Program	B. Pharmacy
Semester	1st
Subject /Course	Pharmaceutical Inorganic and Analytical Chemistry
Subject/Course ID	Pharmaceutical Inorganic and Analytical Chemistry/BP106T
Module No.	03
Module Title	Acid base titrations, Non-aqueous titrations, Precipitation titrations and gravimetry, Complexometric titration and Redox titrations
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LO	Particular
1.	**Interpret** the principles of acid–base titrations, indicator theories, neutralization curves, and standardization procedures for the quantitative analysis of pharmaceutical substances.
2.	**Differentiate** aqueous and non-aqueous titration techniques by selecting appropriate solvents, titrants, and analytical methods for the estimation of weakly acidic and weakly basic drugs.
3.	**Apply** the principles of precipitation titrations and gravimetric analysis to perform quantitative estimation using Mohr's, Volhard's, Modified Volhard's, Fajans methods, and gravimetric techniques.
4.	**Analyze** the role of EDTA, metal ion indicators, masking and demasking agents in complexometric titrations for the accurate estimation of pharmaceutical compounds.
5.	**Evaluate** oxidation–reduction reactions and select appropriate redox titration methods, including permanganometry, cerimetry, iodimetry, iodometry, and potassium iodate titrations, for pharmaceutical analysis.

Module Content Table

Sr. no.	Topic
1.	**Acid base titrations** Theories of acid base indicators, classification of acid base titrations. Preparation and standardization of titrants viz. hydrochloric acid and sodium hydroxide. Theory involved in titrations of strong, weak, and very weak acids and bases, neutralization curves. Assay of Ammonium hydroxide.
2.	**Non-aqueous titrations** Types of solvents used, acidimetric and alkalimetric titration using non-aqueous solvents. Preparation and standardization of acidic and basic titrants. Estimation of weakly acidic and basic substances using non-aqueous titrants, estimation of Sodium benzoate
3.	**Precipitation titrations and gravimetry** Principle and steps involved in gravimetric analysis, Mohr's method, Volhard's, Modified Volhard's, Fajans method. Estimation of barium sulphate by gravimetry.
4.	**Complexometric titrations** Classification, metal ion indicators, masking and demasking reagents, preparation and standardization of disodium EDTA. Estimation of Magnesium sulphate and Calcium gluconate*.
5.	**Redox titrations** Concepts of oxidation and reduction, Types of redox titrations viz. Permanganometry, Cerimetry, Iodimetry, Iodometry and titrations with potassium iodate

Acid base titrations

As discussed in previous chapter Acids and bases are two fundamental types of chemical compounds defined by their behavior in water. Acids release hydrogen ions (H^+) and taste sour, whereas bases accept hydrogen ions and taste bitter. They interact through a pH scale and neutralize each other to form water and salts.

Quantitative chemical analysis is the branch of analytical chemistry that deals with the determination of the amount or concentration of a chemical substance present in a sample. It helps in measuring how much of a particular component is present in a mixture or compound. The result is usually expressed in terms of percentage, molarity, normality, grams, or milligrams. Quantitative analysis is widely used in pharmaceutical industries, medical laboratories, food analysis, environmental studies, agriculture, and research laboratories.

Objectives of Quantitative Chemical Analysis

- To determine the exact amount of a substance present in a sample.
- To check purity and quality of chemicals.
- To estimate active ingredients in pharmaceutical preparations.
- To detect impurities in compounds.
- To maintain quality control in industries.

A **titration** is a quantitative chemical analysis method used to determine the unknown concentration of an analyte by reacting it with a known concentration of a reagent, called the titrant. It relies on precise volume measurements to identify the exact point where the chemical reaction is complete.

"**Analyte"** The solution with an unknown concentration that you want to measure.

"**Titrant"** A standard solution with a precisely known concentration.

'**Indicator'** A substance (often a dye) that changes color at the endpoint to signal that the reaction is complete.

'**Burette'** A long, graduated glass tube used to dispense the titrant drop-by-drop with high precision.

Acid–base titration is a quantitative analytical method used to determine the concentration or strength of an acid or a base solution by reacting it with another solution of known concentration. It is based on the principle of **neutralization**, in which an acid reacts with a base to form salt and water.

In an acid–base titration, the solution of known concentration is called the **standard solution** or **titrant**, while the solution whose concentration is to be determined is called the **analyte**. The titrant is gradually added from a burette to the analyte present in a conical flask until the reaction reaches the **equivalence point**, where the amount of acid and base are chemically equivalent. To detect the completion of the reaction, suitable **acid–base indicators** such as phenolphthalein or methyl orange are used. These indicators change color at a particular pH range, indicating the **endpoint** of the titration.

Basic Principle: The titration is based on the neutralization reaction:

$$\text{Acid} + \text{Base} \rightarrow \text{Salt} + \text{Water}$$

For example:

$$HCl + NaOH \rightarrow NaCl + H_2O$$

At the equivalence point: Number of moles of acid = Number of moles of base

For simple acid–base reactions: $M_aV_a = M_bV_b$

Where M_a = molarity of acid, V_a = volume of acid, M_b = molarity of base, V_b = volume of base

Theories of Acid - Base Indicators

An acid-base indicator is a weak acid or a weak base. **Examples** of indictors used in acid base reactions – Litmus, Phenolphthalein, Methyl orange, thymol blue, methyl yellow, methyl orange, bromophenol blue, bromocresol green, methyl red, bromothymol blue, phenol red, neutral red, phenolphthalein, thymolphthalein, alizarin yellow.

Table: pH range and colour of indicators

Indicators	pH range	Colour for weak acid	Colour for weak base
Methyl orange	4-6	Orange	Yellow
Bromophenol blue	6-7	Yellow	Blue
Thymol blue	8-9	Yellow	Blue
Phenolphthalein	9-10	Colourless	Pink
Alizarin yellow	10-12	Yellow	Red

An indicator is a substance which is used to determine the end point in a titration. In acid base titrations, organic substances (weak acids or weak bases) are generally used as indicators. They change their colour within a certain pH range. The colour change and the pH range of some common indicators are tabulated below:

Table: Colour change and pH range of some common indicators

Indicator	pH range	Colour change
Methyl Orange	3.2-4.5	Pink to yellow
Methyl red	4.4-6.5	Red to yellow
Litmus	5.5-7.5	Red to blue
Phenol red	6.8-8.4	Yellow to red
Phenolphthalein	8.3-10.5	Colourless to pink

Theory of acid-base indicators: Two theories have been proposed to explain the change of colour of acid-base indicators with change in pH.

1. Ostwald's Theory

This theory was proposed by the German scientist Wilhelm Ostwald. According to Ostwald's theory, acid–base indicators are either: **Weak acids**, or **Weak bases**

Principle: According to this theory, the colour change is due to ionisation of the acid-base indicator. The unionised form has different colour than the ionised form. The ionisation of the indicator is largely affected in acids and bases as it is either a weak acid or a weak base.

- In case, the indicator is a weak acid, its ionisation is very much low in acids due to common H^+ ions while it is fairly ionised in alkaline solution.
- Similarly, if the indicator is a weak base, its ionisation is large in acids and low in alkaline due to common OH^- ions.

Considering two important indicators phenolphthalein (a weak acid) and methyl orange (a weak base), Ostwald theory can be illustrated as follows:

Phenolphthalein: It can be represented as HPh. It ionises in solution to a small extent as:

$$HPh \leftrightarrow H^+ + Ph^-$$

Colourless Pink

Applying law of mass action,

$$K = [H^+]\,[Ph^-]/\,[HpH]$$

- The un-dissociated molecules of phenolphthalein are colourless while Ph^- ions are pink in colour.
- In presence of an acid the ionisation of HPh is practically negligible as the equilibrium shifts to left hand side due to high concentration of H^+ ions. Thus, the solution would remain colourless.
- On addition of alkali, hydrogen ions are removed by OH^- ions in the form of water molecules and the equilibrium shifts to right hand side.

- Thus, the concentration of Ph- ions increases in solution and they impart pink colour to the solution.

Methyl Orange: It is a very weak base and can be represented as MeOH. It is ionized in solution to give Me^+ and OH^- ions.

$$MeOH \leftrightarrow Me^+ + OH^-$$

Yellow Red

Applying law of mass action, $K = [Me^+][OH^-]/[MeOH]$

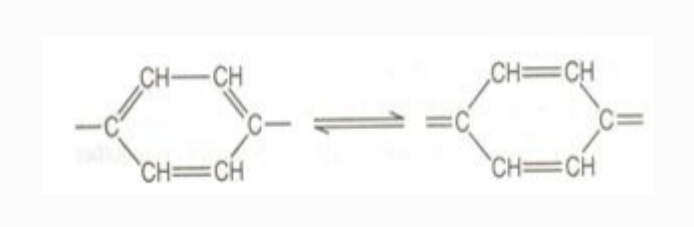
- In presence of an acid, OH^- ions are removed in the form of water molecules and the above equilibrium shifts to right hand side. Thus, sufficient Me^+ ions are produced which impart red colour to the solution.
- On addition of alkali, the concentration of OH^- ions increases in the solution and the equilibrium shifts to left hand side, i.e., the ionisation of MeOH is practically negligible. Thus, the solution acquires the colour of unionised methyl orange molecules, i.e., yellow.

This theory also explains the reason why phenolphthalein is not a suitable indicator for titrating a weak base against strong acid. The OH^- ions furnished by a weak base are not sufficient to shift the equilibrium towards right hand side considerably, i.e., pH is not reached to 8.3. Thus, the solution does not attain pink colour.

2. Quinonoid theory

According to this theory:

i) The acid-base indicators exist in two tautomeric forms having different structures. Two forms are in equilibrium. One form is termed benzenoid form and the other quinonoid form.

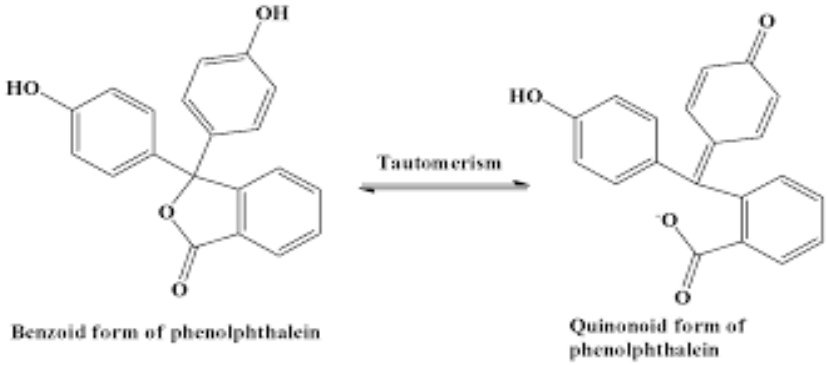


ii) Two forms have different colours. The color change in due to the interconversion of one tautomeric form into other.

iii) One form mainly exists in acidic medium and the other in alkaline medium. Thus, during titration medium changes from acidic to alkaline or vice versa. The change in pH converts one tautomeric form into other and thus, the colour changes occurs.

a. Phenolphthalein

Phenolphthalein has benzoid form in acidic medium and thus, it is colourless while it has quinonoid form in alkaline medium which has pink colour.

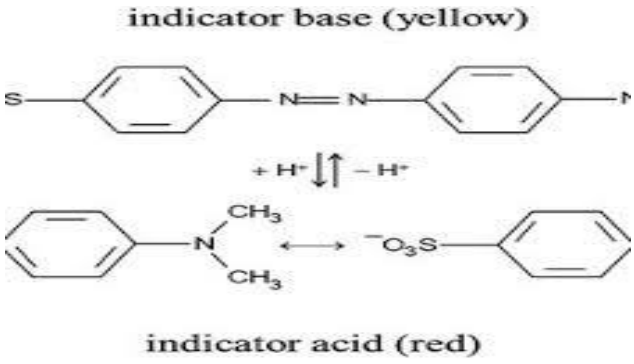


Benzoid form of phenolphthalein

Quinonoid form of phenolphthalein

b. Methyl Orange

Methyl Orange has quinonoid form in acidic solution and benzenoid form in alkaline solution. The colour of benzenoid form is yellow while that of quinonoid form is red.



Classification of Acid Base Titrations

Acid–base titrations are quantitative analytical methods based on the neutralization reaction between an acid and a base. These titrations are classified according to the strength of the acid and the base used in the reaction. The strength of the reacting acid and base affects the pH at the equivalence point, the shape of the titration curve, and the choice of indicator. Acid–base

titrations are widely used in pharmaceutical analysis, chemical laboratories, food industries, and water analysis. The different types of acid–base titrations are:

1. Strong acid vs Strong base titration
2. Weak acid vs Strong base titration
3. Strong acid vs Weak base titration
4. Weak acid vs Weak base titration

1. Strong acid vs Strong base titration: Strong acid reacts with a strong alkali to form salt and water.

A strong acid–strong base titration involves the reaction between a completely ionized strong acid and a completely ionized strong base. Since both are fully dissociated in aqueous solution, the neutralization reaction occurs rapidly and completely.

At the end of the reaction, no molecule of acid or base exists as every molecule in the reaction has completely reacted to form a salt. Hence the endpoint or equivalence point is precise and sharp. Example or these types of acids are HCI, H_2SO_4, HNO_3, HBr, $HCIO_4$ (perchloric acid), H_3PO_4, etc. The examples or strong bases are NaOH, $MgOH_2$, Al_2OH_2, etc.

Neutralization occurs rapidly and the pH at equivalence point is approximately 7 (there is sharp change in pH near end point). Indicators such as phenolphthalein or methyl orange can be used.

Examples:

- hydrochloric acid with sodium hydroxide
- nitric acid with potassium hydroxide

Neutralization Reaction:

$$HCl + NaOH \rightarrow NaCl + H_2O$$

2. Strong Acid vs Weak Base: Here a strong base reacts with weak add to form salt and water. In this titration strong acid reacts with weak base. The weak base does not ionize completely in water. But since the reaction uses a strong acid, the pH at the endpoint will be towards acidic, i.e., below 7.

Example: Hydrochloric acid vs Ammonium Chloride

$$HCl + NH_4OH \longrightarrow NH_4Cl + H_2O$$

Here the salt formed NH_4Cl is slightly acidic. So, indicators changing color at lower pH's are employed. Methyl orange is generally used. Salt formed undergoes hydrolysis making the solution acidic.

During the reaction, a known concentration of strong acid is taken in a burette and allowed to react drop by drop with the base in a beaker.

3. Weak Acid vs Strong Base: Here the reaction happens between a weak acid and strong base. The weak acid ionizes partially in solution.

The salt formed is slightly basic, so the pH at the end point is above 7(sharp rise in pH near the end point). The indicator used is one which produces changes in color at higher pH (Phenolphthalein).

Example: Acetic acid (CH_3COOH) vs Sodium hydroxide (NaOH)

$$CH_3COOH + NaOH \longrightarrow CH_3COONa + H_2O$$

4. Weak Acid V/S Weak Base: Here both acid and base are weak. So mostly they are avoided due to imprecise endpoints. At the endpoint, the pH will be seven theoretically or change in pH near equivalence is very small. End point is not sharp and cannot be determined accurately. Cannot be measured precisely like that in strong acid and strong base case.

An extra amount of titrant is needed to reach the endpoint due to the imprecise reaction.

$$H_2CO_3 + NH_4OH \longrightarrow NH_4OH + H_2O$$

The endpoint is neutral as the salt is neutral but due to excess titrant added they could be in favour of it.

Table: Choice of indicators in titration

Type of titration	**pH**	**Indicator**
Strong acid vs Strong base	2-10	Indicators like: Phenolphthalein, Methyl orange, Methyl red can be used
Strong acid vs Weak base	2-6	Methyl orange, Methyl red

Weak acid vs Strong base	8-10	Phenolphthalein, Thymol Phthalein
Weak acid vs Weak base	-	Mixed indicators like neutral red methylene blue for dilute ammonia or ethanoic acid Like: Bromocresol green: Methyl green (pH 4.3) Bromomethyl blue: Neutral red (7.2)

Preparation and Standardization of Titrants

1. Hydrochloric acid (HCl)

Hydrochloric acid (HCl) (secondary solution) is one of the most commonly used titrants in volumetric analysis. It is a strong acid and dissociates completely in aqueous solution to produce hydrogen ions. Standard hydrochloric acid solution is widely used in acid-base titrations for the estimation of alkalis such as sodium hydroxide, sodium carbonate, borax, and other basic substances.

Since concentrated hydrochloric acid is volatile and its exact concentration changes on storage, it cannot be used directly as a primary standard solution. Therefore, hydrochloric acid solutions are prepared approximately and then standardized against a primary standard substance such as sodium carbonate (Na_2CO_3) or borax.

Preparation of 0.1 N Hydrochloric Acid Solution

Principle: Normality of hydrochloric acid depends upon the amount of HCl dissolved in water. Concentrated hydrochloric acid is diluted carefully with distilled water to obtain approximately 0.1 N solution.

Concentrated HCl contains approximately: 36–37% w/w HCl. This yields molarity of roughly 12M with the density of 1.18-1.19 g/ml approx. pH is typically around 1.1-1.0.

Using dilution formula:

$$N_1V_1=N_2V_2$$

Where: $N_1=12$, $N_2=0.1$, $V_2=1000$

Therefore, $12\times V_1=0.1\times 1000$

$$V_1=8.3\ mL$$

Hence, about 8.3 mL of concentrated hydrochloric acid is required to prepare 1000 mL of 0.1 N HCl.

Procedure for preparation: Take about 500 mL of distilled water in a 1000 mL volumetric flask. Measure accurately about 8.3 mL of concentrated hydrochloric acid using a measuring cylinder. Slowly add the acid into water with constant stirring. Allow the solution to cool. Make up the volume up to 1000 mL with distilled water.

Important: Acid should always be added to water and not water to acid to avoid splashing and excessive heat generation.

Preparation of Sodium carbonate

Principle: The prepared hydrochloric acid solution is standardized against a primary standard sodium carbonate solution.

Sodium carbonate is a primary standard because: It is pure, Stable in air, Non-hygroscopic, High molecular weight, can be weighed accurately.

Preparation of 0.1 N Sodium Carbonate

$$\text{Weight} = N \times \text{Eq. wt} \times \text{Volume (L)}$$

Where:

- N=0.1
- Equivalent weight = 53
- Volume = 1 L

Substituting:

$$\text{Weight} = 0.1 \times 53 \times 1 = 5.3 \text{ g}$$

Therefore, **5.3 g** sodium carbonate is required.

Procedure: Accurately weigh 5.3 g sodium carbonate. Transfer into a 1000 mL volumetric flask. Dissolve in distilled water and make up the volume to 1000 mL.

Standardization of Hydrochloric Acid

Indicator used is methyl orange and color change is yellow in alkaline medium and orange-pink at end point.

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

Procedure: Rinse and fill burette with HCl solution. Pipette out 25 mL sodium carbonate solution into conical flask. Add 2–3 drops methyl orange. Titrate against HCl and continue till yellow color changes to orange-pink.

Calculation: Using the normality equation:

$$N_1V_1 = N_2V_2$$

Where:

- N_1 = Normality of sodium carbonate solution
- V_1 = Volume of sodium carbonate solution
- N_2 = Normality of hydrochloric acid
- V_2 = Volume of hydrochloric acid used

2. Sodium Hydroxide (NaOH)

Sodium hydroxide (NaOH) is one of the most commonly used alkaline titrants in volumetric analysis. It is widely employed for the assay of acids, acidimetric titrations, pharmaceutical analysis, and quantitative chemical analysis. Sodium hydroxide is a strong base and completely dissociates in aqueous solution to furnish hydroxyl ions. Because sodium hydroxide absorbs moisture and carbon dioxide from the atmosphere, it cannot be used as a primary standard substance. Therefore, its solution must be prepared approximately and then standardized against a primary standard acid such as oxalic acid or potassium hydrogen phthalate (KHP).

Preparation of Sodium Hydroxide Solution: Sodium hydroxide solution is prepared by dissolving a calculated quantity of sodium hydroxide pellets in freshly boiled and cooled purified water. Freshly boiled water is used to remove dissolved carbon dioxide because carbon dioxide reacts with sodium hydroxide forming sodium carbonate.

$$2NaOH + CO_2 \rightarrow Na_2CO_3 + H_2O$$

Preparation of 0.1 N Sodium Hydroxide Solution

Normality equation: Strength (g/L) = Normality × Equivalent weight

Molecular weight of NaOH is 40

$$\text{Strength} = 0.1 \times 40 = 4 \text{ g/L}$$

Thus, 4 g of sodium hydroxide is required to prepare 1 litre of 0.1 N NaOH solution.

About 4 g of sodium hydroxide pellets are accurately weighed quickly because NaOH is hygroscopic. The pellets are dissolved in a small quantity of freshly boiled and cooled purified water in a beaker. After complete dissolution, the solution is transferred into a 1000 mL volumetric flask. The beaker is washed several times with purified water and washings are added to the flask. The volume is finally made up to the mark with freshly boiled and cooled water and mixed thoroughly.

Standardization of Sodium Hydroxide Solution

Principle: The prepared sodium hydroxide solution is standardized using a primary standard acid such as oxalic acid. Oxalic acid is suitable because it is pure, stable, non-hygroscopic, and can be accurately weighed.

During titration, sodium hydroxide neutralizes oxalic acid according to the reaction:

$$H_2C_2O_4 + 2NaOH \rightarrow Na_2C_2O_4 + 2H_2O$$

Phenolphthalein indicator is used because the endpoint occurs in alkaline medium. The color changes from colorless to pale pink.

