UNIT 2

Acids, Bases and Buffers

Buffers:

Buffers are aqueous solutions that **resist significant changes in pH** upon addition of small amounts of acid or base.
They are crucial in pharmaceutical formulations and physiological systems to maintain **stable pH environments**.

Types of Buffers:

1. **Acidic Buffers**: Weak acid + its salt with a strong base
   Example: Acetic acid + Sodium acetate
2. **Basic Buffers**: Weak base + its salt with a strong acid
   Example: Ammonium hydroxide + Ammonium chloride

Buffer Equation:

Henderson–Hasselbalch Equation:

This equation relates the pH of a buffer to the concentration of acid and its conjugate base (or base and its conjugate acid):

- For **acidic buffers**:

$$pH = pKa + \log([Salt]/[Acid])$$

- For **basic buffers**:

$$pOH = pKb + \log([Salt]/[Base])$$

This equation is useful in:

- Designing buffer solutions at a desired pH
- Understanding the effect of changing salt/acid ratio on pH

Buffer Capacity (β):

Definition:
Buffer capacity is the **ability of a buffer to resist changes in pH** when acid or base is added.
It is quantitatively defined as:

$$\beta = dB/d(pH)$$

Where:

- *dB* = small amount of strong acid or base added per liter
- *d(pH)* = resulting change in pH

Key Points:

- Buffer capacity is **maximum** when **pH = pKa**.
- It depends on the **concentration** of buffer components (higher concentration = higher buffer capacity).
- The effective buffering range is usually **pKa ± 1**.

Pharmaceutical Importance:

- Buffers are used in **eye drops, injections, oral solutions**, and **biological preparations**.
- Maintain **drug stability**, **bioavailability**, and **patient comfort**.
- Examples: Citrate buffer in blood collection tubes, phosphate buffer in injections.

Buffers in Pharmaceutical Systems

Importance of Buffers in Pharmaceuticals:

Buffers are extensively used in pharmaceutical systems to maintain a **stable pH environment** which is critical for:

- **Stability** of drug substances
- **Solubility** of active pharmaceutical ingredients (APIs)
- **Bioavailability**
- **Patient comfort** (e.g., eye drops, injections)
- **Enzyme activity** in biological preparations
- **Control of degradation** reactions like hydrolysis or oxidation

Common Pharmaceutical Buffer Systems:

Buffer Type	Composition	pH Range	Applications
Acetate buffer	Acetic acid + sodium acetate	3.6 – 5.6	Eye drops, oral liquids
Phosphate buffer	NaH_2PO_4 + Na_2HPO_4	5.8 – 8.0	Parenteral preparations, ophthalmics
Citrate buffer	Citric acid + sodium citrate	3.0 – 6.2	Blood collection tubes, injections
Borate buffer	Boric acid + sodium borate	7.0 – 9.2	Ophthalmic preparations
Tris buffer	Tris (hydroxymethyl aminomethane)	7.0 – 9.0	Biochemical & enzyme-based formulations

Preparation of Buffers

Steps in Buffer Preparation:

1. **Select the appropriate weak acid/base pair** based on the required pH and compatibility with drug substances.
2. Use the **Henderson–Hasselbalch equation** to calculate the required ratio of salt to acid (or base).
3. **Dissolve** the acid and its salt (or base and its salt) in distilled water.
4. **Adjust the pH** using small amounts of strong acid or base if necessary.
5. Make up the volume to the desired final concentration.

Example: Preparation of Acetate Buffer (pH 4.5)

- Mix **0.2 M acetic acid** and **0.2 M sodium acetate** in equal volumes.
- Use Henderson–Hasselbalch:

$pH=pKa+\log([Salt]/[Acid])=4.76$

To get pH 4.5, slightly increase the amount of acetic acid.

Stability of Buffer Solutions

Factors Affecting Buffer Stability:

1. **Microbial contamination:** Especially in aqueous buffers. Use preservatives like benzalkonium chloride or autoclave sterilization.
2. **Temperature:** Some buffers are heat-sensitive (e.g., Tris buffer breaks down on heating).
3. **Light exposure:** Some buffer components (e.g., phosphate) can degrade in light.
4. **Carbon dioxide absorption:** CO_2 can lower pH, especially in alkaline buffers like borate.
5. **Evaporation:** Leads to increased concentration and pH shift.

