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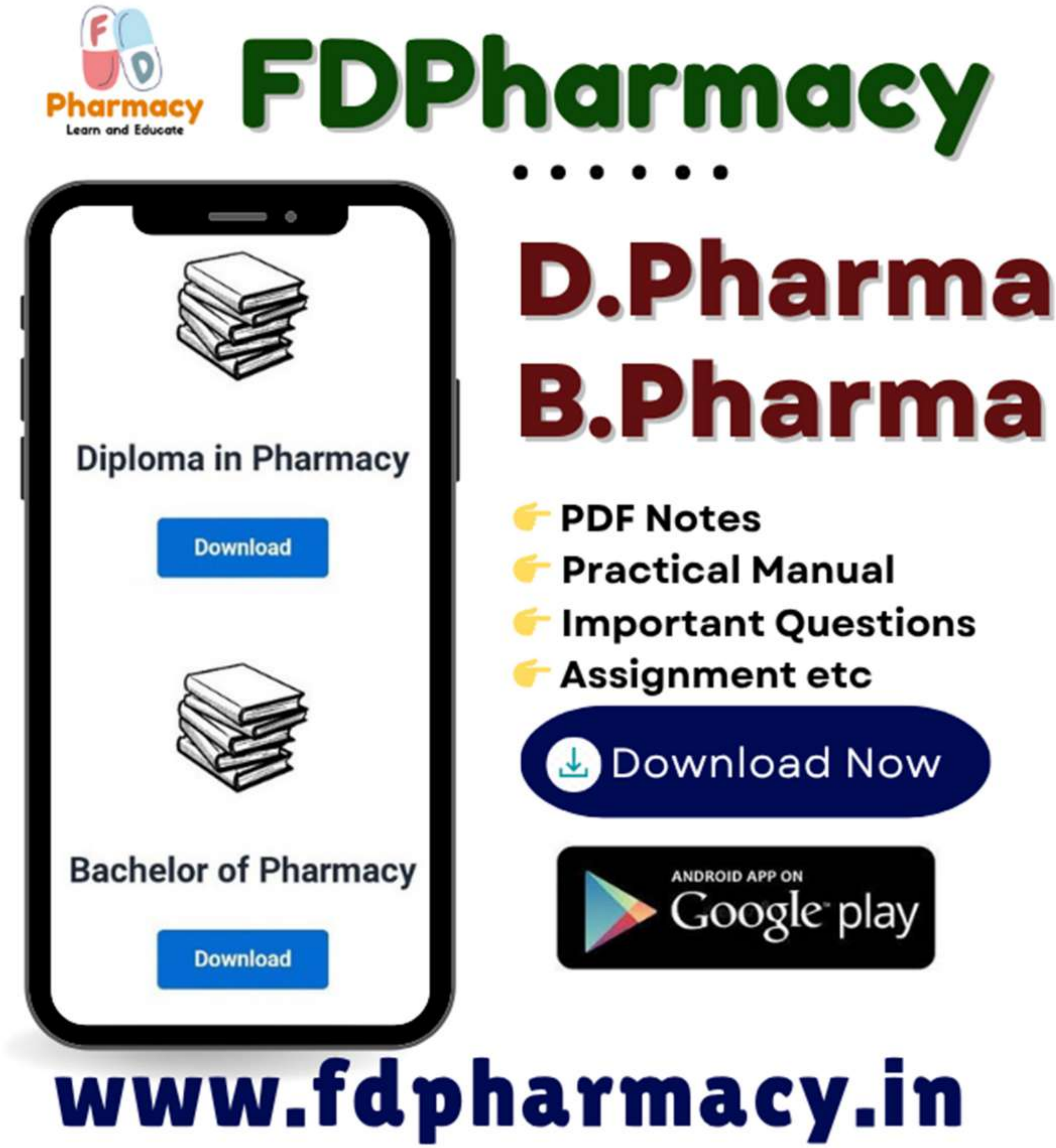
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PHARMACEUTICAL INORGANIC CHEMISTRY

UNIT 2

TOPIC :

- **Major extra and intracellular electrolytes :** Functions of major physiological ions, Electrolytes used in the replacement therapy: Sodium chloride*, Potassium chloride, Calcium gluconate* and Oral Rehydration Salt (ORS), Physiological acid base balance.