Molecular weight of oxalic acid dihydrate $H_2C_2O_4 \cdot 2H_2O = 126$

Equivalent weight = 63

For 0.1 N solution: Strength = $0.1 \times 63 = 6.3$ g/L

Thus, 6.3 g of oxalic acid dihydrate is dissolved in water and diluted to 1000 mL.

Procedure for Standardization: The burette is rinsed and filled with sodium hydroxide solution. A pipette is used to transfer 10 mL or 20 mL of standard oxalic acid solution into a clean conical flask. Two to three drops of phenolphthalein indicator are added. The solution is titrated against sodium hydroxide solution with constant swirling until a faint pink color appears which persists for about 30 seconds. The burette reading is noted.

Reaction Involved:

$$H_2C_2O_4 + 2NaOH \rightarrow Na_2C_2O_4 + 2H_2O$$

Neutralization Curves and theories involved in titrations of strong, weak and very weak acids and bases

Acid–base titrations are important quantitative analytical methods based on neutralization reactions between acids and bases. In these titrations, a solution of known concentration called the titrant reacts with another solution of unknown concentration until the equivalence point is reached. The equivalence point is the stage at which chemically equivalent amounts of acid and base have reacted completely.

Equivalence point: The equivalence point is the precise moment when the amount od added titrant is stoichiometrically equal to the amount of analyte in the sample.

Stage comes when:

- All acid is completely neutralized by base

or

- All base is completely neutralized by acid.

This stage is called the equivalence point.

The theory of acid–base titration depends upon:

1. Degree of ionization of acids and bases
2. Change in hydrogen ion concentration during titration
3. Hydrolysis of salt formed
4. Shape of neutralization curve
5. Choice of suitable indicator

The strength of acids and bases greatly influences the pH change during titration and determines the nature of the neutralization curve.

Neutralization Curve: A neutralization curve or titration curve is a graph obtained by plotting the pH of the solution against the volume of titrant added during the titration.

The curve provides information regarding initial pH of solution, buffer region, equivalence point, endpoint which suitable indicator to be used and sharpness of pH change. The shape of the curve differs according to the strengths of acids and bases involved.

1. Strong Acid–Strong Base Titration

In strong acid–strong base titration, both the acid and the base ionize completely in aqueous solution. Therefore, the concentration of hydrogen ions and hydroxyl ions remains high and the neutralization reaction proceeds rapidly and completely.

A common example is the titration of hydrochloric acid with sodium hydroxide.

Reaction:

$$HCl + NaOH \rightarrow NaCl + H_2O$$

The ionic form of the reaction is:

$$H^+ + OH^- \rightarrow H_2O$$

At the beginning, the solution contains excess hydrogen ions because of the strong acid and hence the pH remains very low. As sodium hydroxide is added gradually, hydrogen ions are neutralized and the pH starts increasing slowly. Near the equivalence point, a very sharp rise in pH occurs because even a small addition of base changes the hydrogen ion concentration rapidly. At the equivalence point, the amount of acid becomes chemically equal to the amount of base and the solution becomes neutral.

In the beginning curve is flat because of strong acid present as we add strong base all the H^+ ion get neutralized and there is sharp rise in pH. The neutralization curve for strong acid–strong base titration shows a steep vertical rise at the equivalence point, making the endpoint very sharp and easy to detect.

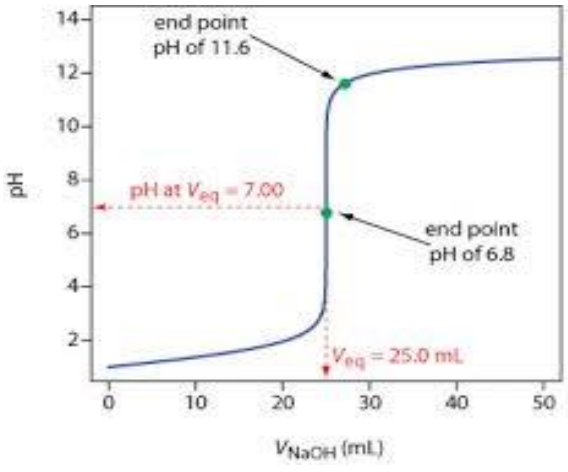


Fig. Strong acid vs strong base

2. Weak Acid-Strong Base titration

In this type of titration, a weak acid is titrated with a strong base. A common example is acetic acid (CH_3COOH) titrated with sodium hydroxide.

The reaction is:

$$CH_3COOH + NaOH \rightarrow CH_3COONa + H_2O$$

A weak acid is only partially ionized in water; therefore, the initial pH of the solution is higher than that of a strong acid. As sodium hydroxide is added, the acid starts converting into its salt, sodium acetate. During this stage, the solution acts as a buffer and resists sudden changes in pH.

As the titration approaches the equivalence point, the pH rises more rapidly. However, the rise is not as sharp as in the strong acid–strong base titration. At the equivalence point, the solution contains sodium acetate, which undergoes hydrolysis and makes the solution slightly basic. Therefore, the pH at the equivalence point is greater than 7, usually around 8 to 9.

Phenolphthalein is the most suitable indicator for this titration because it changes color in the basic pH range. The neutralization curve shows a gradual rise in pH at first, followed by a moderately steep increase near the equivalence point.

$$CH_3COOH + OH^- \rightarrow CH_3COO^- + H_2O$$

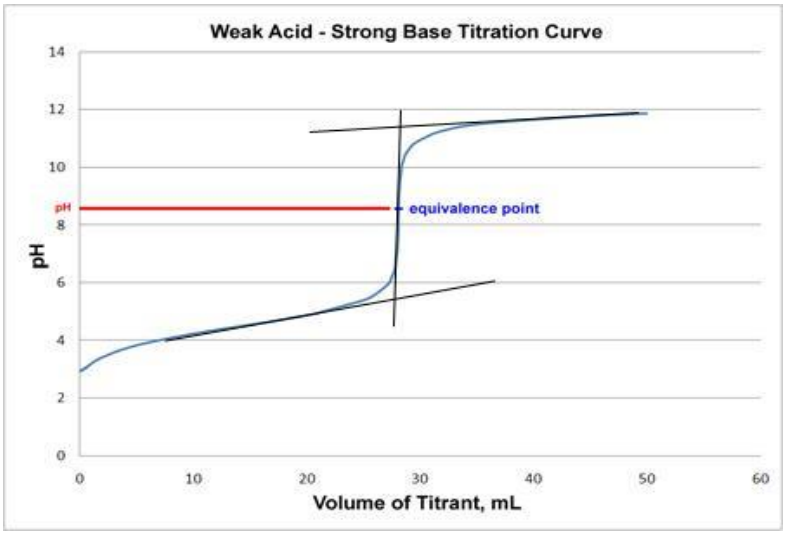


Fig. Weak acid vs strong base

3. Strong Acid - Weak Base titration

A strong acid–weak base titration is a type of acid–base titration in which a strong acid reacts completely with a weak base to form salt and water. A common example is the titration of hydrochloric acid (HCl) with ammonium hydroxide (NH_4OH).

The reaction involved is:

$$HCl + NH_4OH \rightarrow NH_4Cl + H_2O$$

In this titration, hydrochloric acid is completely ionized in water and produces a large concentration of hydrogen ions (H^+) because it is strong acid. Therefore, the solution initially has a very low pH.

$$HCl + H_2O \rightarrow H_3O^+ + Cl^-$$

Ammonium hydroxide is a weak base and ionizes only partially in solution. As the weak base is added slowly from the burette, the hydrogen ions of the acid react with hydroxide ions of the base to form water (H_3O^+ is start consumed by NH_3)

At the equivalence point moles of NH_3 added is equal to moles of HCl in the analyte, the pH change becomes slightly faster, but the rise is not very sharp compared to a strong acid–strong base titration. At equivalence point, solution only has ammonium ions NH_4 and Cl^-. Where ammonium ion NH_4 is conjugate acid of weak base NH_3. Thus, NH_4 will react with H_2O to produce hydronium ions making the solution acidic.

$$NH_4^+ + H_2O \rightarrow NH_3 + H_3O^+$$

The pH at the equivalence point is generally less than 7, usually between 5 and 6. After the equivalence point, excess ammonium hydroxide is present in the solution and the pH rises slowly into the basic region. Since the endpoint occurs in the acidic range, methyl orange is considered a suitable indicator for this titration.

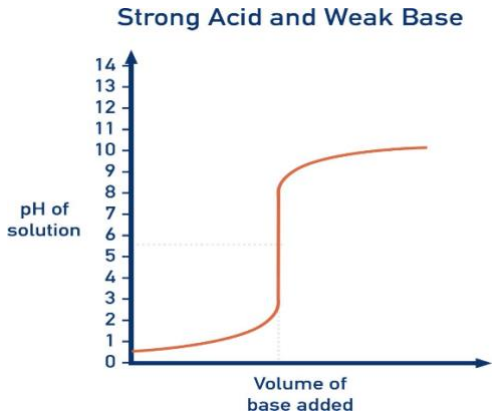


Fig. Strong acid vs weak base

4. Weak Acid - Weak Base titration

A weak acid–weak base titration is a type of acid–base titration in which both the acid and the base are weak electrolytes and ionize only partially in aqueous solution. A common example is the titration of acetic acid (CH_3COOH) with ammonium hydroxide (NH_4OH).

The reaction taking place during the titration is:

$$CH_3COOH + NH_4OH \rightarrow CH_3COONH_4 + H_2O$$

The ionization reactions of the weak acid and weak base are:

$$CH_3COOH \rightleftharpoons CH_3COO^- + H^+$$

$$NH_4OH \rightleftharpoons NH_4^+ + OH^-$$

Since both the acid and the base ionize only partially, the concentration of hydrogen ions and hydroxide ions in the solution is comparatively low. Therefore, the pH change during the titration is very gradual.

At the beginning of the titration, the solution is weakly acidic due to the presence of acetic acid. As ammonium hydroxide is added slowly from the burette, the hydrogen ions of the acid react with hydroxide ions of the base to form water. Because both substances are weak, the neutralization occurs slowly.

During the titration, there is no sharp increase in pH. The pH rises gradually throughout the process. Near the equivalence point, the curve does not show a steep vertical rise as observed in strong acid–strong base titrations.

At the equivalence point, the solution mainly contains ammonium acetate (CH_3COONH_4). The pH at this point depends upon the relative strengths of the weak acid and weak base. If both have nearly equal strength, the solution becomes almost neutral and the pH remains close to 7. Since the endpoint is not sharp, ordinary indicators do not give accurate results in this titration. Therefore, instrumental methods such as pH meter or conductometric methods are generally preferred.

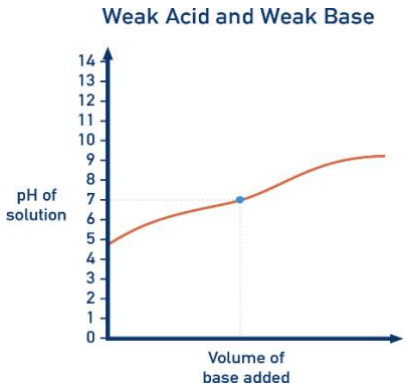


Fig. Weak acid vs weak base

Assay of Ammonium Hydroxide

Ammonium hydroxide (NH_4OH) is a weak alkaline solution formed when ammonia gas dissolves in water. It is commonly used in pharmaceutical preparations, chemical analysis, laboratories, and industries. The assay of ammonium hydroxide is performed to determine its strength or percentage purity. The assay is carried out by acid–base titration using a standard solution of hydrochloric acid because hydrochloric acid reacts completely with ammonium hydroxide.

Principle: Ammonium hydroxide is a weak base and hydrochloric acid is a strong acid. When ammonium hydroxide solution is titrated with standard hydrochloric acid solution, neutralization occurs and ammonium chloride along with water is formed.

$$NH_4OH + HCl \rightarrow NH_4Cl + H_2O$$

Ionization of ammonium hydroxide:

$$NH_4OH \rightleftharpoons NH_4^+ + OH^-$$

Ionization of hydrochloric acid:

$$HCl \rightarrow H^+ + Cl^-$$

Since hydrochloric acid is completely ionized, the hydrogen ions react with hydroxide ions released by ammonium hydroxide to produce water. At the endpoint of the titration, the amount of hydrochloric acid added becomes chemically equivalent to the amount of ammonium hydroxide present in the solution. **Methyl orange** is commonly used as the indicator in this assay because the equivalence point of strong acid–weak base titration lies in the acidic range. In alkaline medium it turns colour of the solution turns yellow and in acidic medium orange to pink

Procedure: Pipette out a measured quantity of ammonium hydroxide solution, usually 10 mL, into a clean conical flask. Add about 20–30 mL of distilled water to dilute the solution. Then add 2–3 drops of methyl orange indicator. Fill the burette with standard hydrochloric acid solution. Note the initial burette reading carefully. Now add hydrochloric acid slowly from the burette into the conical flask while continuously swirling the flask. During the titration, hydrochloric acid reacts with ammonium hydroxide and neutralization occurs. Initially, the solution remains yellow due to the alkaline nature of ammonium hydroxide. Continue adding hydrochloric acid dropwise near the endpoint until the color changes from yellow to light orange or faint pink permanently.

The assay is calculated using the neutralization formula:

$$N_1V_1 = N_2V_2$$

Where N_1 = Normality of HCl, V_1= Volume of HCl used, N_2= Normality of ammonium hydroxide, V_2= Volume of ammonium hydroxide taken

Example Calculation

Suppose: Volume of ammonium hydroxide taken = 10 mL

Normality of HCl = 0.1 N

Volume of HCl used = 12 mL

Using the formula:

$$N_1V_1 = N_2V_2$$

$$0.1 \times 12 = N_2 \times 10$$

$$N_2 = 1.2/10$$

$$N_2 = 0.12$$

Thus, the normality of ammonium hydroxide solution is 0.12 N.

Points to Remember:

- ✓ Acid–base titrations are based on the **neutralization reaction** between an acid and a base.
- ✓ At the equivalence point, the number of **gram equivalents of acid equals the gram equivalents of base**.
- ✓ The endpoint should be as close as possible to the equivalence point for accurate results.
- ✓ The choice of indicator depends upon the **pH of the equivalence point**.
- ✓ Acid–base indicators are generally **weak organic acids or weak organic bases** that exhibit different colours in acidic and alkaline media.
- ✓ According to **Ostwald's theory**, the colour change is due to the ionization of the indicator.
- ✓ According to the **Quinonoid theory**, colour change occurs because of structural transformation between the benzenoid and quinonoid forms.
- ✓ **Phenolphthalein** changes from colourless to pink in the pH range of **8.2–10.0**.
- ✓ **Methyl orange** changes from red to yellow in the pH range of **3.1–4.4**.
- ✓ **Methyl red** changes from red to yellow in the pH range of **4.4–6.2**.
- ✓ Phenolphthalein is suitable for **weak acid–strong base** titrations.
- ✓ Methyl orange is suitable for **strong acid–weak base** titrations.
- ✓ Hydrochloric acid is **not a primary standard** and is standardized against **anhydrous sodium carbonate**.
- ✓ Sodium hydroxide is **not a primary standard** because it absorbs moisture and carbon dioxide from the atmosphere.
- ✓ Sodium hydroxide is standardized using **oxalic acid** or **potassium hydrogen phthalate (KHP)**.
- ✓ Sodium hydroxide solution should always be stored in **polyethylene bottles** with tightly closed stoppers.
- ✓ Strong acid–strong base titrations have an equivalence point near **pH 7**.
- ✓ Weak acid–strong base titrations have an equivalence point **above pH 7**.
- ✓ Strong acid–weak base titrations have an equivalence point **below pH 7**.
- ✓ Weak acid–weak base titrations do not produce a sharp endpoint and are rarely performed.
- ✓ Neutralization curves help in selecting a suitable indicator.
- ✓ Ammonium hydroxide is assayed by titration with standard hydrochloric acid using **methyl red or methyl orange** as the indicator.

Case Based Learning (CBL)

A pharmaceutical quality control laboratory receives a sample of **ammonium hydroxide solution** from the manufacturing department. During routine analysis, the analyst notices that the concentration of the solution appears lower than the labeled claim. To verify its strength, the analyst performs an acid–base titration using **standard hydrochloric acid** and selects an appropriate indicator based on the expected pH at the equivalence point.

Students are asked to determine the correct titration method, choose the suitable indicator, and explain why standardization of hydrochloric acid is necessary before the assay.

Questions

1. Why should hydrochloric acid be standardized before use?
2. Which indicator is most suitable for this assay and why?
3. What is the principle of acid–base titration?
4. Why is ammonium hydroxide considered a weak base?
5. What errors may occur if an unsuitable indicator is used?

Problem-Based Learning (PBL)

Problem: A student performs the assay of ammonium hydroxide using **phenolphthalein** instead of **methyl orange** and obtains inaccurate results.

MCQs

1. Which indicator is most suitable for ammonium hydroxide estimation?

   A. Phenolphthalein
   B. Methyl Orange ✔
   C. Starch
   D. Potassium chromate

2. Hydrochloric acid is standardized using:

   A. Sodium carbonate ✔
   B. Oxalic acid
   C. EDTA
   D. Potassium dichromate

3. Neutralization titration is based on:

   A. Oxidation
   B. Acid–base reaction ✔
   C. Complex formation
   D. Precipitation

4. The endpoint should be:

   A. Far from equivalence point
   B. Close to equivalence point ✔
   C. Above pH 10
   D. Below pH 2

5. Ammonium hydroxide is:

   A. Strong acid
   B. Weak base ✔
   C. Strong base
   D. Neutral salt

Non – Aqueous Titrations

Non-aqueous titrations are those in which the titrations of weakly acidic or basic substances are carried out using nonaqueous solvents so as to get sharp end point. Most of the titrations are performed in the aqueous media, means water is used as solvent. There may be difficulty if reactant is insoluble in water or reactant is reactive with water or the analyte (sample) is either too weak acid or too weak base. It is mainly used for the assay of weak acids and weak bases that cannot be accurately titrated in aqueous medium because they are either poorly soluble in water or only slightly ionized in water. In non-aqueous media, the strength of acids and bases can be increased or decreased by selecting a suitable solvent, thereby giving a sharp and clear end point.

Principle: In aqueous solution, very weak acids or bases do not ionize sufficiently; therefore, the concentration of hydrogen ions or hydroxyl ions is too low to produce a sharp end point. By using a suitable non-aqueous solvent, the ionization of the substance can be enhanced.

For example, acetic acid acts as an acidic solvent and increases the basic nature of weak bases. Hence weak bases can be titrated easily with a strong acid such as perchloric acid in glacial acetic acid.

Advantages of Non-aqueous Titrations

Non- aqueous titration has following advantages -

- It is useful for the titrations of very weak acids or bases.
- Many organic acids which are not soluble in water can be dissolved in non-aqueous solvents. Thus, titration of these organic acids is very easy.
- It can be used for titration of mixture of acids as well.
- These titrations show sharp end point with internal indicator.
- It is simple, qualitative and selective method.
- It is a highly accurate method.
- Preferably non-aqueous titration is used for biological matters.
- It is very important in pharmacopoeial assays.

Applications of Non-aqueous Titration: Non-aqueous titration has various uses in numerous fields. Specially, in medicinal field non- aqueous titration is very useful. We have listed here few applications of non-aqueous titration.

- Non – aqueous titration is used to know the purity of assays.
- It is used for determination of concentration expressions.
- It is used in determination of hydrophobic compounds, phenobarbitone, diuretics, steroids.
- It is used in the determination of composition of antitubercular drugs and adrenergic drugs.

Disadvantages of Non-aqueous Titration: Non – aqueous titration has following disadvantages.

- Solvents used in non-aqueous titration are not stable compared to aqueous solvents.
- In non-aqueous titration, non-aqueous solvents are required calibration after every use.
- In non-aqueous titrations temperature corrections are necessary.

Reasons for Non aqueous titrations:

- The reactant is insoluble in water.
- The reactant is reactive with water (Undergoes chemical decomposition in water).
- The sample is too weak acid or too weak base (water due to its amphoteric nature compete with the sample).

Water should not be used even in minute quantities

- If we are doing titration of weak acid, water will act as strong acid as compared to sample and donates proton to base.
- If we are doing titration of weak base, water will act as strong base as compared to sample and accepts proton from acid.

Types of Solvents used in Non- Aqueous Solvents

The solvent plays an important role in non-aqueous titrations because it affects the strength and ionization of acids and bases.

Non-aqueous solvents are classified into four main types:

1. Protogenic Solvents

2. Protophilic Solvents

3. Amphiprotic Solvents

4. Aprotic Solvent

1. Protogenic Solvents

These solvents donate protons (H^+). They increase the basic strength of solutes. They have high dielectric constant and ionized because of strength and ability to donate protons. Also enhances basicity of weak bases.

They exert a 'levelling effect' on increases the basic nature of weak base.

Weakly basic substances react with protogenic solvents and due to that increase, the basicity.

- $HCl \rightarrow H^+ + Cl^-$
- $CH3COOH \rightarrow CH_3COO^- + H^+$
- $H_2SO_4 \rightarrow H^+ + HSO_4$

For example: Acetic acid, sulphuric acid, formic acid

2. Protophilic Solvents

These solvents are basic in nature and enhance acidity of weak acids. These solvents attracts protons. They accept proton from acid to form solvated proton. All the protophilic solvents have a lone-pairs. They increase the acidic nature of weak acid. The concept of basic nature is according to Lewis concept.

Acid + Basic solvent → Solvated proton + Conjugated base of acid

For example: Acetone, ether, pyridine, liquid ammonia, Ethylenediamine and Dimethylformamide (DMF).