Storage Recommendations:

- Store in **airtight amber bottles** to prevent CO_2 and light entry.
- Preferably store at **cool temperatures** (2–8°C).
- **Label** with preparation date and pH.
- Use freshly prepared buffer for **parenteral or ophthalmic** formulations.

Quality Control Tests for Pharmaceutical Buffers:

- **pH determination** using pH meter
- **Sterility test** for injectable buffers
- **Microbial limit test** for oral or ophthalmic buffers
- **Osmolality measurement** for physiological compatibility

Applications in Formulations:

- **Ophthalmic drops** (e.g., timolol eye drops use phosphate buffer)
- **Injectables** (e.g., insulin injections are formulated with phosphate buffer)
- **Oral liquids** (e.g., multivitamin syrups use citrate buffer)
- **Biologicals** (e.g., enzyme and protein drugs stabilized with Tris or phosphate buffers)

Buffered Isotonic Solutions

Definition:

A **buffered isotonic solution** is a solution that:

- Maintains a **constant pH** (due to the buffer system)

- Has the **same osmotic pressure as body fluids** (isotonicity), which is essential to avoid irritation or damage to body tissues.

Significance in Pharmaceuticals:

- Used in **parenteral**, **ophthalmic**, **nasal**, and **intrathecal** preparations.
- Prevents **cell shrinkage (hypertonic)** or **cell swelling (hypotonic)** due to osmotic imbalance.
- Ensures **stability** and **comfort** in dosage forms administered directly into body tissues.
- Maintains drug **solubility and bioavailability**.

Osmotic Pressure and Isotonicity

- **Isotonic solution**: Same osmotic pressure as that of **blood plasma or tears** (~0.9% NaCl equivalent).
- **Hypotonic solution**: Lower osmotic pressure; causes **cell swelling** and **lysis**.
- **Hypertonic solution**: Higher osmotic pressure; causes **cell shrinkage** and **irritation**.

Examples of Isotonic Solutions:

Solution	Tonicity	Notes
0.9% Sodium chloride (Normal saline)	Isotonic	Commonly used IV fluid
5% Dextrose in water	Isotonic	Provides calories and hydration
Lactated Ringer's solution	Isotonic	Used for fluid and electrolyte replenishment

Preparation of Buffered Isotonic Solutions:

To formulate such a solution, you need to ensure:

- The **buffer system** gives the desired pH.
- The **total osmotic pressure** matches that of body fluids (adjusted using tonicity agents like NaCl).

Methods of Adjusting Isotonicity

There are several methods to adjust the isotonicity of a pharmaceutical solution:

1. Class I Methods (Addition Method):

You add a sufficient amount of a **tonicity agent** (usually sodium chloride) to make the solution isotonic.

Example:
If a drug solution is not isotonic, you calculate the amount of NaCl needed using **NaCl equivalent method (E-value)**.

Amount of NaCl required=(0.9%)−(E-value×amount of drug)

- **E-value**: Amount of NaCl that has the same osmotic effect as 1 gram of the drug.

2. Class II Methods (Freezing Point Depression):

This method uses the **freezing point depression** (ΔT_f) to determine how much solute is needed to make the solution isotonic.

- Normal isotonic solution has a **freezing point of -0.52°C**.
- Use:

Amount of adjusting substance=0.52−ΔTf of drug/0.576

3. White-Vincent Method (Volume Adjustment):

This method determines the **volume of isotonic solution that can be prepared** with a given amount of drug.

$V=w\times E\times 111.1$

Where:

- *V* = volume of isotonic solution
- *w* = weight of drug in grams
- *E* = NaCl equivalent

Then adjust to that volume using sterile water.

4. Cryoscopic Method:

Based on the **freezing point lowering principle**, as body fluids freeze at –0.52°C. The solution is isotonic when its freezing point depression equals that of blood plasma.

5. Sprowls Method:

A variation of the White-Vincent method, where **precalculated E-value tables** are used for rapid formulation.

