UNIT 3

Gastrointestinal Agents – Acidifiers

Acidifiers are substances used to increase acidity in the stomach or urine. In the context of gastrointestinal use, **acidifiers are employed to treat achlorhydria or hypochlorhydria**, which are conditions where there is insufficient secretion of hydrochloric acid in the stomach.

Dilute Hydrochloric Acid (Dil. HCl)

Chemical Information

- **Formula**: HCl in water (approximately 10% w/v solution)
- **Appearance**: Clear, colorless liquid with a pungent odor
- **Storage**: Stored in well-closed, corrosion-resistant containers (typically glass or polyethylene bottles)

Properties

- Strong inorganic acid
- Completely dissociates in aqueous solution to release **H^+** and **Cl^-** ions
- Highly corrosive and must be handled with care

Medicinal Uses

- Used as a **gastric acidifier** to treat **achlorhydria** (absence of hydrochloric acid in gastric secretions)
- Aids in **digestion** by maintaining the acidic environment in the stomach necessary for the activation of **pepsinogen to pepsin**
- Supports the absorption of nutrients like iron and calcium, which require an acidic medium

Dose and Administration

- Administered in a **diluted form**, usually mixed with water, and taken orally.
- Often combined with digestive enzymes in formulations marketed as **digestive aids**

Precautions

- Overuse may lead to **gastric irritation** or worsen **gastritis** or **ulcer conditions**
- Should not be given in patients with active peptic ulcer disease
- Must be administered with caution and only under medical supervision

Pharmaceutical Considerations

- Included in **official monographs** like the **Indian Pharmacopoeia**
- Tested for **acid strength**, **purity**, and **absence of toxic impurities** like heavy metals

Ideal Properties of Antacids

Antacids are substances that neutralize excess gastric hydrochloric acid in the stomach, providing relief from hyperacidity and its associated symptoms such as heartburn, acid indigestion, and ulcers. The ideal antacid should fulfill the following criteria:

1. Efficient and Rapid Acid Neutralization

- It should rapidly neutralize gastric HCl and maintain the pH between **3.5 to 4.5**, which is sufficient to relieve pain without impairing digestion.

2. Prolonged Action

- It should provide **sustained buffering action** and not be easily washed away from the stomach.

3. Non-Systemic Effect

- It should act **locally in the stomach** without being absorbed systemically, thus avoiding systemic alkalosis.

4. No Gas Formation

- It should **not liberate CO_2**, which can cause **bloating** or **belching**, as seen with sodium bicarbonate.

5. Minimal Laxative or Constipating Effects

- It should not cause **diarrhea** (as with magnesium salts) or **constipation** (as with aluminum salts).

6. Palatability

- It should be **tasteless or pleasant tasting**, odorless, and have a smooth mouthfeel if in suspension.

7. Chemical Compatibility

- Should not interfere with **other drugs** or cause precipitation of gastric contents.

8. Stability

- It should be **chemically stable**, not degrade upon storage or exposure to air and moisture.

9. Non-Toxic and Safe

- It should be **non-toxic** in the doses administered and **free from heavy metal impurities**.

Combinations of Antacids

To overcome the side effects and limitations of single-agent antacids, **combinations** are frequently used in commercial preparations. These combinations are designed to **balance** the action and **minimize adverse effects**.

1. Magnesium + Aluminum Salts

- **Example**: Magnesium hydroxide + Aluminum hydroxide gel
- **Rationale**: Magnesium salts are **laxative**, aluminum salts are **constipating** – their combination **neutralizes each other's side effects**
- Provide a **balanced and sustained** antacid effect

2. Antacid + Antifoaming Agent

- **Example**: Aluminum hydroxide + Magnesium trisilicate + **Simethicone**
- **Simethicone** reduces **surface tension** of gas bubbles and helps relieve **flatulence and bloating**

3. Antacid + Local Anesthetic

- **Example**: Antacids + **Oxethazaine**
- Oxethazaine provides **pain relief** by numbing the gastric mucosa in conditions like **gastritis and ulcers**

4. Antacid + Alginates

- **Example**: Antacids + **Sodium alginate**
- Alginates form a **viscous gel or raft** that floats on the stomach contents and prevents **acid reflux** into the esophagus

5. Antacid + Enzymes

- **Example**: Antacids + **Digestive enzymes** (like pepsin or diastase)
- Useful in **dyspepsia** and **indigestion**, helps aid **protein digestion**

