SNS COLLEGE OF PHARMACY AND HEALTH SCIENCES

Coimbatore -641035

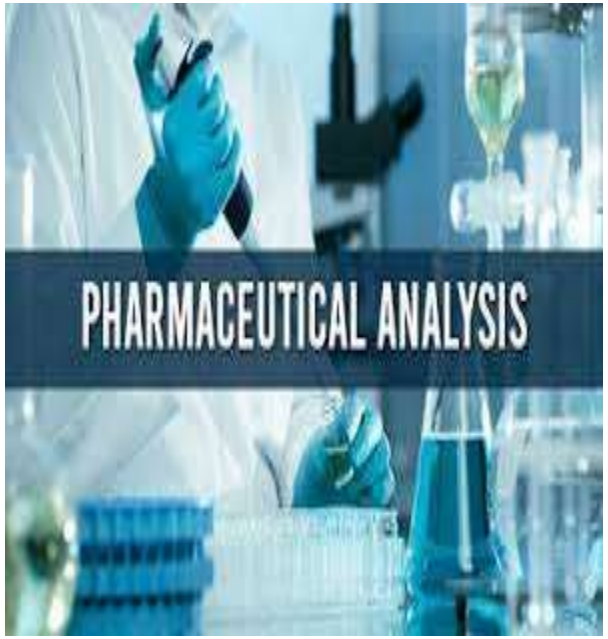
COURSE NAME: BP102T-PHARMACEUTICAL ANALYSIS (Theory)

I YEAR / I SEMESTER

SUB TOPIC: UNIT I-PHARMACEUTICAL ANALYSIS

INTRODUCTION:-

- **Definition:** Pharmaceutical Analysis is the branch of pharmacy that deals with the identification, quantification, and purification of drugs and pharmaceutical substances.
- Involves the application of chemical, physical, and instrumental techniques to analyze drugs.
- Ensures the quality, safety, and efficacy of pharmaceutical products.



Scope of Pharmaceutical Analysis:-

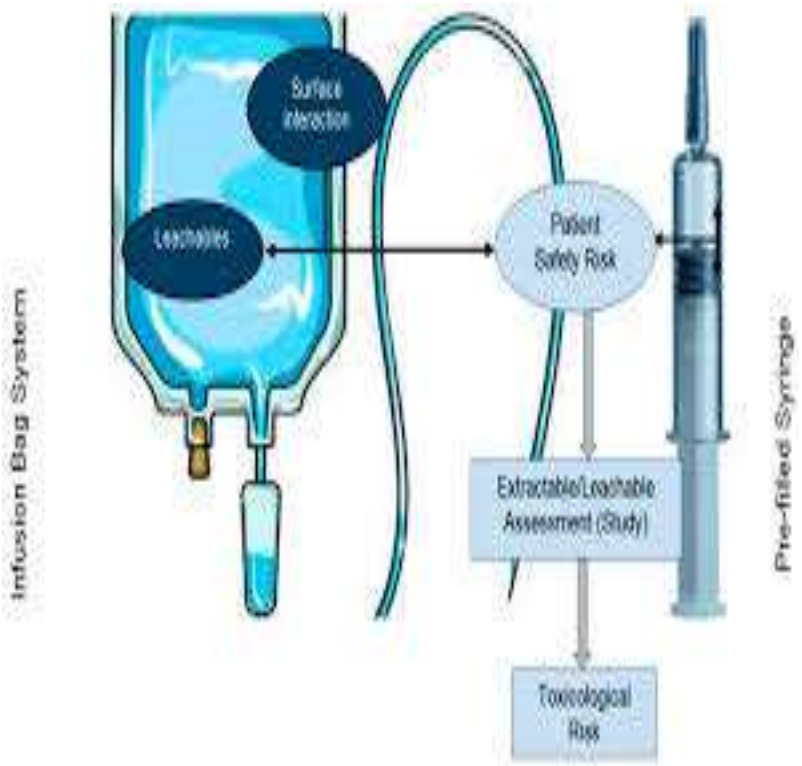
- **Quality Control**: Ensures drugs meet standards for purity, potency, and safety.
- **Drug Development**: Supports formulation, stability testing, and validation of new drugs.
- **Regulatory Compliance**: Meets guidelines set by agencies like FDA, WHO, and ICH.
- **Research and Innovation**: Develops new analytical methods for complex drug molecules.
- **Forensic Analysis**: Detects counterfeit or adulterated drugs.