Applications of Buffered Isotonic Solutions:

- **Eye drops**: Must be isotonic to prevent lacrimation or eye irritation (e.g., phosphate-buffered saline)
- **Injectables**: Intravenous fluids must match blood osmolarity to avoid hemolysis or phlebitis.
- **Nasal sprays**: Prevent mucosal irritation and support drug absorption.
- **Biological drug preparations**: For protein or enzyme stability and compatibility with body fluids.

Measurements of Tonicity

Definition

Tonicity refers to the **osmotic pressure exerted by a solution** relative to body fluids like blood plasma, tears, or cerebrospinal fluid.
It determines whether the solution will cause **cells to shrink (hypertonic)**, **swell (hypotonic)**, or remain unaffected (**isotonic**).

Why Measure Tonicity?

- To **ensure compatibility** of dosage forms (especially parenteral, ophthalmic, nasal).
- To **avoid cellular damage** like hemolysis, irritation, or inflammation.
- To **maintain therapeutic efficacy** and patient safety.

Methods for Measurement of Tonicity

1. Freezing Point Depression Method (Cryoscopic Method)

- **Principle:** Body fluids (like blood plasma and lacrimal fluid) have a freezing point of **–0.52°C**.
- A solution is **isotonic** if it also freezes at **–0.52°C**.
- **Measurement:** Compare the freezing point of the test solution with that of body fluids.

$\Delta T_f = 0.52^\circ C - \text{Measured Freezing Point}$

- Instruments: Cryoscope
- **Commonly used** for parenteral and ophthalmic preparations.

2. Vapour Pressure Method (Osmometry)

- **Principle:** Solutions with higher solute concentration have **lower vapour pressure**.
- **Osmometers** measure vapour pressure to estimate the **osmotic concentration**.
- It gives **osmolarity** (mOsmol/L), which can be correlated to isotonicity.

3. Hemolytic Method (Biological Method)

- **Principle:** Red blood cells (RBCs) react to changes in osmotic pressure.
- **Procedure:**
  - RBCs are suspended in the test solution.
  - The degree of hemolysis is observed.
    - **Complete hemolysis** → Hypotonic
    - **Cell shrinkage** → Hypertonic
    - **No effect** → Isotonic
- This method is **biological** and is useful for checking **blood-compatible** solutions.

4. Colligative Property-Based Calculations

- Based on **osmotic pressure**, **freezing point depression**, **boiling point elevation**, or **vapour pressure lowering**.
- For isotonicity calculations, **freezing point depression** is most commonly used.

5. Osmolarity/Osmolality Measurement

- **Osmolarity**: Osmoles of solute per litre of solution (mOsmol/L).
- **Osmolality**: Osmoles of solute per kilogram of solvent (mOsmol/kg).
- Normal osmolarity of human plasma is **~275–295 mOsmol/L**.
- Instruments: **Osmometers**
- Used to ensure pharmaceutical solutions fall within the physiological osmolarity range.

6. Isotonicity Testing Using Red Cell Method

- In pharmacopoeial testing (especially Indian and British Pharmacopoeias), a **test involving suspension of RBCs** is used to confirm the tonicity of injections and eye drops.
- The **appearance and sedimentation** of RBCs are compared with that in **0.9% NaCl solution**.

Summary of Measurement Techniques

Method	Nature	Accuracy	Common Use
Freezing Point Depression	Physical	High	Ophthalmic, Parenterals
Vapour Pressure Osmometry	Physical	High	Research labs
Hemolytic Method	Biological	Moderate	Injectable solutions
Colligative Properties	Theoretical	Moderate	Formulation calculations
Osmolality Measurement	Instrumental	Very High	Hospital & QC laboratories

Major Extra- and Intracellular Electrolytes

Electrolytes are inorganic ions that **dissociate in body fluids** to produce ions capable of conducting electricity. These are essential for maintaining **homeostasis**, **nerve conduction**, **muscle function**, **acid-base balance**, and **fluid balance**.

They are broadly classified based on their **location** in the body:

Extracellular Electrolytes (outside the cells):

1. **Sodium (Na^+)**
2. **Chloride (Cl^-)**
3. **Bicarbonate (HCO_3^-)**
4. **Calcium (Ca^{2+})**
5. **Magnesium (Mg^{2+})** (partly)

Intracellular Electrolytes (inside the cells):

1. **Potassium (K^+)**
2. **Magnesium (Mg^{2+})**
3. **Phosphate (HPO_4^{2-}, $H_2PO_4^-$)**
4. **Sulfate (SO_4^{2-})**

Functions of Major Physiological Ions

1. Sodium (Na^+)

- **Main extracellular cation**.
- Maintains **osmotic balance**, **blood volume**, and **blood pressure**.
- Required for **nerve impulse conduction** and **muscle contraction**.