3. Amphiprotic Solvents

These types of solvents possess both protophillic and protogenic characteristics. These solvents are acidic as well as basic in nature (can accept or donate the protons).

Acetic acid is mostly employed as a solvent for the titration of basic substances and its dissociation can be depicted as shown below:

$$CH_3COOH \rightarrow H^+ + CH3COO^-$$

For example: Water, alcohol, acetic acid.

PERCHLORIC ACID: It is a very strong acid and when it is made to dissolve in acetic acid, the latter can behave as a base and forms an 'onium ion' after combining with protons donated by the perchloric acid.

$$HClO_4 \rightarrow H^+ + ClO_4^-$$

$$CH_3COOH + H+ \rightarrow CH_3COOH_2^+$$

Onium ion

As the $CH_3COOH_2^+$ ion can instantly donate its proton to a base, therefore, a solution of perchloric acid in glacial acetic acid, behaves as a strongly acidic solution.

4. Aprotic Solvent

They are essentially basic in nature and normally react with acids to form solvated protons. These solvents are neither accept or donate proton. They cannot react with analyte. These solvents generally used for titration of weak acids.

Due to low dielectric constant do not react with either acids or bases and therefore do not favour ionization and they are used for dilution. **Example:** Carbon Tetrachloride, Toluene, Benzene.

Aprotic solvents are neutral, chemically inert substances such as benzene and chloroform.

Selection of solvent: The selection of solvent in non-aqueous titration based on:

Solubility of drug: The weak acidic or basic drug should be soluble in the solvent which at the same time must be miscible with the titrant.

Nature of drug: The solvent is used according to the nature of drug, whether it is weak acid or weak base.

Unreactive: The solvent should be unreacted with the drug.

Some Examples of Non-Aqueous Solvents

A very large number of inorganic solvents have been used for non-aqueous titrations, but a few have been used more frequently than others. Some of the most widely applied solvents systems are discussed below. In all instances pure, dry analytical reagent quality solvent should be used to assist in obtaining sharp end points.

1. Glacial Ethanoic (Acetic) Acid:

Glacial ethanoic acid is the most frequently used non-aqueous solvent. Before it is used it is advisable to check the water content. This may be between 0.1% and 1.0%. *Acetonitrile:* Acetonitrile (methyl cyanide, cyanomethane) is frequently used with other solvents such as chloroform and phenol and especially, with ethanoic acid. It enables very sharp end points to be obtained in the titration of metal ethanoates when titrated with perchloric acid.

2. Alcohol:

Salt of organic acids, especially of soaps are best determined in mixtures of glycols and alcohols or mixtures of glycols and hydrocarbons. The most common combinations are ethylene glycol (dihydroxy ethane) with propan-2-ol or butan-1-ol. The combinations provide admirable solvents for both the polar and non-polar ends of the molecules.

3. Dioxane:

Dioxane is another popular solvent, which is often used in place of glacial ethanoic acid when mixtures of substances are to be quantified. Unlike ethanoic acid, dioxane is not a levelling solvent and separate end points are normally possible, corresponding to the individual components in the mixtures.

4. Dimethylformamide:

Dimethylformamide (DMF) is a protophillic solvent, which is frequently employed for titrations between, for instance, benzoic acid and amides, although end points may sometimes be difficult to obtain.

Levelling Effect

The **levelling effect** refers to the phenomenon where the strength of weak ac or weak bases increases in the presence of suitable solvent. By choosing the right solvent the strength of weak acids or bases are increased which makes the titration accurate.

In **basic solvent** (like ammonia), weak acids become stronger because the solvent accepts proton easily.

In an **acidic solvent** (like acetic acid), weak bases become stronger because the solvent donates protons.

For example: Acetic acid behave like a strong acid in ammonia solution due to this effect.

Differentiating solvents: Differentiating solvents allow acids and bases to show different strength. The degree of dissociation varies depending on solvent used. **For example**, in glacial acetic acid HI act as a strong acid, HBr is moderate and HCl is weaker. This is called **differential effect**.

Types of Non-Aqueous Titrations

1. Acidimetric Non-Aqueous Titration

Acidimetric non-aqueous titration involves the titration of weak organic bases using a standard solution of a strong acid in a non-aqueous solvent. The most commonly used titrant is **0.1 M perchloric acid ($HClO_4$) in glacial acetic acid**.

Many organic bases such as alkaloids, amines, and antihistamines are weakly basic and do not ionize completely in water. When dissolved in glacial acetic acid, their basic properties are enhanced, allowing accurate titration with perchloric acid.

Principle: Glacial acetic acid acts as a protogenic solvent and increases the proton-accepting tendency of weak bases. Perchloric acid behaves as a strong acid in this medium and readily donates protons to the base.

Let B represent a weak base:

$$B + HClO_4 \rightarrow BH^+ + ClO_4^-$$

The base accepts a proton from perchloric acid and forms a salt.

Indicator: Crystal violet (0.5 % in acetic acid)

Colour change: From violet to light green.

2. Alkalimetric Non-Aqueous Titration

Alkalimetric non-aqueous titration involves the titration of weak organic acids using a standard solution of a strong base in a non-aqueous medium. Common titrants include sodium methoxide, potassium methoxide, and tetrabutylammonium hydroxide.

Weak acids such as barbiturates, sulfonamides, and phenols are often insufficiently ionized in water. In non-aqueous solvents, their acidic character is enhanced, resulting in accurate titration.

Principle: Basic solvents increase the dissociation of weak acids. The acid reacts quantitatively with the strong base present in the non-aqueous medium.

General Reaction

Let HA represent a weak acid:

$$HA + NaOCH_3 \text{ (sodium methoxide)} \rightarrow NaA + CH_3OH$$

The weak acid reacts with sodium methoxide to form a salt and methanol.

Indicator: Thymol Blue (0.5 % in methanol)

Colour change: From Pink to Blue

Details	Acidimetry	Alkalimetry
Samples:	Basic drugs such as: Ephedrine, Adrenaline, Caffeine, Acyclovir.	Acidic drugs such as: Nalidixic acid, Flurouracil.
Solvent:	Protogenic solvents such as: glacial acetic acid	Protophilic solvents such as: DMF
Titrant:	Perchloric acid $HClO_4$	Sodium methoxide.
Indicator:	Crystal violet (0.5% in glacial acetic acid) Color change from violet to yellowish green.	Thymol blue (0.5 % in methanol) Color change from pink to blue

Indicators

Indicators used in non-aqueous titrations are substances that undergo a distinct color change at or near the equivalence point in a non-aqueous medium. Since the dissociation behavior of acids, bases, and indicators differs significantly from that in water, ordinary aqueous indicators may not function satisfactorily in non-aqueous solvents. The colour corresponding to the correct end point may be established by carrying out a potentiometric titration (end point is

determined by measuring the change in electrode potential during titration) while simultaneously observing the colour change of the indicator.

Therefore, special indicators are selected according to the solvent system and titration conditions to obtain a sharp and accurate end point.

The choice of indicator depends on the nature of the titration, the solvent used, and the strength of the acid or base involved.

Characteristics of an Ideal Non-Aqueous Indicator: A suitable non-aqueous indicator should:

- Be soluble in the selected solvent.
- Produce a sharp and distinct color change.
- Remain chemically stable in the non-aqueous medium.
- Not interfere with the titration reaction.
- Change color very close to the equivalence point.

Indicators Used in Acidimetric Non-Aqueous Titrations

In acidimetric titrations, weak organic bases are titrated with perchloric acid in glacial acetic acid. The commonly used indicators are basic dyes that undergo color changes upon protonation.

1. Crystal violet: 0.5 % w/v solution in glacial acetic acid. Colour change: Violet through blue Green – Greenish yellow. This indicator is used in reaction Pyridine titrated with perchloric acid.

2. Methyl Red: 0.2 % w/v solution in dioxin. Colour change: Yellow to Red

3. Quenaldine Red: Used as an indicator for drug determinations in dimethylformamide solution. A 0.1% w/v solution in ethanol gives a colour change from purple red to pale green.

4. Malachite Green: Malachite green is suitable for titration of many weak organic bases. Color Change is from Green to Yellow.

Indicators Used in Alkalimetric Non-Aqueous Titrations

In alkalimetric titrations, weak organic acids are titrated using sodium methoxide or other strong bases in non-aqueous media.

1. Thymol blue: Used extensively as an indicator for titrations of substances acting as acids in dimethyl formamide solution. A 0.2% w/v solution in methanol gives a sharp colour change from yellow to blue at the end point.

2. Azo Violet: Azo violet is widely used because of its clear color transition for Weakly acidic pharmaceutical compounds. Color Change is from Yellow to Violet.

Table: Acidimetric Assays: Non-aqueous Titrations different Indicators

S. No.	Name of Substance	Indicator Employed
1.	Amantadine hydrochloride	Crystal violet
2.	Chlorpromazine hydrochloride	Methyl orange
3.	Clonidine hydrochloride	α -Naphthol benzein
4.	Cyproheptadiene.HCl	Crystal violet
5.	Dehydroemetine.HCl	Crystal violet
6.	Ephedrine hydrochloride	Crystal violet
7.	Imipramine hydrochloride	Crystal violet
8.	Isoprenaline hydrochloride	Crystal violet
9.	Lignocaine hydrochloride	Crystal violet

Table: Alkalimetric Assays: Non-aqueous Titrations different Indicators

S. No.	Name of Substance	Indicator Employed
1.	Acetazolamide	Potentiometric determination
2.	Bendrofluazide	Azo violet
3.	Allopurinol	Thymol blue
4.	Mercaptopurine	Thymol blue
5.	Amylobarbitone	Quinaldine Red
6.	Nalidixic acid	Thymolphthalein

Preparation and Standardization of titrants

A. Acidic Titrant: Perchloric Acid (0.1 M) in Glacial Acetic Acid

Principle: Perchloric acid is a strong acid and is the most commonly used acidic titrant in non-aqueous acidimetric titrations. It is used for the assay of weak organic bases such as alkaloids, amines, antihistamines, and local anesthetics. Glacial acetic acid serves as the solvent because it enhances the basicity of weak bases and provides a sharp endpoint.

(i) Preparation of 0.1 N Perchloric Acid

Materials Required: 8.5 ml of perchloric acid (70.0 to 72.0%), 1 litre of glacial acetic acid, 30 ml of acetic anhydride.

Procedure: 1. Gradually mix 8.5 ml of perchloric acid to 900 ml of glacial acetic acid with vigorous and continuous stirring.

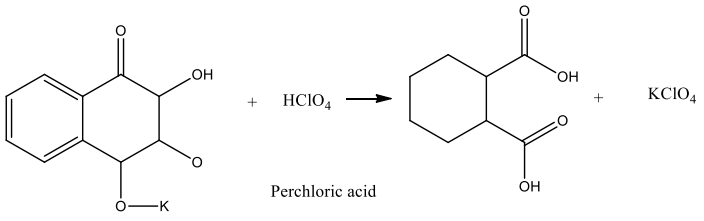
2. Now add 30 ml acetic anhydride and make up the volume to 1 litre with glacial acetic acid and allow to stand for 24 hours before use.

3. The acetic anhydride reacts with the water (approx. 30%) in perchloric acid and some traces in glacial acetic acid thereby making the resulting mixture practically anhydrous.

$$H_2O + (CH_3CO)_2O \rightarrow 2CH_3COOH$$

Acetic anhydride Acetic acid

(ii) Standardization of 0.1 N Perchloric acid: Standardization of acid titrant may be carried out with the any substance which is a strong base and which is available in a known purity. Potassium hydrogen phthalate (KHP) is used as a primary standard because of its high purity. During titration, crystalline precipitate of $KClO_4$ appears, but this does not interfere with location of end point.



Therefore,

$$204.14 \text{ gm } C_8H_5O_4K \equiv HClO_4 \equiv 1000 \text{ ml N or}$$

$$0.02041 \text{ gm of } C_8H_5O_4K \equiv 1 \text{ ml of 0.1 N } HClO_4$$

Chemical Formula: $KHC_8H_5O_4$

Molecular Weight: 204.22 g/mol

Procedure: Weigh accurately about 0.5 gm of potassium hydrogen phthalate in a 100 ml conical flask. Add 25 ml of glacial acetic acid and attach a reflux condenser fitted with a silica-gel drying tube. Warm until the salt gets dissolved completely. Cool and titrate with 0.1 N perchloric acid by making use of either of the following two indicators:

(a) acetous crystal violet- 2 drops, end point Blue to Blue Green (0.5% w/v).

(b) acetous oracet blue B- 2 drops, end point Blue to Pink

Calculation:

$$M_1V_1=M_2V_2$$

or

$$\text{Molarity of } HClO_4 = \frac{\text{Weight of KHP} \times 1000}{\text{Molecular Weight of KHP} \times \text{Volume of } HClO_4}$$

Table: Choice of indicators

Indicator	Colour Change		
	Basic	**Neutral**	**Acidic**
Crystal Violet (0.5 percent in glacial acetic acid)	Violet	Blue-green	Yellowish-green
α-Naphtholbenzein (0.2 % in glacial acetic acid	Blue or blue-green	Orange	Dark-green
Oracet Blue B (0.5% in glacial acetic acid)	Blue	Purple	Pink
Quinaldine Red (0.1 % in methanol)	Magenta		Almost colorless

Effect of temperature on assays: It is always advisable to carry out standardization and titration preferably at the same temperature. In a situation where these temperature parameters cannot be achieved, the volume of titrant may be corrected by the application of the following formula:

$$Vc = V[1 + 0.001 (t1 + t2)]$$

where, Vc = Corrected volume of titrant, V = Volume of titrant measured, t1 = Temperature at which titrant was standardized, t2 = Temperature at which titration was performed.

B. Basic Titrant: Sodium Methoxide (0.1 M)

Principle: Sodium methoxide is the most commonly used basic titrant in non-aqueous alkalimetric titrations. It is employed for the determination of weak organic acids such as barbiturates, sulfonamides, and phenolic compounds.

(i) Preparation of 0.1 M Sodium Methoxide

Composition:

- Sodium metal: 2.3 g
- Methanol (anhydrous): sufficient quantity to produce 1000 mL

Procedure: Take about 700 mL of anhydrous methanol in a dry flask. Carefully add 2.3 g of freshly cut sodium metal in small pieces. Allow complete dissolution. After cooling, dilute with anhydrous methanol to 1000 mL and mix well. Store in a tightly closed container protected from moisture.

$$2Na + 2CH_3OH \rightarrow 2CH_3ONa + H_2\uparrow$$

Sodium reacts with methanol to form sodium methoxide and hydrogen gas.

(ii) Standardization of Sodium Methoxide

Primary Standard: Benzoic Acid

Chemical Formula: C_6H_5COOH

Molecular Weight: 122.12 g/mol

Procedure: Accurately weigh about 0.4–0.5 g of benzoic acid and dissolve it in dimethylformamide (DMF) or methanol. Add 2–3 drops of thymol blue or azo violet indicator and titrate with sodium methoxide solution until the endpoint color appears.

$$C_6H_5COOH + CH_3ONa \rightarrow C_6H_5COONa + CH_3OH$$

Benzoic acid reacts quantitatively with sodium methoxide to form sodium benzoate.

Indicators used: Thymol Blue, Azo Violet, Alizarin Yellow R

Calculation: $M_1V_1=M_2V_2$

or

$$\text{Molarity of Sodium Methoxide} = \frac{\text{Weight of Benzoic Acid} \times 1000}{\text{Molecular Weight of Benzoic Acid} \times \text{Volume of Sodium Methoxide}}$$

Estimation of weakly acidic and basic substances using non-aqueous titrations

Estimation of Ephedrine HCl

Ephedrine is a weak organic base and is not completely ionized in aqueous medium. Therefore, it is assayed by non-aqueous titration using **0.1 M perchloric acid in glacial acetic acid**. Glacial acetic acid enhances the basic nature of ephedrine, allowing it to react quantitatively with perchloric acid. The endpoint is detected using crystal violet indicator.

Ephedrine itself is a weak organic base because it contains a nitrogen atom that can accept a proton (H^+). **Ephedrine hydrochloride** is the hydrochloride salt of ephedrine, formed by reaction with hydrochloric acid:

$$\text{Ephedrine} + HCl \rightarrow \text{Ephedrine HCl}$$

Although the salt contains hydrochloric acid, the drug molecule (ephedrine) retains its **basic character**. Therefore, in pharmaceutical analysis, ephedrine hydrochloride is assayed as a **weak base**.

Principle: During non-aqueous titration of Ephedrine HCl the chloride ion behaves as a weak proton acceptor (weak basic drug). In this titration, it is replaced as acetate ion by adding Mercuric Acetate in Glacial acetic acid. A titration is performed against perchloric acid using crystal violet as an indicator.

Procedure:

Preparation of 0.1M solution of $HClO_4$ and its standardization: Dissolve 8.5 ml of 72 % $HClO_4$ in about 900 ml glacial acetic acid with constant stirring, add about 30 ml acetic anhydride and make up the volume (1000 ml) with glacial acetic acid and keep the mixture for 24 hours. Acetic anhydride absorbed all the water from $HClO_4$ and glacial acetic acid and renders the solution virtually anhydrous. $HClO_4$ must be well diluted with glacial acetic acid before adding acetic anhydride because reaction between HClO4 and acetic anhydride is explosive.

Standardization of $HClO_4$: To 500 mg of potassium acid phthalate add 25 ml of glacial acetic acid and add few drops of 5 % w/v crystal violet in glacial acetic acid as indicator. This solution is titrated with 0.1 M $HClO_4$. The colour changes from blue to blue green.

A blank titration is performed and this volume is subtracted from the volume of perchloric acid needed by the sample.

Factor: Each ml of 0.1 M perchloric acid 0.02017 gm of ephedrine hydrochloride.

Assay Procedure:

Weigh accurately about 0.17 g, dissolve in 10 ml of mercuric acetate solution.

↓

warming gently, add 50 ml of acetone and mix.

↓

Titrate with 0.1 M perchloric acid, using 1 ml of a saturated solution of methyl orange in acetone as indicator, until a red colour is obtained.

↓

Carry out a blank titration.

Calculations:

% Ephedrine Hydrochloride = $\frac{\text{X ml x Molarity (Calculated)} x\ 0.02017 \text{ x } 100}{M\ (Given)\ x\ wt.\ of\ sample\ (in\ gm)}$

Estimation of Sodium Benzoate

Sodium benzoate is the sodium salt of benzoic acid and is one of the most widely used antimicrobial preservatives in pharmaceutical preparations, foods, and beverages. It appears as a white, odourless or nearly odourless crystalline powder or granules and is freely soluble in water. It is effective against yeasts, moulds, and some bacteria, particularly in acidic media.

Chemical Information

- **Chemical Name:** Sodium Benzoate
- **Chemical Formula:** $C_7H_5NaO_2$ or C_6H_5COONa
- **Molecular Weight:** 144.11 g/mol
- **Category:** Antimicrobial preservative

Principle: Sodium benzoate is estimated by non-aqueous titration where it is dissolved in anhydrous glacial acetic acid which enhances the strength of weak base sodium benzoate. This solution is titrated with 0.1 M Perchloric acid using 1-naptholbenzein as an indicator.

Procedure:

Preparation of 0.1 M solution of $HClO_4$ and its standardization: Dissolve 8.5 ml of 72 % $HClO_4$ in about 900 ml glacial acetic acid with constant stirring, add about 30 ml acetic anhydride and make up the volume (1000 ml) with glacial acetic acid and keep the mixture for 24 hours. Acetic anhydride absorbed all the water from $HClO_4$ and glacial acetic acid and renders the solution virtually anhydrous. $HClO_4$ must be well diluted with glacial acetic acid before adding acetic anhydride because reaction between $HClO_4$ and acetic anhydride is explosive.

Standardization of $HClO_4$: To 500 mg of potassium acid phthalate add 25 ml of glacial acetic acid and add few drops of 5 % w/v crystal violet in glacial acetic acid as indicator. This solution is titrated with 0.1 M $HClO_4$. The colour changes from blue to blue green.

Factor: 1 ml of 0.1 M perchloric acid is equivalent to 0.01441 g of $C_7H_5NaO_2$.

Assay Procedure:

Weigh accurately 0.25 g sodium benzoate.

↓

Dissolve in 20 ml of glacial acetic acid

↓

Warm it to if necessary

↓

Cool

↓

Titrate with 0.1 M perchloric acid using 0.05 ml of 1-naptholbenzein solution as an indicator.

↓

Carry out blank titration.

Calculations:

$$\% \text{ Assay} = \frac{V \times M \times MW \times 100}{1000 \times W}$$

Where:

- **V** = Volume of perchloric acid used (mL)
- **M** = Molarity of perchloric acid
- **MW** = Molecular weight of sodium benzoate (144.11)
- **W** = Weight of sample taken (g)

Estimation of Phenobarbital

Principle: Phenobarbital is a weakly acidic barbiturate. It is only slightly ionized in water and therefore is assayed by non-aqueous titration using sodium methoxide in a non-aqueous solvent.

$$C_{12}H_{12}N_2O_3 + CH_3ONa \rightarrow C_{12}H_{11}N_2O_3Na + CH_3OH$$

Phenobarbital reacts with sodium methoxide to form sodium phenobarbital and methanol.

Procedure: Accurately weigh about 0.25 g of phenobarbital and dissolve it in 50 mL of dimethylformamide (DMF). Add 2–3 drops of thymol blue indicator and titrate with 0.1 M sodium methoxide until the color changes from yellow to blue.