Aluminum Hydroxide Gel

Chemical Information

- **Formula**: $[Al(OH)_3]$
- **Form**: A white, viscous suspension
- **Nature**: Amorphous gelatinous precipitate containing variable amounts of hydrated aluminum oxide

Properties

- Practically insoluble in water and alcohol
- Reacts with hydrochloric acid in the stomach to form soluble aluminum chloride
- Slowly neutralizes gastric acid
- **Does not produce CO_2**, hence no belching
- Has a **constipating effect**

Medicinal Uses

- Acts as a **non-systemic antacid**
- Provides **prolonged acid-neutralizing** action
- Used in treatment of **hyperacidity, peptic ulcers, and GERD**
- Sometimes used to **bind phosphate** in patients with chronic kidney disease (to reduce serum phosphate)

Advantages

- Minimal systemic absorption
- Low potential for alkalosis
- Soothing effect on gastric mucosa

Disadvantages

- Can **cause constipation**
- May delay gastric emptying
- Interferes with absorption of drugs like tetracyclines, iron, and digoxin

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Magnesium Hydroxide Mixture

Chemical Information

- **Formula**: $Mg(OH)_2$
- **Form**: White suspension in purified water (Milk of Magnesia)
- Also referred to as **Magnesium Hydroxide Mixture IP**

Properties

- Reacts rapidly with hydrochloric acid to form soluble magnesium chloride and water
- Acts as a **fast-acting antacid**
- Also used as an **osmotic laxative** in higher doses
- Slightly alkaline in nature

Medicinal Uses

- Used as a **non-systemic antacid**
- Employed in the **treatment of acid indigestion, gastritis, and peptic ulcers**
- At higher doses, used as a **mild laxative**
- Often combined with aluminum hydroxide gel to balance GI effects

Advantages

- Quick onset of action
- Useful in patients with constipation

Disadvantages

- May **cause diarrhea** due to osmotic effect
- Should be avoided in **renal impairment** (due to risk of hypermagnesemia)

Cathartics

Cathartics are agents that promote bowel evacuation. Depending on their intensity, they are categorized as:

- **Laxatives**: Mild action, suitable for regular use
- **Purgatives**: Stronger action, used to treat constipation
- **Drastic purgatives**: Very strong, used in poisoning or surgical preparation

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1. Magnesium Sulphate

Chemical Formula: $MgSO_4 \cdot 7H_2O$

Common Name: Epsom salt

Properties

- Colorless crystalline solid
- Soluble in water; solution has a bitter taste
- Acts as an **osmotic purgative**

Mechanism of Action

- Increases osmotic pressure in the intestine
- Retains water in the intestinal lumen
- Promotes bowel evacuation within 2–6 hours

Medicinal Uses

- Used as a **saline cathartic**
- For **constipation**, **poisoning** (to flush out toxins), and **bowel preparation**
- Also used in **preeclampsia** (as anticonvulsant), and **hypomagnesemia**

Dose

- 10–20 g in water, orally as a purgative

Precautions

- Avoid in patients with **renal impairment**
- May cause **dehydration** or **electrolyte imbalance**

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2. Sodium Orthophosphate

Chemical Formula: $Na_3PO_4 \cdot 12H_2O$

Other Name: Tribasic sodium phosphate

Properties

- White crystalline powder
- Freely soluble in water
- Alkaline in nature

Mechanism of Action

- Acts as a **saline cathartic**
- Draws water into the intestine by osmotic action
- Increases intestinal volume and stimulates peristalsis

Medicinal Uses

- Used for **evacuation of bowels**
- Commonly employed in **pre-colonoscopy bowel preparation**
- Also used as a **phosphate supplement**

Dose

- 5–15 g orally, dissolved in water

Precautions

- Excessive use can cause **hyperphosphatemia**, **hypocalcemia**
- Avoid in patients with **renal failure**, **heart conditions**

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3. Kaolin

Nature: Hydrated aluminum silicate

Appearance: Fine white powder

Properties

- Insoluble in water
- Inert and non-absorbable
- Adsorptive properties

Mechanism of Action

- **Not a cathartic**, but rather a **protective and adsorbent**
- Adsorbs toxins, bacteria, and gases from GI tract
- Useful in **diarrhea**, **dysentery**

Medicinal Uses

- Used in the treatment of **mild diarrhea**
- Combined with pectin or bismuth salts in anti-diarrheal mixtures