- Regulated by the **aldosterone hormone**.
- Daily requirement: ~2–3 grams.

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2. Potassium (K^+)

- **Principal intracellular cation**.
- Vital for **nerve impulse transmission**, **muscle contraction**, especially **cardiac muscle**.
- Helps in **intracellular enzyme function** and **acid-base balance**.
- Imbalance can lead to **arrhythmia** or **muscle weakness**.
- Regulated by **aldosterone** and renal excretion.

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3. Chloride (Cl^-)

- **Major extracellular anion**.
- Maintains **osmotic pressure**, **acid-base balance**, and forms **hydrochloric acid in the stomach**.
- Assists in **electroneutrality** by balancing sodium and potassium.
- Deficiency may cause **alkalosis** or **muscle cramps**.

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4. Bicarbonate (HCO_3^-)

- Major **buffer anion** in blood.
- Maintains **physiological pH (7.35–7.45)** by buffering excess acids.
- Involved in **carbon dioxide transport** from tissues to lungs.
- Controlled by **kidneys and lungs** in the bicarbonate-carbonic acid buffer system.

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5. Calcium (Ca^{2+})

- Mostly found in **bones and teeth**, but a small amount is crucial in **plasma**.
- Functions in **blood coagulation**, **neuromuscular activity**, **enzyme activation**, and **hormone release**.
- Essential for **muscle contraction**, especially the **heart**.
- Regulated by **parathyroid hormone**, **vitamin D**, and **calcitonin**.

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6. Magnesium (Mg^{2+})

- Predominantly **intracellular**, found in **bone and soft tissues**.
- Cofactor in over **300 enzymatic reactions** including ATP metabolism.
- Helps in **neuromuscular transmission**, **cardiac function**, and **DNA/RNA synthesis**.
- Low levels can cause **neuromuscular hyperexcitability**.

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7. Phosphate (HPO_4^{2-}, $H_2PO_4^-$)

- Mainly found in **intracellular fluid**, bones, and teeth.
- Important for **energy transfer (ATP, ADP)**, **nucleic acids**, and **phospholipids**.
- Involved in **buffering systems** and **cellular metabolism**.
- Regulated by **parathyroid hormone** and **vitamin D**.

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8. Sulfate (SO_4^{2-})

- Present in **intracellular fluid**, required for **protein structure (disulfide bonds)**.
- Component of **mucopolysaccharides**, **hormones**, and **enzymes**.
- Helps in **detoxification in the liver** through sulfonation.

Electrolytes Used in Replacement Therapy

Electrolyte replacement therapy is used to **restore normal body fluid composition**, especially in conditions like **dehydration**, **electrolyte imbalance**, **diarrhea**, **vomiting**, **burns**, and **shock**. The commonly used electrolyte salts in replacement therapy include:

1. Sodium Chloride (NaCl)*

Category: Electrolyte replenisher and plasma expander
IP Status: Official in Indian Pharmacopoeia

General Properties:

- Colorless, crystalline powder
- Soluble in water, saline taste
- Normal saline = 0.9% w/v solution of NaCl

Medicinal Uses:

- Maintains **osmotic balance** and **extracellular fluid volume**
- Used in **IV infusions** as normal saline for dehydration

- Treats **hyponatremia** and **hypochloremia**
- Used for **wound cleaning**, **eye drops**, **nasal sprays**

Assay (As per IP):

- Based on **argentometric titration** using **silver nitrate** and potassium chromate indicator (Mohr's method)

2. Potassium Chloride (KCl)

Category: Potassium supplement, electrolyte replenisher
IP Status: Official in IP

General Properties:

- White crystalline powder
- Freely soluble in water
- Taste: Saline and bitter

Medicinal Uses:

- Used to correct **hypokalemia** (low potassium levels)
- Supports **cardiac function**, **nerve transmission**, and **muscle contraction**
- Administered orally or IV (with caution due to risk of hyperkalemia)
- Commonly included in **ORS** and electrolyte combinations

