.9 to 95.0) and in 29 of those treated with omeprazole (72.5 percent; 95 percent confidence interval, 58.6 to 86.4; P=0.28). At nine weeks, ulcer healing was confirmed in 43 of the patients receiving antibacterial therapy and in 37 of those receiving omeprazole (P=1.0). The mean (±SD) duration of pain during the first week of treatment was 1.9±2.6 days in the omeprazole group, as compared with 3.6±3.0 days in the antibacterial-treatment group (P=0.004). One year after treatment, recurrent gastric ulcers were detected in 1 of 22 patients (4.5 percent) in the antibacterial-treatment group and in 12 of 23 (52.2 percent) in the omeprazole group (P=0.001). *H. pylori* was detected in the 1 patient with a recurrent ulcer who had received antibacterial treatment and in 10 of the 12 patients with recurrent ulcers who had received omeprazole.

Conclusions. In patients with *H. pylori* infection and gastric ulcers unrelated to the use of nonsteroidal antiinflammatory drugs, one week of antibacterial therapy without acid suppression heals the ulcers as well as omeprazole and reduces the rate of their recurrence. (N Engl J Med 1995;332:139-42.)

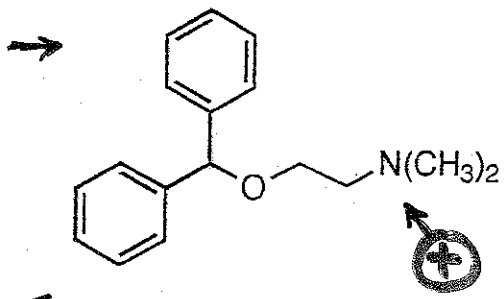
Traitement actuel

- Amoxicilline
- Clarithromycine
- metronidazole

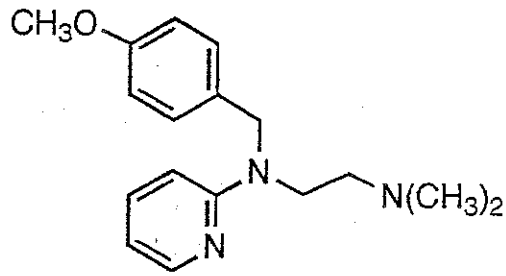
+/- sous-nitrate de bismuth

Récepteurs de l'histamine

Antagoniste H_1

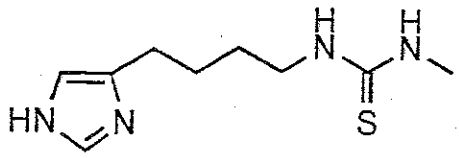


Diphenhydramine



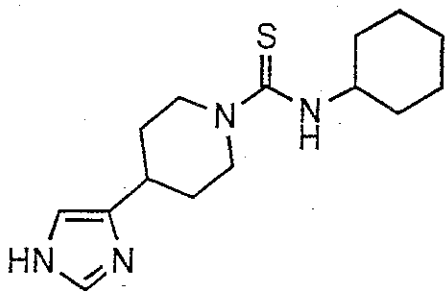
Mepyramine

Antagoniste H_2

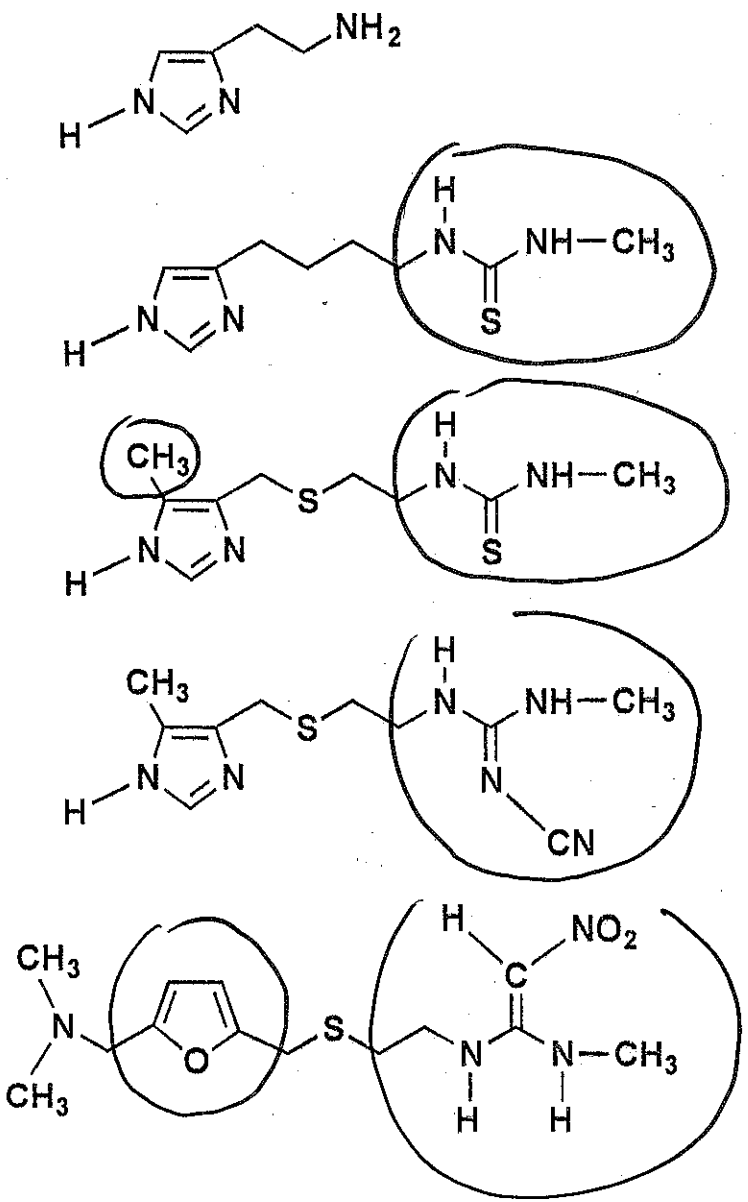


Burimamide

Antagoniste H_3



Thioperamide



histamine

H_1 + H_2

↓

burimamide

H_2-selective (thiourée)

↓

metiamide

10 x more active
side effects !

↓

cimetidine

same activity
side effects ↓↓ cyanoimines

↓

ranitidine

activtity ↑
side effects ↓

- diamines nitro ether
- furane

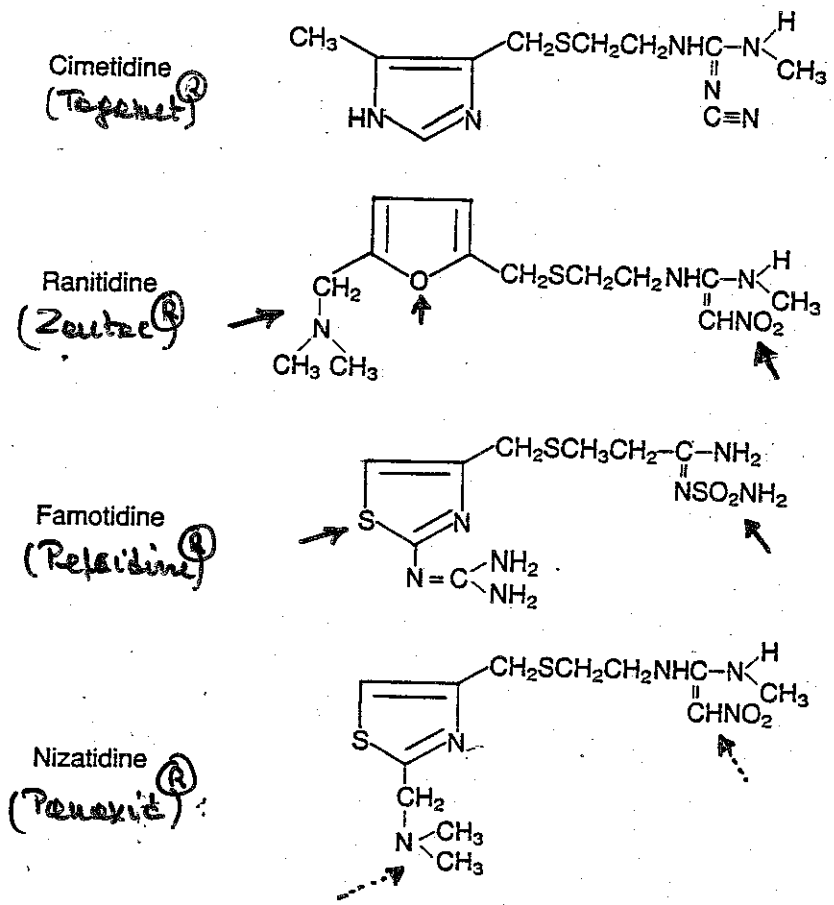


Figure 26.4 Chemical structures of the H_2-receptor antagonists.

