UNIT-VI

Gastrointestinal Drugs

Gastro Intestinal Tract is concerned with the function of ingesting and absorbing nutrients and excreting unabsorbed and waste products.

Here we will discuss prototype drugs used to treat three common medical conditions involving the gastrointestinal (GI) tract:

1. **Peptic ulcers and gastroesophageal reflux disease**
2. **Diarrhea**
3. **Constipation**
4. **Emesis**

Drugs Used To Treat Peptic Ulcer Disease

Antimicrobial Agents
➔Metronidazole

H2 – Histamine Receptor Blockers
➔Cimetidine

Proton Pump Inhibitors
Omeprazole

Prostaglandins Analogue
➔Misoprostol

Antacids
➔Aluminum Hydroxide

Mucosal Protective Agents
➔Sucralfate

Available Brands in the Market

Flagyl Tab. (Metronidazole)
Klint Tab. (Metronidazole)
Cimet Tab. (Cimetidine)
Ulcirex Tab. (Cimetidine)
Risek Cap. (Omeprazole)
Omega Cap. (Omeprazole)
Cytotec Tab. (Misoprostol)
Misoclear Tab. (Misoprostol)
Dijex-MP Syrup. (Aluminum Hydroxide)
Dimeco Syrup (Aluminum Hydroxide)
Sucmed Tab. (Sucralfate)
Sucfate Tab. (Sucralfate)

Metronidazole (Antimicrobial Agents)

Patients with peptic ulcer disease (both duodenal and gastric ulcers) who are infected with H. pylori, which is a Gram- negative, microaerophilic bacterium found in the stomach requires antimicrobial treatment. (See Antiprotozoals Drugs in Chemotherapy topic)

Cimetidine (H2 – Histamine Receptor Blockers)

Mechanism Of Actions

The histamine H2-receptor antagonists cimetidine, act selectively on H2 receptors in the stomach, blood vessels, and other sites, but they have no effect on H1 receptors. They are competitive antagonists of histamine and are fully reversible.

Therapeutic Uses

Peptic Ulcers
Histamine H2-receptor antagonists are equally effective in promoting the healing of duodenal and gastric ulcers.

Acute Stress Ulcers
These drugs are typically given as an intravenous infusion to prevent and manage acute stress ulcers associated with high-risk patients in intensive care units.

Gastroesophageal Reflux Disease
Gastroesophageal reflux disease is a chronic symptom of mucosal damage caused by stomach acid coming up from the stomach into the esophagus.
Low doses of H2 antagonists, currently available for over-the-counter sale, appear to be effective for the prevention and treatment of heartburn (gastroesophageal reflux).

Pharmacokinetics
Cimetidine and the other H2 antagonists are given orally, distribute widely throughout the body and are excreted mainly in urine. Cimetidine normally has a short serum half-life, which is increased in renal failure.

Adverse Effects
The most common side effects are headache, dizziness, diarrhea, and muscular pain.

Omeprazole (Proton Pump Inhibitors)

Mechanism Of Actions
Proton pump inhibitors act by irreversibly blocking the H+/K+ ATPase, or more commonly just gastric proton pump of the gastric parietal cell.

Therapeutic Uses
Proton pump inhibitors are used in the treatment of peptic ulcer, these agents suppressing acid production and healing peptic ulcers. These agents are also successfully used with antimicrobial agents for the peptic ulcer treatment.

Pharmacokinetics
All these agents are delayed-release formulation and effective orally. Metabolites of these agents are excreted in urine and feces.

Adverse Effects
These agents are generally well tolerated. Increased concentration of viable bacteria in the stomach has been reported with continued use of these agents.

Misoprostol (Prostaglandins Analogue)

Mechanism Of Action
Misoprostol seems to inhibit gastric acid secretion by a direct action on the parietal cells through binding to the prostaglandin receptor. It Increases secretion of mucus and bicarbonate.

Therapeutic Action
It is an effective anti-ulcer agent. It is clinically effective only at higher doses that diminish gastric acid secretion.

Adverse Effects
The most common adverse effects of misoprostol are uterine contractions, diarrhea and nausea.

Aluminum Hydroxide (Antacids)

An antacid is a substance, which neutralizes stomach acidity.

Mechanism Of Action
Antacids are weak bases that react with gastric acid to form water and a salt to diminish gastric acidity.

Therapeutic Uses
Aluminum hydroxide antacids are used in the treatment of peptic ulcer disease, and they may also promote healing of duodenal ulcers. They are used as last-line therapy for acute gastric ulcers.

Adverse Effects
Aluminum hydroxide tends to cause constipation, stomach pain, loss of appetite, and muscle weakness.

Pharmacokinetics
Aluminum hydroxide mostly excreted in feces. Small amounts absorbed are excreted by the kidneys.

Sucralfate (Mucosal Protective Agents)

These agents have several actions that enhance mucosal protection mechanisms, they are useful in mucosal injury, reducing inflammation, and healing existing ulcers.