Precautions:

- Rapid IV infusion can be **fatal** (cardiac arrest), hence diluted and slowly infused
- Should not be given undiluted

Assay (As per IP):

- Based on **precipitation titration** with sodium tetraphenylborate

3. Calcium Gluconate*

Category: Calcium supplement
IP Status: Official

General Properties:

- White, crystalline, odorless powder
- Slightly soluble in water

- Contains about 9% elemental calcium

Medicinal Uses:

- Used in **hypocalcemia**, **calcium deficiency**, **tetany**, **osteoporosis**, and **cardiac arrest**
- Given orally or via **slow IV injection**
- Also used as **antidote for magnesium sulfate toxicity**
- Stabilizes **neuromuscular and cardiac function**

Assay (As per IP):

- Complexometric titration with **EDTA** using **murexide indicator**

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4. Oral Rehydration Salt (ORS)

Category: WHO-approved fluid and electrolyte replenisher
Composition (WHO formula):

- Sodium chloride – 2.6 g
- Potassium chloride – 1.5 g
- Sodium citrate – 2.9 g
- Glucose anhydrous – 13.5 g
- Dissolved in 1 liter of potable water

Medicinal Uses:

- Used to treat **dehydration due to diarrhea**, vomiting, heat stroke
- Glucose aids sodium absorption via **SGLT (sodium-glucose transport)**
- Maintains **electrolyte and fluid balance**, especially in children

Advantages:

- Safe, economical, and life-saving in **diarrheal diseases**
- Reduces the need for hospitalization

Types:

- **Standard ORS** – used for all ages
- **Low-osmolarity ORS** – reduces stool output and vomiting

Physiological Acid-Base Balance

The acid-base balance is essential for **normal biochemical functioning** of the human body. The body must maintain a **narrow pH range of 7.35 to 7.45** in the blood. Even slight deviations can affect enzyme activity, oxygen transport, and cellular function. The maintenance of this balance is called **homeostasis**.

Sources of Acids and Bases in the Body

- **Acids:**
  - **Volatile acid** – Carbonic acid (H_2CO_3), formed from CO_2 and water.
  - **Fixed acids** – Lactic acid, sulfuric acid, phosphoric acid, and ketone bodies.
- **Bases:**
  - Primarily **bicarbonate (HCO_3^-)** and other anionic buffers.

Mechanisms that Maintain Acid-Base Balance

The body employs **three major systems** to regulate pH:

1. Buffer Systems (Immediate Response)

Buffers resist changes in pH by neutralizing excess acids or bases. Major physiological buffer systems include:

- **Bicarbonate Buffer System (HCO_3^- / H_2CO_3):**
  Most important in **extracellular fluid**
  $CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$
- **Phosphate Buffer System ($H_2PO_4^-$ / HPO_4^{2-}):**
  Important in **intracellular fluids** and **renal tubules**
- **Protein Buffer System (e.g., hemoglobin):**
  Proteins act as **amphoteric molecules** that can accept or donate H^+ ions
  Effective in **intracellular and blood plasma buffering**

2. Respiratory Regulation (Within Minutes)

- The **lungs regulate blood pH** by controlling the level of **carbon dioxide (CO_2)**.
- CO_2 is exhaled, reducing carbonic acid levels and increasing pH.
- **Hyperventilation** causes loss of CO_2 → **Respiratory alkalosis**

- **Hypoventilation** causes retention of CO_2 → **Respiratory acidosis**

3. Renal Regulation (Slow but Long-Lasting)

- The **kidneys regulate pH** by excreting **H^+ ions** and reabsorbing **HCO_3^-**.
- They also produce **ammonia** to bind with H^+ and excrete it as **NH_4^+**.
- This mechanism is **slow (hours to days)** but very effective.