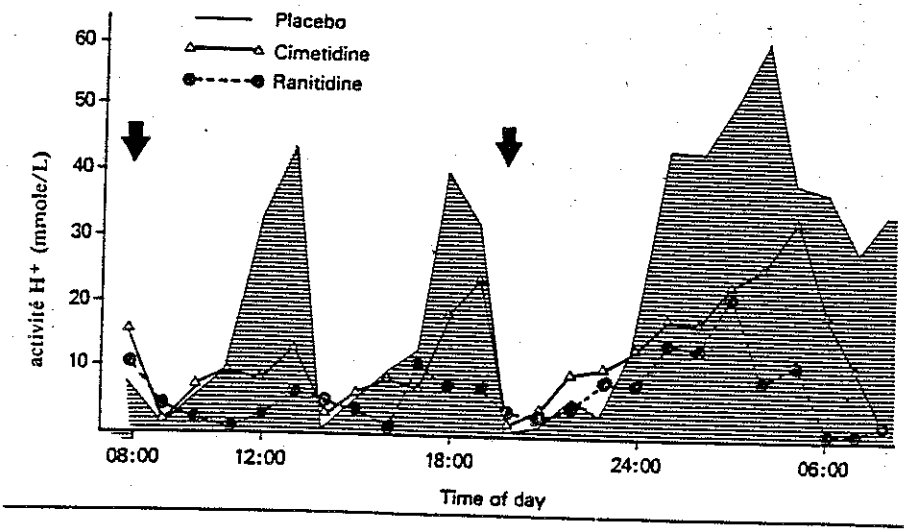
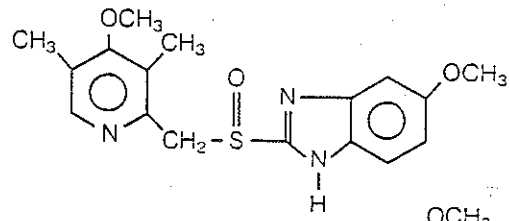


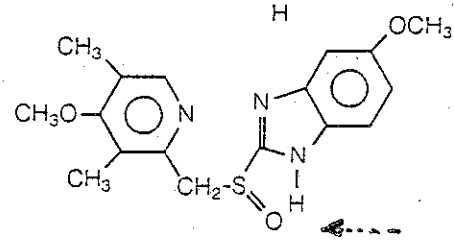
Figure 2. Effet de la ranitidine (150 mg/2 fois par jour) et de la cimétidine (400 mg/2 fois par jour) sur l'activité H^+ mesurée pendant 24 h.

D'après Damman, H.G. *et al.* (1984). «Effects of histamine H_2 receptor antagonists and other agents on intragastric acidity and acid secretion». *In: Ranitidine therapeutic advances*, edited by J.J. Misiewicz and J.R. Wood, Excerpta Medica, Amsterdam, 126-139. Reproduction de la Figure 5 avec l'autorisation de Excerpta Medica, Amsterdam.

Omeprazole
(schematic chemical
structure)

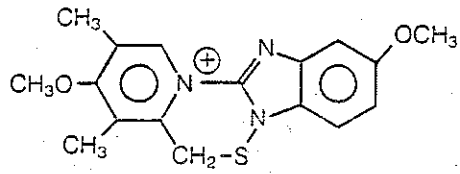


Omeprazole
(sterically adjusted
chemical structure)



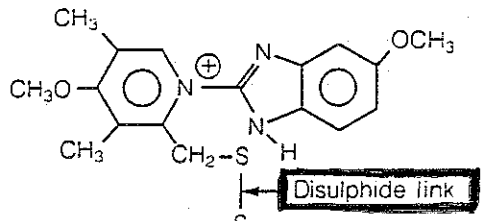
Step 1
(H^+)

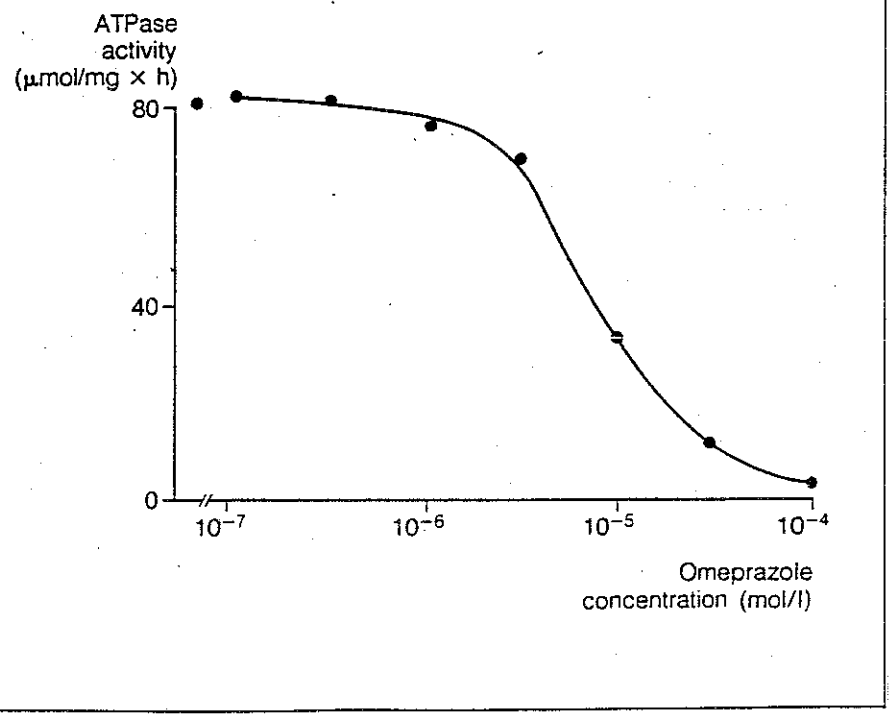
Active inhibitor
(sulphenamide)



Step 2
(Enzyme - SH)