Body Fluid

- Body fluid is the liquid present in the human body that helps in the transport of nutrients, gases, hormones, and waste materials, and also helps to maintain body functions like temperature, pH, and hydration.
- About 60% of total body weight in adults is water.
- Varies with age, sex, and body composition.

Types of body fluids

1. **Intracellular Fluid (ICF) :** Intracellular fluid is the fluid present inside the cells of the body. It makes up about two-thirds of total body fluid. Helps in cellular metabolism and chemical reactions
2. **Extracellular Fluid (ECF) :** Extracellular fluid is the fluid present outside the cells. Makes up about one-third of total body fluid. Helps in transport of nutrients, gases, and waste.

   Types of Extracellular Fluid (ECF)

   - **Interstitial Fluid :** Fluid found between the cells in tissues.
   - **Plasma (Intravascular Fluid) :** Fluid part of the blood
   - **Transcellular Fluid :** Specialized fluid found in specific body spaces.

Electrolytes

→ Electrolytes are substances that, when dissolved in water (or body fluids), dissociate into ions and conduct electricity.

→ **Examples**: Sodium chloride (NaCl), Potassium chloride (KCl), Calcium chloride ($CaCl_2$)

→ Electrolytes presents inside body can be divided into two categories :

i. Intracellular Electrolytes (Present Inside Cell)
ii. Extracellular Electrolytes (Present Outside Cell)

Functions of Major Physiological Ions

1. Sodium (Na^+)

- Maintains extracellular fluid volume and osmotic pressure
- Helps in nerve impulse transmission
- Involved in muscle contraction
- Regulates acid–base balance through Na^+/H^+ exchange
- It also protects body against excessive fluid loss.
- Low level of sodium leads to Hypoatremia.
- High level of sodium leads to Hypernatremia.

2. Potassium (K^+)

- Major intracellular cation
- Regulates membrane potential for nerve and muscle cells
- Essential for heart rhythm and muscle contraction
- Aids in protein synthesis and enzyme activity
- It also helps in transmission of nerve impulse
- Low level of potassium leads to Hypokalemia.
- High level of potassium leads to Hyperkalemia.

3. Calcium (Ca^{2+})

- Important for bone and teeth structure
- Necessary for muscle contraction, including cardiac muscle

- Plays a role in blood coagulation
- Involved in nerve impulse transmission
- Activates various enzymes and hormones
- It helps in contraction of vaious smooth muscles.
- Low level of calcium leads to Hypocalcemia.
- High level of calcium leads to Hypercalcemia.

4. Magnesium (Mg^{2+})

- Cofactor for over 300 enzymatic reactions
- Stabilizes ATP structure
- Required for neuromuscular function
- Helps in protein and DNA synthesis
- It also plays important role in Mycardial function.
- Low level of magnesium leads to Hypomagnesia.
- High level of magnesium leads to Hypermagnesia.

5. Chloride (Cl^-)

- Maintains osmotic balance and electrical neutrality
- Essential component of gastric juice (HCl)
- Helps regulate acid–base balance in blood
- The main source of chloride is common salt which is used in cooking.
- Low level of chloride leads to Hypochloremia.
- High level of chloride leads to Hyperchloremia.

6. Bicarbonate (HCO_3^-)

- Major buffer of blood pH
- Maintains acid–base balance
- Produced by carbonic anhydrase from CO_2 and water
- It also protects tissues of central nervous system.

7. Phosphate (PO_4^{3-})

- Component of ATP, DNA, RNA
- Involved in energy metabolism

- Helps buffer body fluids
- Vital for bone mineralization
- Main dietary source for phosphate is Milk, Nuts etc.
- Low level of phosphate leads to Hypophosphatemia.
- High level of phosphate leads to Hyperphosphatemia

8. Sulphate

- It is present in very small amount in extracellular fluid.
- They play vital role in Detoxification Mechanism.
- It also helps in various biological process.

