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

Pharmaceutical Analysis – Methods of Expressing Concentration

Methods of Expressing Concentration

1. Percentage Concentration
- w/w – Weight by Weight
- w/v – Weight by Volume
- v/v – Volume by Volume

2. Molarity (M)
- Moles of solute per liter of solution
- Used in solution preparations

3. Molality (m)
- Moles of solute per kilogram of solvent
- Temperature independent

4. Normality (N)
- Equivalents of solute per liter of solution
- Used in titration analysis

5. Parts per million (ppm)
- Used for very dilute solutions
- e.g., trace elements in water

6. Mole Fraction (X)
- Ratio of moles of one component to total moles

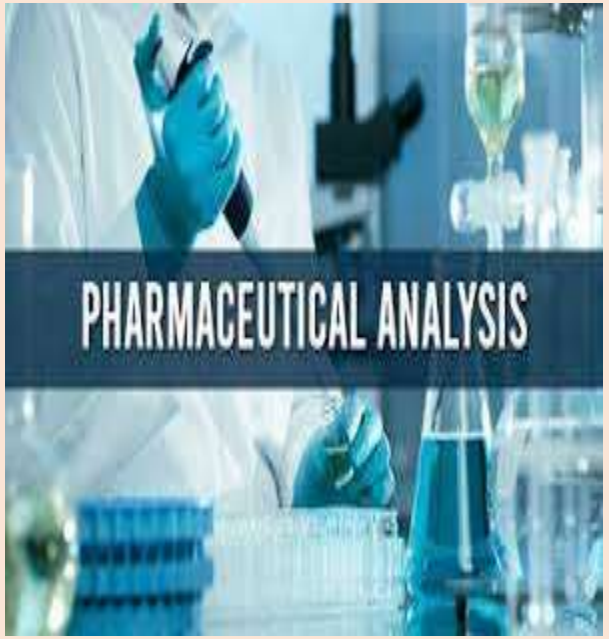
Understanding Pharmaceutical Analysis Through Design Thinking:-

Content:-

- **Key Techniques**:
  - **Spectroscopy** (UV-Vis, NMR): Identifies molecular structures for drug verification.
  - **Chromatography** (HPLC, GC): Separates and quantifies components to ensure purity.
  - **Mass Spectrometry**: Analyzes molecular mass for drug metabolism studies.
- **Design Thinking Application**:
  - **Empathize**: Address needs of analysts (speed, accuracy) and patients (safety).
  - **Ideate & Prototype**: Develop user-friendly tools, e.g.,HPLC systems.
  - **Impact**: Faster, cost-effective analysis with enhanced drug quality and safety.
- **Visuals**:
- Compact design thinking cycle graphic (Empathize, Define, Ideate, Prototype, Test).
- Design Thinking Solution (e.g., Spectroscopy - Data interpretation).
- Emphasize how design thinking optimizes analytical processes by focusing on user needs.
- Highlight practical outcomes like improved efficiency and drug safety.

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:-

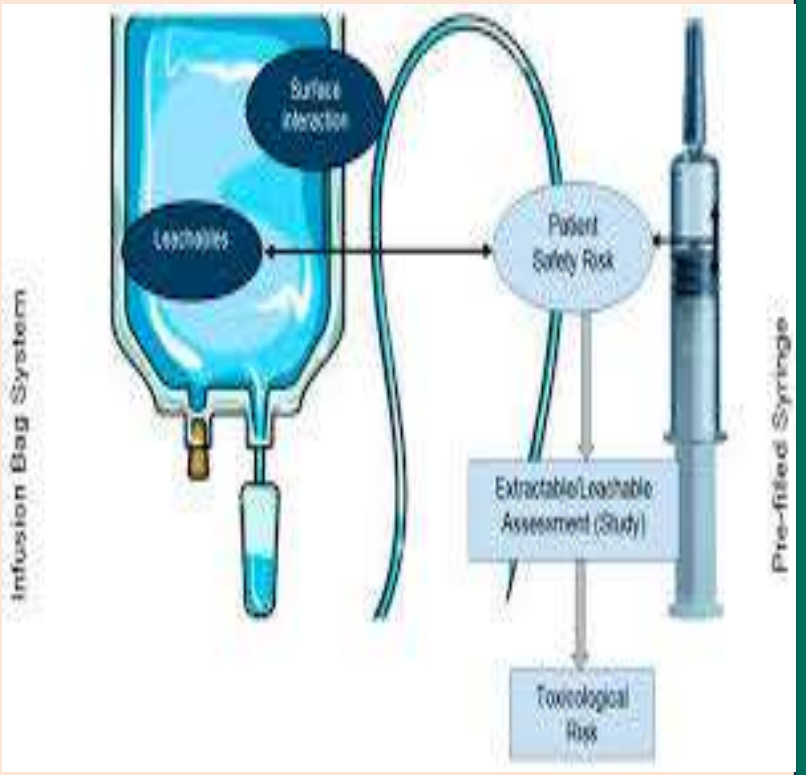
- **Quality Control**: Ensures drugs meet standards for purity, potency, and safety.
- **Drug Development**: Supports formulation, stability testing, and validation of new drugs.
- **Regulatory Compliance**: Meets guidelines set by agencies like FDA, WHO, and ICH.
- **Research and Innovation**: Develops 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.