1 mL of 0.1 M Sodium Methoxide≡23.22 mg of Phenobarbital

Calculation

Percentage Assay Formula

$$\% \text{ Assay} = V \times F \times 100 / W \times 1000$$

Where:

- **V** = Volume of sodium methoxide used (mL)
- **F** = Factor (23.22 mg/mL)
- **W** = Weight of sample taken (g)

Points to Remember:

- ✓ Non-aqueous titrations are used for substances that are **weak acids or weak bases** and cannot be accurately titrated in water.
- ✓ Non-aqueous solvents increase the strength of weak acids and weak bases, producing a sharp endpoint.
- ✓ **Protogenic solvents** donate protons (e.g., glacial acetic acid).
- ✓ **Protophilic solvents** accept protons (e.g., dimethylformamide).
- ✓ **Amphiprotic solvents** can both donate and accept protons (e.g., methanol).
- ✓ **Aprotic solvents** neither donate nor accept protons (e.g., benzene, chloroform).
- ✓ **Glacial acetic acid** is the most commonly used non-aqueous solvent.
- ✓ Perchloric acid is used as the titrant in **acidimetric non-aqueous titrations**.
- ✓ Sodium methoxide is used as the titrant in **alkalimetric non-aqueous titrations**.
- ✓ Perchloric acid is standardized using **potassium hydrogen phthalate**.
- ✓ Sodium methoxide is standardized using **benzoic acid**.
- ✓ Crystal violet, malachite green, azoviolet, and thymol blue are commonly used indicators.
- ✓ Weak bases are estimated using perchloric acid in glacial acetic acid.
- ☑ Weak acids such as sodium benzoate are estimated using sodium methoxide.

Case Based Learning (CBL)

Case

A pharmaceutical company receives a batch of **sodium benzoate** for quality testing. When an analyst attempts to estimate it using aqueous sodium hydroxide, no sharp endpoint is observed. The senior analyst recommends performing the assay by **non-aqueous titration** using **sodium methoxide** in methanol.

Students must explain why aqueous titration fails and why a non-aqueous medium provides accurate results.

Questions

1. Why are non-aqueous titrations used?
2. Why is sodium benzoate difficult to estimate in water?
3. Which titrant is used?
4. What solvent is commonly employed?
5. What are the advantages of non-aqueous titrations?

Problem-Based Learning (PBL)

Problem

An analyst uses water instead of glacial acetic acid while estimating a weak base, resulting in an indistinct endpoint.

MCQs

1. Non-aqueous titration is mainly used for:
   A. Strong acids
   B. Weak acids and weak bases ✔
   C. Neutral salts
   D. Sugars
2. The commonly used acidic solvent is:
   A. Glacial acetic acid ✔
   B. Water
   C. Acetone
   D. Benzene
3. Perchloric acid is used for:
   A. Weak bases ✔
   B. Weak acids
   C. Chlorides
   D. Sulphates
4. Sodium methoxide is used to estimate:
   A. Weak acids ✔
   B. Weak bases
   C. Oxidizing agents
   D. Chlorides
5. The major advantage of non-aqueous titration is:
   A. Lower sensitivity
   B. Sharp endpoint ✔
   C. Higher precipitation
   D. Lower accuracy

Precipitation Titration and Gravimetry

Precipitation titration and gravimetric analysis are important quantitative analytical techniques used for the determination of various chemical substances. Both methods are based on the formation of a sparingly soluble precipitate when a suitable reagent reacts with the analyte. These techniques are widely employed in pharmaceutical, chemical, environmental, and industrial laboratories for accurate quantitative analysis.

In **precipitation titration**, the concentration of an analyte is determined by measuring the volume of a standard solution required to produce a complete precipitation reaction. The endpoint of the titration is detected using suitable indicators or instrumental methods. Common examples include the determination of chloride, bromide, and iodide ions using silver nitrate solution.

Gravimetric analysis, on the other hand, is based on the measurement of mass. In this method, the analyte is converted into an insoluble precipitate of known composition, which is then filtered, washed, dried or ignited, and accurately weighed. The amount of analyte present is calculated from the mass of the precipitate obtained. Gravimetry is considered one of the most accurate and reliable methods of quantitative chemical analysis.

Both **precipitation titration** and **gravimetry** are closely related because they rely on the same fundamental principle of precipitate formation. However, precipitation titration is a volumetric method that measures the volume of titrant consumed, whereas gravimetry is a weight-based method that measures the mass of the precipitate formed. These methods provide accurate, precise, and reproducible results and therefore occupy an important place in pharmaceutical and analytical chemistry.

Precipitation titration and gravimetry are closely related because **both are based on the formation of an insoluble precipitate from a chemical reaction**. The main difference lies in how the amount of analyte is measured.

Common Principle: In both methods, the analyte reacts with a reagent to form a sparingly soluble precipitate.

For example, for chloride ion:

$$Ag^{+} + Cl^{-} \rightarrow AgCl \downarrow$$

The same reaction can be used in both precipitation titration and gravimetric analysis.

In Precipitation Titration: The amount of analyte is determined by measuring the **volume of titrant** required to completely precipitate the analyte.

Example: A chloride solution is titrated with silver nitrate.

$$Ag^{+} + Cl^{-} \rightarrow AgCl\downarrow$$

The endpoint is detected using an indicator (Mohr's, Volhard's, or Fajans method).

- Measure **volume of $AgNO_3$ used**
- Calculate chloride concentration from titration data

In Gravimetry: The analyte is precipitated completely, and the precipitate is collected, dried, and weighed.

Example: Chloride is precipitated as silver chloride. The AgCl precipitate formed is filtered, dried, and weighed.

- Measure **mass of AgCl formed**
- Calculate chloride content from the mass

Advantages of Precipitation Titration

- Simple and rapid method.
- Good accuracy and precision.
- Suitable for determination of halide ions.
- Requires simple apparatus.
- Widely applicable in pharmaceutical and water analysis.

Limitations of Precipitation Titration

- Limited to substances forming insoluble precipitates.
- Endpoint detection may sometimes be difficult.
- Interfering ions may affect accuracy.
- Requires controlled pH conditions.

Factors Affecting Solubility of the Precipitate

1. Common ion effect on solubility (C.I.): The presence of a common ion decreases the solubility of a precipitate. According to Le Chatelier's principle, the addition of an ion already present in the equilibrium shifts the equilibrium towards the formation of more precipitate.

$$AgCl \rightleftharpoons Ag^{+} + Cl^{-}$$

Addition of sodium chloride increases the concentration of Cl^{-} ions and decreases the solubility of silver chloride. It leads to decreases solubility. Precipitation becomes more complete and endpoint becomes sharper.

2. Effect of Temperature: The solubility of most precipitates increases with an increase in temperature, although some precipitates may show little change. Silver chloride becomes slightly more soluble at higher temperatures. Higher temperature generally increases solubility or may dissolve part of the precipitate. Controlled temperature is required for accurate titration.

3. Effect of pH: The pH of the solution can significantly affect the solubility of precipitates, especially those derived from weak acids or weak bases. Silver chromate used in Mohr's method is affected by pH.

In acidic medium:

$$CrO_4^{2-} + H^{+} \rightleftharpoons HCrO_4^{-}$$

The concentration of chromate ions decreases, affecting endpoint detection. Acidic conditions may increase solubility of some precipitates. While alkaline conditions may produce unwanted precipitates. That is why proper pH control is essential.

4. Complex Formation: Some ions form soluble complex ions with the precipitating ion, thereby increasing the solubility of the precipitate. Example: Silver chloride dissolves in excess ammonia:

$$AgCl + 2NH_3 \rightarrow [Ag(NH_3)_2]^{+} + Cl^{-}$$

Solubility increases greatly due to complex formation and titration results become inaccurate.

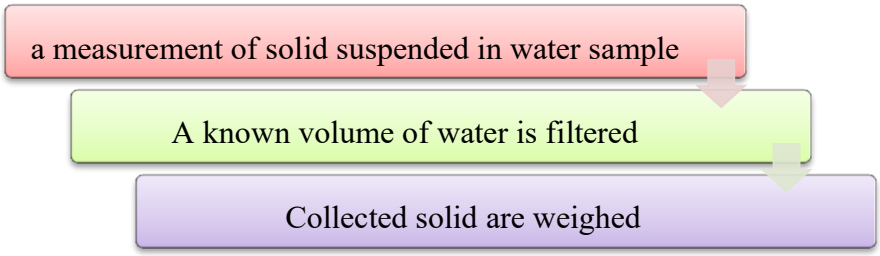
5. Nature of the Solvent: The solvent affects the dielectric constant and ionization of substances. A solvent with a high dielectric constant generally increases the dissociation of ionic compounds. Solubility depends on the polarity of the solvent. The solubility of most inorganic compounds is reduced by the addition of organic solvents such as methanol, ethanol, propan-1-ol and acetone. **For example**, the addition of about 20 % ethanol renders the solubility of lead sulphate practically negligible, thus permitting quantitative separation.

6. Particle Size of the Precipitate: Small particles have a larger surface area and are generally more soluble than larger particles. Fine precipitates dissolve more readily as compared to larger crystals are less soluble and more stable. Digestion helps in forming larger crystals.

7. Presence of Foreign Substances: Impurities may either increase or decrease the solubility of the precipitate by adsorption or complex formation. Impurities interfere with precipitation and affect endpoint detection which leads to reduces accuracy of analysis.

Gravimetric analysis

Gravimetry is the process of measuring or weighing a compound or element in a pure form as possible after some form of chemical treatment.



Advantages

1. It is accurate and precise.
2. Possible sources of errors are readily checked.
3. It is absolute method.
4. It is relatively inexpensive.

   It is a macroscopic method usually involving relatively large samples. Gravimetric analysis is concerned with weighing of substance that can either be precipitated from solution or volatilized and absorbed.

Classification: Gravimetry may be classified into two major types:-

- Precipitation Method
- Volatilization Method

Precipitation Method

In this method the analyte is converted into insoluble product and then filtered, washed and heated. **Examples:**

- Chloride as silver chloride (AgCl)
- Sulfate as barium sulfate ($BaSO_4$)

Volatilization Method

In this method the analyte is heated and analyte and its decomposition product are collected. The resulting loss of mass is determined. When we use thermal or chemical energy to remove a volatile species, this method is known as volatilization gravimetry. **Example:**

Determination of moisture content:

$$H_2O\ (l) \rightarrow H_2O\ (g)$$

The loss in weight corresponds to water content.

Principle:

The principle of gravimetric analysis is based on the quantitative conversion of the analyte into a sparingly soluble precipitate (pure form) of known chemical composition by precipitation reaction. The precipitate is filtered, washed, dried or ignited to constant weight, and weighed accurately. The mass of the precipitate is then used to calculate the amount of analyte present in the sample.

Example: For estimation of sulfate ions:

$$Ba_2^{+} + SO_4^{2-} \rightarrow BaSO_4\downarrow$$

The sulfate ions are precipitated as barium sulfate, which is filtered, dried, and weighed.

Steps Involved In Gravimetry

Preparation of the sample solution

↓

Precipitation Process

↓

Digestion of Precipitates

↓

Filtration of Precipitates

↓

Washing of Precipitates

↓

Drying of Precipitate

↓

Ignition

↓

Treatment of Ash

1. Preparation of Sample Solution

The sample is dissolved completely in a suitable solvent to obtain a homogeneous solution. An ideal sample would be identical in all its properties with the bulk of material which it is taken. The points considered in this step are:

- Cost of test.
- Value of Product.
- End use of Product.
- Accuracy of test method.
- Nature of materials.

Take a clear beaker

↓

Transfer the weighed sample to the beaker

↓

Add sufficient water or alkali to the sample to get clear solution, if heating is necessary

↓

Heat the solution to get clear solution

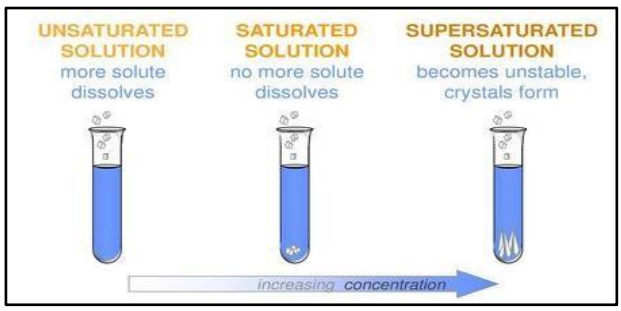
2. Precipitation

A suitable precipitating reagent is added slowly to convert the analyte into an insoluble precipitate. Some factors determine the successful analyses of precipitates are as follows.

a. The precipitates must be insoluble.
b. It can be readily separated from solution by filtration.
c. It should be of high purity.

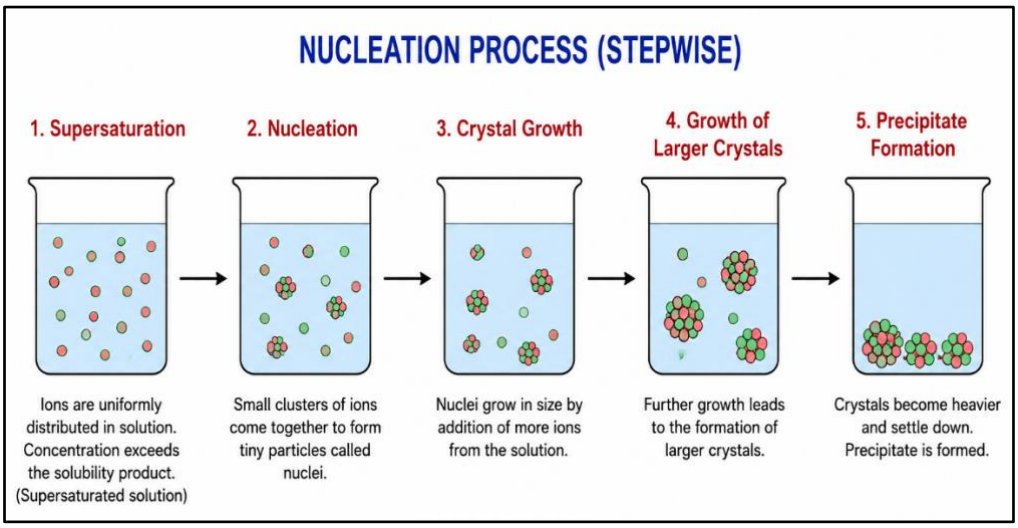
The precipitate formation takes place in 3 steps: Supersaturation, Nucleation and Precipitate Particle growth.

(i) Saturated solution: A mixture that contains the maximum possible amount of solute (the dissolved substance) that a solvent can dissolve at a given temperature and pressure. Any additional solute to this point will not dissolve and will settle at the bottom.



Supersaturation: Supersaturated solution contain higher concentration of solute. It contains greater amount of dissolved substance than undissolved substance. This is achieved by heating the saturated solution. This stage appears for short period of time because it is unstable. It is primary phase of crystallization and precipitation.

(ii) Nucleation: It is the initial process of crystal formation. It involves the aggregation of small groups of ions or molecules to form primary nuclei of sub microscopic dimensions. The number of nuclei form depends on the degree of supersaturation.



Precipitation particle growth/ Crystal growth: The particle grows with the addition of ions of the precipitate until the system come to equilibrium. It is achieved after nucleation. It is observed in two cases

- Diffusion of the ions to the surface of growing crystals.
- Deposition of this diffused ion on crystal surface.

The nucleation can be predicted by Von Weimarn Ratio

$$\text{Von Weimarn Ratio} = \frac{(Q-S)}{S}$$

Q- Concentration of reactant before precipitation.

S- Solubility of the precipitate in the medium from it is precipitated.

Conditions of precipitates

- Precipitation carried out in dilute solution.
- Mixing or stirring should be slow and continuous that decrease supersaturation and increase degree of large crystal growth.
- The precipitates are affected by hot solution
- The precipitates should be washed with dilute solution of electrolyte.

Contamination of Precipitates.

When the precipitates are separate out from the solution, it is not always pure i.e. the precipitates are contaminated with some amount of impurities. The amount of impurity depend upon nature and condition of precipitate. The sources of contamination of precipitates affecting the gravimetry are:

- Post precipitation
- Co-precipitation

Post Precipitation- It involves the deposition of 2nd substance (impurity) on the analyte precipitates when allowed to keep in contact with mother liquor.

Example: Calcium oxalate precipitate out in the presence of magnesium ion satisfactorily without any interference. But if the precipitates remain in contact with mother liquor for long time, then magnesium oxalate precipitates on calcium oxalate. It can be avoided by filtering the precipitates within one or two hours of precipitations.

Co-Precipitation – It involve the inclusion of soluble substance in the precipitates during its formation.

The major types of co-precipitation include:

1. Adsorption
2. Mixed crystal contamination due to isomorphic inclusion.
3. Occlusion.
4. Mechanical entrapment of Non-isomorphic substance.

Adsorption- It depends on surface area of precipitates particle. Colloidal particles with their large surface area adsorb different types of impurities on primary layers.

Mixed crystal contamination- It occurs due to substitution in the precipitate lattice with impurity ion.

Occlusion- It occurs during the formation of precipitate when foreign ion in the counter ion layer gets trapped within the rapidly growing crystals.

Mechanical Entrapment- It occurs when several crystals growing together come closer to each other and trap a portion of solution in pockets between crystals.

Contamination of precipitates can be avoided by **Homogenous precipitation technique.**

Homogenous Precipitation- It is an effective technique in chemical precipitation where the precipitating agents are synthesized inside the solution instead of adding it mechanically. It gives filterable dense and relatively pure precipitates.

3. Digestion of Precipitates

The precipitates are left hot for 30 minutes to one hour in order for the particles to be digested (raised temperature increases the rate of digestion). It involves dissolution of small particles and reprecipitate on large one, resulting in particle growth and better precipitation characteristics (smaller particles of precipitate converted to larger one in the presence of mother liquor). This is called as **Ostwald Ripening.**

Mother liquor is a solution that contains precipitates.

4. Filtration of Precipitates

It is a process which helps to separate the insoluble precipitate from the mother liquor. Filtration of the precipitates can be carried out using filter papers, sintered glass crucible with porous septum.

Different type of filter paper is used:

a. Quantitative Filter Paper: This filter paper is used for the gravimetric analysis has very low ash content. Lower value of ash content is usually achieved by washing with hydrochloric acid and hydrogen fluoride during its manufacturing,

b. Whatman Filter Papers: These are generally available with filter paper no. 30, 31, 32, 40, 41, 42, 50, 52, and 54. The no. 42 filter paper is used for very fine particles and no. 41 is used for gelatinous precipitates. The size of the filter paper is based on the bulk of the precipitate and not the volume of the solution to be filtered.

5. Washing of Precipitates

It is necessary to wash a gravimetric precipitate as it will be contaminated with non-volatile compounds such as the excess of precipitating reagent added. Washing of the precipitate can

be done by using warm water or with the suitable solvent for removing impurities from precipitates.

Following point must be considered during washing:

- Several washing with small volume of wash liquid are more efficient in removing soluble contaminants than the same total volume used only in one washing.
- Minimum amount of the wash liquid should be used because no precipitate is absolutely insoluble.
- The wash liquid employed for washing must have following properties.

i. It should not dissolve the precipitate.

ii. It should not react with precipitate.

iii. It should not form any volatile or insoluble products with the precipitate.

iv. It should be easily volatile at room temperature.

v. It should not contain any substance which is likely to interfere with subsequent determination in filtrate.

6. Drying or Ignition of Precipitate

Drying or Ignition is used to remove the water from the precipitate which occurs during washing. The drying can be done out in an electric oven by heating at 110°C to 120°C for 1 to 2 hours.

Ignition can be done at much higher temperature, which is usually required if precipitate must be converted to a more suitable form for weighing.

7. Treatment of Ash

During, ignition the small fraction of the precipitate may get reduced by the carbon of the paper into the compound (or metal) altogether different from the compound in which determination is sought. The ash, therefore is treated with suitable reagents to get back the form (compound) in which it is finally to be weight. This step is called the ash treatment.

Weighing and calculation

After drying, take residue (precipitate) in room temperature and weigh accurately on analytical balance.

$$\% \text{ purity of substance} = \frac{E \times S}{W} \times 100$$

Where, E = weight of residue (precipitate)

S = Gravimetric factor

W = Weight of sample

Types of Precipitation Titration

Precipitation titrations are volumetric analytical methods in which the analyte reacts with the titrant to form a sparingly soluble precipitate. These titrations are based on precipitation reactions and are mainly used for the determination of halide ions such as chloride, bromide, iodide, cyanide, and thiocyanate ions. The most commonly used precipitating reagent is **silver nitrate ($AgNO_3$)** because it forms insoluble salts with many anions.

Based on the method used for endpoint detection, precipitation titrations are classified into:

1. Mohr's Method,

2. Volhard's Method, and

3. Fajans Method.

1. Mohr's Method

It is one of the most important method of precipitation titration. The method was developed by Karl Friedrich Mohr in 1856. This method is a direct precipitation titration used for the determination of chloride and bromide ions. It employs **standard silver nitrate solution as the titrant** and **potassium chromate as the indicator**.

Principle: This method involves the titration of silver nitrate against the halides (chloride ions) in neutral solution using 2% of solution of **potassium chromate** as an indicator. After all chloride ions have been precipitated, the first excess silver ion reacts with chromate ions to form a reddish-brown precipitate of silver chromate. The end product is determined by the appearance of brick red coloured precipitate due to formation of silver chromate and silver chloride.