Mechanism Of Action
Sucralfate creates a physical barrier that impairs diffusion of HCl and prevents degradation of mucus by pepsin and acid. It also stimulates prostaglandin release as well as mucus and bicarbonate output, and it inhibits peptic digestion.

Therapeutic Uses
Sucralfate effectively heals duodenal ulcers and is used in long-term maintenance therapy to prevent their recurrence.

Pharmacokinetics
Little of the drug is absorbed systemically. It is very well tolerated; it has a very short serum half-life of 1 h and is excreted almost completely by the kidneys.

Adverse Effects
Less serious side effects of sucralfate may include stomach pain, constipation, diarrhea, nausea, and vomiting.

Prototype Drugs Used To Treat Diarrhea

Increased motility of the gastrointestinal tract and decreased absorption of fluid are major factors in diarrhea. Most common antidiarrheal drugs used to treat acute diarrhea include antimotility agents, and adsorbents.

Antimotility Agents
➔Loperamide

Adsorbents
➔Aluminum Hydroxide

Available Brands in the Market

Imodium Tab. (Loperamide)
Floramex Tab. (Loperamide)
Dijex-MP Syrup. (Aluminum Hydroxide)
Dimeco Syrup (Aluminum Hydroxide)

Loperamide (Antimotility Agents)

Loperamide is widely used to control diarrhea. They inhibit acetylcholine release and decrease peristalsis. At the usual doses, they lack analgesic effects. Side effects include drowsiness,

abdominal cramps, and dizziness. They should not be used in young children or in patients with severe colitis.

Aluminum Hydroxide (Adsorbents)

Adsorbent agents, such as aluminum hydroxide are used to control diarrhea. Presumably, these agents act by adsorbing intestinal toxins or microorganisms and/or by coating or protecting the intestinal mucosa. They can interfere with the absorption of other drugs.

Prototype Drug Used To Treat Constipation

Laxatives are commonly used for constipation to accelerate the movement of food through the gastrointestinal tract. Most common and important laxatives are listed below.

Irritants And Stimulants
➔Castor oil

Saline And Osmotic Laxatives
➔Lactulose

Stool Softeners
➔Docusate

Available Brands in the Market

Castor Oil
Duphalc Syrup (Lactulose)
Lilac Syrup (Lactulose)
Abolitium Tab. (Docusate)

Castor Oil (Irritants And Stimulants)

This agent is broken down in the small intestine to ricinoleic acid, which is very irritating to the stomach and promptly increases peristalsis. This agent is used for the treatment of constipation.

Lactulose (Saline And Osmotic Laxatives)

Lactulose is a semisynthetic disaccharide sugar that also acts as an osmotic laxative. It is a product that cannot be hydrolyzed by intestinal enzymes. Oral doses are degraded in the colon by colonic bacteria into lactic, formic, and acetic acids. This increases osmotic pressure, causing fluid accumulation, colon distension, and soft stools.

Docusate (Stool Softeners)

Stool softeners emulsified with the stool produce softer feces and ease passage. They may take days to become effective and are often used for prophylaxis rather than acute treatment. Stool softeners should not be taken with mineral oil because of the potential for absorption of the mineral oil.

Antiemetics

Vomiting is a protective reflex mechanism for eliminating irritant of harmful substances from upper GIT.

Causes Of Vomiting

- **Pregnancy**
- **Motion sickness**
- **GI obstruction**
- **Peptic ulcer**
- **Drug toxicity**
- **Renal failure**
- **Hepatitis**

Prototype Drug Used To Treat Emesis

D_2 Receptor Antagonist
➔Metoclopramide
➔Domperidone

Sedative Hypnotics
➔Barbiturates
➔Benzodiazepines
(See in Anxiolytic And Hypnotic Drugs)

Antimuscarinics
➔Scopolamine

H1 Receptor Antagonists
➔Meclizine
➔Dimenhydrinate

Available Brands in the Market

Metoclopramide Syrup (Metoclopramide)
Emetus Tab. (Domperidone)
Gravinate Syrup (Dimenhydrinate|)

Metoclopramide (D_2 Receptor Antagonist)

Mechanism Of Action
Metoclopramide centrally block dopamine D_2 receptors in CTZ, it also enhances action of acetylcholine at muscarinic nerve ending in gut.

Therapeutic Uses
Metoclopramide is used in the treatment of nausea and vomiting associated with GI disorders, before emergency anesthesia and in gastroesophageal reflux.

Adverse Effects
Restlessness, diarrhea

Dimenhydrinate (H1 Receptor Antagonists)

Mechanism Of Action
Dimenhydrinate is a H1 antihistaminic or antiemetic agent.

Therapeutic Uses
It provides relief of symptoms of vomiting, allergic reactions such as rash, watery eyes, runny nose, itchy eyes and sneezing. It may also be used to treat motion sickness, relief of anxiety or tension and sleeplessness.

Adverse Effects
Dizziness, Headache, Drowsiness, and Fatigue