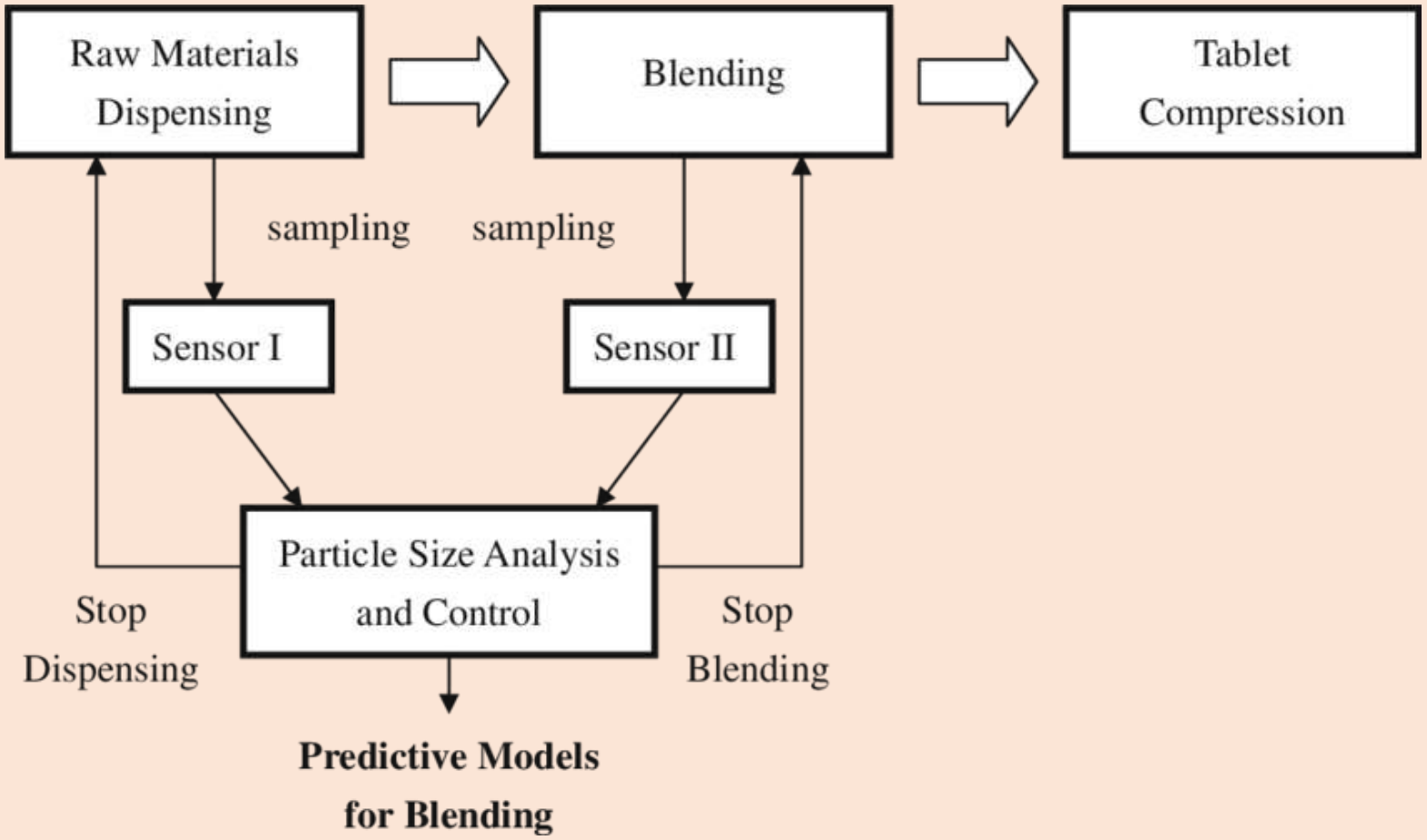
Normality (N):

- 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.