Techniques in Pharmaceutical Analysis:

- **Chemical Methods:** Titrimetry, gravimetry for drug quantification.Spectroscopic
- **Methods:** UV-Vis, IR, NMR for structural analysis.
- **Chromatographic Methods:** HPLC, GC for separation and identification.
- **Electrochemical Methods:** Potentiometry, conductometry for ion analysis.
- **Applications:** Used in raw material testing, in-process control, and final product analysis.

Importance in Pharmacy:-

- **Ensures Patient Safety**: Verifies absence of harmful impurities in drugs.
- **Enhances Drug Efficacy**: Confirms correct dosage and active ingredient content.
- **Supports Industry Standards**: Aligns with Good Manufacturing Practices (GMP).
- **Career Opportunities**: Roles in quality control, R&D, regulatory affairs, and academia.
- **Future Trends**: Automation, AI, and advanced analytical tools in pharmaceutical analysis.



Different techniques of analysis:-

- **High-Performance Liquid Chromatography (HPLC):** Separates and quantifies drug components.
- **Gas Chromatography (GC):** Used for volatile compounds.
- **Thin Layer Chromatography (TLC):** Quick method for drug purity checks.
- **UV-Visible Spectroscopy**: Analyzes drug absorption in UV/visible range.
- **Infrared (IR) Spectroscopy:** Identifies functional groups in drug molecules.
- **Nuclear Magnetic Resonance (NMR):** Determines molecular structure.

Percentage Concentration:

- **Definition**: Expresses concentration as parts of solute per 100 parts of solution.
- **Types**:
  - **Weight/Weight (w/w)**: Grams of solute per 100 grams of solution.
    - Example: 5% w/w NaCl = 5 g NaCl in 100 g solution.
  - **Weight/Volume (w/v)**: Grams of solute per 100 mL of solution.
    - Example: 0.9% w/v saline = 0.9 g NaCl in 100 mL solution.
  - **Volume/Volume (v/v)**: mL of solute per 100 mL of solution.
    - Example: 70% v/v ethanol solution.
- **Applications**: Common in ointments, creams, and liquid formulations.

Different techniques of analysis:-

Molarity (M):

- **Definition**: Number of moles of solute per liter of solution (mol/L).
- **Formula**: Molarity (M) = Moles of solute / Volume of solution (in liters).
- **Example**: 0.1 M HCl = 0.1 moles of HCl in 1 liter of solution.

Molality (m):

- **Definition**: Number of moles of solute per kilogram of solvent (mol/kg).
- **Formula**: Molality (m) = Moles of solute / Mass of solvent (in kg).
- **Example**: 1 m glucose = 1 mole of glucose in 1 kg of water.