Enzyme - inhibitor complex





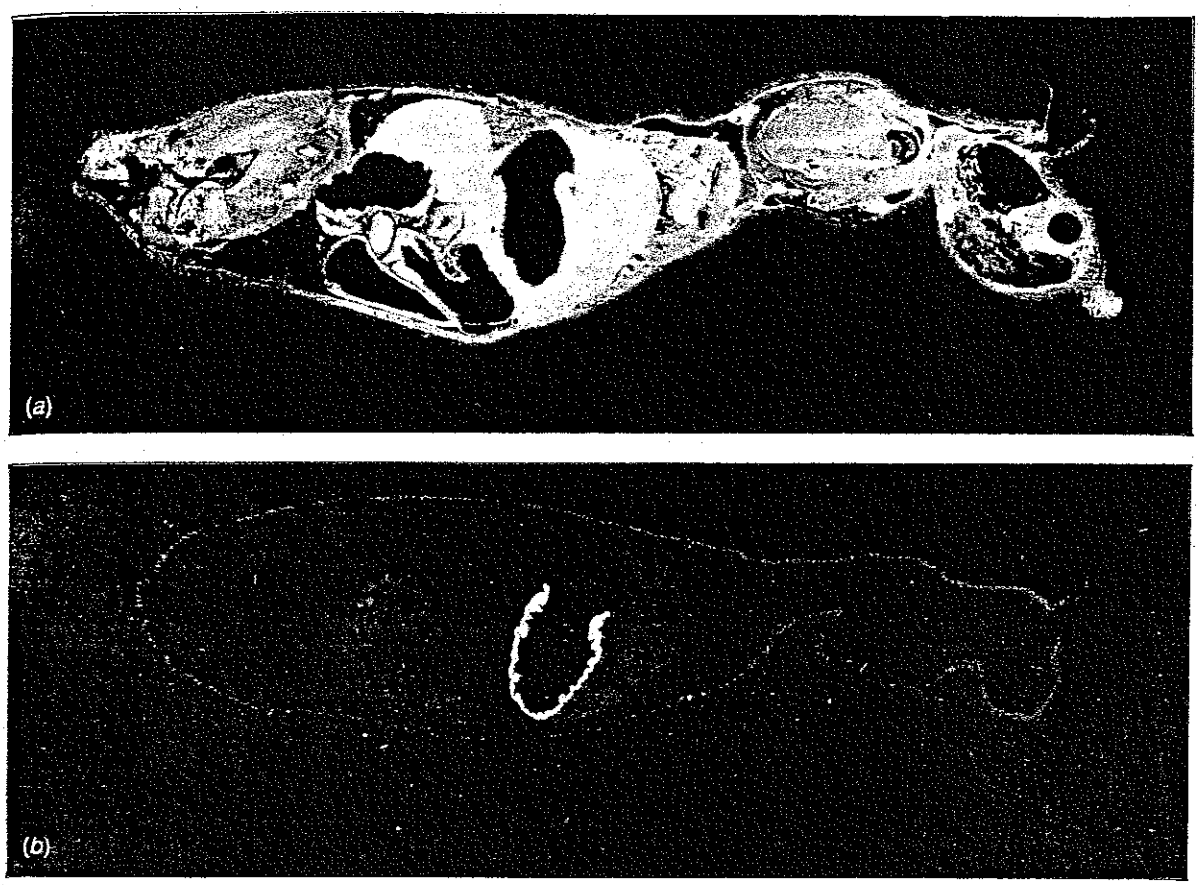


Figure 12
(a) One minute after i.v. injection in the mouse, radiolabelled omeprazole (light areas) is found mainly in the stomach, liver, kidneys and lungs[20].
(b) Sixteen hours after i.v. injection, high levels of radiolabelled omeprazole (acid-activated form) are found only in the stomach[20].

ıre 11 The uncoated ulation of omeprazole pidly absorbed in the (mean ± SEM)[10].

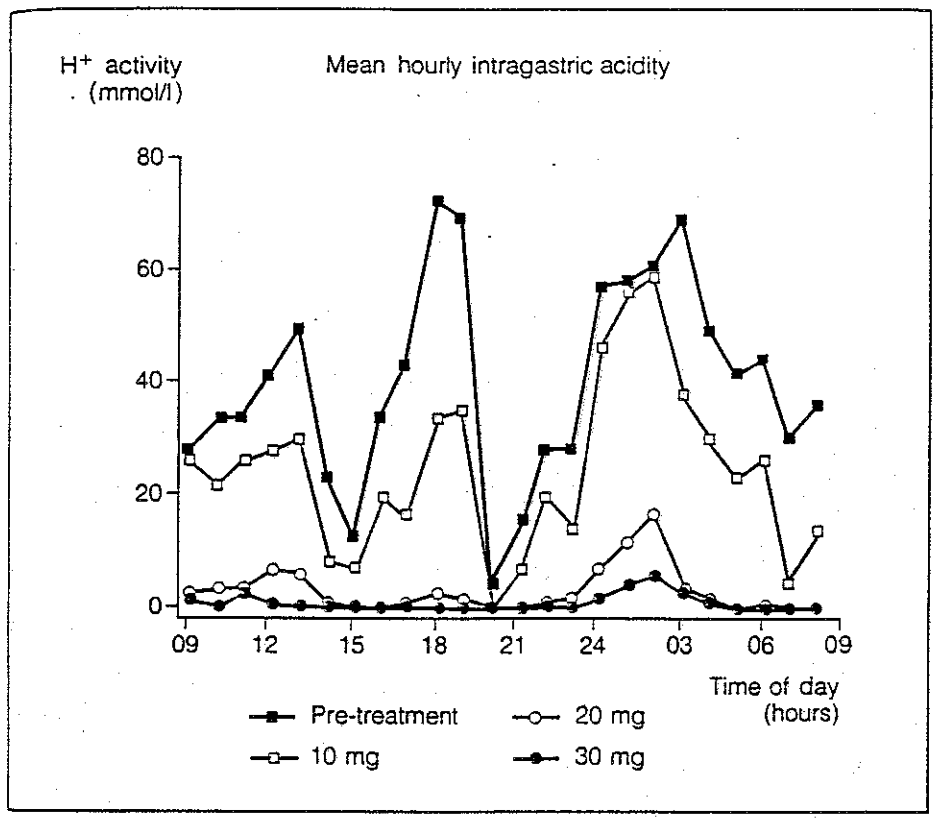


Figure 26 Omeprazole. 20 mg once daily, effectively controls 24-hour intragastric acidity. Graph shows the mean decrease of 24-hour intragastric acidity after 7 days of omeprazole 10 mg, 20 mg or 30 mg once daily in 6 patients with duodenal ulcer in remission[53].

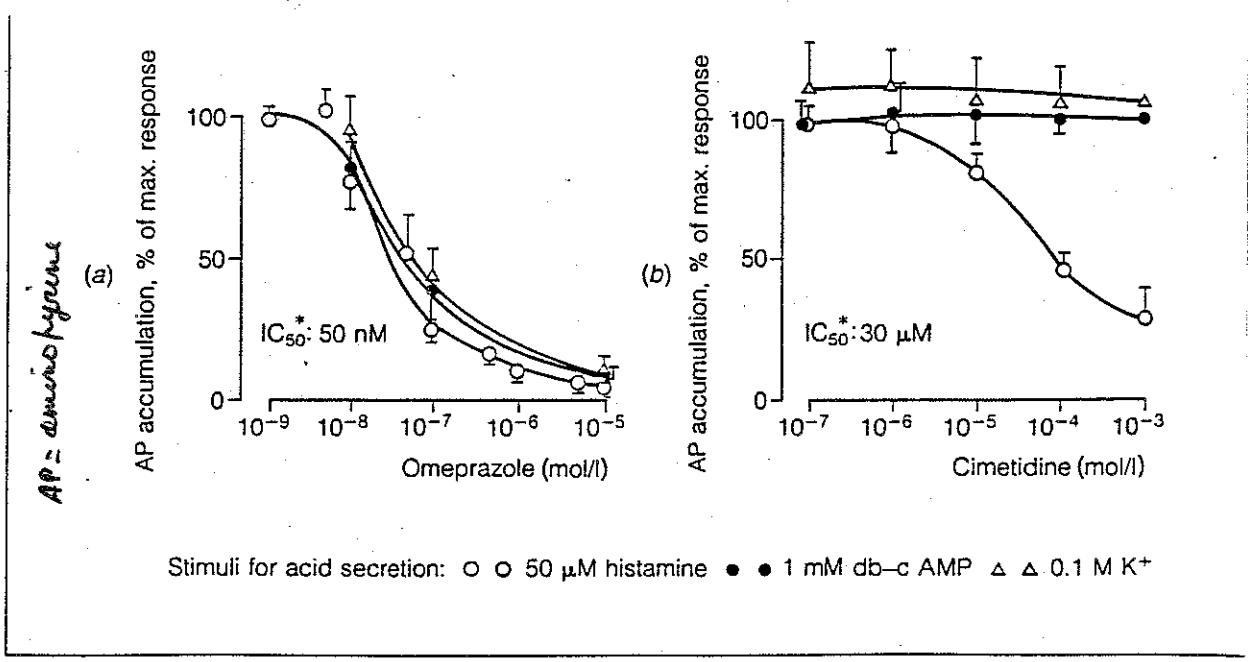
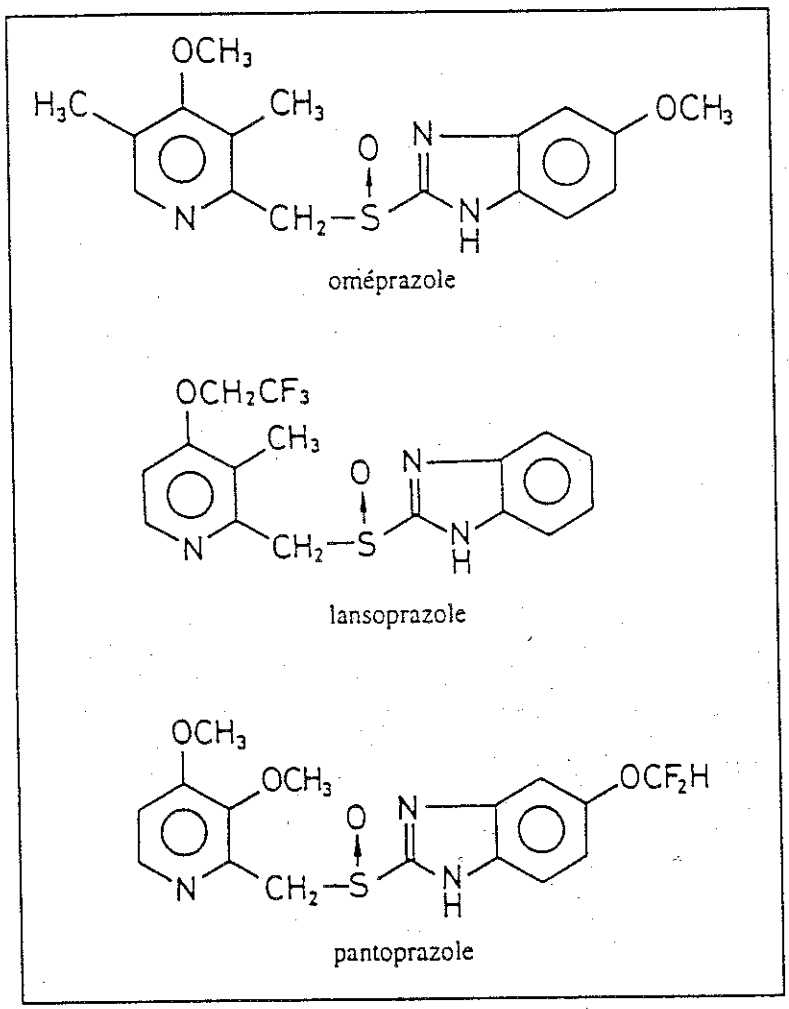