Electrolytes used in the replacement therapy

→ In different abnormal conditions like Diarrhoea, Vomiting, Dehydration electrolytes in our body get imbalance.

→ The main purpose of electrolyte replacement therapy is to overcome the electrolyte imbalance and restore the composition of body fluid and body volume.

→ There are following three compounds which are used as the major source of electrolyte:

- Sodium Chloride
- Potassium Chloride
- Calcium Gluconate

1. SODIUM CHLORIDE (NaCl)

- **Molecular Formula**: NaCl
- **Molecular Weight**: 58.44 g/mol
- **Synonyms**:
  - Rock Salt
  - Table Salt
  - Common Salt

Method of Preparation

Natural Source:

- Obtained from rock salt or sea water.
- The naturally occurring salt is impure and may contain calcium, magnesium, and sulfate impurities.
- Purification:
  - Done by filtration and evaporation to obtain pure sodium chloride.

Laboratory Method:

- Prepared on a small scale by acid–base neutralization reaction:

  HCl (strong acid + $NaOH$ (strong base) → $NaCl$ + H_2O

Properties

Physical Properties:

- **State**: Crystalline or powder
- **Colour**: White or colourless
- **Taste**: Saline (salty)
- **Odour**: Odourless
- **Solubility**:
  - **Soluble** in water
  - **Insoluble** in alcohol

Chemical Properties:

- **Reaction with Silver Nitrate**:

  $NaCl + AgNO_3 \rightarrow AgCl$ (whiteppt) $+ NaNO_3$

- **Reaction with Sulfuric Acid**:

  $2NaCl + H_2SO_4 \rightarrow 2HCl + Na_2SO_4$

Uses

- Used as an electrolyte replenisher in IV fluids
- 0.9% NaCl solution is isotonic with blood
- Used in the preparation of Oral Rehydration Salts (ORS)
- Acts as a taste enhancer in food and formulations
- Used in diuretic formulations
- Used as a diluent in injections and infusions

Assay of Sodium Chloride

Principle:

- Based on Argentometric titration (precipitation titration using silver nitrate).

Procedure:

1. Weigh 1 g of sodium chloride sample.
2. Dissolve in 50 mL of distilled water.
3. Add 50 mL of 0.1 M $AgNO_3$ (silver nitrate).
4. Add 5 mL of 2 M nitric acid (HNO_3) and 2 mL of concentrated $KMnO_4$.
5. Shake well.
6. Titrate the solution with 0.1 M ammonium thiocyanate.
7. Use 2 mL of ferric ammonium sulfate as indicator.
8. End point: Appearance of reddish-brown colour (ferric thiocyanate complex).

2. POTASSIUM CHLORIDE (KCl)

- **Molecular Formula**: KCl
- **Molecular Weight**: 74.55 g/mol
- **Synonyms**:
  - Muriate of Potash
  - Potash
  - Kalium Chloride

Method of Preparation

Natural Source:

- Found naturally as sylvite (KCl) and in carnallite ($KCl \cdot MgCl_2 \cdot 6H_2O$)
- Extracted by mining, then purified by crystallization and evaporation of brine.

Laboratory Method:

- Can be prepared by neutralization reaction:

KOH (Potassium hydroxide) + HCl (Hydrochloric acid) → KCl + H_2O

Properties

Physical Properties:

- **State**: Crystalline powder or granules
- **Colour**: White or colourless
- **Taste**: Salty but slightly bitter
- **Odour**: Odourless
- **Solubility**:
  - **Freely soluble** in water
  - **Insoluble** in alcohol

Chemical Properties:

- **Neutral salt** (does not hydrolyze in water)
- Reacts with **silver nitrate ($AgNO_3$)** to form white precipitate of **silver chloride (AgCl)**:

$$KCl + AgNO_3 \rightarrow AgCl \downarrow + KNO_3$$

Uses

- Used as a potassium replenisher to treat hypokalemia (low potassium levels)
- Important for muscle contraction, especially cardiac function
- Used in oral rehydration salts (ORS)
- Included in IV fluids (very carefully and slowly)
- Acts as a fertilizer in agriculture (not for pharmaceutical grade)

Assay of Potassium Chloride

Principle:

- Based on precipitation titration with silver nitrate ($AgNO_3$).

