

Drugs Acting on GI Tract

Anti-Ulcer Agents

- Ulcers are lesions that develop in the mucosal membrane and extend below the epithelium of stomach or duodenum.
- Ulcers formed in stomach are called stomach ulcers while those in the duodenum are called duodenal ulcers. Both of them together, called peptic ulcers.
- Peptic ulcers occur in that part of GI which is exposed to gastric acid and pepsin.
- Peptic ulcers occur probably due to an imbalance between the aggressive (acid, pepsin) and the defensive (gastric mucus, bicarbonate secretion) factors.
- Ulcers are formed when the aggressive factors dominate over the defensive factors.

Classification

1) Reduction of gastric acid secretion

- a) H₂-antagonists: Cimetidine, Ranitidine, Loxatidine, Famotidine, Roxatidine

- b) Proton Pump Inhibitors: Omeprazole,

Lansoprazole, Pantoprazole, Rabeprazole

- c) Prostaglandin Analogues: Misoprostol, Epracril

- d) Antigastin: Octreotide

- e) Anti-cholinergics: Pirenzepine, Oxyphenonium

- 2) Neutralisation of Gastric Acids (Antacids)

- a) systemic: Sodium bicarbonate, sodium citrate

- b) non-systemic: Magnesium hydroxide, magnesium trisilicate, Calcium carbonate.

- 3) Ulcer-healing drug: Carbenoxolone sodium

- 4) Anti H. pylori drugs: Amoxicillin, Tinidazole, clarithromycin, Metronidazole.

MoA

- H₂-antagonists suppress the normal secretion of acid by parietal cells and the secretion at the time of eating. This is done by two methods:
- 1) Histamine released by Enterochromaffin-like cells (ECL) in the stomach is blocked from binding on parietal cell H₂-receptors, which stimulates acid secretion.

2) In the presence of H_2 -blockers, direct stimulation of parietal cells by gastrin or acetylcholine results in reduced acid secretion.

Therapeutic uses

H_2 -antagonists are used in the treatment of acid-related GI conditions. These include:

- 1) Peptic Ulcer Disease (PUD)
- 2) Dyspepsia \rightarrow discomfort in upper abdomen
- 3) Zollinger Ellison syndrome \rightarrow too much gastric acid secretion
- 4) Gastroesophageal Reflux Disease (GERD)
- 5) Prevention of stress ulcer

Adverse effects may be:

- headache
- dizziness
- rash
- loss of libido \rightarrow desire for sex
- Gynecomastia in males \rightarrow swollen male breast tissue
- Impotence
- temporary loss of sperm count

Major Drugs

1) Cimetidine

It is a histamine H_2 -receptor antagonist that inhibits acid secretion.

Treatment uses in heartburn and peptic ulcers.

Cimetidine is used for the treatment of:

- i) Duodenal ulcers.
- ii) Active gastric ulcers.
- iii) GERD
- iv) Zollinger Ellison syndrome (ZES)

2) Ranitidine

similar pharmacological effects in body as shown by cimetidine.
side effects discussed for both.

Proton Pump Inhibitors

These are the class of drugs that are irreversible inhibitors of the gastric parietal cell proton pump. This act by blocking ($H^+ + K^+ + ATPase$) system.
eg: Omeprazole, Rabeprazole, pantoprazole.

Therapeutic uses are:

- i) Peptic ulcers
- ii) GERD
- iii) ZES

Anticholinergics

Anticholinergic agents block the neurotransmitter acetylcholine in CNS and PNS.

e.g. probanthine, oxyphenonium, pyrenzepine.

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They act selectively on muscarinic M₁ receptors and inhibits gastric secretion without producing typical atropinic side effects.

Prostaglandin Analogs

Prostaglandin reduce the risk of stomach ulcers.

Therapeutic uses

Synthetic prostaglandins are used in:

- chronic gastric and duodenal ulcer
 - NSAID induced ulceration and bleeding
- side effects may be:
- diarrhoea, abdominal cramps, nausea
 - dysmenorrhoea.

Drug example

Misoprostol → reduces the risk of stomach ulcers in patients being treated with NSAIDs (e.g. aspirin, ibuprofen)

Antigastrin Drugs

Gastrin is a hormone that stimulates the secretion of gastric acid (HCl) and helps in gastric motility (movement of food).

Anti-gastrin drugs inhibit the mechanism of gastrin and therefore blocks acid secretion e.g. Octreotide

Therapeutic uses

This medication is used to treat:

- 1) Acromegaly (secretion of too much GH)
- 2) watery diarrhoea caused by cancerous tumours.