Figure 3. Structures chimiques des IPP



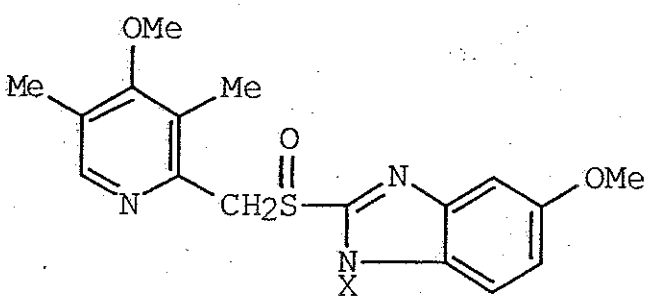
en 2001....

Esomeprazole

Process for the preparation of optically pure crystalline salts of omeprazole. Lindberg, Per Lennart; Von Unge, Sverker. (Astra AB, Swed.). PCT Int. Appl. (1994), 30 pp. CODEN: PIXXD2 WO 9427988 A1 19941208 Designated States W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, \ Designated States RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, ML, MR, NE, SN, TD, TG.

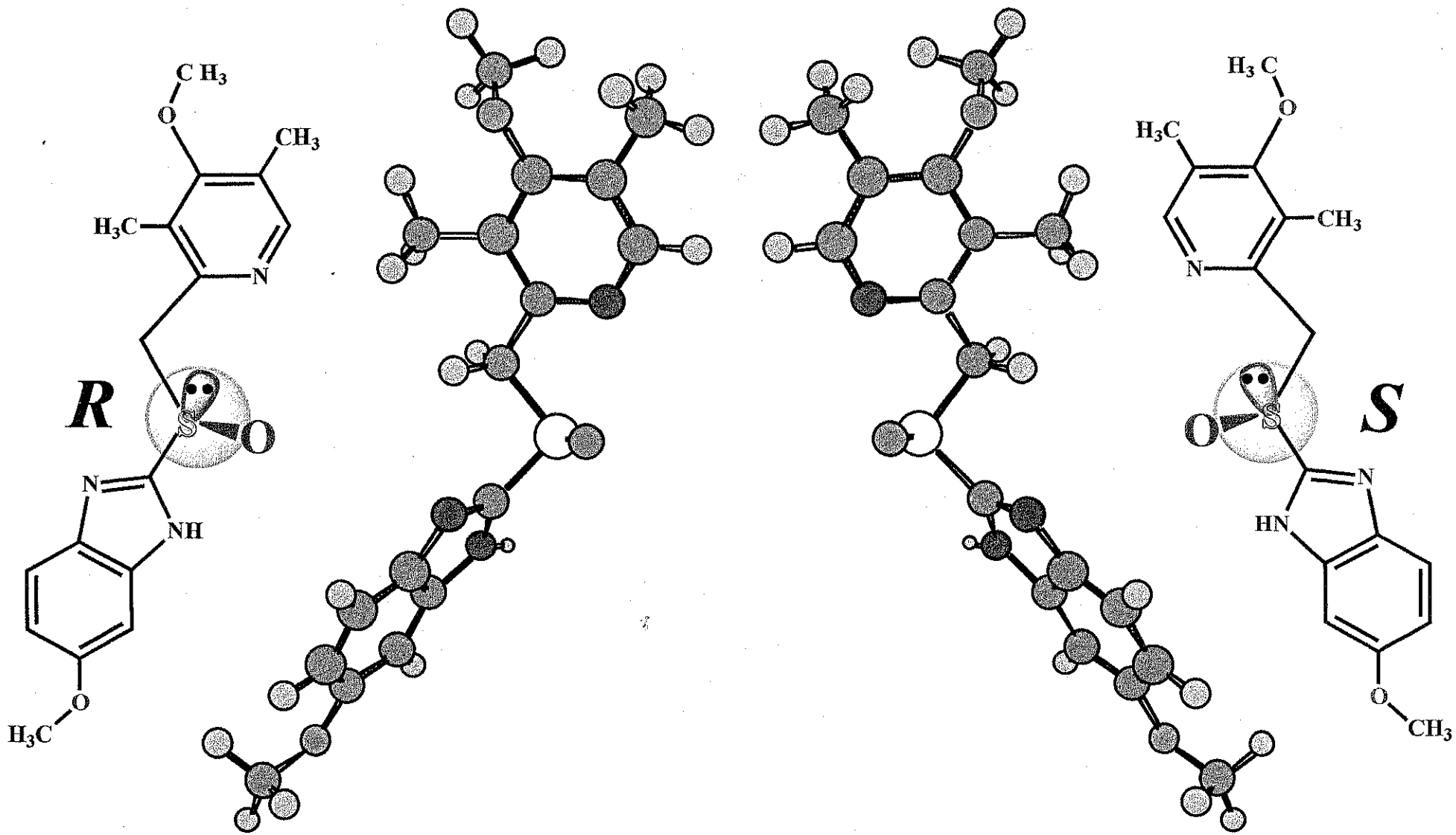
Abstract

Optically pure Na+, Mg2+, Li+, K+, Ca2+, and quaternary alkylammonium salts of (+)-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole or (-)-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole ulcer inhibitors are prepd. from diastereomeric derivs. (I; X = chiral acyloxymethyls) which are sepd. by chromatog. or fractional crystn. and dissolved in an alk. soln. of a protic solvent (e.g., alcs., H2O) or with a base (e.g., NaOH) in an aprotic solvent (e.g., DMF, DMSO). Formulations contg. the chiral omeprazole salts are presented.