During titration: $AgNO_3 + NaCl \rightarrow AgCl\downarrow + NaNO_3$

$$2AgNO_3 + K_2CrO_4 \rightarrow Ag_2CrO_4\downarrow + 2\ KNO_3$$

Silver chromate red colour ppts.

Procedure:

1.2 gm of sodium chloride is dissolved in water then add 50ml of this solution into volumetric flask. Add 1–2 mL of potassium chromate indicator to the prepared solution. Burette is filled with standard silver nitrate solution and initial reading is noted. Content present in the flask is titrated with silver nitrate solution. During titration $AgNO_3$ reacts with NaCl and form AgCl (silver chloride) precipitates. A white precipitate of silver chloride forms during titration. Titration is continued until all the chloride ion used and $AgNO_3$ react with K_2CrO_4 indicator and forms silver chromate precipitate (brick red coloured) indicates end point.

Calculations:

$$N_1V_1 = N_2V_2 \quad \text{or} \quad M_1V_1 = M_2V_2$$

Where, N_1 is Normality of $AgNO_3$, V_1 = Volume of $AgNO_3$, N_2 = Normality of chloride solution, V_2 = Volume of sample

Advantages:

1. It is simple and rapid method.
2. Highly accurate for chloride determination.
3. No filtration is required in this method.

Limitations:

1. Applicable only in neutral or slightly alkaline medium (pH 6.5–10).
2. Not suitable in acidic solutions because chromate converts to dichromate.
3. Carbonates and phosphates interfere.
4. Not suitable for iodide and thiocyanate determination.
5. Endpoint color may be difficult to observe in colored solutions.

Applications

1. It is helpful in the determination of chloride in dextrose injection.
2. Analysis of saline solutions.
3. Pharmaceutical analysis of chloride, bromide and thiocyanate containing compounds.

4. Quality control testing in laboratories.

2. Volhard's Method

This method was designed by germen scientist Jacob volhard's in 1874. This method is used for the estimation of silver by titrating against a standard thiocyanate solution in the presence of ferric salt as indicator.

Principle

Volhard's method is an indirect (back titration) precipitation method used for determining chloride, bromide, iodide, and silver ions. A known excess amount of standard silver nitrate is added to the analyte. The chloride ions precipitate as silver chloride. The excess unreacted silver nitrate is then titrated with standard ammonium thiocyanate using ferric alum as an indicator. At the endpoint, excess thiocyanate reacts with ferric ions to form a reddish-brown ferric thiocyanate complex.

Procedure: The solution of standard 0.1 N $AgNO_3$, 0.1 N NaCl and 0.1N KSCN (potassium thiocyante) will be prepared. Then excess amount of silver nitrate is used for the titration of sodium chloride solution. After the complete precipitation of silver chloride (AgCl), excess amount of silver nitrate is added.

$$AgNO_3 + NaCl \rightarrow AgCl\downarrow + NaNO_3$$

Now the excess amount of silver nitrate is titrated against potassium thiocyanate and also add ferric (Fe^{3+}) salt as indicator. A standard solution of KSCN is added from a burette to a solution of silver nitrate in the presence of nitric acid

$$AgNO_3 + KSCN \rightarrow AgSCN\downarrow + KNO_3$$

In this a precipitate of silver thiocyanate (AgSCN) continues to be formed till the silver get completely precipitates out. After this the addition of further drop of thiocyanate reacts with ferric ion to form a red colored ferric thiocyanate complex. The appearance of reddish brown color indicates the end point.

$$Fe^{3+} + SCN^- \rightarrow [FeSCN]^{2+}$$

Procedure

1. Take a measured volume of sample solution.
2. Add a known excess volume of standard silver nitrate solution.
3. Allow complete precipitation of silver chloride.
4. Add ferric alum indicator.
5. Titrate excess silver nitrate with standard ammonium thiocyanate solution.
6. Endpoint is the appearance of permanent reddish-brown color.
7. Calculate chloride content from the difference between silver nitrate added and thiocyanate consumed.

Calculations

Silver nitrate added: meq $AgNO_3 = N_1V_1$

Silver nitrate remaining: meq $AgNO_3 = N_2V_2$

Silver nitrate consumed by chloride: $(N_1V_1) - (N_2V_2)$

Then: Amount of chloride = $[(N_1V_1) - (N_2V_2)] \times$ Eq. Wt.

Advantages

1. Suitable for colored and turbid solutions.
2. Highly accurate.
3. Applicable to acidic solutions there is no interference from carbonate, phosphate and arsenate.
4. Useful for determining silver ions directly.
5. It is preferred as a suitable method when Mohr's method cannot be used.

Limitations

1. Requires back titration, making the procedure longer.
2. Filtration may sometimes be necessary.
3. Ferric indicator may interfere in some solutions.
4. Requires careful endpoint observation.
5. More reagents are required than direct methods.

Applications

1. Estimation of halides: Analysis of Chlorine, bromine, Iodide in acidic medium.
2. It helps in the determination of silver content in alloys, ores and drug formulation.
3. It is also used in the determination of Aminophylline, Ethionamide, Sodium chloride injection.
4. Food and industrial chemical analysis.

Modified Volhard's Method

Chloroform or other organic liquid are added after adding excess amount of silver nitrate, because precipitates of silver chloride (AgCl) may be solubilised in solution during estimation. So, addition of chloroform will prevent the solubility of silver chloride.

When chloride are analysed the Volhard method has to be slightly modified. During titration the solution is contact with two precipitation simultaneously silver chloride and ammonium thiocyanate which has different solubility. So, after the titration excess of thiocyanate ions are react with AgCl and the red colour of iron thiocyanate complex gradually disappear. Addition of more SCN^- causes restoration of red colour which induced huge error in analysis.

To avoid the error before titration with thiocyanate the solution of few ml of organic liquid chloroform which does not mix with water is added.

This compound will moisten the surface of the precipitates forming on the surface insoluble in water and thus isolating it from the solution. This effectively prevent the exchange of ions between precipitates and solution.

Why Chloroform is Added

In the ordinary Volhard method, silver chloride may react with thiocyanate ions:

$$AgCl + SCN^- \rightarrow AgSCN + Cl^-$$

This side reaction consumes additional thiocyanate and causes positive errors.

When chloroform is added and the mixture is shaken:

- The silver chloride precipitate becomes coated with chloroform.
- The precipitate settles below the aqueous layer.
- Contact between AgCl and thiocyanate ions is minimized.
- A sharper and more accurate end point is obtained.

Thus, chloroform acts as a protective layer around the precipitate.

Principle: A known excess of standard silver nitrate solution is added to the chloride-containing sample. Chloride ions precipitate as silver chloride. Chloroform is then added, which forms a layer around the silver chloride precipitate and prevents its interaction with thiocyanate ions. The excess unreacted silver nitrate is back-titrated with standard potassium thiocyanate solution using ferric ammonium sulfate as indicator.

Procedure

1. Pipette a measured volume of the chloride-containing solution into a conical flask.
2. Acidify with dilute nitric acid.
3. Add a known excess volume of standard silver nitrate solution.
4. Shake thoroughly to ensure complete precipitation of silver chloride.
5. Add about 2–5 mL of chloroform.
6. Shake the flask vigorously so that the silver chloride precipitate becomes coated with chloroform and settles.
7. Add ferric ammonium sulfate indicator.
8. Titrate the excess silver nitrate with standard potassium thiocyanate solution.
9. Continue titration until a permanent reddish-brown color appears in the aqueous layer.

3. Fajans Method

The **Fajans method** is a type of **precipitation titration** in which the end point is detected using an **adsorption indicator**. It is mainly used for the determination of halide ions such as chloride (Cl^-), bromide (Br^-), and iodide (I^-) by titration with a standard silver nitrate ($AgNO_3$) solution.

The method was developed by the Polish chemist Kazimierz Fajans. The titration depends on the adsorption of an indicator onto the surface of the precipitate formed during the reaction.

Principle

In the Fajans method, a precipitate is formed during the titration. Before the equivalence point, the precipitate particles possess a negative charge due to the adsorption of excess anions. After the equivalence point, a slight excess of silver ions causes the precipitate surface to become positively charged.

An adsorption indicator present in the solution is then adsorbed onto the positively charged precipitate surface, producing a distinct color change that indicates the end point. Indicators such as fluorescein, dichloroflourescein, eosin are used.

For example, during the titration of chloride ions with silver nitrate:

$$Ag^+ + Cl^- \rightarrow AgCl\downarrow$$

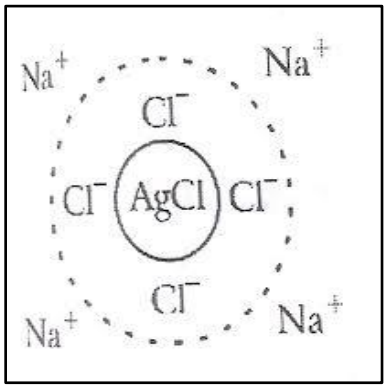
White silver chloride precipitate is formed.

Theory: Firstly, chloride ion is titrated against silver nitrate which forms the silver chloride precipitate.

$$Ag^+ + Cl^- \rightarrow AgCl\downarrow$$

Now excess of chloride ions get adsorbed on the silver chloride precipitate forming uniform layers. Thus, the primary adsorbed layer of chloride ions holds the secondary adsorbed layer of Na^+ ions. The precipitate surface becomes **negatively charged**. Since the adsorption indicator is also negatively charged, it is repelled and no color change occurs.

$$AgNO_3 + NaCl \rightarrow AgCl\downarrow + NaNO_3$$

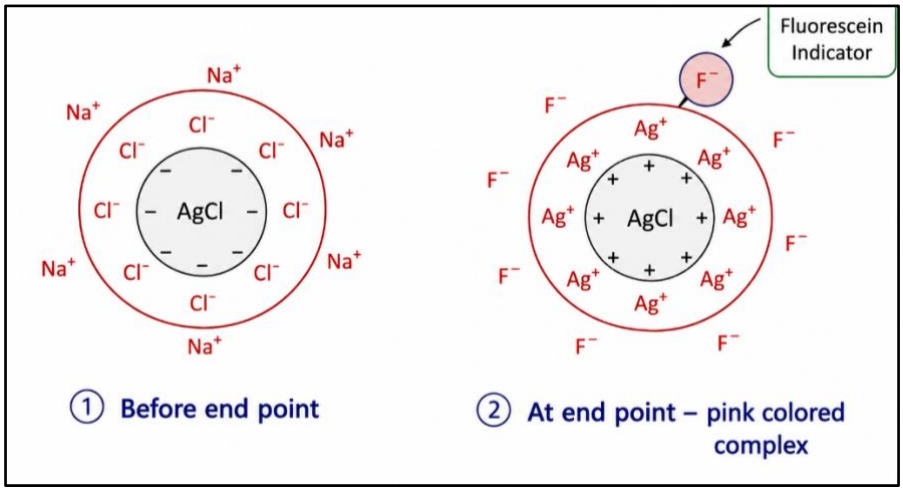


After all chloride ions are consumed at the equivalence point, the silver chloride adsorbs excess of Ag^+ ions as primary adsorbed layer, which further adsorbed the indicator fluorescein ions as

secondary layer. The precipitate surface becomes **positively charged**. The negatively charged adsorption indicator is attracted and adsorbed onto the precipitate surface, producing a characteristic color change.

Due to the adsorption a pink colour complex formed which indicates the end point.

$$Ag^{+} + Fl^{-} \rightarrow AgFl\downarrow \text{ (pink colour)}$$



Titration Procedure

1. Pipette a known volume of chloride solution into a conical flask.
2. Add a few drops of dichlorofluorescein indicator.
3. Titrate with standard silver nitrate solution.
4. White silver chloride precipitate forms continuously.
5. Near the equivalence point, add $AgNO_3$ dropwise with constant stirring.
6. The first permanent pink coloration of the precipitate indicates the end point.
7. Note the burette reading and calculate the chloride concentration.

Calculation

$$N_1V_1 = N_2V_2$$

Where:

- N_1 = Normality of $AgNO_3$
- V_1 = Volume of $AgNO_3$ used
- N_2 = Normality of chloride solution
- V_2 = Volume of chloride solution taken

Strength of Chloride Solution

$$\text{Strength (g/L)} = N \times \text{Equivalent Weight}$$

Equivalent weight of NaCl = 58.5

Advantages

1. Simple and rapid method.
2. No filtration required.
3. Sharp and distinct end point.
4. High accuracy for dilute solutions.
5. Suitable for chloride, bromide, and iodide estimations.
6. Requires only a small amount of indicator.

Limitations

1. Not suitable for colored or turbid solutions.
2. End point may be difficult to observe in concentrated solutions.
3. Requires a precipitate with a large surface area.
4. Presence of other absorbable ions may interfere.
5. pH must be carefully controlled.

Applications

1. Determination of chloride in pharmaceutical preparations.
2. Analysis of drinking water and wastewater.
3. Estimation of bromide and iodide ions.
4. Quality control in chemical industries.
5. Laboratory analysis of halide-containing samples.
6. Environmental monitoring of water samples.

Estimation of Barium Sulphate

Gravimetric analysis is a quantitative analytical method in which the analyte is converted into a pure, stable, insoluble compound of known composition. The precipitate is filtered, washed, dried or ignited, and weighed. From the mass of the precipitate, the amount of analyte present is calculated.

Principle: In the estimation of barium, a soluble barium salt solution is treated with dilute sulphuric acid (H_2SO_4) or a soluble sulphate solution. Barium ions react with sulphate ions to form a highly insoluble white precipitate of barium sulphate.

$$BaCl_2 + H_2SO_4 \rightarrow BaSO_4\downarrow + 2HCl$$

Theory: When sulphate ions are added to a hot dilute solution containing barium ions, nuclei of barium sulphate are formed. These nuclei grow into larger crystals during digestion. Large crystals are easier to filter and contain fewer impurities. The precipitate is allowed to digest on a water bath or hot plate, filtered through an ashless filter paper, washed to remove impurities, ignited in a crucible, and weighed as pure barium sulphate. Since the composition of $BaSO_4$ is known, the amount of barium present can be calculated from the weight of the precipitate.

Procedure:

1. Preparation of Solution: Take a known volume of the barium chloride containing solution in a beaker. Add a few drops of dilute hydrochloric acid and dilute with distilled water.

2. Heat the solution nearly to boiling. Add dilute sulphuric acid slowly with constant stirring until precipitation is complete. A dense white precipitate of barium sulphate is formed.

$$BaCl_2 + H_2SO_4 \rightarrow BaSO_4\downarrow + 2HCl$$

3. Keep the mixture on a hot water bath or hot plate for about 30–60 minutes. Digestion allows small particles to dissolve and re-deposit on larger crystals, producing a coarse crystalline precipitate.

4. Filter the precipitate through a weighed ashless filter paper.

5. Wash the precipitate several times with hot distilled water until free from chloride ions.

6. Transfer the filter paper containing the precipitate to a previously weighed crucible. Dry and ignite gradually at 800–900°C until constant weight is obtained. During ignition, the filter paper burns away and pure barium sulphate remains.

7. Cool the crucible in a desiccator and weigh accurately. Repeat heating, cooling, and weighing until constant weight is obtained.

Calculation:

Percentage of Barium

$$\text{Percent purity of substance} = \text{Weight of Ba} / \text{Weight of Sample} \times 100$$

Applications

1. Determination of barium in pharmaceutical substances.
2. Analysis of barium-containing minerals.
3. Water analysis for barium content.
4. Quality control of barium salts.
5. Teaching and research laboratories for gravimetric analysis.

Points to Remember:

- ✓ Gravimetric analysis is based on the accurate measurement of the **mass of a pure precipitate**.
- ✓ The precipitate should be pure, stable, insoluble, easily filterable, and of known composition.
- ✓ The main steps in gravimetric analysis are **precipitation, digestion, filtration, washing, drying or ignition, and weighing**.
- ✓ Digestion increases crystal size and reduces impurities in the precipitate.
- ✓ High supersaturation produces small crystals, while low supersaturation produces large crystals.
- ✓ Large crystals are easier to filter and wash than fine crystals.
- ✓ Barium sulphate is estimated gravimetrically by precipitation with **barium chloride**.
- ✓ Barium sulphate is dried or ignited before weighing.
- ✓ Mohr's method is used for the estimation of chloride ions.
- ✓ Mohr's method requires a **neutral medium**.
- ✓ Potassium chromate is the indicator in Mohr's method.
- ✓ The endpoint in Mohr's method is the formation of a **brick-red silver chromate precipitate**.
- ✓ Volhard's method is a **back titration** carried out in an acidic medium.
- ✓ Ferric ammonium sulphate is the indicator in Volhard's method.
- ✓ Modified Volhard's method uses **chloroform or nitrobenzene** to prevent dissolution of silver chloride.
- ✓ Fajans method employs an **adsorption indicator** such as fluorescein.
- ✓ The endpoint in Fajans method is detected by adsorption of the indicator on the precipitate surface.

Case Based Learning (CBL)

Case

A water testing laboratory analyzes chloride content using **Mohr's method**. During the experiment, the technician acidifies the solution before titration. The endpoint becomes unclear, and inaccurate results are obtained.

Students are required to identify the mistake and explain the importance of maintaining the correct pH during precipitation titrations.

Questions

1. Why should Mohr's method be performed in neutral medium?
2. Which indicator is used?
3. What is the endpoint?
4. Why are acidic conditions unsuitable?
5. Compare Mohr's and Volhard's methods.

Problem-Based Learning (PBL)

Problem

While estimating chloride ions by **Mohr's method**, a student performs the titration in an acidic medium. The endpoint is not distinct, and the calculated chloride content is inaccurate.

MCQs

1. Mohr's method uses:
   A. Ferric alum
   B. Potassium chromate ✔
   C. Starch
   D. EBT
2. Mohr's titration is carried out in:
   A. Acidic medium
   B. Neutral medium ✔
   C. Alkaline medium
   D. Alcoholic medium
3. Volhard's method is:
   A. Direct titration
   B. Back titration ✔
   C. Complexometric titration
   D. Gravimetric analysis
4. Fajans method uses:
   A. Methyl orange
   B. Adsorption indicator ✔
   C. EBT
   D. Starch
5. Gravimetric analysis is based on:
   A. Volume
   B. Weight of precipitate ✔
   C. Colour
   D. pH

COMPLEXOMETRIC TITRATION

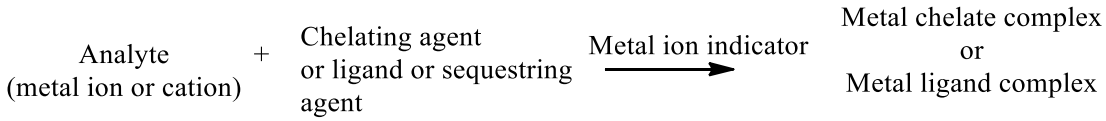
Complexometric titration is a type of volumetric analysis in which the reaction between a metal ion and a complexing agent is used to determine the concentration of metal ions in a solution. The method is based on the formation of a stable, water-soluble complex between the metal ion and a ligand. A **ligand** is a substance capable of donating one or more pairs of electrons to a metal ion, resulting in the formation of a coordination compound or complex.

The most commonly used complexing agent in complexometric titrations is **Ethylenediaminetetraacetic Acid (EDTA)**. EDTA is a hexadentate ligand that can bind with metal ions through six donor atoms, forming very stable 1:1 metal-EDTA complexes regardless of the charge of the metal ion. Due to its strong chelating ability, EDTA is widely employed in the quantitative determination of metal ions such as calcium, magnesium, zinc, copper, lead, and many others.

Complexometric titrations are usually carried out in a buffered medium because the stability of metal-EDTA complexes depends on the pH of the solution. Indicators known as **metallochromic indicators**, such as Eriochrome Black T (EBT), Murexide, and Xylenol Orange, are used to detect the end point. These indicators form weak colored complexes with metal ions. During titration, EDTA displaces the indicator from the metal-indicator complex, causing a distinct color change that signals the end point.

Complexometric titrations are highly accurate, rapid, and selective methods for the determination of metal ions. They are extensively used in pharmaceutical analysis, water hardness determination, food analysis, environmental monitoring, and industrial quality control. Because of their simplicity and precision, complexometric titrations have become one of the most important analytical techniques in quantitative chemical analysis.

- Complexometric titration (sometimes chelatometry) is a form of volumetric analysis in which the titration based on complex formation between the analyte and titrant and these colored complexes is used to indicate the end point of a titration.



  Complexometric titrations are particularly useful for the determination of a mixture of different metal ions in solution. An indicator with a marked color change is usually used to detect the end-point of the titration.

