



GASTROINTESTINAL AGENTS

Drugs used in the treatment of GI disorders are known as GI Agents. It includes many different classes of drugs that are used to treat gastrointestinal disorders.

They can be classed as: **antacids, acidifying agents, adsorbents, cathartics, protectives**, etc.

ANTACIDS

Antacids (anti - against; acidus - acid) are **weak alkaline compounds** used **to neutralize hydrochloric acid** in the stomach. Antacids are the substances which reduce gastric acidity resulting in an **increase in the pH of stomach and duodenum**. Gastric acidity occurs due to excessive secretion of HCl in stomach due to various reasons.

When hyperacidity occurs the result can range from:

- i. Gastritis (a general inflammation of gastric mucosa)
- ii. Peptic ulcer or oesophageal ulcer (lower end of oesophagus)
- iii. Gastric ulcer (stomach)
- iv. Duodenum ulcer



Classification of antacids

Antacids are mainly classified into two categories:-

- (i) Systemic (absorbable) antacids.
- (ii) Non-systemic (non-absorbable) antacids.

(i) Systemic antacids:

These types of antacids are **soluble and absorbable** and produce systemic alkalosis. It shows the most rapid onset of action and provides faster relief of symptoms. However, they may cause an "acid rebound". It is inappropriate for patients affected with hypertension or kidney failure.

e.g. Sodium bicarbonate.

Rebound acidity, also known as acid rebound, refers to the phenomenon where there is an overproduction of stomach acid following the discontinuation of acid-suppressing medications. This increased acid production can lead to a temporary worsening of symptoms, often causing the individual to experience more severe heartburn or indigestion than before starting the medication.

(ii) Non-systemic antacids:

These types of antacids are **not absorbed into systemic circulation** and does not produce systemic alkalosis. These antacids though less prone to cause a rebound effect. These antacids



are more potent and effective in a semi liquid or liquid form than in a capsule or tablet. The usually high presence of aluminium and magnesium hydroxides in non-absorbable antacids can be effectively used to prevent significant stress ulcer bleeding in post-operative patients or those with severe burns.

e.g. Aluminium hydroxide gel, Magnesium hydroxide, etc.

NAME	MOLECULAR FORMULA	PHARMACEUTICAL FORMULATIONS	MARKET PREPARATIONS	STORAGE CONDITIONS	USES
Aluminium hydroxide gel Non-systemic antacid	$Al(OH)_3$	<ul style="list-style-type: none">- Oral Suspensions- Tablets	<ul style="list-style-type: none">- Alterna gel- Amphojel- Nephrox- Gelusil- Tricreama lte- Trioosgel	Store in air-tight containers Avoid freezing. It can be dispensed in blue/ amber colored bottles.	<ul style="list-style-type: none">- Used as an antacid and protective in treating peptic ulcers, gastritis, peptic oesophagitis.- It is also used in cases of acute hyperacidity.



					<ul style="list-style-type: none">- It relieves the symptoms of dyspepsia.- It acts as antiseptic and astringent.- To adsorb pepsin due to adsorbent properties.
Magnesium hydroxide Non-systemic antacid	$Mg(OH)_2$	<ul style="list-style-type: none">- Suspensions- Tablets	<ul style="list-style-type: none">- Ex-Lax of Milk of Magnesia- Milk of Magnesia- Pedia-Lax Chewable	Store in air-tight containers	<ul style="list-style-type: none">- Used as an antacid and laxative.- It is used in the treatment of heartburn, stomach upset and indigestion.
Magaldrate Non-systemic antacid	$Al_5Mg_{10}(OH)_{31}(SO_4)_2 \cdot xH_2O$	<ul style="list-style-type: none">- Suspensions- Tablets	<ul style="list-style-type: none">- Riopan	Store in air-tight containers at room	<ul style="list-style-type: none">- To treat gastric & duodenal ulcers, GERD.



				temperature between 15-30°C.	
Sodium bicarbonate Systemic antacid	NaHCO_3	<ul style="list-style-type: none">- Tablets- Injection	<ul style="list-style-type: none">- Nabico- Zeitabin- Sellymin- Brioschi- Neut- Sodium bicarbonate	Store in airtight containers Store in well closed containers	<ul style="list-style-type: none">- treatment of metabolic acidosis in severe renal disease, uncontrolled diabetes, and circulatory insufficiency due to shock or severe dehydration.- to relieve heartburn, sour stomach, or acid indigestion by neutralizing



					excess stomach acid
Calcium carbonate Non-systemic antacid	CaCO ₃	- Suspensions - Tablets	- Mixocal Calcium carbonate - Calcio carbonato 600mg - Tums Chewy delights	Store in well closed, air-tight containers.	- Antacid - Relieves pain of gastric/duodenal ulcer

COMBINATION OF ANTACIDS

There are three complications usually seen when antacids are used.

- First, many antacids exert an action on the bowel. For example: **some have a mild laxative effect (e.g. Magnesium hydroxide)** and **some are constipating (e.g. aluminium hydroxide)**.



- Secondly if the cation (the metallic ion) is absorbed, **systemic alkalosis** (a condition in which the alkalinity of body fluids and tissues is abnormally high) may be produced (e.g. **sodium bicarbonate**). **Calcium ions** may produce **hypercalcaemia** (the presence in the blood of an abnormally high concentration of calcium). **Magnesium and aluminum** cause **precipitation of phosphate in the gastrointestinal tract** and depletion of phosphorus.
- Finally, antacids **may affect the absorption of other drugs** which may be administered alone with antacids such as **anticholinergics and antibiotics**. These drugs may be adsorbed by the antacids.
- Antacids may also **alter the pH of gut gastric contents** thereby **delaying the absorption of weak acids and speeding the absorption of basic drugs**.