Adverse effects may be

- Headache
- Gallstones
- High or low blood sugar
- slow heart rate
- skin reactions like pruritus → itching
- Hyperbilirubinaemia (high bilirubin)
- Dyspnoea (difficulty in breathing)
- Pancreatitis
- Hepatitis

Antacids

neutralise gastric acid and increase pH of gastric contents.

Commonly used antacids are trisilicate salts of magnesium and aluminium.

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Antacids do not decrease the production of acid, they only increase the pH by neutralising it.

Therapeutic Uses

- Antacids reduce the acid irritation of ulcers.
- relieves pain due to ulcers.

Adverse effects may be:

- systemic alkalosis (excess alkali in body)
- gastric distention (flatulence)
- milk-alkali syndrome
- rebound acidity

Systemic Antacids

(1) Sodium Bicarbonate

water-soluble, strong base. It has a short duration effect. It is a potent neutraliser and pH may rise above 7.

2) Sodium Citrate

similar action like sodium bicarbonate.

Non-systemic Antacids

- 1) Magnesium Hydroxide
- 2) Magnesium trisilicate
- 3) Aluminium hydroxide gel
- 4) Magaldrate
- 5) Calcium carbonate

Anti-H. pylori Drugs

Helicobacter pylori are gram-negative bacteria which live in GIT. If they remain for many years, they cause ulcers.

The drugs used for inhibiting the growth of Helicobacter pylori are:

- i) Amoxicillin
- ii) Clarithromycin
- iii) Tnidazole.

Drugs for Constipation & Diarrhoea

Constipation is a condition in which a person has uncomfortable or infrequent bowel movements. This results in the passage of small amounts of hard, dry stool, usually fewer than three times a week.

Dry stool is the result of absorption of large part of water from the food content in colon.

The other symptoms of constipation are:

- stomach pain
- Loosing appetite
- Bloating and cramps in abdomen.

Causation

- 1) not eating enough fibre (fruits, vegetables, cereals)
- 2) ignoring the urge to pass stool
- 3) not taking enough fluids
- 4) lack of exercise
- 5) Problems with intestinal function
- 6) Changes in lifestyle, such as travel, pregnancy, and old age.
- 7) Some medication side effects

Laxatives

→ These are the foods, drugs or compounds taken to induce bowel movement or to loosen the stool. These are basically given to treat constipation.

→ Laxatives in high doses can cause diarrhoea and hasten the elimination of undigested food in large intestine. Hence, used in mild doses.

MOA

- Laxatives cause accumulation of fluid in gut lumen
- 1) stimulation of adenylyl cyclase, thus increasing water and electrolyte secretion.
 - 2) inhibition of $\text{Na}^+ \text{K}^+ \text{ATPase}$ of villous cells, thus impairing electrolyte and water absorption.

Classification

Bulk forming

- Bran
- Psyllium
- Ispaghula
- Methylcellulose

Stool Softner

- Docusate (Doss)
- Liquid paraffin

1.

Bulk-forming Laxatives

First line treatment for constipation.

They may be natural (agar, psyllium) or synthetically prepared (methylcellulose, carboxy methylcellulose).

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Bulk-forming agents act as dietary fibres. The non-digestible and non-absorbable food swell in the presence of water and form a viscous solution softening the faecal mass and increasing its bulk.

Faecal volume is further increased by the growth of colonic bacteria which consume these materials as nutrients. The intestinal transit time is accelerated because the enlarged faecal volume stretches the intestinal wall and stimulates peristalsis.

→ This increases bowel movements

Therapeutic uses

- laxatives are helpful in/for:
- diverticulosis, irritable bowel syndrome (IBS)
- fibre supplements.

Adverse effects

- Oesophageal obstruction occurs if there are swallowed in the absence of sufficient fluids.

Drugs1) Dietary Fibre - Bran

Bran is a by-product of flour and consists of around 40% dietary fibre. It absorbs water in the intestines, swells, increases water content of faeces, softens it and facilitates colonic transit.

2) Psyllium (Plantago) and Ispaghula

These agents contain natural colloidal mucilage which absorbs water and forms a gelatinous mass.

3) Methylcellulose

4-6gm dose per day is adequate.

2.

Stool Softener

They use surfactant as ingredient to help water mix with the faecal mass, thereby softening it to pass easily from the intestine.

Docusate is the only approved stool softener available as calcium or sodium salt.

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Docusate being an anionic surfactant lowers the surface tension at the oil-water interface of stool, thus allows the water to enter stool. As a result, the faecal matter becomes soft and helps in natural defecation.

Adverse effects

- 1) Mild GI cramping pains
- 2) Feeling of discomfort
- 3) Hepatotoxicity

Purgatives

or cathartics

These have stronger action and facilitate the elimination of watery or more fluid stools.

