



# Antiulcer Drugs



Website



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Pharmacology 3 | U 2

**ANTI-ULCER DRUGS PHARMACOLOGY**

**Aggressive**  
Acid, Pepsin, Bile  
H. pylori

**Defensive**  
Mucus, Bicarbonate,  
PGs, NO

**GI Secretions :-**

- 1) Porensymes - Porensin (Chief Cell)  
Pepsinogen (Peptic Cells)
- 2) Acid (parietal Cells), IF (Oxyntic Cells)
- 3) Mucus & HCO<sub>3</sub><sup>-</sup> → G mucosa
- 4) Cytoprotective PGE → ↑ Mucus & HCO<sub>3</sub><sup>-</sup> Sec.
- 5) Bile / Alcohol → Destroy mucus layer

**Regulatory Molecule**

- # Gastrin → Stimulatory hormone - (GR) → +
- # Ach → Stimulatory NTs → (M1R) → + → Acid Sec.
- # Histamine → Stim. local hormone → (H2R) → +
- # PGE<sub>2</sub> → Inhibitory local hormone - (PGR) → -

**Goal for Treatment -**

- ↳ Relief pain
- ↳ Ulcer healing
- ↳ ↓ Complication
- ↳ ↓ Relapse

**1. Acid Neutralization - Anta-Acids**

- ⓐ Systemic - NaHCO<sub>3</sub>, Sod. Citrate
- ⓑ Non Systemic → Mg(OH)<sub>2</sub>, Al(OH)<sub>3</sub>, Mg. Trisillicate.

**2. Anti-Secretory / Anti Gastric**

- ⓐ Anti-Ach → Pirenzepine, Propanthelin,
- ⓑ H<sub>2</sub>-blockers → Cimetidine, Ranitidine, Famotidine, Roxatidine
- ⓒ H<sup>+</sup>K<sup>+</sup> pump Inhibitors (PPIs) - Omeprazole, Rebeprazole, Lansoprazole, ilaprazole
- ⓓ PGs → Misoprostol, Cisaprost  
↳ Cytoprotective Action

**3. Ulcer Protective - Sucralfate**  
Coloidal Bismuth Subcitrate (CBS)

**4. Anti H. pylori** → Amoxicillin, Clarithromycin, Metronidazole

**5. Anti Gastrin - Proglumide**

**6. Antacid Combination with -**

- Alginate
- Simecane
- ↑ Viscosity & Adherence of mucus

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### H<sub>2</sub> RECEPTOR BLOCKERS (ANTI-ULCER DRUGS)

Cimetidine, Ranitidine, Roxatidine, Famotidine

MOA = Competitive Antagonist (GSPCR) / Partially noncompetitive Antagonist (H<sub>2</sub>R)

Response ↓

- # Gastric → ↓ Acid Secretion
- # Heart → ↓ HR (Bradycardia)
- # Broncha - Spasm +
- # Uterine - Contraction
- # BP ↑ → At high dose

H<sub>2</sub> blocker ↓ gastric secretion induced by histamin & also ↓ by Ach, Gastrin, Alcohol & Insulin

Also reduce gastric volume, pepsin & (IF)

They do not affect GI Motility

Use = Antiulcerogenic effect, ↓ Gastric Ulcer induced by stress, NSAIDs, cholinergic & histamin.

ADR\* High IV Dose → Can release histamine  
 ↳ Bradycardia, Arrhythmia, cardiac arrest  
 ↳ Confusion, hallucination, convulsion  
 ↳ Always given slowly

# Headach, dizziness, Bowel upset, dry mouth

# Only in cimetidine :-

- ① Anti Androgenic effect - Gynaecomastia
- ② ↑ prolactin secretion
- ③ ↓ Estradiol degradation in Liver
- ④ Masked hep. Metabolic Enz Inhibitor
- ⑤ Cross placenta & poorly in BBB

Drug Interaction

- # ↓ Metabolism of - Theophyllin, phenytoin, Barbiturate, Sulfonylurea, Warfarin & lead to their toxic effect
- # Antacids ↓ Absorption of H<sub>2</sub> blocker, So need to 2h gap if necessary

P<sub>kinetic</sub>\*

"Ranitidine" (Furan ring) - 5 time more potent and lesser side effect

"Famotidine" - "Thiazole ring"

Use →

- ① Ulcer
- ② Zollinger-Ellison Syndrome
- ③ GERD
- ④ prophylaxis of Aspiration Pneumonia

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### PROTON PUMP INHIBITORS PHARMACOLOGY

PPIs - Omeprazole, Esomeprazole, Lansoprazole, Pantoprazole, Rabeprazole, Ilaprazole

MOA = H<sup>+</sup>K<sup>+</sup>ATPase pump Inhibitors (Irreversible)

"Omeprazole" - Benzimidazole, Prototype drug

- # Omp suppress the acid secretion dose dependently
- # PPIs do not effects (very little) on pepsin, IF, Gastric juice volume unlike H<sub>2</sub> blockers.
- # They do not affect cholinergic and histaminergic transmission
- # They abolish HCl secretion, both in resting as well as stimulated by foods.
- # Omp. inactive at neutral pH, At < 5 pH

Omeprazole

Sulphenic acid + Sulphenamide

react covalently with

-SH group of H<sup>+</sup>K<sup>+</sup>ATPase pump (in apical membrane of parietal cell)

PPIs → Inactivate Irreversibly → ↓ H<sup>+</sup> → ↓ HCl

P<sub>kinetics</sub> - All PPIs administered orally in enteric coated form.

Omp → 50% BA at stomach due to acidic pH, if pH rises → Abs/BA ↑ 3-4 times

- BA ↓ by food (thus taken in empty stomach)
- = Metabolized by CYP-2C19 & 3A4

# Inhibits CYP2C19 & alter the metabolism of others like ↓ Oxd<sup>n</sup> of Diazepam, Phenytoin, Warfarin

ADR - Long term use can cause →

- # Atrophic Gastritis (Carcinoid tumors)
- # ↓ Testosterone level # Erectile dysfunction
- # Gynaecomastia
- # ↓ Ca<sup>2+</sup> Abs - Osteoporosis

Uses - # Peptic Ulcer

- # Zollinger Ellison Syndrome (First choice)
  - ↳ Tumor → (H) Gastrin → ↑ Acid Secretn
- # GERD # Aspiration Pneumonia

Esomeprazole → S-enantiomer of Omp, High BA & t<sub>1/2</sub> better control GERD

Lansoprazole - Partially reversible inhibitor, lesser Cyp Inhibitor

Pantoprazole → "Acid Stable" High BA. (S-pantoprazole)

Rabeprazole → Fast acid Suppression, Higher pKa - Fast ionised at site and convert it active form

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