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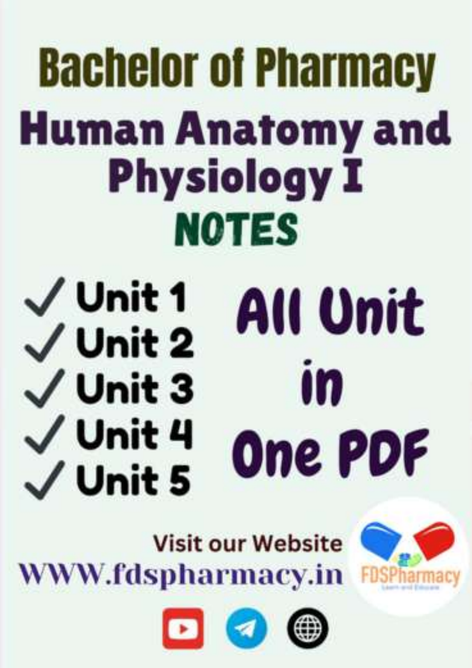
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PHARMACEUTICAL ANALYSIS I

UNIT 3

TOPIC :

- **Gravimetry :** Principle and steps involved in gravimetric analysis. Purity of the precipitate: co-precipitation and post precipitation, Estimation of barium sulphate.
  Basic Principles,methods and application of diazotisation titration

Gravimetric

- Gravimetric analysis is a quantitative analytical technique where the amount of an analyte (substance being measured) is determined by converting it into a pure, stable, and weighable solid form (precipitate).

Principle of Gravimetric Analysis :

- Gravimetric analysis is based on the precipitation of the analyte as a pure, stable, and insoluble compound from a solution, which is then filtered, dried (or ignited), and weighed.
- The amount of the analyte is determined from the mass of the precipitate using stoichiometric calculations.

Steps Involved in Gravimetric Analysis

Preparation of the Solution

- A known volume of the sample solution is taken.
- The solution must be clear and free from interfering substances.
- pH is adjusted if necessary to favor precipitation of the analyte.

Example: Use dilute HCl to avoid co-precipitation of carbonates in Ba^{2+} estimation.

Precipitation

- A suitable precipitating reagent is added slowly with constant stirring to form a solid precipitate of the analyte.
- Conditions such as temperature, pH, and concentration are controlled to ensure complete and selective precipitation.

Example: Add dilute H_2SO_4 to Ba^{2+} solution to form $BaSO_4$.

Digestion of the Precipitate

- The mixture is heated (typically near boiling) and allowed to stand for 30–60 minutes.
- This allows smaller particles to dissolve and reprecipitate on larger crystals (Ostwald ripening).
- Improves filterability and purity of the precipitate.

Filtration

- The precipitate is separated from the solution using filter paper or a sintered glass crucible.
- Special care is taken to avoid loss of any solid during transfer.
- Hot filtration may be used for gelatinous or fine precipitates.

Washing the Precipitate

- The precipitate is washed several times with distilled water or a specific wash solution.
- This step removes adsorbed impurities like co-precipitated ions or excess reagents.
- Must ensure that the wash liquid does not dissolve the precipitate.

 Example: Use dilute HCl to wash $BaSO_4$ (to prevent solubility loss).

Drying or Ignition

- The washed precipitate is dried in an oven (100–120°C) or ignited in a muffle furnace (up to 1000°C), depending on the analysis.
- Drying removes moisture, and ignition converts the precipitate to a stable, weighable form.

 Example: $BaSO_4$ is usually ignited to ensure complete conversion and stability.

Weighing

- After drying or ignition, the precipitate is cooled in a desiccator to avoid moisture absorption.
- The constant weight is noted using a precise analytical balance.

Calculation

- The mass of the pure precipitate is used to calculate the amount of analyte using stoichiometric relationships.

  Amount of analyte = Weight of precipitate × Molar mass of analyte / Molar mass of precipitate

  ⍰ *Example:* $BaSO_4$ → used to calculate amount of Ba^{2+} in the sample.

Purity of the Precipitate

→ When the Precipitate is separated out from the solution, it is not always pure the precipitate is contaminated with some amount of impurities.

→ These amount of impurities depends upon the nature and condition of precipitate.

→ It is mainly of two types :

- Co-Precipitation
- Post Precipitation

1. Co-Precipitation :

→ Co-precipitation is the process in which impurities are carried down along with the main precipitate during a chemical precipitation reaction, even though these impurities are normally soluble under the reaction conditions.

Types of Co-Precipitation

- **Surface Adsorption :** In surface adsorption, impurity ions get adsorbed (stick) on the outer surface of the precipitate particles.
- **Occlusion :** In occlusion, impurities get trapped or enclosed inside the crystal structure of the growing precipitate during rapid precipitation.
- **Inclusion (Isomorphous Replacement) :** In inclusion, impurity ions of similar size and charge replace the ions of the main precipitate and become part of the crystal lattice.

Example:

- In the precipitation of $BaSO_4$ (used for estimating barium), nitrate or chloride ions may get adsorbed on the precipitate if not washed properly — this is co-precipitation.

2. Post-Precipitation

→ Post-precipitation is the process in which impurities present in the solution begin to precipitate later (after the main precipitate has formed) and get deposited over the surface of the primary precipitate. These impurities are not originally part of the main precipitate, but settle after some time, contaminating the solid.