MoA

All the purgatives act by increasing the water content of faeces by:

- 1) Purgative drugs reduce the total water and electrolyte absorption.
- 2) Increasing propulsion rate, thereby allowing less time for absorption of salt and water.

Classification1) Stimulant Purgatives

- a) anthraquinones: Senna and cascara sagrada.
- b) diphenylmethanes: Phenolphthalein, Bisacodyl
- c) Fixed oil: castor oil.

2) Osmotic purgatives

- a) Magnesium salts: Sulphate and hydroxide
- b) sodium salts: sulphate and phosphate
- c) sodium potassium tartrate
- d) lactulose

Anti-Diarrhoeal Drugs

WHO defines diarrhoea as - the passage of more liquid or loose stools three or more times per day.

Generally, diarrhoea is a gastrointestinal infection that can be caused either by viral, bacterial or any parasitic organism.

The infection spreads via:

- contaminated food and drinking water
- person-to-person due to improper hygiene.

Diarrhoea causes:

- dehydration (lack of fluids)
- increased motility and secretions of the GI tract. This causes decreased fluid absorption which results in loss of electrolytes and water.

Treatment of diarrhoea

- 1) Maintenance of fluid and electrolyte balance
oral rehydration solution - preparations of sodium chloride and glucose.

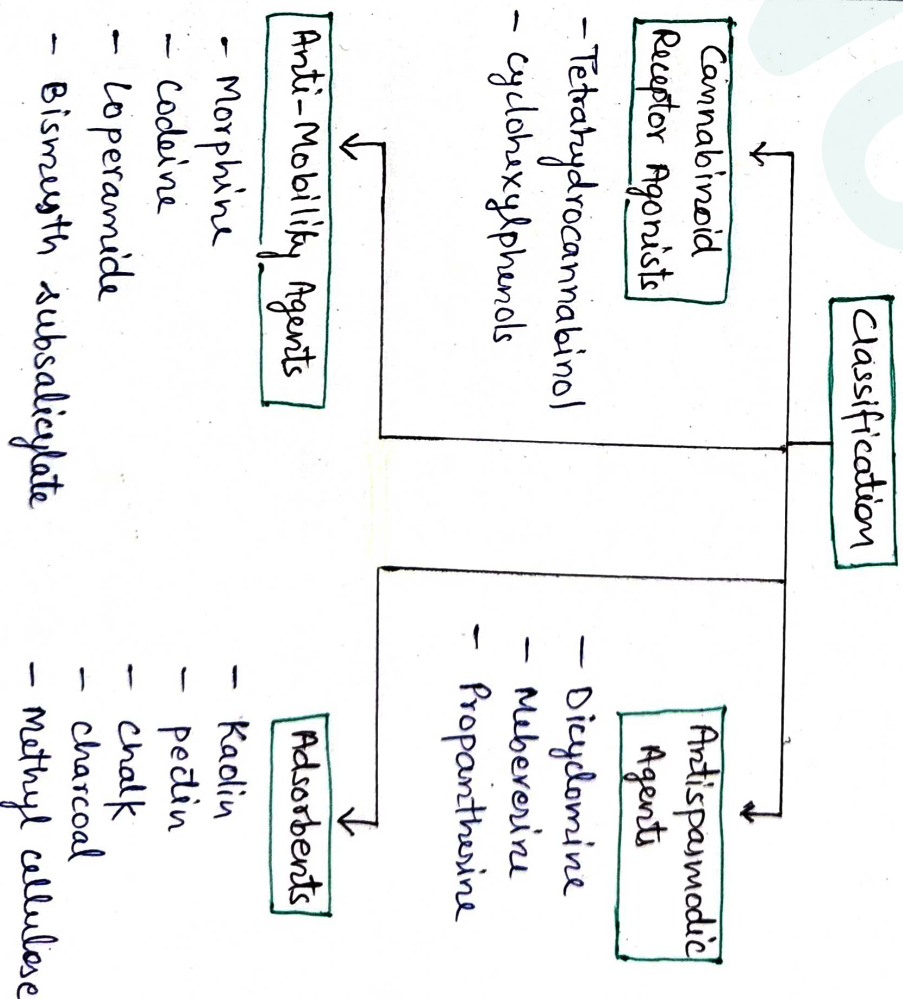
- 2) Use of anti-infective agents

Campylobacter species is the commonest bacterial organism causing diarrhoea.

Erythromycin or ciprofloxacin may be given.

- 3) Non-Anti-microbial Antidiarrhoeal Agents

These agents modify fluid and electrolyte transport.



Anti-Motility Agents

These agents decrease the ability of intestine to contract. e.g. opiates and muscarinic receptor antagonists.