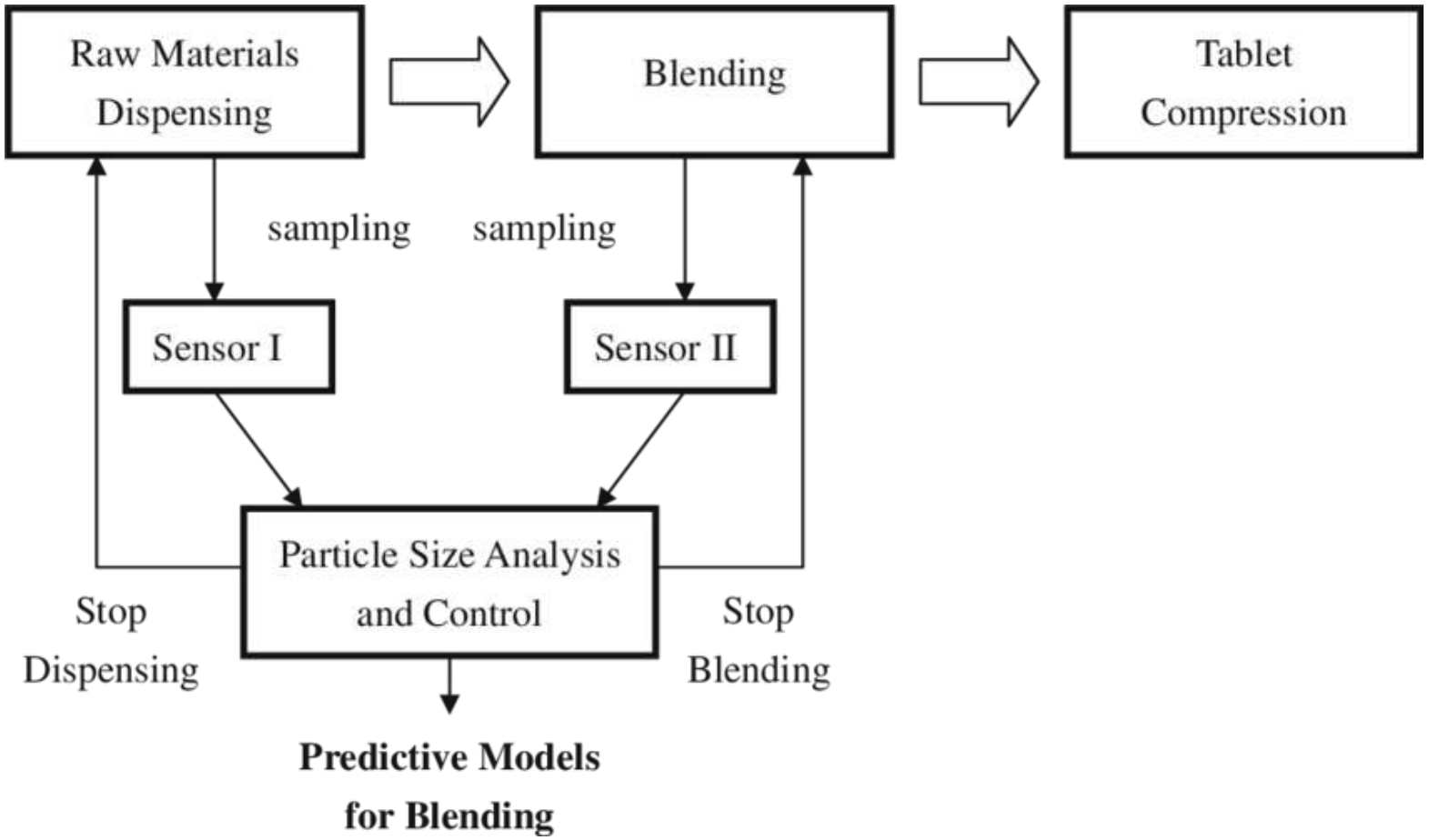
Normality (N):

- Number of gram-equivalents of solute per liter of solution.
- Formula: Normality (N) = Gram-equivalents of solute / Volume of solution (in liters).
- Example: 0.5 N H_2SO_4 = 0.5 equivalents of H_2SO_4 in 1 liter.
- Used in acid-base and redox titrations.

Parts Per Million (ppm):

- Mass of solute per million parts of solution (mg/kg or mg/L).
- Example: 1 ppm = 1 mg of solute in 1 kg of solution.
- Used for trace impurities in drugs or water analysis.

Percentage Concentration:



Primary Standards:

- **Definition**: Highly pure substances used directly as reference materials in analytical procedures.
- **Characteristics**:
  - High purity (≥99.98% pure).
  - Stable under storage conditions.
  - Non-hygroscopic and non-reactive.
  - Known composition and stoichiometry.
- **Examples**:
  - Sodium carbonate (Na_2CO_3) for acid-base titrations.
  - Potassium hydrogen phthalate (KHP) for standardization of bases.

Secondary Standards:

- **Definition**: Substances standardized against a primary standard for use in analytical procedures.
- **Characteristics**:
  - Less pure than primary standards but reliable after standardization.
  - May be hygroscopic or less stable.
  - Standardized using a primary standard before use.
- **Examples**:
  - Sodium hydroxide (NaOH) standardized against KHP.
  - Hydrochloric acid (HCl) standardized against Na_2CO_3.

Comparison Table: Primary vs. Secondary Standards:

- Pure chemical substances used to prepare standard solutions
- High stability, purity, and accuracy
- Non-hygroscopic and easy to weigh
- Examples: Sodium chloride, Potassium hydrogen phthalate
- Directly used for standardization of solutions

- Solutions standardized against primary standards
- Lower purity and stability compared to primary standards
- More prone to contamination or degradation
- Examples: Standardized NaOH, HCl solutions
- Used for routine analytical work after standardization

Preparation and Standardization of Various Molar Oxalic Acid.