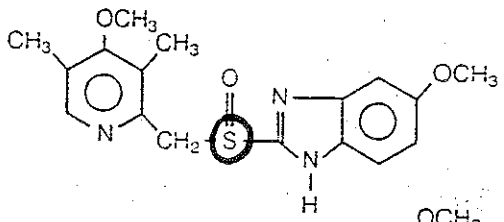
I

- quel est l'atome chiral ?
- l'est-il encore après formation des sulfénamides ?



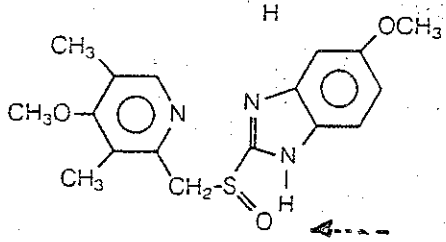
PrPVB

Omeprazole
(schematic chemical
structure)



O = atome chiral

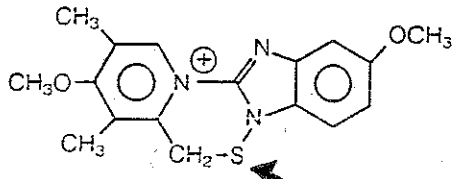
Omeprazole
(sterically adjusted
chemical structure)



Step 1
(H^+)

à pH acide

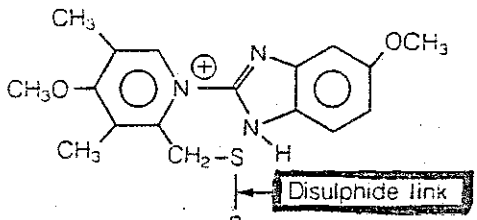
Active inhibitor
(sulphenamide)

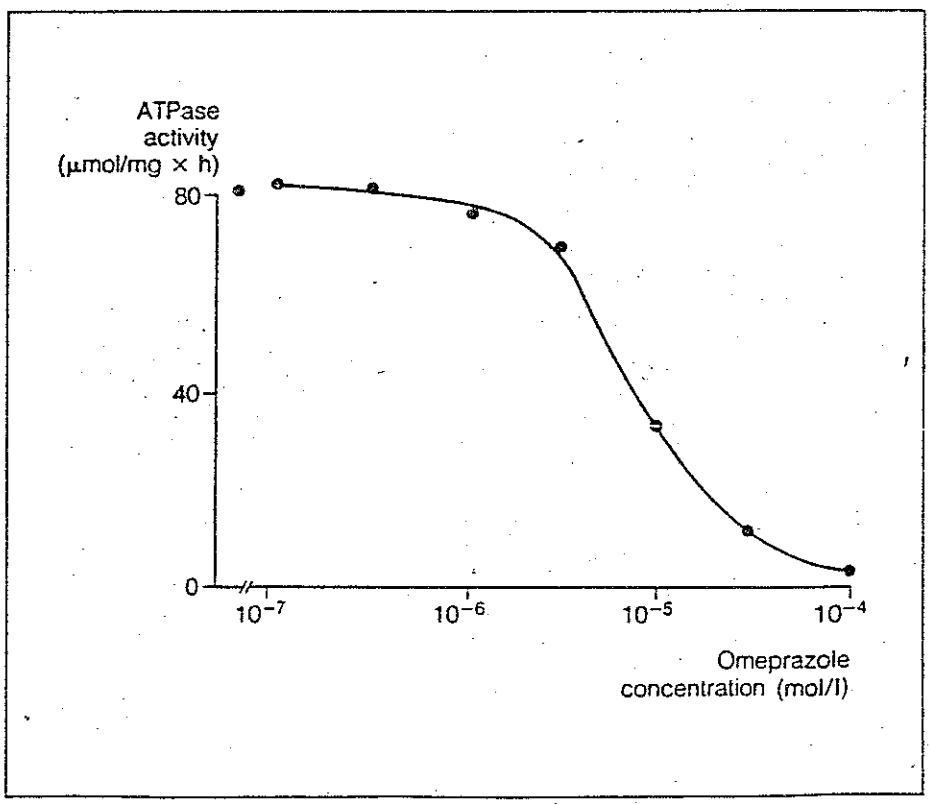


Step 2
(Enzyme - SH)

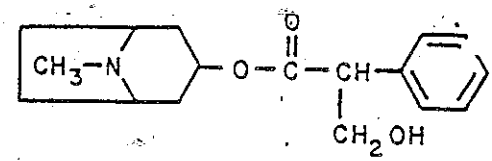
ceci n'est plus chiral

Enzyme - inhibitor complex

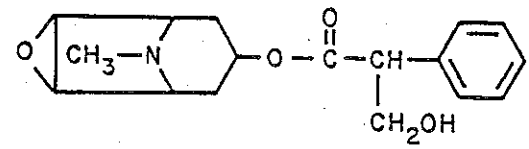




Alcaloïdes naturels

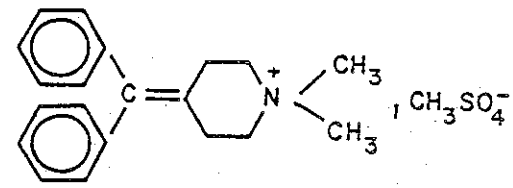


Atropine

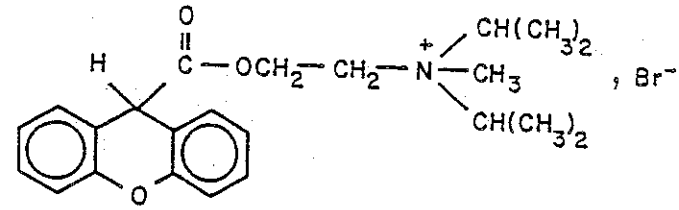


Scopolamine

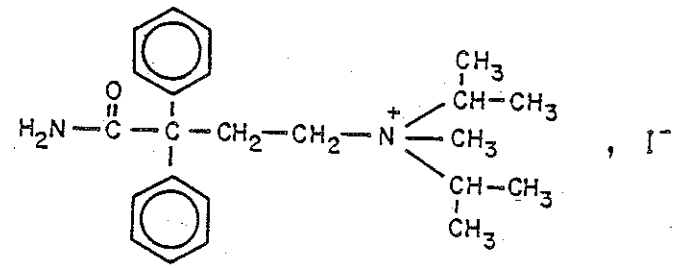
Dérivés ammoniums quaternaires



diphémanil méthylsulfate
(Prantal)



propanthéline bromure



isopropamide iodure
(Priamide)

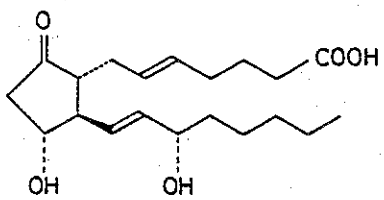
Fig. 4. Structure des principaux anticholinergiques antisécrétoires.

Tableau 1: Choix des cytoprotecteurs

Principes actifs (DCI)*	Spécialités (B, CH, F)	Formes galéniques	Doses journalières
sous-nitrate de bismuth[1]	Bismuth Tulasne (CH)	sachet 6.5 g	20 g
sous-citrate de bismuth[1]	De-Nol (B)	compr. 120 mg	600 mg
	Duosol (CH)	compr. 120 mg	600 mg
sucralfate*	Ulcar (F)	compr. 1 g	4 g
	Ulcogant (B, CH)	compr. 1 g sachet 1 g	4 g
misoprostol*	Cytotec (B, CH, F)	compr. 200 µg	800 µg

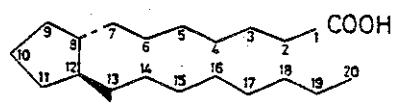
[1] A l'exclusion des associations contenant plus de deux principes actifs.