Acid-Base Disorders

Imbalance in acid-base regulation leads to four major clinical conditions:

Type	Cause	Compensation
Metabolic Acidosis	Loss of bicarbonate (diarrhea), excess acid (diabetes, renal failure)	Hyperventilation to remove CO_2
Metabolic Alkalosis	Excess bicarbonate (antacids), loss of acid (vomiting)	Hypoventilation
Respiratory Acidosis	Hypoventilation (COPD, asthma) → CO_2 retention	Renal reabsorption of HCO_3^-
Respiratory Alkalosis	Hyperventilation (anxiety, fever) → CO_2 loss	Renal excretion of HCO_3^-

Normal Blood Gas Values

Parameter	Normal Range
pH	7.35 – 7.45
pCO_2	35 – 45 mmHg
HCO_3^-	22 – 26 mEq/L
pO_2	80 – 100 mmHg

Dental Products: Dentifrices

Dentifrices are preparations used **with a toothbrush** to **clean and polish natural teeth**. They are designed to promote **oral hygiene**, remove **dental plaque**, food debris, and **surface stains**, and deliver **active agents** for therapeutic or cosmetic benefits.

Types of Dentifrices

1. **Toothpastes** – Most commonly used, semi-solid preparation.
2. **Tooth powders** – Finely divided powders (less commonly used now).
3. **Gels** – Transparent or translucent forms, may contain fluoride or whiteners.
4. **Mouthwashes and rinses** – Adjunct to dentifrices for antimicrobial action.
5. **Medicated dentifrices** – Contain therapeutic agents like fluoride, triclosan, chlorhexidine.

Ideal Properties of Dentifrices

- Non-irritating, pleasant taste
- Able to **clean teeth effectively**
- Compatible with dental tissues and restorative materials
- Stable and non-toxic
- **pH near neutral** (to avoid enamel erosion)
- Contain **anticaries, antimicrobial, and antiplaque** agents

Formulation of Dentifrices

A typical toothpaste formulation contains the following components:

Ingredient	**Purpose**
Abrasives	Remove debris, stains (e.g., calcium carbonate, hydrated silica, dicalcium phosphate)
Humectants	Prevent drying (e.g., glycerin, sorbitol, propylene glycol)
Binding agents	Maintain consistency (e.g., sodium carboxymethyl cellulose, xanthan gum)
Surfactants/foaming agents	Help loosen debris (e.g., sodium lauryl sulfate)
Sweeteners and flavors	Improve taste (e.g., saccharin, mint oil, menthol)
Preservatives	Prevent microbial growth (e.g., methylparaben, benzoates)
Coloring agents	Aesthetic appeal
Therapeutic agents	Fluoride (anticaries), triclosan (antibacterial), desensitizers, whiteners
Water	Solvent

Role of Fluoride in Dentifrices

- Most toothpastes contain **1000–1500 ppm fluoride**.
- Fluoride strengthens enamel by converting hydroxyapatite to **fluorapatite**, making teeth more resistant to acid attack.
- Also inhibits bacterial metabolism (especially *Streptococcus mutans*), reducing dental caries.

Medicinal Uses

- Prevention of **dental caries**
- Reduction of **plaque and gingivitis**
- Relief of **dentin hypersensitivity**
- Whitening or stain removal
- Delivery of **desensitizing agents**, **fluoride**, or **antibacterials**

Examples of Common Dentifrices

1. **Calcium carbonate-based toothpastes** – abrasive and cleansing agent
2. **Sodium monofluorophosphate or sodium fluoride** – anticaries
3. **Potassium nitrate** – desensitizing agent
4. **Triclosan** – antimicrobial
5. **Zinc compounds** – reduce halitosis and plaque

Role of Fluoride in the Treatment of Dental Caries

Fluoride is a **key agent** in the **prevention and treatment of dental caries (tooth decay)**. Its inclusion in various dental products such as **toothpastes, mouthwashes, drinking water, tablets, and varnishes** has significantly reduced the incidence of dental caries worldwide.

Mechanism of Action of Fluoride

1. **Remineralization of Enamel:**
   - Enamel is primarily made of **hydroxyapatite crystals ($Ca_{10}(PO_4)_6(OH)_2$)**.
   - During acid attack by bacterial fermentation of sugars, enamel demineralizes.
   - Fluoride helps in **remineralization** by forming **fluorapatite ($Ca_{10}(PO_4)_6F_2$)**, which is more **resistant to acid dissolution** than hydroxyapatite.