Procedure:

- Dissolve a known quantity of KCl in water.
- Add nitric acid to acidify the solution.
- Titrate with 0.1 M $AgNO_3$ using potassium chromate as an indicator.
- End point: Formation of red precipitate **of** silver chromate (Ag_2CrO_4)

3. CALCIUM GLUCONATE

- **Molecular Formula**: $C_{12}H_{22}CaO_{14}$
- **Molecular Weight**: 430.37 g/mol
- **Synonyms**:
  - Gluconic acid calcium salt
  - Calcium D-gluconate

Method of Preparation

Laboratory Preparation:

- Prepared by neutralizing gluconic acid (or sodium gluconate) with calcium carbonate ($CaCO_3$) or calcium hydroxide ($Ca(OH)_2$).

  2C6H12O7 (Gluconic acid) + CaCO3 → (C6H11O7)2Ca + CO2 + H2O

- The product is then filtered and crystallized to obtain pure calcium gluconate.

Properties

Physical Properties:

- **Appearance**: White, crystalline powder or granules
- **Taste**: Slightly bitter
- **Odour**: Odourless
- **Solubility**:
  - Sparingly soluble in water
  - Insoluble in alcohol and ether

Chemical Properties:

- Stable in dry air
- On heating, decomposes and may form calcium carbonate
- Does not react with silver nitrate like chlorides
- Compatible with calcium salts and weak acids

Uses

- Acts as a calcium replenisher in hypocalcemia (low blood calcium)
- Used in calcium deficiency diseases like:
  - Rickets
  - Osteomalacia
  - Tetany
- Used in treatment of:
  - Calcium channel blocker overdose
  - Hyperkalemia (as a cardiac stabilizer)
  - Magnesium sulfate toxicity (e.g., in eclampsia)
- Used in intravenous injections to correct acute hypocalcemia

Assay of Calcium Gluconate

Principle:

- Based on complexometric titration using EDTA (disodium salt)

Procedure:

- Dissolve an accurately weighed sample in water.
- Add buffer solution (pH 10).
- Use Eriochrome Black T or Murexide as indicator.
- Titrate with standard 0.05 M EDTA until colour changes (end point).

ORS – Oral Rehydration Salt

- ORS stands for Oral Rehydration Salt
- Also known as Oral Rehydration Therapy (ORT)
- ORS is a type of fluid replacement therapy used mainly for treating dehydration caused by diarrhea.
  It is a simple, cheap, and highly effective method to prevent or treat fluid and electrolyte loss.

Uses

- Treats dehydration caused by:
  - Diarrhea
  - Vomiting
  - Heatstroke
- Restores electrolyte balance
- Prevents shock and severe complications in children and adults

Principle of ORS

→ Glucose enhances the intestinal absorption of sodium and water by sodium-glucose co-transport mechanism, helping to rehydrate the body and restore electrolyte balance.

WHO-Recommended Formula of ORS (per 1 liter of water)

Component	Amount (g/L)
Sodium chloride (NaCl)	2.6 g
Potassium chloride (KCl)	1.5 g
Trisodium citrate dehydrate	2.9 g
Glucose (anhydrous)	13.5 g
Total weight	**20.5 g**

Equipment Needed

- 1 liter boiled and cooled drinking water
- A clean glass (200 mL)
- A clean vessel for mixing
- A clean spoon for mixing and feeding

Procedure

- Wash hands thoroughly
- Take 1 liter of clean water in a vessel
- Open the ORS packet
- Pour the entire contents into the water
- Stir well using a clean spoon
- Pour the solution into a clean glass
- Feed the child/adult small amounts frequently (every few minutes)

