

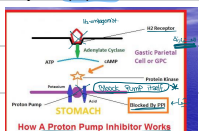
سيزو ميرا مقنط  
مستوي مده

Very efficacious and safe drugs.  
 • Omeprazole (oral).  
 • Rabeprazole (oral).  
 • Lansoprazole (oral and IV).  
 • Pantoprazole (oral and IV).  
 • Esmoprazole (oral and IV).  
 • Formulated as a **prodrug** which is released in the intestine.

# \* Proton Pump Inhibitors

## Pharmacokinetics

They are **lipophilic** weak bases (pKa 4-5)



After **intestinal absorption**, they **diffuse across lipid membranes** into **acidified compartments** such as the **parietal cell canaliculus**.

The **prodrug** becomes **protonated** and concentrated more than **1000-fold** within the **parietal cells**.

it **undergoes** a molecular conversion to the **active form** which covalently binds the **H+/K+ ATPase enzyme** and **inactivates it**.

Rabeprazole has **immediate release**  
**omeprazole** have **faster onsets** of action.  
 • Should be **given one hour** before meal.  
 • Have **short half lives** but effect lasts for **24 hours** due to **irreversible inhibition**.

## Pharmacodynamics

**Inhibit both fasting and meal-stimulated secretion** because they **block the final common pathway of acid secretion** (90-98% of 24-hour secretion)

## \* Clinical uses:

- Gastroesophageal Reflux (GERD)  
 - PPI most effective in all forms of this Disease.
- Nonulcer Dyspepsia  
 - Modest activity - 10-20% beneficial than placebo

## Peptic Ulcer Disease:

heal more than 40% of cases within 4-6 weeks

**H. pylori**  
 - eradicate H. pylori by Dual antimicrobial activity.  
 ↓ MIC of antibiotic

**NSAIDs**  
 - promote ulcer healing despite continued NSAIDs

**Rebleeding peptic ulcer**  
 - oral or IV

**Triple therapy**  
 - PPI (X2X1)  
 - Clarithromycin (X2X1)  
 - Amoxicillin (X2X1) or bismuth subsalicylate

Parent ulcer complications  
 - High pH enhance the platelet aggregation

الاستروجين  
 مضاد مستقبلات  
 NSAIDs

**Stress- Related Gastritis:**  
 - oral immediate omeprazole administered via nasogastric tube

Gastrinoma and other Hypersecretory Conditions:  
 - high doses of omeprazole

## Adverse Effects

Increased **serum gastrin** ↑ levels:  
**Hyperplasia** of ECL cells.  
**Carcinoid tumors** in rats.  
 Increase **proliferative** rate of colonic mucosa.  
**Chronic inflammation** in gastric body.  
**Atrophic gastritis** and intestinal metaplasia

## Drug Interactions:

- May affect **absorption of drugs** due to **decreased gastric acidity** like **digoxin** and **ketoconazole**.  
 و تأثيره يمنع امتصاصه في الامعاء
- Omeprazole** can **inhibit metabolism of drugs** such as **diazepam** and **phenytoin**.  
 أي يمنع على الكبد دخولها معي
- Rabeprazole** and **pantoprazole** have **no significant interaction**.  
 لا بنته د بيبيل ماله اثر

ملين  
 laxatives  
 ديوكس  
 Antidiarrheal

# \* Drugs of GI Motility

## \* Laxatives

- Nonpharmacologic Remedies
- Bulk-Forming Laxatives:
- Stool Surfactant Agents ( Softeners):

High fiber diet.  
 • Adequate fluid intake.  
 • Regular exercise.  
 • Responding to nature's call.

Are **indigestible, hydrophilic colloids** that **absorb water**, forming a **bulky, emollient gel** that **distends the colon** and **promotes peristalsis**.  
 • Can cause **bloating and flatus**.

**Natural Plant Products:**  
 • Psyllium.  
 • Sterculia "Normacol"  
 • Methylcellulose.

**Synthetic Fibers:**  
 • Polycarbophil.

They permit water and lipids to penetrate.  
 • Given orally or rectally.  
 • **Docusate**.  
 • **Glycerin suppository**.  
 • **Mineral oil**:  
 - Clear viscous oil that lubricates fecal material, retarding water absorption from the stool.  
 - Used to prevent and treat fecal impaction.  
 - **Aspiration** can cause **lipoid pneumonia**.  
 - Can impair absorption of fat-soluble vitamins.

## Osmotic Laxatives (Purgatives):

**Soluble nonabsorbable** compounds that result in **increased stool liquidity** due to an obligate increase in **fecal fluid**.

**Magnesium oxide (Milk of Magnesia)**  
 Can cause **hypermagnesemia**.  
 • Large doses of magnesium citrate and sodium phosphate can cause **Purgation**: rapid bowel evacuation within 1-3 hours. This might cause **volume depletion**.