Principle: In this titration, the metal ions are titrated with a complexing agents (ligands) or a chelating agent or EDTA. It involves the transformation of simple metal ions into complex ion

and metal ion indicator used for the determination of end point by changing the colour. It is also known as chilometric titration.

$$\text{Metal ion + Ligands} \longrightarrow \text{Complex}$$

$$\text{Metal ion indicator}$$

$$M^{2+}, M^{3+} + [H_2X]^{2-} \longrightarrow [MX]^{2-} + 2H^{+}$$

Theory of complexometric titration:

- lon formed reversibly by the attachment of metal ion with chelating agents, with no redox change in the reaction is called **complex ion**.

$$Cu^{+2} + 4\,(NH_3) \longrightarrow Cu\,(NH_3)_4{}^{+2}$$

$$Fe^{+3} + 6CN^{-} \longrightarrow Fe\,(CN)_6{}^{-3}$$

- A **complexing or chelating agent** is an electron donating ion or molecule which is usually called as a **ligand**. Ligands have ability to form one or more covalent bonds with central metal ion to produce a complex which has different properties from those of the free metal ion.
- Bonds in complexes are either ordinary covalent bonds or co-ordinate covalent bonds.
- In complexometric analysis, a simple ion is transformed into a complex ion and the equivalent point is determined by using metal indicators or electrometrically.
- Metal atom having few electrons in the outer most electron shell loses these electrons by transfer to other atoms and thus acquire stable electron configuration. Non-metal atoms having less than eight electrons in outer shell, tends to gain electrons and thus acquire stable electron configuration of next higher inert gas. This type of chemical bond formed by electron transfer from one atom to another is called **electrovalent or a polar bond.**
- Some atoms complete their octet of electrons by mutual sharing of electrons between atoms. A chemical bond formed by sharing of electrons between atoms each of which contribute an electron to the shared pair is known as **covalent or non- polar bond**.
- A chemical bond formed by the sharing of a pair of electrons both of which are contributed by one atom is called a **co-ordinate covalent or semi-polar bond.**

- The number of ligands that can attach to a central ion is called the co-ordination number of that ion. The maximum co-ordination number is related to the position of the element in the periodic system.
- Generally, the co-ordination number exhibited is twice the electrovalence or oxidation number of that ion. **e.g.** $Ag(NH_3)^+$, $Cu(NH_3)_4^{+2}$.

Ligand and its classification

A **ligand** is an ion or molecule that donates one or more pairs of electrons to a central metal atom or metal ion to form a **coordinate covalent bond**. Ligands contain at least one atom with a lone pair of electrons, such as N, O, S, P, or halogen atoms. The metal ion acts as a Lewis acid (electron acceptor), while the ligand acts as a Lewis base (electron donor).

Example:

$$[Cu(NH_3)_4]^{2+}$$

In this complex, ammonia (NH_3) acts as a ligand and donates its lone pair of electrons to the Cu^{2+} ion.

Ligands can be classified into following different types,

1. Unidentate ligand: Ligands that are bound to metal ion only at one place are called unidentate ligands (one toothed). For example, NH_3 is a unidentate ligand capable of complexing with cupric ions. Halide ions, cyanide ions and NH_3 are common examples of unidentate ligands.

2. Bidentate ligand: Many ligands contain two groups, capable of binding with metal ions. The ligand molecule or ion has a lone pair of electrons, then the molecule has two donor atom and it may be possible to form two coordinate bonds with the metal ion. Such ligands are known as bidentate ligands or chelating agents.

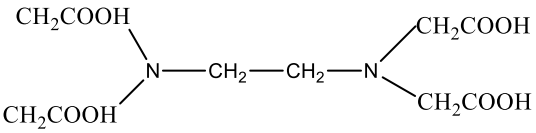
3. Polydentate ligand: When several donor atoms are present in a single ligand as with ethylene diamine tetra-acetic acid, the ligand is said to be polydentate ligand. Ethylene diamine tetra acetic acid (EDTA) is an example of multidentate ligand.

Chelate and Chelating agents:

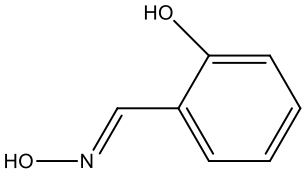
Chelate (Ligand): Bi or polydentate ligand containing two or more donor atoms combines with a single metal ion and forms a chelate complex. Thus, a chelate can be described as a heterocyclic ring structure in which a metal atom is a member of the ring.

Chelating agents (Complexing agents):

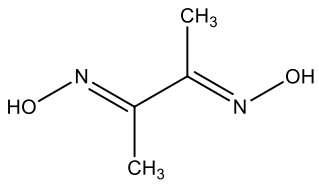
- Ligands having more than one electron donating groups are called **chelating agents**.
- The most effective complexing agent in ligands are amino and carboxylate ions.
- The solubility of metal chelates in water depends upon the presence of hydrophilic groups such as COOH, SO_3H, NH_2 and OH.
- When both acidic and basic groups are present, the complex will be soluble over a wide range of pH. When hydrophilic groups are absent, the solubilities of both the chelating agent and the metal chelate will be low, but they will be soluble in organic solvents.
- The term **sequestering agent** is generally applied to chelating agents that form water-soluble complexes with bi- or poly-valent metal ions. Thus, although the metals remain in solution, they fail to give normal ionic reactions. Ethylenediaminetetra-acetic acid (EDTA) is a typical sequestering agent forming soluble complexes, whereas, dimethylglyoxime and salicylaldoxime are chelating agents, forming insoluble complexes.



Ethylene diamine tetraacetic acid



Salicylaldoxime



Dimethyl glyoxime

Why EDTA used as titrant in complexometry?

EDTA (ethylene diamine tetraacetic acid) is the most widely used chelating agent in analytical chemistry. Ethylene diamine tetraacetic acid is a hexadentate ligand containing 4 carboxyl group and 2 amino group that can acts as electron pair donors, or lewis bases. The ability of EDTA to donate its six lone pairs of electrons for the formation of coordinate covalent bonds

to metal cations makes EDTA a hexadentate ligand. It is insoluble in water but its di-sodium salt is water soluble.

EDTA has the widest general application in complexometric analysis because of the following important properties:

- It forms very stable, 1:1 complexes with most metal ions.
- Its dilute solutions are very stable.
- It is sensitive to solution conditions, particularly PH
- It forms strain less five-membered rings.
- It is cheaper

Classification of Complexometric titrations

There are five types of complexometric titrations namely

1) Direct titration:

This method is similar to simple acid base titrations. Here standard chelating solution (EDTA) is titrated with analyte (metal ion solution which is buffered) until the end point is reached which is detected by suitable indicator. Precipitation of metal hydroxide is prevented by adding some auxiliary complexing agents. Metal indicators such as mordant red 7 are used in these titrations. Examples of substances estimated by direct titration: Magnesium salts such as magnesium carbonate, bismuth salts such as bismuth nitrate, calcium salts such as calcium chloride, zinc oxide etc.

The titration mixture should be suitably buffered to obtain stable complex.

2) Alkalimetric titration:

When the reaction of metal ion with di-sodium EDTA (Na_2H_2Y) takes place, it liberates two equivalent of hydrogen ion.

$$M^{+n} + H_2Y^{-2} \rightleftharpoons (MY)^{n-4} + 2H^+$$

These liberated protons are estimated by reaction with standard alkali solution. A solution mixture containing bismuth and lead ions can be successfully titrated by first titrating the bismuth at pH = 2 with xylenol orange as indicator, then adding hexamine to raise the pH to about 5, and titrating the lead. The solution of the metal to be determined must be accurately neutralized before titration.

3. Back Titration:

It is similar to volhards method. In this method a known excess of amount of EDTA is used for the titration of metal ion solution. Then the excess EDTA is titrated with a standard metal solution.

This technique is used for:

- Metals which can precipitated as hydroxide in alkaline solution of buffer
- Metals which are insoluble in nature for e.g. calcium sulphate
- Compound which do not react with EDTA titrant
- If the analyte reaction with EDTA is too slow
- If the analyte blocks the indicator.

For e.g. in determination of Mn^{+2}, this metal cannot be directly titrated with EDTA because of precipitation of $Mn(OH)_2$. Hence here excess of known volume of EDTA is added to an acidic solution of Mn^{+2} salt and then ammonia buffer is added to adjust the pH 10 and excess EDTA is back titrated with a standard Zn^{+2} solution using Eriochrome black T as indicator.

This method is used for the determination of: Calcium phosphate, $Al(OH)_3$ gel (aluminium hydroxide), Aluminium Sulphate.

4. Replacement titration (Displacement or substitution):

In this method the metal ion to be analyzed is displace the metal from the metal ligand complex. It is used when direct and indirect titration give sharp end point.

If there is no suitable indicator for a metal (i.e. indicator does not gives sharp end point), then analyte is treated with excess Mg $(EDTA)^{-2}$ to displace Mg^{+2} and then titrate the displaced Mg^{+2} with standard EDTA:

$$M^{+n} + MgY^{-2} \longrightarrow MY^{n-4} + Mg^{+2}$$

The formation constant of MY^{n-4} must be greater the formation constant of MgY^{-2} otherwise, displacement will not happen.

Example of displacement titration is the determination of Mn^{+2}, where, Mg-EDTA complex is added so that Mn^{+2} displaces Mg^{+2} from Mg-EDTA complex and the freed Mg^{+2} is then titrated directly with a standard EDTA solution. This displacement takes place because Mn^{+2} forms a more stable complex with EDTA.

By this method Calcium, lead, mercury may be determined using Eriochrome black T indicator.

Calcium displaces magnesium ion and forms a stable complex with EDTA as calcium- EDTA complex. The displaced and liberated magnesium ions are then titrated with standard EDTA solution using mordant black as indicator.

$$Ca^{2+} + \text{Mg-EDTA} \longrightarrow \text{Ca-EDTA} + Mg^{2+}$$

5. Indirect titration (Determination of anions):

It is used for the determination of ions such as anions, which do not react with EDTA or anions that are precipitated with the metal.

For example: Barbiturates do not react with EDTA but are quantitatively precipitated in alkaline solution by mercuric ions as 1 : 1 complex.

Method: Barbiturates to be analyzed is taken in a flask and heated with excess of mercury ion in alkaline solution. When precipitated Hg-barbiturate complex is formed, it is filtered and dissolved in excess of standard EDTA solution. The unreacted EDTA solution is then back titrated with a standard Zn solution.

Metal Ion Indicators for End Point Detection (Metallochromic):

Metal ion indicators, also known as **metallochromic indicators or pM indicators**, are organic dyes that form weak, colored complexes with metal ions. They are mainly used in **complexometric titrations**, particularly those involving EDTA, to detect the end point of the titration. These indicators exhibit different colors in their free form and metal-bound form, allowing visual detection of the completion of the reaction.

During titration, the indicator first forms a colored complex with the metal ion. As EDTA is added, it forms a more stable complex with the metal ion and displaces the indicator. The released indicator shows a different color, indicating the end point.

Before equivalent point the colour of the solution is because of metal-indicator complex. As the titrant (Chelate) is added, metal-indicator complex breaks and there is a formation of chelate-metal complex which liberates indicator in free form. After an equivalent point all indicator gets free and this free indicator has different color.

Ideal requirements of metal indicators for satisfactory detection of end point are:

- Chemically it should be stable.
- It forms 1:1 complex with metal.
- The colour reaction should be specific or selective.
- The indicator must be very sensitive to metal ions so that the colour change occurs as near to equivalence point as possible.
- The colour contrast between the free indicator and the metal-indicator complex should be readily observed.
- The indicator should form M-indicator complex as rapidly as possible.
- M-Ind complex should be less stable than M-Ligand complex.
- The metal-indicator complex must be sufficiently stable otherwise sharp colour change is not obtained.
- It should be selective for particular metal ion being titrated.
- All the above requirements must be fulfilled within the pH range at which the titration is performed.

Theory (Mechanism) of metal indicators:

The metal indicators, used are various organic compounds that form highly colored complex with metal ions and show no color or different color in absence of metal ion. A metal ion indicator (In) forms a colored complex with a metal ion (M):

$$M^{n+} + In \rightleftharpoons M\text{-}In \text{ (metal ion indicator complex red colour)}$$

When EDTA is added, it forms a more stable metal-EDTA complex:

$$M\text{-}In + EDTA \rightarrow M\text{-}EDTA + In \text{ (Indicator shows blue color)}$$

Since the free indicator and metal-indicator complex have different color, a distinct color change occurs at the end point.

Metal indicators used in complexometric titration:

Mordant Black II is a metallochromic indicator used in complexometric titrations for the determination of metal ions. It forms colored complexes with metal ions and helps in detecting the end point during EDTA titrations. The indicator is particularly useful for calcium and magnesium estimations. In alkaline medium, Mordant Black II forms a colored complex with

metal ions. As EDTA is added, the metal ions preferentially form a more stable complex with EDTA, releasing the free indicator and producing a distinct color change. Mordant Black II is valued for its sensitivity and clear end-point detection in complexometric analysis.

Eriochrome Black T (EBT) is one of the most widely used metallochromic indicators in complexometric titrations. It is especially important in the determination of calcium and magnesium ions and in the estimation of water hardness. The titration is usually carried out at pH 10 using an ammonia-ammonium chloride buffer. Eriochrome Black T forms a wine-red complex with metal ions. During titration, EDTA complexes the metal ions more strongly than the indicator does, causing the indicator to be released in its free form.

This results in a sharp color change from wine red to blue, indicating the end point. Because of its reliability, sensitivity, and distinct color change, Eriochrome Black T is extensively used in pharmaceutical, environmental, and industrial analysis.

Methyl Thymol Blue (MTB) is another useful metallochromic indicator that forms colored complexes with various metal ions, including calcium, magnesium, and zinc. It is frequently employed in complexometric analyses because of its sensitivity and sharp end point. The color change generally observed is from blue to yellow, although the exact color transition may vary depending on the metal ion and the pH of the solution.

Thymol Blue is primarily known as an acid-base indicator, but under suitable conditions it can also function as a metallochromic indicator. It is used in certain specialized complexometric titrations involving metal ions. The color changes observed with Thymol Blue depend upon both the pH of the solution and the nature of the metal ion present.

Xylenol Orange is a versatile metallochromic indicator employed in the determination of several metal ions such as aluminium, lead, bismuth, thorium, and zinc. It is generally used in acidic media and forms red-colored complexes with metal ions.

At the end point of the titration, when the metal ions are completely complexed by EDTA, the indicator reverts to its free form and the solution changes from red to yellow.

Table: Various metal indicators used in complexometric titration:

Sr. No.	Name of the indicator	Colour Change		pH range	Metals detected
		Metal-indicator complex color	Free indicator Color		
1.	Mordant black-II	Red	Blue	10	Ca, Ba, Mg, Cd, Mn, Pb, Hg
	Eriochrome black T				
	Solochrome black-T				
2.	Murexide (Ammonium purpurate)	Blue	Red-violet	10-11	Cu, Ni, Co, Ca
3.	Xylenol orange	Red	Lemon- Yellow	1-2	Bi, Thorium
				4-5	Pb
				5-6	Hg, Cd
				8-9	Zn
4.	Methyl Blue	Blue	Yellow	4-5	Pb, Zn, Cd, Hg
	Thymol Blue	Blue	Grey	10-12	
5.	Alizarin	Red	Yellow	4.3	Pb, Zn, Cu, Mg
6.	Catechol-Violet	Violet	Red	4-7	Mn, Mg, Fe, Pb

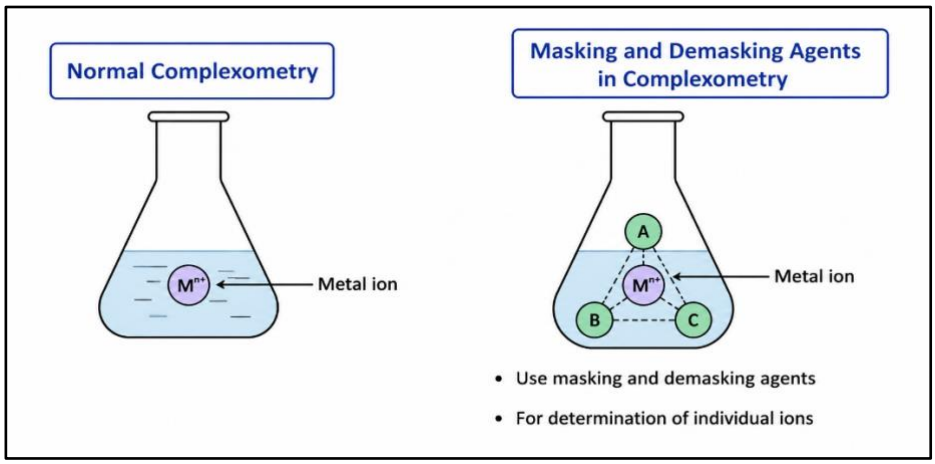
INSTRUMENTAL METHOD FOR DETECTING END POINT

The following instrument methods are employed in the detection of end point during Complexometric titration, these are:

1. Potentiometric titration
2. Photometric titration
3. Amperometric titration

Masking and Demasking Agents

In complexometric titrations, especially those involving EDTA, many metal ions present in a solution can react with the titrant simultaneously. This can lead to interference, inaccurate results, and difficulty in determining a specific metal ion. To overcome these problems, **masking and demasking agents** are used.



Principle:

The use of masking and demasking agents in complexometry is well explained by the analysis of 3 metals, Cu, Cd and Ca.

1. Direct titration of the mixture with the EDTA gives the sum of the 3 metals.

2. Cu and Cd may be masked with the addition of cyanide to the solution, leaving only Ca ion.

3. When formaldehyde or chloral hydrate is added to the cyanide containing mixture, only Cd is demasked and the EDTA titrates the sum of Ca and Cd. In this manner, the concentration of three ions is determined by 3 individual titrations.

Step 1: Titration without Masking Agent

Initially, the solution contains **Ca^{2+}, Cd^{2+} and Cu^{2+}**. If EDTA is added directly, all three metal ions react with EDTA.

Reactions:

$$Ca^{2+} + EDTA^{4-} \rightarrow [Ca\text{-}EDTA]^{2-}$$

$$Cd^{2+} + EDTA^{4-} \rightarrow [Cd\text{-}EDTA]^{2-}$$

$$Cu^{2+} + EDTA^{4-} \rightarrow [Cu\text{-}EDTA]^{2-}$$

Total amount of **Ca^{2+} + Cd^{2+} + Cu^{2+}** is determined.

Step 2: Titration in the Presence of a Masking Agent

A **cyanide ion (CN^-)** is added as the masking agent. It forms stable complexes with **Cd^{2+}** and **Cu^{2+}**, but does not react with **Ca^{2+}**.

Masking reactions:

$$Cd^{2+} + 4CN^- \rightarrow [Cd\ (CN)4]^{2-}$$

$$Cu^{2+} + 4CN^- \rightarrow [Cu\ (CN)4]^{2-}$$

$$Ca^{2+} + CN^- \rightarrow \text{No reaction}$$

Now only calcium remains free.

EDTA reaction:

$$Ca^{2+} + EDTA^{4-} \rightarrow [Ca\text{-}EDTA]^{2-}$$

Only **Ca^{2+}** is determined.

Step 3: Titration after Demasking

A demasking agent (formaldehyde, HCHO) is added. It reacts with cyanide ions and releases **Cd^{2+}** from its cyanide complex, while Cu^{2+} remains masked because its cyanide complex is much more stable.

Demasking reaction:

$$[Cd\ (CN)_4]^{2-} + HCHO \rightarrow Cd^{2+} + \text{products}$$

$$[Cu\ (CN)_4]^{2-} + HCHO \rightarrow \text{No reaction}$$

The released cadmium is then titrated with EDTA.

$$Cd^{2+} + EDTA^{4-} \rightarrow [Cd\text{-}EDTA]^{2-}$$

Copper remains masked throughout this step. **Cd^{2+}** is determined separately, while **Cu^{2+}** remains masked.

Masking Agent

A **masking agent** is a substance that selectively binds to an interfering ion (impurity), forming a stable, soluble complex. This "masks" the ion, making it inactive or unavailable to react with the analytical reagent (like an EDTA titrant). Common masking agents include **cyanide ion (CN^-)**, which masks metal ions such as copper, zinc, cadmium, nickel, and silver by forming highly stable cyanide complexes.

Masking may be defined as the process in which a substance without physical separation of it or its reaction products is so transformed that it does not interfere into a particular reaction.

a. Masking by precipitation: It is a technique in which an interfering metal ion is converted into an insoluble precipitate so that it is removed from the solution and cannot react with EDTA during a complexometric titration. The precipitated ion remains unavailable for complex formation and therefore does not interfere in the determination of the desired metal ion.

This method is particularly useful when the interfering ion can be selectively precipitated without affecting the ion being analyzed. After precipitation, the desired metal ion remains in solution and can be titrated accurately with EDTA.

Examples:

1. Lead ions (Pb^{2+}) can be masked by adding sulphate ions, forming insoluble lead sulphate:

$$Pb^{2+} + SO_4^{2-} \rightarrow PbSO_4 \downarrow$$

2. Barium ions (Ba^{2+}) can be masked by precipitation as barium sulphate:

$$Ba^{2+} + SO_4^{2-} \rightarrow BaSO_4 \downarrow$$

3. Calcium ions (Ca^{2+}) can be masked by precipitation as calcium oxalate:

$$Ca^{2+} + C_2O_4^{2-} \rightarrow CaC_2O_4 \downarrow$$

b. Masking by complex formation: Masking agents form more stable complexes with the interfering metal ions. The most important aspect is that the masking agent must not form complexes with the metal ion under analysis. The different masking agents used are enlisted below:

1. **Ammonium fluoride** will mask aluminium, iron and titanium by complex formation.

2. **Ascorbic acid** is a convenient reducing agent for iron (III) which is then masked by complexing as the very stable hexacyanoferrate (II) complex. This latter is more stable and less intensely coloured than the hexacyanoferrate (III) complex.

3. **Dimercaprol (2,3-Dimercaptopropanol)** Cations of mercury, cadmium, zinc, arsenic, tin, lead and bismuth react with dimercaprol in weakly acidic solution to form precipitates which are soluble in alkaline solution. All these complexes are stronger than the corresponding edetate complexes and are almost colourless.

4. **Potassium cyanide** reacts with silver, copper, mercury, iron, zinc, cadmium, cobalt and nickel ions to form complexes in alkaline solution which are more stable than the corresponding edetate complexes, so that other ions, such as lead, magnesium, manganese and the alkaline earth metals can be determined in their presence.