Cannabinoid Receptor Agonists

It acts by reducing the motility of gut, most probably by reducing the release of acetylcholine from enteric nerves.

Absorbents

These agents act in three possible mechanisms:

- i) adsorbing microorganisms
- ii) by altering the intestinal flora
- iii) by coating and protecting the intestinal mucosa.

Antispasmodic Agents

These help in reducing spasm in the gut. They are particularly used in irritable bowel movement (IBS) and diverticular disease.

Appetite Stimulants & Suppressants

Appetite is the desire to eat.

Causes of loss of appetite may be:

- psychological disorders (stress, depression, anxiety)
- gastrointestinal disorders (PUD, GERD)
- Chronic diseases (COPD, cystic fibrosis, Parkinson's)
- medications (chemotherapy, laxatives)
- slowed metabolism
- Hormonal change

Appetite stimulants, also known as **orexigenic** agents, **hunger-mimetics** or **hyperphagics**, are the hormones or compounds that increase appetite

Drugs Used

1) Cyproheptadine

The lateral hypothalamus usually exerts endogenous opiates which help in stimulating hunger.

2) Megestrol Acetate

It is a synthetic progestin. It is used to stimulate appetite and promote weight gain in people with cancer and **cachexia**, **muscle mass loss**

Appetite Suppressants

Also known as anorectic drugs. They reduce appetite to result in lower food consumption and weight loss.

The drugs act upon the CNS and make it believe that the body is not in need of food.

MOA

Centrally acting adrenergic agents

stimulate the release of nor-epinephrine, dopamine from the storage site in the nerve terminal which is situated in the lateral hypothalamus feeding centre

↓
decrease appetite

Drug

Diethylpropion

Diethylpropion is a microsomal triglyceride transfer protein (MTP) inhibitor which functions to produce weight loss.

Digestants

Digestants are the substances which facilitate or promote digestion of food. They contain combination formulations of amylolytic, proteolytic and lipolytic enzymes.

Drugs

- 1) Pepsin → It is used in combination with HCl in case of gastric achlorhydria.
- 2) Papain → It is a proteolytic enzyme present in raw papaya which helps in digestion of food.
- 3) Pancreatin → It is a mixture of pancreatic enzymes containing amylase, trypsin, lipase.
- 4) Diastase and Takadiastase → These are amylolytic enzymes present in *Aspergillus oryzae*.
- 5) Methyl Polysiloxane → It is a silicon polymer.
- 6) Bile and bile acids → Liver secretes about 1000 ml of bile per day. Bile acids emulsify the intestinal fats.

Carminatives

They provide soothing effect by relieving stomach and intestinal pain caused due to flatulence (gas). Carminativum is a word which involves any herb or herbal preparation meant for preventing gas formation in GI tract.

Drugs

Carminatives include preparations containing mixtures of essential oils and herbal spices.

Herbal drugs having carminative action includes:

- Angelica
- Ajwain
- Anise seed
- Asafoetida
- Basil calamus
- Cardamom, Cinnamon
- Coriander

Synthetic drugs

Simethicone is used to lower the surface tension of gas bubbles.

Emetics

Vomiting or emesis is a protective mechanism of the body in which the harmful substances are eliminated from the stomach and duodenum. Emetics are the drugs which induce vomiting in some specific conditions like ingestion of poison, migraine pain, etc.

Emetics should not be used in:

- acid and alkali poisoning
- CNS stimulant drug poisoning
- petroleum poisoning
- unconscious patients

Drugs

- 1) Mustard → One teaspoonful of mustard with warm water can be given to produce vomiting.
- 2) Ammonium carbonate → This is a very safe and effective emetic. It is given as highly diluted and in milk.
- 3) Apomorphine → It is injected hypodermically in special cases.
- 4) Sulphate of zinc → causes little nausea or depression.
- 5) Sulphate of copper → rapid action.

Anti-Emetics

Anti-emetics are drugs, effective against vomiting.

These are used to treat:

- motion sickness
- side effects of opioid analgesics
- general anaesthetics

Classification

- 1) Anticholinergics
It acts by blocking conduction of nerve impulses of vomiting centre. e.g. Hyoscine, Dicyclanine
- 2) H₁-antihistamines
They are useful in motion sickness, morning sickness, e.g. Promethazine, Cinnarizine
- 3) Neuroleptics
They act by blocking D₂ receptors and antagonise apomorphine induced vomiting, e.g. Prochlorperazine
- 4) Prokinetic Drugs
Promote GI transit and speed gastric emptying.
e.g. Metoclopramide, Domperidone, Cisapride

5) Adjuvant Anti-emetics

relieves pain

e.g. Cannabinoids, Dexamethasone

Benzodiazepines