Example:

- During barium sulphate ($BaSO_4$) estimation, if the solution contains iron (Fe^{3+}) or calcium, they may slowly form ferric hydroxide or calcium sulphate after the main $BaSO_4$ precipitate has formed.

Estimation of Barium Sulphate ($BaSO_4$)

Principle:

→ Barium ions (Ba^{2+}) react with sulphate ions (SO_4^{2-}) from dilute sulphuric acid to form insoluble barium sulphate ($BaSO_4$).
This precipitate is filtered, dried or ignited, weighed, and from its mass, the amount of barium is calculated.

Chemical Reaction:

$$Ba^{2+} + SO4^{2-} \rightarrow BaSO4_4 \downarrow \text{ (White precipitate)}$$

$BaSO_4$ is a **white, stable, and insoluble** compound — ideal for gravimetric estimation.

Requirements:

- Barium chloride ($BaCl_2$) solution (known concentration)
- Dilute sulphuric acid (H_2SO_4)
- Distilled water
- Glassware: beaker, funnel, porcelain crucible, filter paper/sintered crucible
- Heating source, muffle furnace (for ignition), analytical balance, desiccator

Procedure:

1. Take a known volume of $BaCl_2$ solution in a beaker.
2. Heat the solution gently to about 70–80°C.
3. Add dilute H_2SO_4 slowly with stirring until no further precipitation occurs.
4. Digest the mixture on a hot water bath for 30–60 minutes to allow particle growth.
5. Filter the hot mixture through ashless filter paper or sintered glass crucible.

6. Wash the precipitate with hot distilled water to remove chloride and excess reagents.
7. Dry the precipitate in an oven or ignite in a muffle furnace (~800°C) until constant weight.
8. Cool in a desiccator and weigh accurately.
9. Repeat drying and weighing until constant weight is achieved.

Calculations:

Let the weight of **$BaSO_4$** obtained = W grams
Molar mass of **$BaSO_4$ = 233.39 g/mol**
Molar mass of **Ba^{2+} = 137.33 g/mol**

$$\text{Amount of } Ba^{2+} = W \times 137.33 \; / \; 233.39$$

You can also calculate % Ba^{2+} or amount in mg depending on your sample and report format.

Diazotisation titration

→The diazotization titration is nothing but the conversion of the primary aromatic amine to a diazonium compound.

→This process was first discovered in 1853 and was applied to the synthetic dye industry.

→The reaction mechanism was first proposed by Peter Griessin.

→In this method, the primary aromatic amine is reacted with the sodium nitrite in acidic medium to form a diazonium salt.

→This method is first used in the determination of dyes.

Principle

- The principle involved in this method is that the primary aromatic amine present in the sample reacts with the sodium nitrite in the presence of acid such as hydrochloric acid to obtain a diazonium salt.The first involved is addition of sodium nitrite to hydrochloric acid cause formation of nitrous acid

$$R-NH_2 + NaNO_2 + HCl \longrightarrow R-\underline{N}\equiv N-Cl + NaCl + H_2O$$

- Sodium nitrite is added to the solution of amine in the presence of acid at 0–5 °C. The amine reacts with the nitrous acid to form nitrosamine, which is followed by the tautomerisation and the water molecule is lost to form the diazonium ion. This diazonium ion is stabilized by the displacement of the positive charge at the ortho and para positions of the ring.

$$C_6H_5NH_2 + NaNO_2 + HCl \longrightarrow C_6H_5N = NCl + NaCl + H_2O$$

Methods of Diazotisation Titration:

→ There are two main methods depending on the nature of the compound:

A. Direct Diazotisation Titration:

- The sample solution (containing primary aromatic amine) is cooled to 0–5°C.
- Titrated directly with standard $NaNO_2$ solution.
- End point: Appearance of blue color on starch-iodide paper indicates excess nitrous acid.

B. Back Titration Method:

- Used when the sample is not easily soluble or the reaction is slow.
- A known excess of $NaNO_2$ is added to the amine in acidic solution.
- The mixture is allowed to stand in the cold.
- The unreacted $NaNO_2$ is back titrated using standard potassium iodide (KI) and starch indicator (iodometric titration).

Procedure:

Step 1: Preparation

- Pipette a known volume (e.g., 25 mL) of the sulphanilamide solution into a clean conical flask.
- Add about 10–15 mL of dilute HCl (to acidify the solution).
- Place the flask in an ice bath to cool the contents to 0–5°C.
- Allow the solution to stand in the ice bath for 5–10 minutes for full cooling.

Step 2: Titration

- Fill the burette with standard sodium nitrite solution ($NaNO_2$).
- Begin titrating slowly from the burette into the amine solution, maintaining the temperature at 0–5°C throughout the titration.

- After every few drops, remove a drop of the reaction mixture using a glass rod and place it on a starch-iodide paper.

Step 3: End Point Detection

- Continue the titration until a blue spot appears on the starch-iodide paper. This indicates that free nitrous acid is present (end point reached).

Step 4: Repeat and Calculate

- Repeat the titration to get concordant readings (within ±0.1 mL difference).
- Record the volume of $NaNO_2$ used and calculate the amount of primary amine.

Applications of Diazotisation Titration:

Pharmaceutical Use:

- Estimation of sulpha drugs:
    - Sulphanilamide
    - Sulphadiazine
    - Sulphaguanidine
- Quality control in drug manufacturing.

Analytical Chemistry:

- Estimation of aromatic amines in chemical samples.
- Assay of amines in dyes and intermediates.