5. **Triethanolamine** forms a colourless complex with aluminium, a yellow complex with iron (III), the colour of which is almost discharged by adding sodium hydroxide solution, and a green manganese (III) complex which oxidizes mordant black II.

Demasking agents

Demasking agent is a substance used to release a metal ion that has previously been masked. It destroys or removes the masking complex, freeing the metal ion so that it can react with EDTA and be determined separately.

Demasking is useful for the **sequential determination of different metal ions** present in the same solution. First, interfering ions are masked; later, specific ions are demasked and titrated individually. Selective cations like zinc or cadmium can be demasked by adding formaldehyde-acetic-acid solution or, better with chloral hydrate. Such cations can be titrated with EDTA after selective demasking.

$$[Zn(CN)_4]^{-2} + 4H^+ + 4HCHO \longrightarrow Zn^{+2} + 4HO\text{-}CH_2\text{-}CN$$

Examples:

1. **Formaldehyde** demasks Zn^{2+} ions from their cyanide complexes by reacting with cyanide ions.
2. **Chloral Hydrate** demasks Zn^{2+} and Cd^{2+} ions from cyanide complexes.
3. **Acetone** removes cyanide ions and releases metal ions such as Zn^{2+} for titration.
4. **Boric Acid** demasks Al^{3+} ions from fluoride complexes by forming fluoroborate complexes.
5. **Mercuric Chloride ($HgCl_2$)** demasks metal ions from cyanide complexes because mercury forms a more stable cyanide complex.
6. **Hydrogen Peroxide (H_2O_2)** can destroy certain masking complexes and release the metal ions.

Preparation and Standardization of Disodium EDTA

Disodium ethylenediaminetetraacetate (Disodium EDTA or $Na_2H_2Y \cdot 2H_2O$) is the most commonly used titrant in complexometric titrations because it forms stable 1:1 complexes with most metal ions. Since EDTA is not available in a sufficiently pure form for direct use as a primary standard, its prepared solution must be standardized against a standard metal ion solution before use.

Preparation of 0.05 M Disodium EDTA Solution

Principle: Disodium EDTA dissolves readily in distilled water to produce a stable solution. The prepared solution is approximately 0.05 M and is standardized before use.

Procedure:

1. Accurately weigh 18.61 g of disodium EDTA dihydrate.
2. Transfer it into a clean beaker containing about 500 mL of distilled water.
3. Stir until the EDTA dissolves completely.
4. Transfer the solution into a 1000 mL volumetric flask using a funnel.
5. Wash the beaker several times with distilled water and add the washings to the flask.
6. Make up the volume to 1000 mL with distilled water.
7. Mix thoroughly and store the solution in a clean, tightly closed polyethylene or glass bottle.

Standardization of Disodium EDTA Solution

Principle: The prepared EDTA solution is standardized against a standard zinc sulfate solution or standard calcium carbonate solution. EDTA reacts quantitatively with metal ions in a **1:1** molar ratio. The end point is detected using Eriochrome Black T (EBT) indicator in an ammonia-ammonium chloride buffer (pH 10).

Reaction:

$$Zn^{2+} + EDTA^{4-} \rightarrow [Zn{-}EDTA]^{2-}$$

or

$$Ca^{2+} + EDTA^{4-} \rightarrow [Ca{-}EDTA]^{2-}$$

Procedure:

1. Pipette 25.0 mL of standard zinc sulfate solution into a conical flask.
2. Add 5 mL of ammonia-ammonium chloride buffer (pH 10).
3. Add 2–3 drops of Eriochrome Black T indicator.
4. The solution develops a wine-red color.
5. Titrate with the prepared EDTA solution until the color changes from wine red to pure blue.
6. Repeat the titration until concordant readings are obtained.

Calculation

Formula

$$M_1V_1=M_2V_2$$

Where:

- **M_1** = Molarity of standard zinc/calcium solution
- **V_1** = Volume of standard solution
- **M_2** = Molarity of EDTA solution
- **V_2** = Volume of EDTA consumed

Therefore,

$$M_{EDTA} = \frac{M_{standard} \times V_{standard}}{V_{EDTA}}$$

Applications:

- Standardization of EDTA solution.
- Determination of water hardness.
- Estimation of calcium and magnesium.
- Pharmaceutical analysis of metal-containing formulations.
- Determination of various metal ions by complexometric titration.

Estimation of Magnesium Sulphate

Principle: Magnesium sulphate dissociates in aqueous solution to produce Mg^{2+} ions. During the titration, magnesium ions react with disodium EDTA in a 1:1 molar ratio to form a stable magnesium-EDTA complex. The titration is carried out at pH 10 using an ammonia-ammonium chloride buffer**.** Eriochrome Black T (EBT) is used as the indicator. Initially, the indicator forms a wine-red complex with magnesium ions. As EDTA is added, it forms a more stable complex with magnesium, releasing the free indicator, and the color changes from **wine red to blue**, indicating the end point. Reaction involved in this titration is as follows.

$$Mg^{2+} + EDTA \longrightarrow Mg\text{-}EDTA + 2H^{+}$$

Magnesium ion — Disodium edetate — Mg-disodium edetate complex

Procedure:

1. Weigh accurately about 0.3 g of magnesium sulphate in a conical flask and dissolve in 50ml of distilled water.
2. Add 10 ml of strong ammonia-ammonium chloride solution.
3. Add 2 drops of mordant black II mixture as an indicator.
4. Then fill the burette with standardized disodium edetate solution.
5. Start titration with the disodium edetate untill reach the endpoint.
6. The approach of the endpoint is suggested by the change of pink colour to blue.
7. Record the readings of burette. Repeat the titration three times to get precise readings.
8. Take mean of them and calculate the percentage purity of magnesium sulphate.
9. Equivalent factor of magnesium sulphate for 1ml of 0.05M disodium edetate is 0.00602.

Applications

- Assay of magnesium sulphate in pharmaceutical formulations.
- Quality control of magnesium-containing preparations.
- Determination of magnesium in water and industrial samples.
- Routine analysis in pharmaceutical and analytical laboratories.

Estimation of Calcium Gluconate

Principle: This is a replacement titration. Magnesium forms complex with mordant black II mixture indicator which shows first colour.

Mg^{2+} + In^{-} ⟶ Mg-In

Magnesium ion + Indicator ⟶ Magnesium indecator complex (coloured I)

Magnesium-indicator complex is much more stable than calcium-indicator complex therefore calcium has not any effect on magnesium-indicator complex. On titration against disodium edetate complex of calcium and disodium edetate is formed.

Ca^{2+} + EDTA Disodium edetate ⟶ Ca- EDTA Calcium-disodium edetate complex

Calcium ion

When calcium is totally consumed, next drop of disodium edetate breaks the magnesium-indicator complex and make complex with magnesium by liberating free indicator. End point is detected by observing second colour at that time.

Mg-In + EDTA Disodium edetate ⟶ Mg- EDTA Magnesium-disodium edetate complex + In Free indicator (coloured 2)

Magnesium indecator complex (coloured I)

Procedure:

1. Weigh accurately about 0.5 g of calcium gluconate in a conical flask and dissolve in 50 ml of warm water.

2. Allow to cool.

3. Add 5 ml of 0.05 M magnesium sulphate.

4. Add 10 ml of strong ammonia-ammonium chloride solution.

5. Add 2 drops of mordant black II mixture as an indicator.

6. Then fill the burette with standardized disodium edetate solution.

7. Start titration with the disodium edetate until reach the endpoint.

8. Record the reading of burette. Repeat the titration three times to get precise readings.

9.Take mean of them and calculate the percentage purity of calcium gluconate.

10. Repeat the titration again using same procedure without calcium gluconate for blank reading.

11. Equivalent factor of calcium gluconate for 1 ml of 0.05 M disodium edetate is 0.02242.

Applications

- Assay of calcium gluconate in pharmaceutical formulations.
- Quality control of calcium supplements.
- Determination of calcium content in injections and tablets.
- Routine analysis in pharmaceutical and analytical laboratories.

Points to Remember:

- ✓ Complexometric titrations are based on the formation of stable metal–ligand complexes.
- ✓ EDTA is the most commonly used complexing agent.
- ✓ EDTA is a **hexadentate ligand** containing six donor atoms.
- ✓ EDTA forms **1:1 complexes** with most metal ions irrespective of their valency.
- ✓ The stability of metal–EDTA complexes depends on the pH of the solution.
- ✓ Buffer solutions are essential to maintain the required pH during titration.
- ✓ Ammonia–ammonium chloride buffer maintains **pH 10**.
- ✓ Eriochrome Black T (EBT), murexide, and xylenol orange are common metal ion indicators.
- ✓ Eriochrome Black T forms a **wine-red complex** with metal ions.
- ✓ At the endpoint, Eriochrome Black T changes from **wine red to blue**.
- ✓ Murexide is commonly used for calcium estimation.
- ✓ **Masking agents** prevent interfering metal ions from reacting with EDTA.
- ✓ Cyanide, fluoride, triethanolamine, and tartrate are common masking agents.
- ✓ **Demasking agents** release the masked metal ions for selective estimation.
- ✓ Disodium EDTA is standardized using standard zinc or calcium solutions.
- ✓ **Magnesium sulphate** is estimated using EDTA with Eriochrome Black T at pH 10.
- ✓ **Calcium gluconate** is estimated using EDTA with murexide in alkaline medium.

Case Based Learning (CBL)

Case

A pharmaceutical laboratory estimates **magnesium sulphate** using EDTA. The analyst forgets to add the ammonia–ammonium chloride buffer, resulting in an indistinct endpoint.

Students should identify the role of the buffer, explain the function of EDTA, and discuss the importance of maintaining the correct pH.

Questions

1. Why is a buffer required?
2. What is the role of EDTA?
3. Which indicator is used?
4. What colour change occurs at the endpoint?
5. What is meant by masking?

Problem based learning

Problem

A student estimates **magnesium sulphate** using EDTA but forgets to add the **ammonia–ammonium chloride buffer**. The endpoint is unclear, and the titration result is inaccurate.

MCQs

1. The main function of the buffer is to maintain:

   A. pH ✔
   B. Temperature
   C. Pressure
   D. Volume

2. EDTA forms:

   A. 1:1 metal complexes ✔
   B. 1:2 complexes
   C. 2:1 complexes
   D. 3:1 complexes

3. The indicator used for magnesium estimation is:

   A. Murexide
   B. Eriochrome Black T ✔
   C. Starch
   D. Methyl orange

4. Murexide is mainly used for estimating:

   A. Calcium ✔
   B. Iron
   C. Copper
   D. Zinc

5. Masking agents are used to:

   A. Increase acidity
   B. Eliminate interference from other metal ions ✔
   C. Produce precipitates
   D. Change the indicator colour

REDOX TITRATIONS

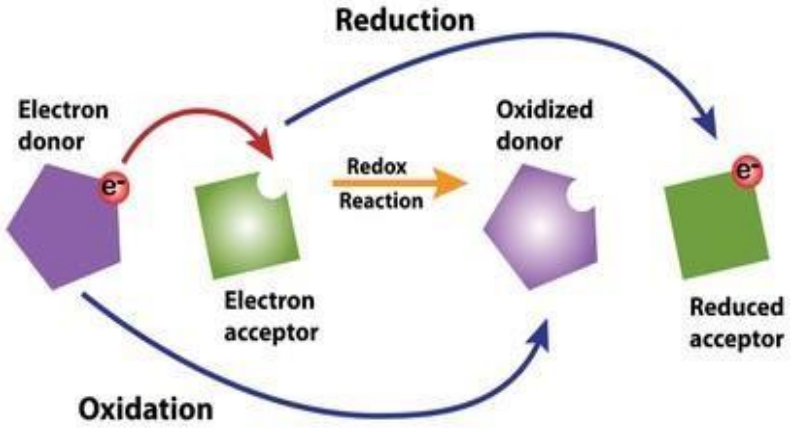
An oxidation-reduction titration or redox titration is one in which the substance to be determined is either oxidised or reduced by means of the solution with which the titration is made. In spite of this, titrimetric determinations based on oxidation-reduction reactions are most widely used methods in the quantitative analysis of inorganic as well as organic compounds. In order to understand the theory of redox titrimetry, we must know such terms as oxidation, reduction, oxidising agent or oxidant and reducing agent or reductant.

Redox titrations (Oxidation-Reduction titrations) are volumetric analytical methods based on **oxidation-reduction (redox) reactions** between an oxidizing agent and a reducing agent. In these titrations, one substance undergoes **oxidation** (loss of electrons), while the other undergoes **reduction** (gain of electrons). The end point is detected either by a suitable redox indicator or by the appearance of a permanent color due to the titrant itself.

Redox titrations are widely used in pharmaceutical analysis, environmental analysis, food analysis, and industrial quality control for the quantitative determination of oxidizing and reducing substances.

As an example, during the combustion of wood, oxygen from the air is reduced, gaining electrons from the carbon. Although oxidation reactions are commonly associated with the formation of oxides from oxygen molecules, oxygen is not necessarily included in such reactions, as other chemical species can serve the same function.

The reaction can occur relatively slowly, as in the case of rust, or more quickly, as in the case of fire. There are simple redox processes, such as the oxidation of carbon to yield carbon dioxide (CO_2) or the reduction of carbon by hydrogen to yield methane (CH_4), and more complex processes such as the oxidation of glucose ($C_6H_{12}O_6$) in the human body.



Concept of Oxidation-Reduction

Oxidation and reduction are complementary chemical processes that occur simultaneously in many chemical reactions. These reactions involve the transfer of electrons from one substance to another and are collectively known as oxidation-reduction (redox) reactions. In pharmaceutical analysis, redox reactions form the basis of redox titrations, where the concentration of an oxidizing or reducing agent is determined quantitatively.

Oxidation: Oxidation is the process in which a substance loses one or more electrons**,** resulting in an increase in its oxidation number. Oxidation may also be defined as the addition of oxygen**,** removal of hydrogen**,** or loss of electrons**.**

Examples:

Loss of electrons:

$$Fe^{2+} \rightarrow Fe^{3+} + e^{-}$$

Addition of oxygen:

$$2Mg + O_2 \rightarrow 2MgO$$

Magnesium combines with oxygen and is oxidized to magnesium oxide.

Removal of hydrogen:

$$CH_3CH_2OH \rightarrow CH_3CHO + 2H$$

Ethanol is oxidized to acetaldehyde by the removal of hydrogen.

Reduction: Reduction is the process in which a substance gains one or more electrons, resulting in a decrease in its oxidation number. It may also be defined as the removal of oxygen**,** addition of hydrogen, or gain of electrons.

Example:

Gain of electrons:

$$Ce^{4+} + e^{-} \rightarrow Ce^{3+}$$

Here, ceric ion (Ce^{4+}) gains one electron to form cerous ion (Ce^{3+}). Therefore, Ce^{4+} is reduced.

Removal of oxygen:

$$CuO + H_2 \rightarrow Cu + H_2O$$

Copper oxide loses oxygen and is reduced to copper.

Addition of hydrogen:

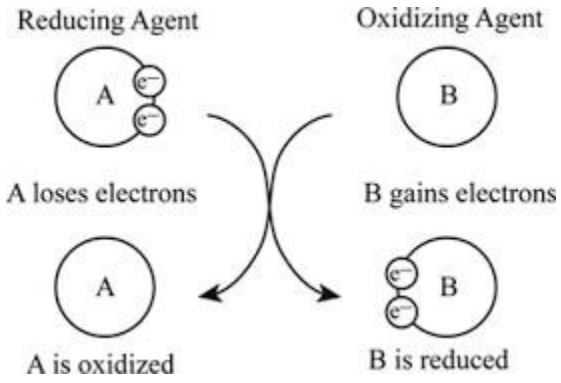
$$CH_2 = CH_2 + H_2 \rightarrow CH_3\ CH_3$$

Ethene gains hydrogen to form ethane and is therefore reduced.

Oxidizing and Reducing Agents

An oxidizing agent, or oxidant, gains electrons and is reduced in a chemical reaction. Also known as the electron acceptor, the oxidizing agent is normally in one of its higher possible oxidation states because it will gain electrons and be reduced. Examples of oxidizing agents include halogens, potassium nitrate, and nitric acid.

A reducing agent**,** or reductant, loses electrons and is oxidized in a chemical reaction. A reducing agent is typically in one of its lower possible oxidation states, and is known as the electron donor. A reducing agent is oxidized, because it loses electrons in the redox reaction. Examples of reducing agents include the earth metals, formic acid, and sulfite compounds.



In redox processes, the reductant transfers electrons to the oxidant. Thus, in the reaction, the reductant or reducing agent loses electrons and is oxidized, and the oxidant or oxidizing agent gains electrons and is reduced. The pair of an oxidizing and reducing agent that are involved in a particular reaction is called a **redox pair**. A **redox couple** is a reducing species and its corresponding oxidizing form, e.g., Fe^{2+}/Fe^{3+}.

Oxidizers

Substances that have the ability to **oxidize** other substances (cause them to lose electrons) are said to be **oxidative** or **oxidizing** and are known as oxidizing agents, oxidants, or oxidizers. That is, the oxidant (oxidizing agent) removes electrons from another substance, and is thus itself reduced. And, because it "accepts" electrons, the oxidizing agent is also called an electron acceptor. Oxygen is the quintessential oxidizer.

Examples:

- Potassium permanganate ($KMnO_4$)
- Potassium dichromate ($K_2Cr_2O_7$)
- Ceric ammonium sulphate (Ce^{4+})
- Iodine (I_2)
- Hydrogen peroxide (H_2O_2)

Reducers

Substances that have the ability to **reduce** other substances (cause them to gain electrons) are said to be **reductive** or **reducing** and are known as reducing agents, reductants, or reducers. The reductant (reducing agent) transfers electrons to another substance, and is thus itself oxidized. And, because it "donates" electrons, the reducing agent is also called an electron donor. Electron donors can also form charge transfer complexes with electron acceptors.

Examples:

- Ferrous sulphate ($FeSO_4$)
- Oxalic acid ($H_2C_2O_4$)
- Sodium thiosulphate ($Na_2S_2O_3$)
- Ascorbic acid (Vitamin C)
- Hydrogen sulphide (H_2S)

Oxidation and Reduction Occur Simultaneously

Oxidation and reduction always occur together because electrons lost by one substance must be gained by another.

Example

$$Ce^{4+} + Fe^{2+} \rightarrow Ce^{3+} + Fe^{3+}$$

In this reaction:

- Fe^{2+} loses an electron and **is** oxidized**.**
- Ce^{4+} gains an electron and **is** reduced**.**
- Fe^{2+} is the reducing agent.
- Ce^{4+} is the oxidizing agent.

Detection of end point

1) By using Redox indicator

a. Redox indicators/Internal Indicators

b. Self-indicators II.

c. External indicator

2) Potentiometric method

a. By using Redox indicator

1. Internal Indicator

An oxidation-reduction indicator is a compound which exhibits different colours in the oxidised and reduced forms.

One of the best redox indicator is the Ferroin, (ortho phenanthroline ferrous ion).

The base combines readily in solution with ferrous salts in the molecular ratio 3 base: 1 ferrous ion forming the intensely red tri ortho phenanthroline ferrous ion. With strong oxidizing agent the ferric complex ion is formed which has a pale blue colour.

$$[Fe\ (C_{12}\ H_8N_2)_3]^{+++} \quad + \quad [Fe\ (C_{12}\ H_8N_2)3]^{++}$$

(Oxidised form = pale blue) (Reduced form = Red)

Examples of Redox Indicators

Indicator name	**Colour change**	
	Oxidized	**Reduced**
Nitro ferroin	Pale blue	Red
Ferroin	Pale blue	Red
N-phenyl anthranilic acid	Purple red	Colourless
Diphenylamine in conc. Sulphuric acid	Red violet	Colourless
Diphenylamine	Violet	Colourless
Starch indicator	Blue	Colourless

2. Self-Indicator

Many times the titrant itself may be so strongly coloured after the end point, in that case titrant acts as self-indicator. One drop of $KMnO_4$ imparts visible colour change to hundred/thousand ml of solution.

E.g. $KMnO_4$ - Pink, Iodine- Brown, Ce(S04)2- Pale yellow

KMnO4 is strongly used as self-indicators. KMnO4 get reduced in the redox titration as:

$$MnO_4 + 8H^+ + 5e^- \longrightarrow Mn^{2+}\ 4H_2O$$

The $KMnO_4$ has dark purple colour due to MnO_4 which on reduction give Mn^{2+} which is colourless, so as at the end point excess drop of $KMnO_4$. It gets dilute in the solution and gives pink colour to the solution.

3. External Indicator

The best- known example of an external indicator in redox process is the spot test for the titration of ferrous ion with $K_2Cr_2O_7$.

Near the equivalence point, drops of solution are removed and brought into contact with dilute freshly prepared potassium ferricyanide solution on a spot plate. The end point is reached when first drop fails to give blue color. These are almost obsolete now-a-days as there are various better internal indicator available, further there is loss of reaction mixture.

Potentiometric Methods

This is physico-chemical method which may be applied to those cases where suitable indicators, are not available. This method is also applied to those cases in which the visual indicator method fails or is of limited accuracy e.g. for coloured solution for very dilute solution.