Important Points

- Use the solution within 24 hours
- Do not boil the solution after mixing
- Discard leftover solution after 24 hours
- Do not add sugar, salt, or other ingredients

Advantages of ORS:

- Low cost, easy to prepare
- Life-saving in acute diarrhea
- Can be used at home or hospital
- Safe for all age groups

Storage

- Keep ORS packets in a **cool, dry place**
- Once prepared, the solution should be **stored in a clean container** and used within **24 hours**

Physiological Acid Base Balance

→ Acid–base balance is a part of the homeostasis process that maintains the body's pH within a normal range.
Most biochemical reactions in the body function only at a specific pH, and even slight deviations can lead to serious physiological disturbances.

- Normal Blood pH: ~7.42
- Survival pH Range: 6.8 – 8.0
- Outside this range may result in coma or death, hence maintaining pH is crucial.

Systems That Regulate pH Balance

1. **Buffer System** – First line of defense
2. **Respiratory System** – Fast, second line of defense
3. **Renal System** – Slow but most effective, long-term regulation

1. Buffer Systems

→ Buffers convert strong acids and bases into weak acids and bases, preventing rapid or drastic changes in pH.

Major Buffer Systems in the Body:

Buffer System	Location
1. Bicarbonate buffer	Blood plasma, kidneys
2. Phosphate buffer	Intracellular fluid, intestine
3. Protein buffer	Blood and plasma

(1) Bicarbonate Buffer System

- Most important buffer in blood
- Operates in plasma and kidneys

Mechanism:

Case I: When H^+ (acid) increases (acidosis):

$$H^+ + HCO_3^- \rightarrow H_2CO_3 \text{ (carbonic acid)}$$

Case II: When H^+ decreases (alkalosis):

$$H_2CO_3 \rightarrow H^+ + HCO_3^-$$

(2) Phosphate Buffer System

- Found in intestinal fluid and intracellular fluid
- Consists of:
  - Na_2HPO_4 (Disodium monohydrogen phosphate – weak base)
  - NaH_2PO_4 (Sodium dihydrogen phosphate – weak acid)

Mechanism:

Case I: When H^+ increases (acidosis):

$$H^+ + Na_2HPO_4 \rightarrow NaH_2PO_4$$

Case II: When H^+ decreases (alkalosis):

$$NaH_2PO_4 \rightarrow Na_2HPO_4 + H^+$$

(3) Protein Buffer System

- Found in blood and plasma
- Proteins contain amino acids, which have:
  - Amino group ($-NH_2$) → acts as base
  - Carboxyl group ($-COOH$) → acts as acid

➢ ***Mechanism:***

Case I: Excess H^+ → Amino group accepts H^+

$$-NH_2 + H^+ \rightarrow -NH_3^+$$

Case II: Low H^+ → Carboxyl group releases H^+

$$-COOH \rightarrow -COO^- + H^+$$

2. Respiratory system

→ The respiratory system plays an important role in maintaining acid–base balance by regulating the level of carbon dioxide (CO_2) in the blood.

→ CO_2 in blood combines with water to form carbonic acid (H_2CO_3):

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

Thus, an increase or decrease in CO_2 directly affects blood pH.

Case	Condition	CO_2 Level	Effect on pH	Respiratory Response
Case I – Acidosis	↑ Acidity in blood	↑ CO_2	↓ pH (more H^+ ions)	↑ **Breathing rate** to remove CO_2
Case II – Alkalosis	↑ Basicity in blood	↓ CO_2	↑ pH (less H^+ ions)	↓ **Breathing rate** to retain CO_2

3. Renal system

→ The renal system (kidneys) is the most powerful and long-term regulator of acid–base balance.
It maintains blood pH by controlling the excretion of hydrogen ions (H^+) and the reabsorption of bicarbonate ions (HCO_3^-).

→ Normal urine pH: ~6.0 (slightly acidic)

→ when the amount of H^+ increases in our body then it is eliminated from our body through Urine, while the bicarbonate ions HCO_3^- reabsorbed in our body and that's how it maintains the acid-base balance.