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:

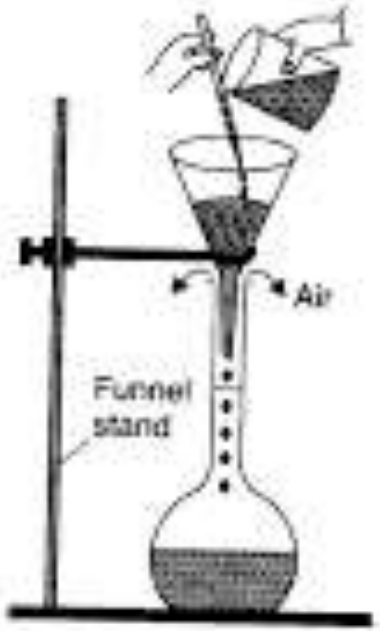


Fig. Transferring solution to measuring flask.

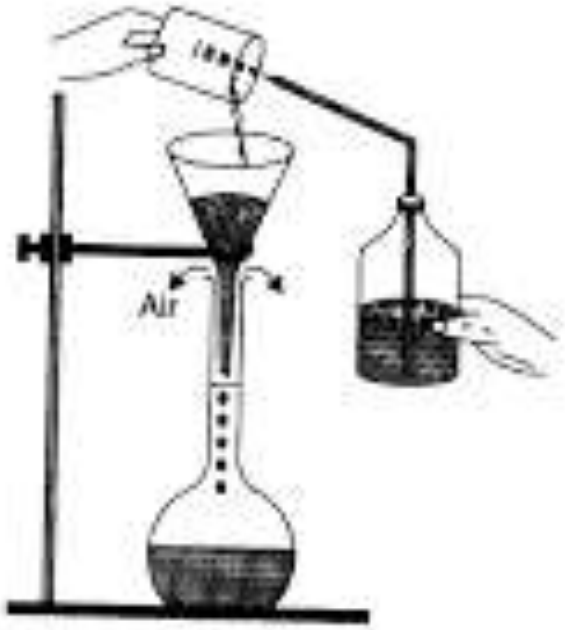


Fig. Transferring last traces of solution to measuring flask.

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.

- 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 $KMnO_4$

Case Study:

Case:

You are working as a quality control analyst in a pharmaceutical company. During the standardization of **0.1N Sodium Hydroxide solution**, you used **0.1N Oxalic Acid** as a primary standard. After performing three concordant titrations, you got slightly varying burette readings.

Questions:

1. Explain the **importance of using a primary standard** for standardization.
2. Describe the **procedure for standardization** of NaOH using oxalic acid.
3. What types of **errors** might have caused variation in readings?
4. Suggest **methods to minimize these errors**.
5. Comment on the **accuracy and precision** of the titration results.

ASSESSMENT:

Choose the most appropriate answer.

1. Which of the following is a primary standard?

a) Sodium hydroxide b) Hydrochloric acid

c) Oxalic acid d) Sodium thiosulphate

2. Which of the following expresses concentration in terms of moles of solute per liter of solution?

a) Normality b) Molarity

c) Molality d) % w/v

3. Which type of error occurs due to defective apparatus or calibration?

a) Personal error b) Systematic error

c) Random error d) Gross error

4. Which Indian Pharmacopoeia edition is currently followed in India?

a) IP 1985 b) IP 1996

c) IP 2018 d) IP 2020

5. Which of the following is a source of impurity in drugs?

a) Manufacturing process b) Storage condition

c) Raw materials d) All of the above

Reference:

1. A.H. Beckett & J.B. Stenlake's, Practical Pharmaceutical Chemistry Vol I & II, Stahlone Press of University of London.