Introduction to Molar and Normal Solutions:

- **Molar Solution**: A solution containing one mole of solute per liter of solution.
  - Formula: Molarity (M) = Moles of solute / Volume of solution (L)
- **Normal Solution**: A solution containing one gram equivalent weight of solute per liter of solution.
  - Formula: Normality (N) = Gram equivalent weight / Volume of solution (L)
- **Oxalic Acid ($C_2H_2O_4 \cdot 2H_2O$)**: A dibasic acid used as a primary standard in titrations.
- **Importance**: Used in volumetric analysis for standardization of bases (e.g., NaOH).

Preparation of Molar Solution of Oxalic Acid:

Definition: 1 M oxalic acid contains 126.07 g of $C_2H_2O_4 \cdot 2H_2O$ per liter.

Procedure:

- Weigh 12.607 g of oxalic acid dihydrate accurately.
- Dissolve in a small amount of distilled water in a volumetric flask.
- Make up the volume to 100 mL (for 0.1 M) or 1 L (for 1 M) with distilled water.
- Mix thoroughly to ensure uniformity.

Precautions:

- Use analytical-grade oxalic acid.
- Ensure complete dissolution before final volume adjustment.

Example: For 0.1 M, dissolve 1.2607 g in 100 mL of water.

Preparation of Normal Solution of Oxalic Acid:

•**Definition**: 1 N oxalic acid contains 1 gram equivalent weight per liter.

- Equivalent weight of oxalic acid = Molecular weight / Basicity = 126.07 / 2 = 63.035 g.

•**Procedure**:

- Weigh 6.3035 g of oxalic acid dihydrate for 1 L of 0.1 N solution.
- Dissolve in distilled water in a volumetric flask.
- Dilute to the mark (100 mL for 0.1 N or 1 L for 1 N).
- Shake well to homogenize.

Preparation:

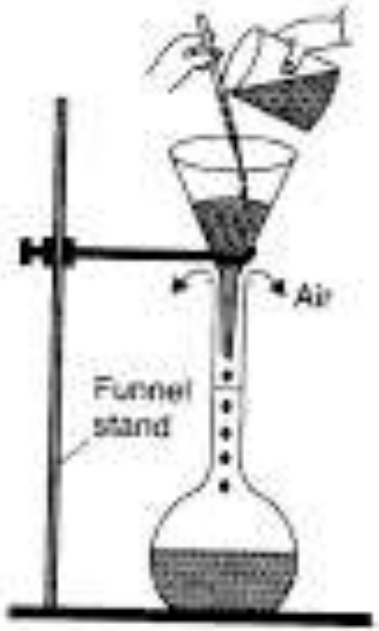


Fig. Transferring solution to measuring flask.

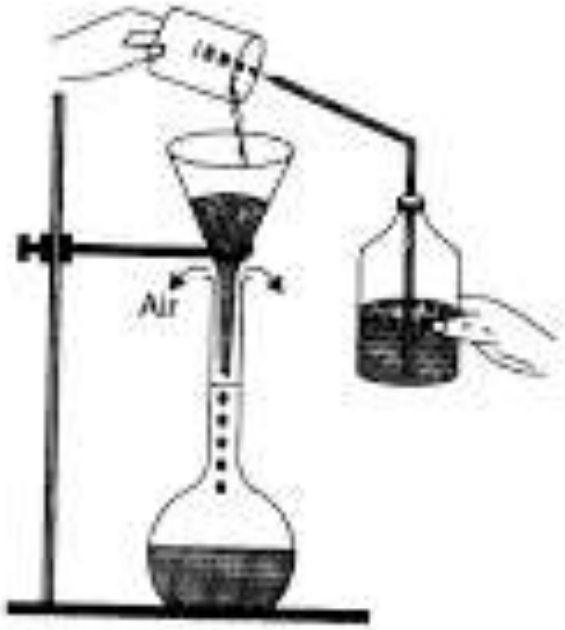


Fig. Transferring last traces of solution to measuring flask.

Standardization of Oxalic Acid Solution:

Purpose: To verify the exact concentration of the prepared solution.

Method: Titration with a standard NaOH solution using phenolphthalein indicator.

Procedure:

Pipette 10 mL of oxalic acid solution into a conical flask.

Add 2-3 drops of phenolphthalein indicator.

Titrate with 0.1 N NaOH until a permanent pink color appears.