Note

- **Not a purgative**, but included here as part of GI-acting agents

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4. Bentonite

Nature: Colloidal hydrated aluminum silicate (volcanic clay)

Appearance: Light grey or cream powder

Properties

- Swells in water to form a **gel-like colloid**
- High adsorptive and suspending capacity

Medicinal Uses

- Used as a **suspending agent** in pharmaceutical preparations
- Has **adsorbent** properties in **diarrhea treatment**
- Like kaolin, not a true cathartic but used in **GI disorders**

Antimicrobials

Definition

Antimicrobials are agents that **kill or inhibit the growth** of microorganisms such as **bacteria, fungi, viruses, and protozoa**. In pharmaceutical sciences, the term typically refers to **chemicals used to treat infections** by targeting pathogens without harming the host significantly.

Mechanism of Action of Antimicrobials

The primary mechanisms include:

1. **Inhibition of cell wall synthesis**
    - Targets peptidoglycan layer in bacterial cell walls.
    - Leads to cell lysis and death.
    - Example: Penicillins, Cephalosporins
2. **Disruption of cell membrane integrity**
    - Alters permeability and causes leakage of cellular components.
    - More common in antifungals.
    - Example: Polymyxins (for bacteria), Amphotericin B (for fungi)
3. **Inhibition of protein synthesis**
    - Binds to bacterial ribosomes (30S or 50S subunits).
    - Prevents proper translation of mRNA into proteins.
    - Example: Tetracyclines, Aminoglycosides, Macrolides
4. **Inhibition of nucleic acid synthesis**
    - Blocks DNA replication or RNA transcription.
    - Example: Fluoroquinolones (inhibit DNA gyrase), Rifampicin (inhibits RNA polymerase)
5. **Antimetabolite activity**
    - Mimic natural substrates in metabolic pathways.
    - Example: Sulfonamides (inhibit folic acid synthesis), Trimethoprim

Classification of Antimicrobials

Antimicrobials can be classified based on various criteria:

1. Based on the Type of Microorganism Targeted

Type	**Example Agents**
Antibacterials	Penicillin, Ciprofloxacin
Antifungals	Ketoconazole, Nystatin
Antivirals	Acyclovir, Zidovudine
Antiprotozoals	Metronidazole, Chloroquine
Anthelmintics	Albendazole, Mebendazole

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2. Based on the Mode of Action

Mode of Action	**Examples**
Inhibit cell wall synthesis	Penicillin, Cephalosporins
Disrupt cell membrane	Polymyxins, Amphotericin B
Inhibit protein synthesis	Tetracyclines, Macrolides
Inhibit nucleic acid synthesis	Rifampicin, Quinolones
Inhibit metabolic pathways	Sulfonamides, Trimethoprim

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3. Based on the Spectrum of Activity

Type	**Description**	**Examples**
Broad-spectrum	Active against a wide range of gram-positive and gram-negative organisms	Tetracycline, Chloramphenicol
Narrow-spectrum	Active against specific type(s) of bacteria	Penicillin (Gram-positive), Isoniazid (Mycobacteria)

4. Based on Source

Source	**Examples**
Natural	Penicillin (from *Penicillium notatum*)
Semi-synthetic	Ampicillin, Amoxicillin
Synthetic	Sulfonamides, Fluoroquinolones

5. Based on Bacteriological Effect

Effect	Action	Examples
Bactericidal	Kill bacteria	Penicillins, Aminoglycosides
Bacteriostatic	Inhibit bacterial growth	Tetracyclines, Sulfonamides

1. Potassium Permanganate ($KMnO_4$)

Category: Inorganic Antimicrobial (Oxidizing Agent)

Appearance: Dark purple crystalline powder with a metallic sheen

Solubility: Soluble in water, forming deep purple solutions

Odour: Odourless

Taste: Astringent and slightly sweet, then metallic and bitter

Mechanism of Antimicrobial Action

- Acts as a **strong oxidizing agent**
- Releases nascent oxygen, which **oxidizes cellular components** like proteins and enzymes of microorganisms
- Leads to microbial death and sterilization

Medicinal Uses

- **Disinfectant and antiseptic** in dilute solutions (1:5000 to 1:10000)
- Used for:
    - **Washing infected wounds and ulcers**
    - **Mouthwash** in stomatitis and gingivitis
    - **Treatment of fungal infections** like athlete's foot
    - **Gargles** in pharyngitis
    - **Antidote** in poisoning by morphine, strychnine (oxidizes the alkaloids)