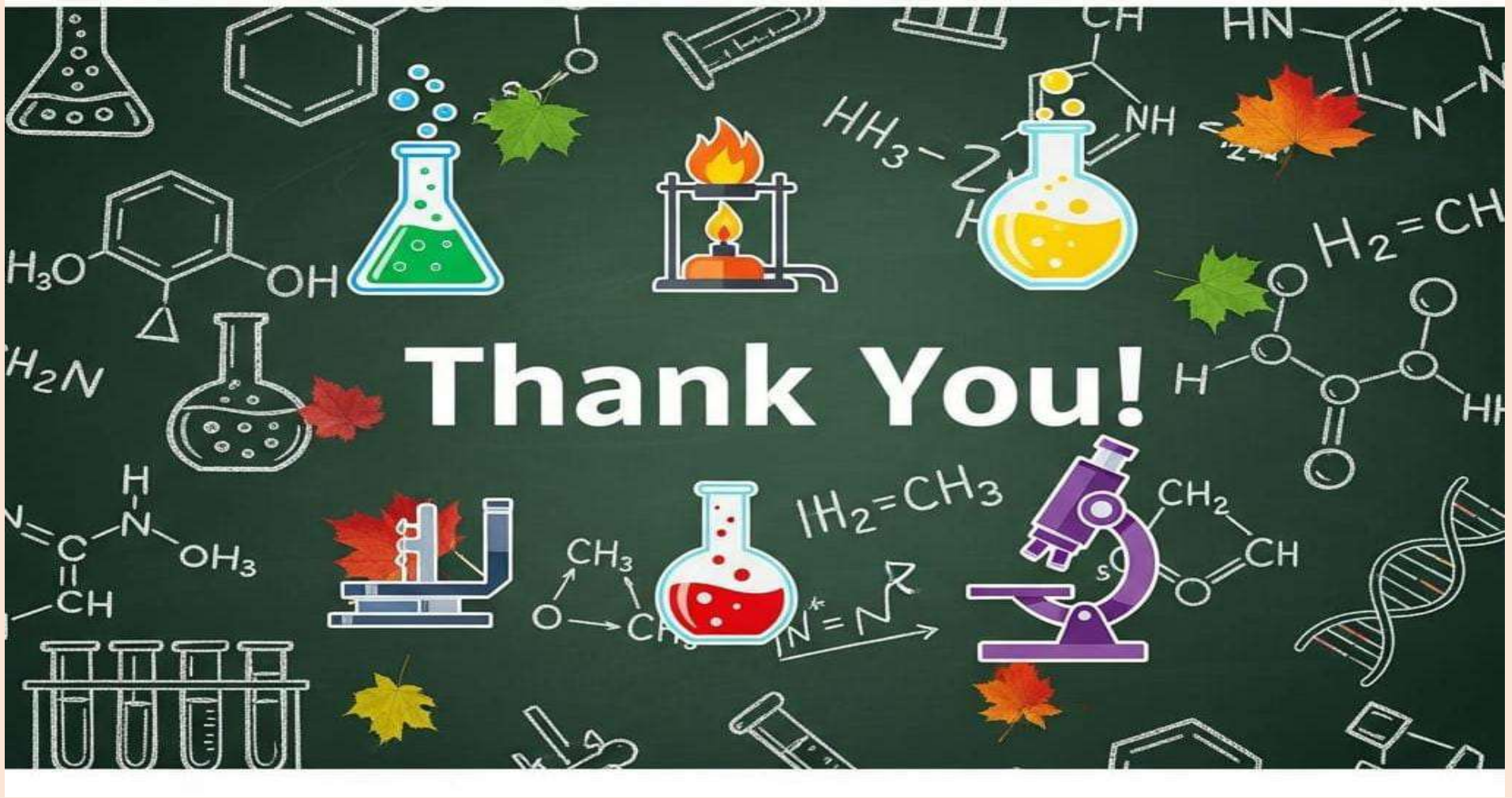
2. A.I. Vogel, Text Book of Quantitative Inorganic analysis.

3. P. Gundu Rao, Inorganic Pharmaceutical Chemistry.

4. Bentleyand Driver's Textbook of Pharmaceutical Chemistry.

5. John H. Kennedy, Analytical chemistry principles.

6. Indian Pharmacopoeia.


Thank You!