2. **Inhibition of Demineralization:**
    - Fluoride ions **adsorb onto the enamel surface** and protect it from acid attack.
    - It reduces the solubility of enamel in acidic pH.
3. **Antibacterial Effect:**
    - Fluoride **inhibits bacterial enzymes** (like enolase), reducing acid production by cariogenic bacteria (*Streptococcus mutans*).
    - Fluoride disrupts the **metabolism and adhesion** of bacteria to the tooth surface.
4. **Enhancement of Enamel Maturation:**
    - In developing teeth, systemic fluoride helps form **stronger, well-mineralized enamel**.

Fluoride Delivery Methods

1. **Topical Fluoride:**
    - **Toothpastes** (1000–1500 ppm fluoride)
    - **Mouth rinses** (225 ppm for daily use or 900 ppm for weekly use)
    - **Fluoride varnishes and gels** (used professionally in high-risk patients)
    - **Fluoride-containing dental materials** (cements, sealants)
2. **Systemic Fluoride:**
    - **Fluoridated drinking water** (optimum: 0.7–1.2 ppm)
    - **Fluoride tablets or drops** (used in non-fluoridated areas, especially in children)
    - **Salt or milk fluoridation** in some countries

Desensitizing Agents

Desensitizing agents are used in the treatment of **dentin hypersensitivity**, which is a short, sharp pain arising from exposed dentin in response to thermal, tactile, or chemical stimuli. Hypersensitivity occurs due to the exposure of dentinal tubules to the oral environment.

Mechanism of Action

- These agents **block or occlude the dentinal tubules**, preventing fluid movement within the tubules and thereby reducing nerve response.
- Some agents **depolarize nerve endings**, preventing the transmission of pain.

Examples

1. **Potassium Nitrate** – Interferes with nerve signal transmission by depolarizing nerve endings.
2. **Strontium Chloride** – Precipitates inside tubules, blocking them.
3. **Fluorides** (e.g., sodium fluoride) – Promote remineralization and occlusion.
4. **Oxalates** – Form calcium oxalate crystals inside the tubules.
5. **Calcium Phosphate-based agents** – Promote tubule sealing via hydroxyapatite formation.

Uses

- Incorporated into **toothpastes** and **varnishes** for routine use.
- Provide symptomatic relief for patients with sensitivity due to gum recession, enamel erosion, or after scaling.

1)Calcium Carbonate

Properties

- Chemical formula: $CaCO_3$
- Appearance: Fine, white, odorless powder
- Practically insoluble in water
- Stable at room temperature

Medicinal Uses

- **Mild abrasive** in **toothpastes**, helps in removing plaque and stains from teeth.
- Used as a **calcium supplement** in treating hypocalcemia.
- Acts as an **antacid** by neutralizing stomach acid.

Pharmaceutical Use

- Used as a **filler**, **diluent**, and **abrasive** in dentifrices.
- Safe and economical ingredient with good polishing ability.

2)Sodium Fluoride

Properties

- Chemical formula: NaF
- Appearance: White crystalline solid
- Soluble in water

Medicinal Uses

- **Caries prevention**: Acts as a topical anticaries agent.
- **Remineralizes enamel** and forms **fluorapatite**.
- Available in **toothpastes (1000–1500 ppm)**, **mouth rinses**, and **varnishes**.
- Also used in **fluoride tablets** for systemic fluoridation in children in non-fluoridated areas.

Dose and Administration

- Commonly used in concentrations between **0.05% to 0.2%** in mouth rinses.
- Incorporated in dental materials for **long-term fluoride release**.

3)Zinc Eugenol Cement

Composition

- Powder: **Zinc oxide**
- Liquid: **Eugenol** (from clove oil)

Mechanism

- A chelation reaction between ZnO and eugenol forms a **hard mass** with sedative and sealing properties.

Properties

- Has **analgesic and antiseptic** properties.
- Provides **thermal insulation** and temporary sealing in dental cavities.

Uses in Dentistry

- Used as a **temporary filling material** and **lining agent** under restorations.
- Acts as a **sedative dressing** for sensitive or inflamed pulps.
- Used in **impression pastes** and **periodontal dressings**.

Advantages

- Non-irritating to pulp
- Soothing to exposed dentin
- Easy to mix and apply

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

ANTACIDS

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**

1)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

2)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

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**

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**

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

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

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

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

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+→2Mn2++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

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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**
- Avoid contamination with organic matter