Storage

- Store in tightly closed containers protected from light and organic substances (to prevent decomposition or fire hazard)

Assay

- Assayed by **redox titration** with standard **oxalic acid** or **sodium oxalate** using **sulfuric acid** as medium.
- Reaction:

$2MnO4^{-}+5C2O42-+16H+\rightarrow 2Mn^{2+}+10CO2+8H2O$

- Endpoint: Decolorization of the pink solution

2. Boric Acid (H_3BO_3)

Category: Weak acid, Mild Antiseptic

Appearance: White crystalline powder or transparent granules

Solubility: Soluble in water, more in hot water

Odour and Taste: Odourless, weak acidic taste

Mechanism of Antimicrobial Action

- Mild **bacteriostatic** and **fungistatic** action
- Inhibits **enzymes** by interacting with hydroxyl groups and proteins
- Useful as **external antiseptic** due to low toxicity and low tissue penetration

Medicinal Uses

- **Eye wash** and **ear drops** (as 2–4% solution)
- **Skin antiseptic** for minor burns, cuts, and abrasions
- Included in **dusting powders**, ointments, and lotions
- Used in **buffer solutions** for ophthalmic preparations
- Historically used for **diaper rash**, but modern usage is more limited due to slow elimination

Toxicity Note

- Toxic if ingested in large amounts or absorbed over large skin surfaces, especially in infants
- **Not used in internal preparations** anymore

Storage

- Store in tightly closed containers, protected from moisture

Iodine (I_2)

Category: Antimicrobial (Halogen group), Disinfectant, Antiseptic

Appearance: Shiny, dark violet-black crystalline solid with a metallic lustre

Solubility: Sparingly soluble in water, freely soluble in alcohol, ether, and potassium iodide solution (due to complex formation)

Odour: Pungent, characteristic

Taste: Strong and acrid

Mechanism of Antimicrobial Action

- Iodine acts by **oxidizing the sulfhydryl (-SH) and phenolic groups** in microbial proteins and enzymes, leading to **denaturation** and microbial cell death.
- It has a **broad-spectrum antimicrobial activity** effective against **bacteria, fungi, viruses, protozoa, and spores**.
- It penetrates quickly into microorganisms and **destroys vital cell components**.

Medicinal Uses

- Used as a **topical antiseptic and disinfectant** for skin, wounds, and surgical sites
- **Treatment of fungal infections** like ringworm and athlete's foot
- **Used in tinctures, ointments, and solutions**
- Internally, **iodine is a nutritional trace element** essential for the synthesis of thyroid hormones

Toxicity and Caution

- Excessive iodine use can cause skin irritation and allergic reactions.
- Chronic exposure can lead to **iodism** (metallic taste, excessive salivation, sore gums).

Preparations of Iodine

1. Tincture of Iodine (Iodine Tincture)

Composition (as per IP):

- Iodine – 2% w/v
- Potassium iodide – 2.5% w/v
- Alcohol – 90% v/v
- Purified water – q.s.

Properties and Uses:

- Alcohol enhances iodine solubility and acts as an additional antiseptic
- Used as a **skin disinfectant before injections/surgery**, or for minor cuts
- Should not be applied to large open wounds (systemic absorption)

2. Lugol's Iodine Solution (Strong Iodine Solution)

Composition:

- Iodine – 5% w/v
- Potassium iodide – 10% w/v
- Purified water – q.s.

Properties and Uses:

- Used **internally as an iodine supplement** or for **thyroid suppression** prior to surgery
- **Disinfectant** for water purification and medical instruments in dilute form

3. Iodine Ointment

Composition:

- Contains **0.5% to 1% iodine** in an appropriate ointment base (e.g., white soft paraffin)

Uses:

- Applied **topically** for chronic wounds, ulcers, and skin infections

4. Iodophors (e.g., Povidone-Iodine)

Definition:

- **Iodine complexes with surface-active agents or polymers**, such as povidone (polyvinylpyrrolidone), forming **stable complexes that release free iodine slowly**.

Advantages:

- **Less irritant and less staining**
- **Prolonged antiseptic action**
- **Broad-spectrum activity**
- Available in scrubs, mouthwashes, vaginal suppositories, ointments

Storage of Iodine and Preparations:

- Store in **tightly closed amber-coloured containers**
- **Protect from light and moisture** and Avoid contamination with organic matter.