Record the volume of NaOH used.

Calculation:

Normality of oxalic acid = (Normality of NaOH × Volume of NaOH) / Volume of oxalic acid

Example: If 10 mL of 0.1 N NaOH neutralizes 10 mL of oxalic acid, the solution is 0.1 N.

Applications and Safety:

Applications of Oxalic Acid Solutions:

- Standardization of NaOH and $KMnO_4$ solutions.
- Determination of metal ions in analytical chemistry.
- Used in redox titrations (e.g., with $KMnO_4$).

Safety Precautions:

- Oxalic acid is toxic; handle with care.
- Wear gloves and safety goggles.
- Avoid inhalation and contact with skin.
- Store solutions in labeled containers.

Preparation of Sodium Hydroxide Solution:

Procedure for 0.1 M/0.1 N NaOH Solution:

- Weigh 4 g of NaOH pellets (analytical grade) accurately.
- Dissolve in a small amount of distilled water (CO_2-free) in a volumetric flask.
- Make up the volume to 1 L (or 100 mL for smaller volumes) with distilled water.
- Mix thoroughly to ensure uniformity.

Precautions:

- Use CO_2-free distilled water to prevent carbonate formation.
- Handle NaOH carefully as it is caustic.

Standardization of Sodium Hydroxide Solution:

Reaction: $2NaOH + C_2H_2O_4 \rightarrow Na_2C_2O_4 + 2H_2O$

Method: Titration with a primary standard (e.g., oxalic acid) using phenolphthalein indicator.

Procedure:

- Pipette 10 mL of 0.1 N oxalic acid ($C_2H_2O_4 \cdot 2H_2O$) into a conical flask.
- Add 2-3 drops of phenolphthalein indicator.
- Titrate with NaOH solution until a permanent pink color appears.
- Record the volume of NaOH used.

Calculation:

Normality of NaOH = (Normality of oxalic acid × Volume of oxalic acid) / Volume of NaOH

Example: If 10 mL of 0.1 N oxalic acid requires 9.8 mL of NaOH, Normality of NaOH = (0.1 × 10) / 9.8 = 0.102 N.

Preparation of Hydrochloric Acid Solution:

Procedure for 0.1 M/0.1 N HCl Solution:

- Use concentrated HCl (≈11.6 M, density ≈1.18 g/mL, 37% w/w).
- Calculate volume needed for 0.1 M: (0.1 × 1000) / 11.6 ≈ 8.62 mL for 1 L.
- Slowly add 8.62 mL of concentrated HCl to ≈500 mL distilled water in a volumetric flask.
- Make up the volume to 1 L with distilled water and mix thoroughly.

Precautions:

- Always add acid to water (not vice versa) to avoid exothermic splashing.
- Use a fume hood due to corrosive fumes.
- Store in a tightly sealed container to prevent evaporation.

Standardization of Hydrochloric Acid Solution:

Reaction: $Na_2CO_3 + 2HCl \rightarrow 2NaCl + H_2O + CO_2$

Method: Titration with a primary standard (e.g., sodium carbonate, Na_2CO_3) using methyl orange indicator.

Procedure:

1. Pipette 10 mL of 0.1 N Na_2CO_3 into a conical flask.
2. Add 2-3 drops of methyl orange indicator (yellow in basic solution).
3. Titrate with HCl solution until the color changes to red-orange (endpoint).
4. Record the volume of HCl used.

Calculation:

1. Normality of HCl = (Normality of Na_2CO_3 × Volume of Na_2CO_3) / Volume of HCl
2. Example: If 10 mL of 0.1 N Na_2CO_3 requires 10.2 mL of HCl, Normality of HCl = (0.1 × 10) / 10.2 ≈ 0.098 N.

pH scale:

Titration Hand Position:

Preparation of Sodium Thiosulphate Solution:

Procedure for 0.1 M/0.1 N $Na_2S_2O_3$ Solution:

- Weigh 24.818 g of sodium thiosulphate pentahydrate ($Na_2S_2O_3 \cdot 5H_2O$) accurately.
- Dissolve in a small amount of boiled and cooled distilled water (to remove dissolved O_2) in a 1 L volumetric flask.
- Add 0.1 g of sodium carbonate (Na_2CO_3) as a stabilizer to prevent decomposition.
- Make up the volume to 1 L with distilled water and mix thoroughly.