Figure 1. Structures chimiques, nomenclature ou DCI des cytoprotecteurs



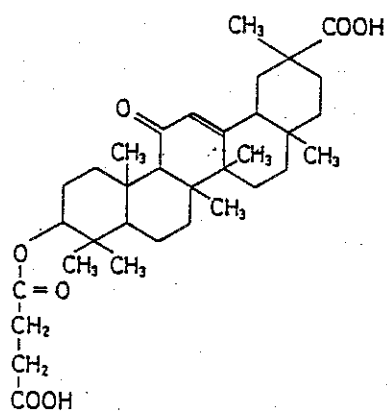
prostaglandine E_2 (dinoprostone)
(double liaison en C_{5-6} et C_{13-14})

Dérivés de la PGE_2
— déhydro (=C_5=) (enprostil)
— méthylé (C_{15}) (arbaprostil)
— méthylé (C_{16}) (trimoprostil)

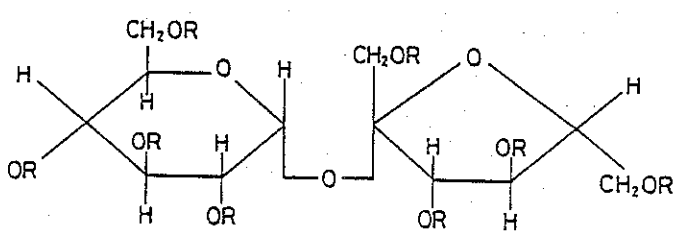


acide prostanoïque (virtuel)
(cf. Figure 3, ch. 36, pour les structures et nomenclatures des prostanoïdes en général)

Dérivés de la PGE_1 (1 seule double liaison en C_{13-14})
— méthylé (C_{15}), estérifié (OCH_3 en C_1) (misoprostol)
— méthylé (C_{15}) (rioprostil)



carbénoxolone



sucralfate

PROTECTIVE FACTORS

Mucus layer. This forms a physical barrier (approximately 500 μm thick) on the surface of the stomach and proximal duodenum, and consists of a mucus gel into which HCO_3^- is secreted. Within the gel matrix the HCO_3^- neutralizes acid diffusing from the lumen. This creates a pH gradient and the gastric mucosa is maintained at a neutral pH, even when the stomach contents are at pH 2. Prostaglandins E_2 and I_2 are synthesized by the gastric mucosa, where they are thought to exert a cytoprotective action by stimulating the secretion of mucus and bicarbonate, and by increasing the mucosal blood flow.

Mucosal strengtheners

Sucralfate is a complex substance formed from sulphated sucrose and aluminium hydroxide. The molecules polymerize below pH 4 to give a very sticky gel which adheres strongly to the base of ulcer craters. The gel presumably protects the ulcerated area by allowing the development of the normal pH gradient caused by the secretion of HCO_3^-. Sucralfate is about as effective as cimetidine in promoting ulcer healing and has very few side-effects.

Bismuth chelate may act in a similar way to sucralfate. It has a strong affinity for mucosal glycoproteins, especially in the necrotic tissue of the ulcer craters, which become coated in a protective layer of polymer–glycoprotein complex. However, bismuth salts eradicate the organism *Helicobacter pylori* and it may be this action which is responsible for ulcer healing. Bismuth may blacken the teeth and stools. Bismuth and sucralfate must be given on an empty stomach or they will complex with food proteins.

Misoprostol is a synthetic analogue of prostaglandin E_1. It promotes healing of peptic ulcers but side-effects, especially diarrhoea, make it unsuitable for this purpose. It seems that the beneficial effects of prostaglandin analogues are due to the decrease in acid secretion that they cause, rather than by any cytoprotective action they may have.

Figure 26.3 Mean gastric pH after a meal with or without antacid given 1 and 3 hours after meals. *(From Sleisenger MH, Fordtran JS (Eds): Gastrointestinal Diseases: Pathophysiology, Diagnosis, Management. Philadelphia, W.B. Saunders, 1983, p717 with permission.)*

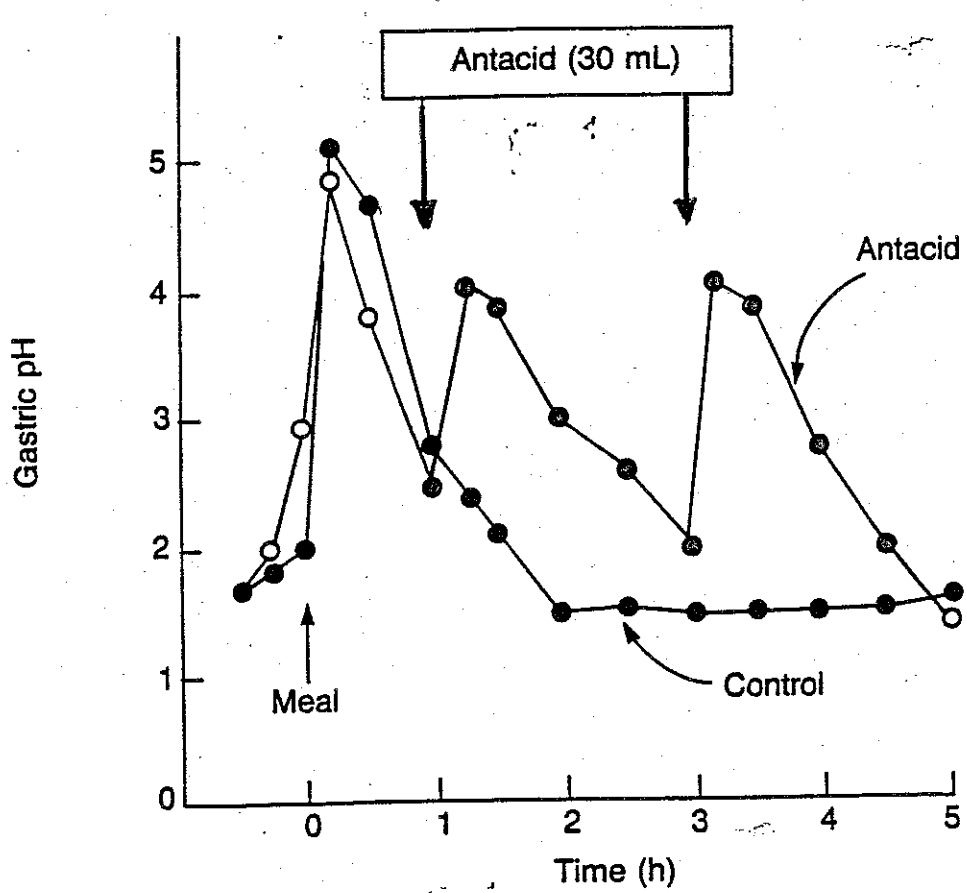


Tableau I: Anti-acides: choix thérapeutique et caractéristiques du mode d'action (capacité anti-acide)