Therefore **because of the defects associated with the antacids, it is apparent that it is wiser to use a combination of antacids** so that the defects can be minimized.

For example: Magnesium hydroxide and Aluminium hydroxide may be combined to balance the constipating effect of the latter with the laxative effect of the former.

On this basis the following combinations are in regular clinical use.

1. Magnesium and aluminium hydroxides (**Magaldrate**)
2. Magnesium and aluminium hydroxides, dimethicone (**Dioval Forte Tabs**)



3. Magnesium and aluminium hydroxides, methylpolysiloxane (**Gelusil MPS**)
4. Aluminium hydroxide gel, magnesium trisilicate (**Gelusil**)
5. Aluminium hydroxide gel, Magnesium hydroxide, magnesium trisilicate (**Gelusil M**)
6. Magnesium hydroxide, dried aluminium hydroxide gel, methylpolysiloxane, sodium carboxymethyl cellulose (**Digene gel**).

ACIDIFYING AGENTS

Acidifiers are the inorganic chemicals that **either produce or become acid**. These are the drugs which are able to **increase the acidity, in GIT**. Thus, **decreasing the stomach pH**. Some of these drugs are used to **increase metabolic acidosis** whereas some of these are used to **increase the gastric hydrochloric acid**.

E.g.: HCl

The pH of stomach is 1.5 -2 when empty and rises to pH 5-6 when food is ingested. The pH of stomach is so low because of the secretion of HCl. Gastric HCl act by **destroying the bacteria in the ingested food and drinks**. It **softens the fibrous food** and **promotes the formation of the proteolytic enzyme pepsin**. This enzyme is formed from pepsinogen at acidic pH (<6). Pepsin helps in the metabolism of proteins in the ingested food.



Achlorhydria:

Lack of HCl in the stomach can cause Achlorhydria.

Two types of achlorhydria are known:

- 1) where the gastric secretion is devoid of HCl, even after stimulation with histamine phosphate
- 2) where gastric secretion is devoid of HCl, but secreted upon stimulation with histamine phosphate.

The cause of achlorhydria in first case may be **subtotal gastrectomy, atrophic gastritis, carcinoma, gastric polyp, etc** while in later case it may be **chronic nephritis, tuberculosis, hyperthyroidism, chronic alcoholism, sprue, pellagra etc**. The symptoms vary with associated disease but they generally include **mild diarrhoea or frequent bowl movement, epigastric pain and sensitivity to spicy food.**

Achlorhydria can be treated by various acidifying agents like ammonium chloride, dilute HCl, Calcium chloride etc.



PROTECTIVES AND ADSORBENTS

Protective and adsorbents are drugs which **adsorb intestinal toxins, bacteria etc, and give a protective coating to the inflamed mucosal walls.**

- Protectives Chemically inert substance used to form a **protective layer in GIT.**
E.g. Bismuth subcarbonate, Aluminium sulphate, Talc, etc.
- Adsorbents Chemically inert substance used for **removing toxic substances from GIT.**
E.g. Kaolin, Activated charcoal, Pectin, etc

These are **chemically inert substances.**

They are used in the **treatment of Diarrhoea or Dysentery**

They **adsorb gases, toxin and bacteria in the GI tract.**

CATHARTICS

Cathartics are therapeutic agents which **facilitate defecation.** They are beneficial in **constipation** and for **expulsion of intestinal parasites.** They may be given for **cleaning bowels before surgery.**

The term laxative is used for mild cathartic whereas purgative is used for strong cathartics.

Laxatives, cathartics and purgatives **act by retaining fluid in the bowel.** They are administered by **oral route or rectal route.**



In normal habits, peristalsis leads to defecation. The peristaltic waves stimulate bowel and relieve its contents.

Constipation can also be caused by many factors like weakness of intestine, intestinal injury and use of certain drugs and diet etc. In constipation, faecal matter becomes dry and hard. Use of laxative or purgative (lubricants) gives relief in constipation by **elimination of bowel contents**.

Classification

The cathartics can be considered under the following class

- Mild purgatives or laxatives
- Strong purgatives

Mild purgatives or laxatives

Mild purgatives or laxatives are those which **promote defecation** causing minimum adverse effects.

- **Bulk producing drugs-** which promote evacuation by **increasing the stools bulk volume and water contents**.
e.g: Isapgol, agar-agar, methylcellulose, bran, psyllium seed, sodium carboxy methylcellulose, etc.
- **Stool softeners-** which penetrate, **lubricate and soften the stool**.



e.g liquid paraffin.

Strong purgatives

Strong purgatives cause complete evacuation of the bowel and constipation usually follows for which a mild purgative is needed. These purgatives should not be used for constipation. They may be given in **worm infection** along with drugs killing worms and **also to remove solid materials from intestines prior to x-ray examinations.**

- **Irritant or stimulant purgatives-** Stimulant laxatives, also known as contact laxatives, **encourage bowel movements by acting on the intestinal wall.** They **increase the muscle contractions** that move along the stool mass.
E.g: senna, aloe, cascara, rhubarb extract, castor oil, podophyllin
- **Saline cathartics (osmotic laxative) -** Saline cathartics are water soluble and are taken with large quantities of water. This **prevents excessive loss of water from body fluids.** They act in the intestine and a full cathartic dose produces a water evacuation within 3-6 hrs.
E.g.: sodium phosphate, potassium sodium tartarate, magnesium hydroxide, magnesium sulphate, sodium sulphate, etc