Precautions:

- Use boiled, cooled water to minimize oxidation by dissolved oxygen.

Standardization of Sodium Thiosulphate Solution:

Reaction: $2Na_2S_2O_3 + I_2 \rightarrow Na_2S_4O_6 + 2NaI$

Method: Titration with a standard iodine solution (I_2) using starch indicator.

Procedure:

- Pipette 25 mL of 0.1 N iodine solution into a conical flask.
- Add 2-3 mL of starch indicator (blue color forms with iodine).
- Titrate with $Na_2S_2O_3$ solution until the blue color disappears (colorless endpoint).
- Record the volume of $Na_2S_2O_3$ used.

Calculation:

- Normality of $Na_2S_2O_3$ = (Normality of I_2 × Volume of I_2) / Volume of $Na_2S_2O_3$
- Example: If 25 mL of 0.1 N I_2 requires 24.5 mL of $Na_2S_2O_3$,
- Normality of $Na_2S_2O_3$ = (0.1 × 25) / 24.5 ≈ 0.102 N.

Preparation of Sulphuric Acid Solution:

Procedure for 0.1 M/0.2 N H_2SO_4 Solution:

- Use concentrated H_2SO_4 (≈18 M, density ≈1.84 g/mL, 98% w/w).
- Calculate volume needed for 0.1 M: (0.1 × 1000) / 18 ≈ 5.56 mL for 1 L.
- Slowly add 5.56 mL of concentrated H_2SO_4 to ≈500 mL distilled water in a volumetric flask.
- Make up the volume to 1 L with distilled water and mix thoroughly.

Precautions:

- Always add acid to water (not vice versa) to avoid violent exothermic reactions.
- Use a fume hood due to corrosive fumes.
- Cool the solution during mixing to prevent overheating.

Standardization of Sulphuric Acid Solution:

Reaction: $H_2SO_4 + Na_2CO_3 \rightarrow Na_2SO_4 + H_2O + CO_2$

Purpose: Determine the exact concentration of H_2SO_4 solution.
Method: Titration with a primary standard (e.g., sodium carbonate, Na_2CO_3) using methyl orange indicator.
Procedure:

Pipette 10 mL of 0.1 N Na_2CO_3 into a conical flask.
Add 2-3 drops of methyl orange indicator (yellow in basic solution).
Titrate with H_2SO_4 solution until the color changes to red-orange (endpoint).
Record the volume of H_2SO_4 used.

Calculation:

Normality of H_2SO_4 = (Normality of Na_2CO_3 × Volume of Na_2CO_3) / Volume of H_2SO_4
Example: If 10 mL of 0.1 N Na_2CO_3 requires 9.9 mL of H_2SO_4, Normality of H_2SO_4 = (0.1 × 10) / 9.9 ≈ 0.101 N.

Preparation of Potassium Permanganate Solution:

Procedure for 0.1 M/0.5 N $KMnO_4$ Solution:

- Weigh 15.803 g of $KMnO_4$ crystals accurately.
- Dissolve in 500 mL of distilled water in a volumetric flask.
- Boil the solution for 15–20 minutes to remove organic impurities and stabilize.
- Cool and make up the volume to 1 L with distilled water; filter if necessary.

Precautions:

- Use distilled water free of reducing agents.
- Store in a dark bottle to prevent decomposition by light.
- Allow the solution to stand for 24–48 hours before use to ensure stability.

Standardization of Potassium Permanganate Solution:

Reaction: $2KMnO_4 + 5H_2C_2O_4 + 3H_2SO_4 \rightarrow 2MnSO_4 + 10CO_2 + 8H_2O + K_2SO_4$

Purpose: Determine the exact concentration of $KMnO_4$ solution.
Method: Titration with a primary standard (e.g., oxalic acid) in acidic medium.

Procedure:

1. Pipette 20 mL of 0.1 N oxalic acid ($H_2C_2O_4 \cdot 2H_2O$) into a conical flask.
2. Add 10 mL of 2 N H_2SO_4 and heat to 70–80°C.
3. Titrate with $KMnO_4$ solution until a permanent pale pink color appears (self-indicator).
4. Record the volume of $KMnO_4$ used.

Calculation:

1. Normality of $KMnO_4$ = (Normality of oxalic acid × Volume of oxalic acid) / Volume of $KMnO_4$


Thank You!