Spécialités (B, CH, F)	Composition en anti-acides en principe indiquée pour la première forme galénique présentée (particularités)	Formes galéniques	Mécanisme		Capacité anti-acides mmol H^+ neutralisées par unité thérapeutique				Cinétique de libération de l'activité anti-acides: % activité anti-acide libérée à 30 min			
			neutralisation (jusqu'à pH)	pouvoir tampon (pH)	pH 3	pH 2	pH 1,5	pH 1	pH 3	pH 2	pH 1,5	pH 1
Alucol (CH)	hydroxyde d'Al hydroxyde de Mg	comprimés, gel										
Alucid (B)	bicarbonate de Na carbonate de Ca dihydroxyaminoacétate d'Al trisilicate de Mg	comprimés										
Andursil (CH)	hydroxyde d'Al carbonate de Mg	comprimés, suspension										
Camalox (CH)	hydroxyde d'Al hydroxyde de Mg carbonate de Ca	comprimés, suspension										
Contracid (F)	hydroxyde de Mg trisilicate de Mg	suspension	2	1,8-1,3	3,4	8,2	17,0	20,4	90	69	93	95
Dops (B, F)	bicarbonate de Na carbonate de Ca hydroxyde de Mg phosphate tricalcique	poudre	6	5,5	32	32	33	39	99	99	100	100
(F)	+ carbonate de Mg	comprimés	6	5,5-4,5	18,0	18,5	20,1	23,8	85	82	82	95
Combacid-Gel (CH)	hydroxyde d'Al carbonate de Mg	suspension										
faible → Gastric Vichy (B, F)	hydroxyde d'Al 187 mg carbonate de Mg 93 mg trisilicate de Mg 233 mg	comprimés	2	1,8-1,3	2,7	5,3	8,1	10,0	70	80	85	90
Gaviscon (B, CH, F)	acide alginique bicarbonate de Na hydroxyde d'Al (gel protecteur)	comprimés, granulé (F), poudre (B)										
	alginate de Na bicarbonate de Na hydroxyde d'Al carbonate de Ca (gel protecteur)	suspension										
élevé → Gelox (F)	hydroxyde d'Al hydroxyde de Mg montmorillonite beidellitique (pansement anti-acide)	suspension	3,5	3,5-3,2	29,7	36,1	39,8	41,8	95	95	95	95
Gelusil (B, CH, F) (CH)	trisilicate de Mg gel d'hydrate d'Al (algeldrate)	comprimés, suspension										
élevé → Maalox (B, F) Maaloxan (CH)	hydroxyde de Mg 400 mg hydroxyde d'Al 400 mg	comprimés, suspension	2	1,8	11,0	17,4	25,3	44,1	71	75	88	92
Mutésa (F) Muthesa (B, CH)	oxyde d'Al et de Mg	suspension, comprimés										
Phosphalugel (B, CH, F)	phosphate d'Al (pansement anti-acide)	gel	2	1,8-1,3	2,4	23,0	32,0	38,8	100	81	91	80
Riopan (CH)	magaldrate	comprimés, suspension	3,0 3,5	3-1,5 3,2-2,5	2,1 3,1	4,5 3,2	12,3 15,0	15,6 15,7	56 69	78 76	78 90	89 100
Smecta (F)	smectite intergrade de nature beidellitique (silicate d'Al et de Mg); gel d'hydroxyde d'Al et de carbonate de Mg codesséchés (pansement anti-acide)	poudre	1,5	1,5-1,0	1,3	2,7	5,5	6,1	100	100	100	100
Valuzid (F)*	hydroxyde d'Al hydroxyde de Mg carbonate de Mg	comprimés, suspension	2,5	2,2-1,5	14,8	19,9	25,3	75,7	68	74	76	90
			2,5	2,2-1,5	4,5	8,2	12,9	20,8	70	75	74	86

* En voie d'être commercialisé.

(Au 5 bis)

Effets 2 daires

TABLEAU I

Transformation des anti-acides

Effets systémiques	CO_3HNa	Estomac :	$CO_3HNa + HCl$	→	ClNa ↓
		Intestin :			résorbé → surcharge sodée Le CO_3HNa pancréatique ne neutralise pas HCl ; il est résorbé et éliminé par le rein. → risque d'alcalose.
	CO_3Ca	Estomac :	$CO_3Ca + 2HCl$	→	Cl_2Ca + CO_3HNa pancréatique
		Intestin :			90 % CO_3Ca insoluble 10 % Cl_2Ca résorbé (Une faible partie de CO_3HNa est résorbée → risque d'alcalose).
Effets non systémiques		Estomac :	$(OH)_2Mg$ $(OH)_3Al + HCl$	→	Cl_3Al → Cl_3Mg
		Intestin : • duodénum • jéjunum • côlon			↓ Formation de composés basiques puis de $(CO_3Al_2$ Savons, PO_4Al insolubles
					↓ $+CO_3^{--}$ → CO_3Mg +acides gras → savons insolubles Possibilité de redissolution de CO_3Mg

AU4

Tableau 3: Utilisations thérapeutiques et posologie des anti-acides

Indications	Effets recherchés	Mécanismes d'action	Posologie, durée
Ulcère duodénal	Cicatrisation	Anti-acide	7 prises/jour, doses fortes, 4 semaines.
	Symptomatologie	Anti-acide	A la demande, 4 semaines.
	Traitement d'entretien; traitement des résistances		Pas d'efficacité puisque pas d'effet sur la sécrétion nocturne.
Ulcère gastrique	Symptomatologie; cicatrisation	Anti-acide: diminution de l'agressivité du reflux duodéno-gastrique	A la demande: posologie élevée 6 semaines.
Œsophagite peptique	Symptomatologie; cicatrisation	Anti-acide: effet sur le sphincter; diminution de l'agressivité des sels biliaires	Fortes doses: à la demande 8 semaines.
Traitement des hémorragies g.i. d'origine ulcéreuse		Anti-acide (pH intragastrique = 7); inhibition de la rétrodiffusion des ions H^+; inhibition de la protéolyse peptique du caillot.	Fortes doses: toutes les heures jusqu'à l'arrêt de l'hémorragie.
Traitement et prévention des lésions aiguës du stress		Anti-acide (pH intragastrique = 7); inhibition de la protéolyse peptique du caillot.	Fortes doses, toutes les heures.

① emploi ancien $\begin{cases} NaHCO_3 \\ CaCO_3 \end{cases}$

② sels d'Al et de Mg (hydroxydes)

① $MgCO_3 + 2HCl \leftrightharpoons MgCl_2 + H_2CO_3$
$Al(OH)_3 + 3HCl \leftrightharpoons AlCl_3 + 3H_2O$ (neutralisation)

② $Al(OH)_3 + TAC \leftrightharpoons$ acylate d'Al (hydrolyse).

TABLEAU II. — **Interactions entre les anti-acides et d'autres médicaments**

Mode d'action des anti-acides	*Médicaments concernés*
Adsorption : réduction du taux plasmatique	Isoniazide, tétracyclines
Modification du pH intragastrique	
— Augmentation de la résorption	Sulfonamide, anticoagulants ?
— Diminution de la résorption	Carbénoxolone, tétracyclines par voie orale, digitaliques, chlorpromazine
Modification de la fonction rénale : élévation du pH urinaire	
– Augmentation de l'excrétion	Salicylates
– Diminution de l'excrétion	Quinidine, amphétamines

Anti-acids

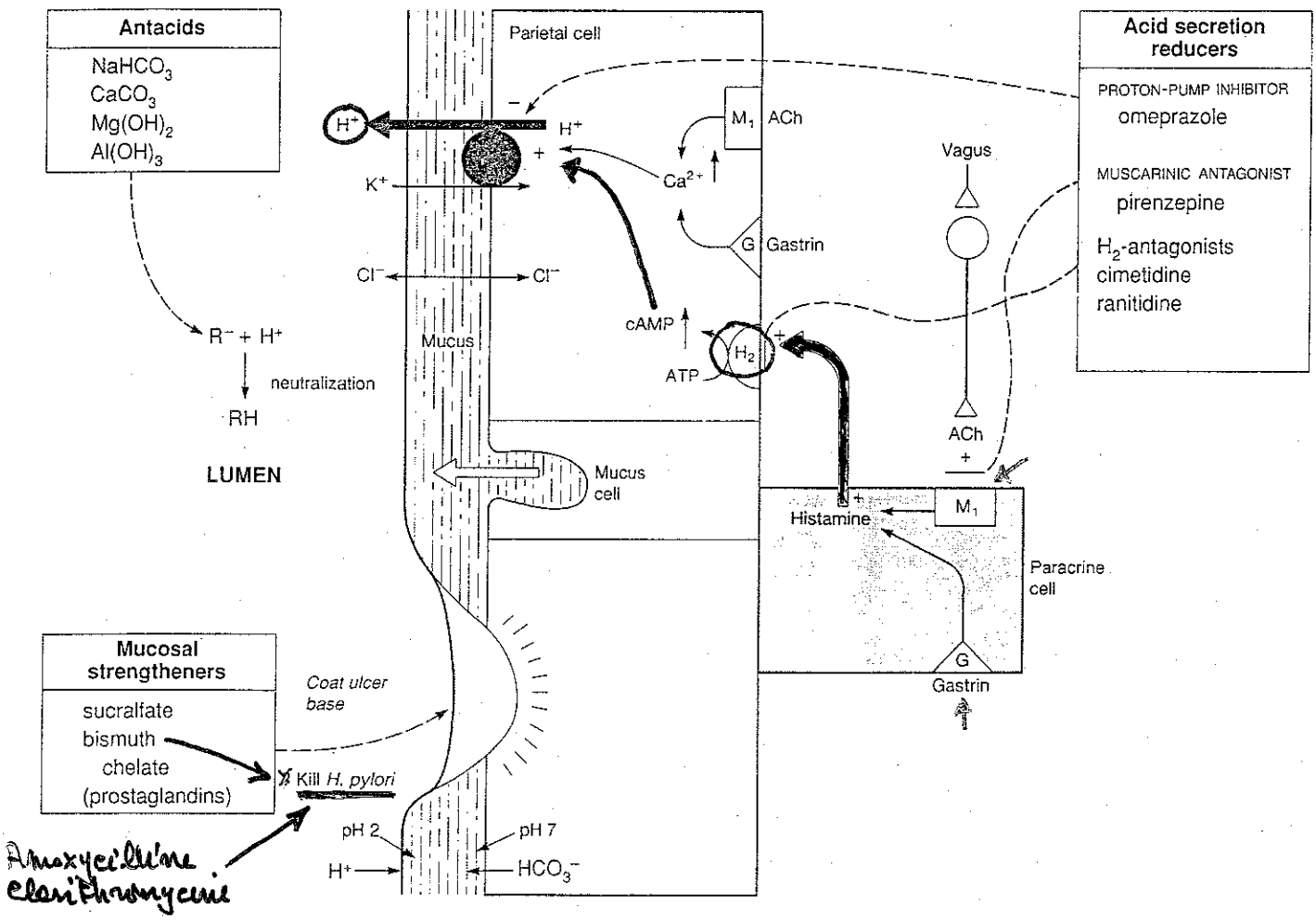
Notions essentielles

- Les anti-acides agissent de façon passive sur le contenu intragastrique en réduisant ou en supprimant totalement la concentration en ions H^+ sécrétés. Ils ne modifient pas les processus sécrétoires.
- Le mode d'action des anti-acides repose sur deux mécanismes possibles souvent associés : neutralisation des ions H^+ avec modification du pH intragastrique et/ou effet tampon, qui correspond à la consommation des ions H^+ sans modification du pH intragastrique.
- L'évaluation in vitro de la capacité anti-acide à différents niveaux de pH correspondant à la sécrétion gastrique permet de calculer la capacité thérapeutique potentielle, c'est-à-dire le nombre de millimoles d'acide qu'une unité thérapeutique peut théoriquement consommer pour réduire les concentrations acides de 100 à 40, 10 ou 1 mmol/l. Cette caractéristique doit être prise en compte pour le choix d'un anti-acide.
- Il n'existe pas de travaux permettant d'établir une relation entre les effets observés in vitro et ceux mesurés in vivo. Ceci doit inciter à la prudence quant à la notion de « puissance » visant à classer les différents médicaments anti-acides. D'autre part, la variabilité des résultats des expérimentations, en fonction en particulier du pH et de la valeur pondérale de la prise d'essai in vitro, renforce la notion qu'il est impossible de classer les anti-acides.
- La propriété pharmacologique essentielle de cette classe de médicaments est de diminuer la concentration en ions H^+ du contenu intragastrique. Cette modification peut entraîner une inhibition de l'activité protéolytique et faciliter l'adsorption des sels biliaires et des lysolécithines ; de ce fait, les anti-acides peuvent exercer un pouvoir protecteur de la muqueuse gastrique contre d'autres facteurs d'agression que l'acide.
- Certains effets additionnels méritent d'être pris en considération : les modifications du pH intragastrique affectent la libération de gastrine, la vidange gastrique et donc l'apport d'ions H^+ dans le duodénum.

Anti acids

- La structure physicochimique des différents anti-acides est responsable de l'intensité du pouvoir anti-acide et de la cinétique de libération des sites de fixation des ions H^+. Elle est également responsable d'effets généraux observés après leur administration, en particulier l'alcalose métabolique, la surcharge en sodium ou en calcium, sous l'effet des anti-acides anioniques ; les anti-acides à base d'aluminium et de magnésium peuvent entraîner des troubles graves en cas d'insuffisance rénale sévère.
- Les anti-acides sont indiqués dans le traitement des troubles liés à l'acidité pathogène, dans la maladie ulcéreuse, le reflux gastro-œsophagien, à titre préventif des hémorragies gastro-intestinales d'origine ulcéreuse ou des complications du stress, ulcérations et hémorragies. Dans ce dernier cas, leur effet thérapeutique est souvent supérieur à celui des antisécrétoires.
- L'administration des anti-acides doit tenir compte d'une part des variations du contenu acide de l'estomac et d'autre part de la vidange gastrique. Les anti-acides doivent en particulier prendre le relais du repas, lui-même anti-acide ; de ce fait, ils doivent être prescrits 1 heure environ après le repas. L'effet anti-acide ne sera efficace que tant que l'anti-acide reste dans le contenu intragastrique, c'est-à-dire non vidangé vers le duodénum. Une nouvelle administration peut être recommandée pour compenser la perte d'anti-acide par la vidange gastrique. La période nocturne s'accompagne d'une hypersécrétion acide dont le mécanisme n'est pas connu et qui nécessite l'administration fréquente, toutes les heures ou toutes les 2 heures, d'anti-acides, ce qui est possible dans le cas de la prévention du stress mais difficile pour un malade ambulatoire.
- Les anti-acides exercent des modifications importantes de la biodisponibilité d'autres médicaments par suite de phénomènes d'adsorption, de modification du pH intragastrique et d'altération de l'excrétion rénale.
- L'emploi des anti-acides constitue un volet important en thérapeutique œsophago-gastroduodénale, mais il est limité en raison du mode d'action en site exclusivement intragastrique. Cette limitation peut justifier qu'ils soient utilisés en association avec les antisécrétoires.

12 Drugs acting on the gastrointestinal tract: I peptic ulcer



The term **peptic ulcer** refers to any ulcer in an area where the mucosa is bathed in the hydrochloric acid and pepsin of gastric juice (i.e. the stomach and upper part of the duodenum). Drugs that are effective in the treatment of peptic ulcer either **reduce gastric acid secretion** (right) or **increase mucosal resistance** to acid–pepsin attack (bottom left).

Acid secretion from the *parietal cells* (⇐) is reduced by **H_2-histamine antagonists** (*cimetidine, ranitidine*), which are the first-line drugs in ulcer treatment. *Pirenzepine*, a cholinergic M_1-muscarinic antagonist with a relatively selective action in the gut, also decreases acid secretion, but less effectively than the H_2-blockers, probably because it does not block gastrin-stimulated acid release. Nevertheless, the rate of healing with pirenzepine is comparable with that obtained with H_2-antagonists. *Omeprazole* can produce virtual antacidity by irreversibly inhibiting the proton pump (●), which transports H^+ ions out of the parietal cells. It is very effective in promoting ulcer healing, even in patients resistant to H_2-antagonists. The '**mucosal strengtheners**' *sucralfate* and *bismuth chelate* increase ulcer healing by binding to the ulcer base (left, □). This provides **physical protection** and allows the secretion of HCO_3^- to re-establish the pH gradient normally present in the mucus layer (▥) which originates from mucus-secreting cells (⇦).

Peptic ulcers, however healed, will often recur without continuous drug administration. There is evidence that the recurrence of ulcers is slower following bismuth chelate administration, but the reason for this is unknown. It may well be due to the antibacterial action of bismuth, because chronic infection of the stomach with *Helicobacter pylori* is probably an aetiological factor in ulcer formation.

Antacids (top left) are bases that raise the gastric luminal pH by neutralizing gastric acid (middle left). They provide effective treatment for many dyspepsias and symptomatic relief in peptic ulcer and oesophageal reflux. Many proprietary mixtures are available which usually contain magnesium or aluminium salts.