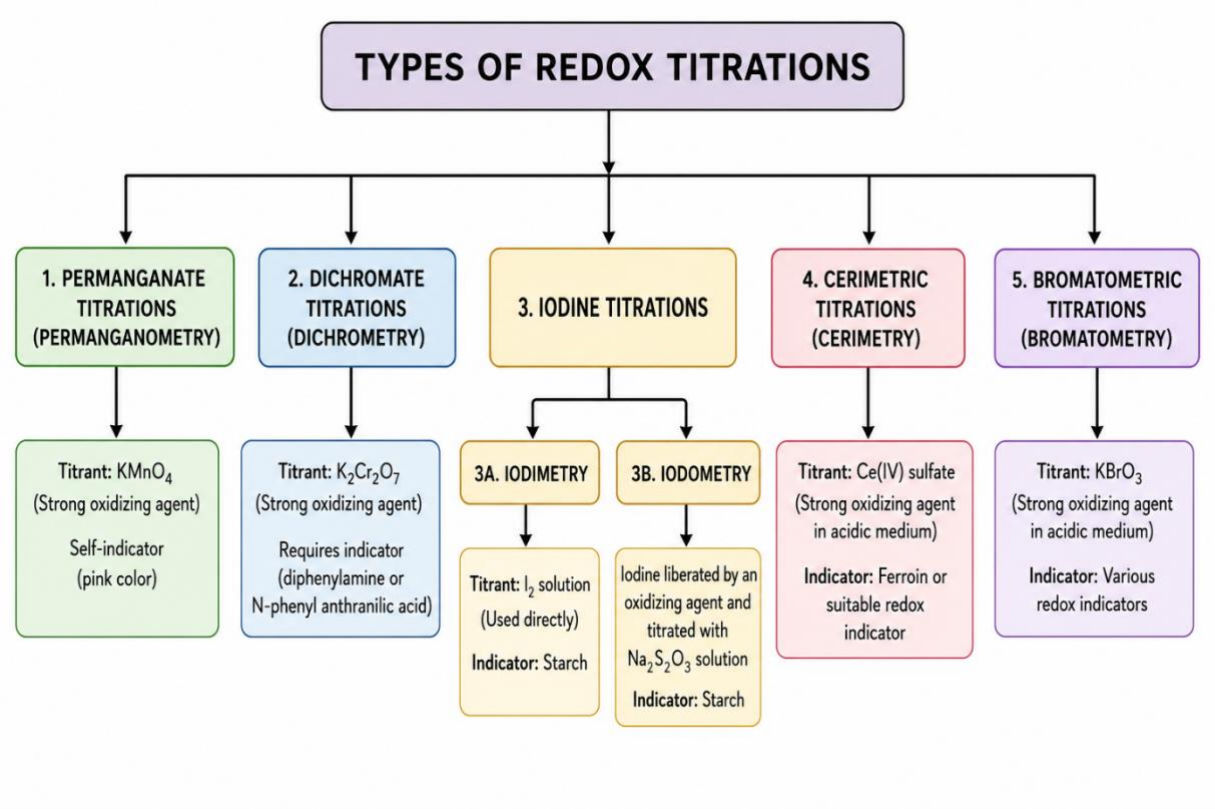
TYPES OF REDOX TITRATION

1. Permanganate Titration

2. lodine Titration

3. Cerimetry

4. Titration with potassium iodate



1) Permanganate Titration (Permanganometry):

Permanganate titration (Permanganometry) is a type of redox titration in which potassium permanganate ($KMnO_4$) is used as the standard oxidizing agent to determine the concentration of reducing substances. It is one of the most widely used oxidation-reduction titration methods in pharmaceutical and chemical analysis. These titrations involving permanganate oxidation is a special case of oxidimetry in which a solution of KMnO4 is used as an oxidant.

The ability of $KMnO_4$, solution to oxidise is due to the conversion of the MnO_4 to Mn^{2+} in acidic solution and to MnO_2 in alkaline, neutral or very weak acidic solution. The MnO_4 is reduced in accordance with the following reactions:

In Acidic solution: Solutions containing MnO_4^- ions (in oxidized state) are purple in colour, solution of salts containing Mn^{2+} (reduced KMnO4) ions are colourless hence a permanganate solution is decolourised when added to the solution of reducing agent as long as latter is present

in the solution. The moment there is an excess of $KMnO_4$ the solution it becomes pink or purple. Thus, permanganate ion can serve as its own indicator, especially in acidic solution.

$$MnO_4 + 8H+ + 5e^- \longrightarrow Mn^{2+} + 4H_2O$$

Why Acidic Medium is Required?

Sulphuric acid is used because it allows complete reduction of permanganate to Mn^{2+}.

- Does not interfere with the reaction.
- Provides sufficient H^+ ions.
- Gives sharp end point.

Why HCl and nitric acid is Not Used?

HCl is oxidized by $KMnO_4$ to chlorine gas. This causes errors and Nitric acid is itself an oxidizing agent and interferes with the titration.

In Alkaline or Neutral solution: In alkaline and neutral solution, MnO_4 reduces in to MnO_2. These MnO_2 is in the form of brown particles, therefore KMnO4 is not used as self-indicator.

Here, diphenylamine (red-violet to colourless) or phenylanthranillic acid (purple-red) is used as an indicator with very dilute solution of $KMnO_4$. $KMnO_4$ solution is used in determination of both oxidizing and reducing agents.

$$MnO_4 + 4H^+ + 3e^- \longrightarrow MnO_2 + 2H_2O$$

Standardization of $KMnO_4$: $KMnO_4$ is not a primary standard because:

- It contains impurities.
- It decomposes on standing.
- It reacts with organic matter.
- It cannot be weighed accurately.

Hence it is standardized against a primary standard such as:

- Sodium oxalate ($Na_2C_2O_4$)
- Oxalic acid dihydrate ($H_2C_2O_4 \cdot 2H_2O$)

Procedure:

1. Prepare approximately 0.1 N $KMnO_4$ solution.
2. Standardize it using standard sodium oxalate or oxalic acid.
3. Fill the burette with standardized $KMnO_4$.
4. Pipette a measured volume of the analyte into a conical flask.

5. Add dilute sulphuric acid.
6. If oxalic acid is used, warm the solution to 60–70°C.
7. Titrate with $KMnO_4$ until a permanent pale pink colour appears.
8. Record the burette reading and calculate the concentration.

Applications: In the estimation of Ferrous sulphate, Assay of Hydrogen peroxide, Determination of Oxalic acid, Estimation of Calcium (after precipitation as calcium oxalate).

2. Cerimetry:

Cerimetric titration (Cerimetry) is a type of redox titration in which cerium (IV) sulphate [$Ce(SO_4)_2$] or ceric ammonium sulphate [$(NH_4)_4Ce(SO_4)_4 \cdot 2H_2O$] is used as the standard oxidizing agent to determine the concentration of reducing substances. It is widely used in pharmaceutical and analytical chemistry due to its high oxidation potential and sharp end point.

It can be used only in acid solution best in 0.5 M or higher concentration. In neutral solution ceric hydroxide (or hydrated cerium (IV) oxide) or basic salts are precipitated.

The solution of cerium (IV) sulphate has intense yellow colour and in hot solutions which are not too dilute, the end point may be detected without an indicator. This procedure requires blank correction, and it is therefore preferable to add a suitable indicator.

Cerimetric titrations generally require an external redox indicator because Ce^{4+} is not a self-indicator. Commonly used indicators are Ferroin indicator**,** Diphenylamine**,** N-Phenyl anthranilic acid**.**

Principle: Cerimetric titrations are carried out in sulphuric acid (H_2SO_4) because Ce^{4+} is stable in acidic medium, the reaction proceeds rapidly and completely. A sharp end point is obtained.

Hydrochloric acid should not be used, as chloride ions may be oxidized.

$$4\ Ce^{4+} + 2Cl^- \longrightarrow 2\ Ce^{3+} + Cl_2$$

Preparation of 0.1 M cerium sulphate:

Molecular weight of cerium sulphate and cerium ammonium sulphate are 333.25 and 632.57 respectively. Weigh 35 gm of cerium sulphate add 56 mL. of sulphuric acid and stir with frequent water addition and gentle warming to dissolve salt completely. Transfer to volumetric flask and cool, dilute to one litre mark with distilled water.

Preparation of 0.1 M cerium ammonium sulphate:

Dissolve 65 gm of cerium ammonium sulphate with the help of gentle heat, in a mixture of 30 mL of H_2SO_4 and 500 mL of water, cool and filter if turbid and dilute it to 1000 mL. of water.

Standardization of Ceric Solution

Cerium (IV) sulphate solution is standardized using primary standards such as:

- Sodium oxalate ($Na_2C_2O_4$)
- Arsenic trioxide (As_2O_3)
- Ferrous ammonium sulphate (FAS)

Standardization with arsenic trioxide

Weigh accurately about 0.2 gm of arsenic trioxide, previously dried at 105 °C for 1 hour and transfer to 500 mL of conical flask. Wash with 25 mL of 8% w/v solution of sodium hydroxide, swirl to dissolve, add 100 mL of water and mix. Add 30 mL of dilute sulphuric acid, 0.15 mL of osmic acid solution, 0.1 mL of ferroin solution and titrate with cerium ammonium sulphate, slowly the pink color changes to vary pale blue.

Method:	Cerimetry
Titrant:	Cerium (IV) sulphate or Ceric ammonium sulphate
Type:	Redox titration
Medium:	Acidic (Dilute H_2SO_4)
Indicator:	Ferroin, Diphenylamine, N-Phenyl anthranilic acid
End Point:	Colour change depending on the indicator
Oxidizing Agent:	Ce^{4+} ions
Electron Transfer:	1 electron ($Ce^{4+} \rightarrow Ce^{3+}$)
Main Applications:	Ferrous salts, arsenic (III), hydrogen peroxide, ascorbic acid, tin (II) compounds

3. Iodine Titration:

Iodine titrations are redox titrations based on the oxidation-reduction reactions involving iodine (I_2) and iodide ions (I^-)**.** Iodine titrations are of two types:

1. Iodimetry (Direct Iodine Titration): in which standard iodine solution is used as a titrant.

2. Iodometry (Indirect Iodine Titration): in which iodine liberated during chemical reaction is titrated.

1. Iodimetry (Direct Iodine Titration): It is a titration in which iodine solution directly titrate with reducing agent using starch as an indicator or iodine act as a self-indicator. This titration is carried out in neutral or slightly alkaline condition.

Preparation of Iodine solution (0.05 M): Take 14 g of iodine and 36 gm of KI (potassium iodide), dissolve it in 100 ml water 3 drops of HCl are added and dilute it to 1000 ml.

Standardization of Iodine solution: Standardization of 12 solution is done with sodium thiosulphate and arsenic trioxide.

Standardization I_2 solution with Sodium thiosulphate ($Na_2S_2O_3$):

Preparation of 0.1 M $Na_2S_2O_3$: Add 25 gm of $Na_2S_2O_3$ and 0.2 gm of Na_2CO_3 in water and make up the volume upto 1000 ml with CO_2 free water.

Standardization: Directly titrate prepared iodine solution against sodium thiosulphate ($Na_2S_2O_3$) until the solution has a pale yellow colour. Add starch solution and continue the titration until the solution is colourless.

Solution of Iodine has intense yellow to brown colour. Addition of 1 drop of 0.1 N I_2 solution gives pale yellow colour to 100 ml water. Thus, Iodine solution serves as its own Indicator.

Reaction:

$$\text{Oxidizing agent: } I_2 + 2e^- \longrightarrow 2I^-$$

$$\text{Reducing agent: } 2S_2O_3^{2-} \longrightarrow S_4O_6^{2-} + 2e^-$$

$$\text{Overall reaction: } I_2 + 2Na_2S_2O_3 \longrightarrow 2NaI + Na_2S_4O_6$$

$$\text{Here, } I_2 = 2Na_2S_2O_3 = 2e^-$$

Standardization I_2 solution with Arsenic Trioxide (AS_2O_3):

This is a best primary standard for Iodine solution.

Weigh accurately 0.15 g of arsenic trioxide previously dried at 105 °C for 1 hour. Dissolve it in 20 ml of 1 M NaOH by warming and dilute with 40 ml of water. Add 0.1 ml of methyl orange solution. Add dropwise dilute HCl until yellow colour changed to pink. Add 2 gm of Na_2CO_3 and dilute with 50 ml of water. Add 3 ml of starch solution. Titrate with iodine until a permanent blue colour is produced.

Each ml of 0.05 M iodine is equivalent to 0.004946 g of AS_2O_3.

Reaction:

AS_2O_3 is dissolved in water to give arsenious acid (H_3AsO_3)

$$AS_2O_3 + 3H_2O \longrightarrow 2H_3AsO_3$$

Reduction: $As_2O_3 + 3H_2O \longrightarrow 2H_3AsO_3$

Oxidation: $5\,[H_3AsO_3 + 3H_2O \longrightarrow 2\,H_3AsO_4 + 2H^+ + 2e^-]$

Overall reaction: $5[H_3AsO_3 + I_2 + H_2O \longrightarrow HASO_4^{2-} + 4H^+ + 2I^-$

Iodometry (Iodometric titration):

Iodometry is an indirect redox titration used to estimate **oxidizing agents**.

In this method:

- The oxidizing agent liberates iodine from potassium iodide.
- The liberated iodine is titrated with **standard sodium thiosulphate solution**.

Principle: The oxidizing agent oxidizes iodide to iodine. Iodine dissolves in the iodide-containing solution to give triiodide ions, which have a dark brown color. The triiodide ion solution is then titrated against standard sodium thiosulphate solution to give iodide using starch indicator till blue colour changes to colourless.

Oxidizing agent + KI → Iodine liberated

The liberated iodine reacts with sodium thiosulphate.

Reaction:

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

Conditions for Iodometric Titrations:

1. Titration must be carried out in acidic conditions.

2. In highly alkaline conditions, NaOI (Sodium hypo-iodide) is formed which is a strong oxidizing agent as compared to iodine.

$$2NaOH + I_2 \rightarrow NaOI + NaI + H_2O$$

3. Reaction mixture must be kept in dark to decrease volatilization of iodine (light accelerates the side reaction in which I- ions are oxidized to I_2 by atmospheric oxygen.

4. Titration must be carried out in closed flask and in cold conditions to prevent volatilization of iodine.

5. Iodine is very slightly soluble in water, so there is need to add excess of KI to dissolve the 1_2.

Sodium thiosulphate is standardized using: Potassium dichromate, Potassium iodate, Potassium bromate

I. Preparation of 0.1 M Sodium Thiosulphate Solution: Dissolve 25 g of sodium thiosulphate and 0.2 g of sodium carbonate in carbon dioxide free water and dilute to 1 litre with water.

II. Standardization of Sodium Thiosulphate: Dissolve accurately weighed 0.200 gm of potassium bromate in water to produce 250 ml to 50 ml of this solution. Add 2 gm of potassium iodide and 3 ml of 2M hydrochloric acid and titrate with sodium thiosulphate solution using starch indicator until blue colour disappears.

Factor: Each ml of 0.1 M sodium thiosulphate is equivalent to 0.002784 gm of KBrO3

Principle: Potassium bromate reacts with potassium bromide (KBr) in the presence of dilute hydrochloric acid to liberate bromine (Br_2). The liberated bromine reacts with excess potassium iodide (KI) to liberate iodine (I_2). The liberated iodine is then titrated with standard sodium thiosulphate solution using starch as the indicator.

Reactions Involved

Step 1: Liberation of Bromine

$$KBrO_3 + 5KBr + 6HCl \rightarrow 3Br_2 + 6KCl + 3H_2O$$

Step 2: Liberation of Iodine

$$Br_2 + 2KI \rightarrow 2KBr + I_2$$

Since **$3Br_2$** are produced,

$$3Br_2 + 6KI \rightarrow 6KBr + 3I_2$$

Step 3: Titration of Iodine

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

IODIMETRIC TITRATION	IODOMETRIC TITRATION
It is direct titration of iodine	It is an indirect titration of 1_2. (1_2 liberates in the reaction between KIO_3+ KI)
Iodine is used as a titrant.	Iodine is not used as a titrant but KIO_3, are used as titrant which reacts with KI.
It is carried out in neutral or slightly alkaline solution, because it forms **hypoiodate ion** from I_2 which is strong oxidizing agent.	It is carried out in slightly acidic condition. In strongly alkaline solution **hypoiodide ion** is formed. $2NaOH + I_2 \longrightarrow NaOI + NaI + H_2O$
It is used for analysis of reducing agent. 1_2 is oxidizing agent (Titrant). Arsenic oxide & $Na_2S_2O_3$ are reducing agent. (Analyte)	It is used for analysis of oxidizing agent. $Na_2S_2O_3$ is reducing agent. (Titrant) $K_2Cr_2O_7$ & KIO_3 are oxidizing agent (Analyte)

4. Titrations with potassium Iodate

Potassium iodate (KIO_3) is a strong oxidizing agent and is widely used in redox titrations, particularly in iodometric titrations. It is an excellent primary standard because it is highly pure, stable, non-hygroscopic, and has a high molecular weight, allowing it to be weighed accurately without further purification.

Potassium iodate is mainly used for:

- Standardization of sodium thiosulphate solution.
- Determination of reducing agents through indirect iodometry.
- Pharmaceutical and analytical chemistry.

Principle: Potassium iodate itself is not used as the direct titrant. In an acidic medium, it reacts with potassium iodide (KI) to liberate a known amount of iodine (I_2). The liberated iodine is then titrated with standard sodium thiosulphate ($Na_2S_2O_3$) using starch as the indicator.

Thus, potassium iodate indirectly helps determine the concentration of sodium thiosulphate or other reducing agents.

Step 1: Liberation of Iodine

$$KIO_3 + 5KI + 3H_2SO_4 \rightarrow 3I_2 + 3K_2SO_4 + 3H_2O$$

Step 2: Titration of Liberated Iodine

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

Procedure: Pipette 25 mL of standard potassium iodate solution into a clean conical flask. Add about 2 g of potassium iodide (KI)**.** Add 10–15 mL of dilute sulphuric acid (or dilute hydrochloric acid). Swirl the flask. Iodine is liberated, and the solution becomes yellowish-brown**.** Fill the burette with standard sodium thiosulphate solution. Titrate the liberated iodine until the brown colour becomes pale yellow**.** Add 2–3 mL of freshly prepared starch solution**.** The solution turns deep blue due to the starch–iodine complex. Continue adding sodium thiosulphate dropwise until the blue colour disappears completely, producing a colourless solution.

Applications

1. Standardization of sodium thiosulphate solution.
2. Determination of reducing agents by iodometry.
3. Estimation of **ascorbic acid (Vitamin C)**.
4. Determination of **sulphites**.
5. Estimation of **arsenites**.
6. Pharmaceutical quality control.

Points to Remember:

- ✓ **Redox** (short for reduction–oxidation reaction) is a chemical reaction in which the oxidation states of atoms are changed. Any such reaction involves both a reduction process and a complementary oxidation process, two key concepts involved with electron transfer processes. Redox reactions include all chemical reactions in which atoms have their oxidation state changed; in general, redox reactions involve the transfer of electrons between chemical species.
- ✓ **Oxidation** is the loss of electrons or an increase in oxidation state by a molecule, atom, or ion.
- ✓ **Reduction** is the gain of electrons or a decrease in oxidation state by a molecule, atom, or ion.
- ✓ An **oxidizing agent**, or **oxidant**, gains electrons and is reduced in a chemical reaction. Also known as the electron acceptor, the oxidizing agent is normally in one of its higher possible oxidation states because it will gain electrons and be reduced. Examples of oxidizing agents include halogens, potassium nitrate, and nitric acid.
- ✓ A **reducing agent,** or **reductant**, loses electrons and is oxidized in a chemical reaction. A reducing agent is typically in one of its lower possible oxidation states, and is known as the electron donor. A reducing agent is oxidized, because it loses electrons in the redox reaction. Examples of reducing agents include the earth metals, formic acid, and sulfite compounds.
- ✓ **Self indicators:** The $KMnO_4$ solutions are quite deeply coloured and a slight excess of this reagent in a titration is easily detected. Thus in the titration of oxalic acid, ferrous ammonium sulphate, hydrogen peroxide etc., with $KMnO_4$, as soon as the reaction is complete, and a drop of the latter is in excess, a light pink colour is itself developed, indicating that the reaction is complete and the end point has reached.
- ✓ **Specific indicator:** This is a substance which reacts in a specific manner with one of the reagents in a titration to exhibit a colour. Thus starch produces a deep blue colour with iodine; thiocyanate ion produces a red colour with Fe (III) ion.

Case Based Problem

Case

A quality control analyst performs a **permanganate titration** using **hydrochloric acid** instead of **sulphuric acid**. During the experiment, chlorine gas is evolved, and the titration results are inaccurate. The supervisor asks the trainee to identify the cause of the error and recommend the correct experimental conditions.

Students are expected to explain why sulphuric acid is preferred, discuss the role of potassium permanganate as a self-indicator, and describe how the incorrect acid affects the reaction.

Questions

1. Why is sulphuric acid preferred over hydrochloric acid in permanganometry?
2. Why is potassium permanganate called a self-indicator?
3. What is the endpoint of a permanganate titration?
4. Why is hydrochloric acid unsuitable?
5. Differentiate between iodimetry and iodometry.

Problem based learning

Problem

During a **permanganate titration**, a student uses **hydrochloric acid** instead of **dilute sulphuric acid**. Chlorine gas is produced, and the endpoint becomes unreliable, resulting in an incorrect assay.

MCQs

1. The preferred acid in permanganometry is:
   A. Hydrochloric acid
   B. Nitric acid
   C. Dilute sulphuric acid ✔
   D. Acetic acid

2. Potassium permanganate acts as:
   A. Self-indicator ✔
   B. Adsorption indicator
   C. Acid–base indicator
   D. Fluorescent indicator

3. Sodium thiosulphate is standardized using:
   A. Sodium hydroxide
   B. Potassium iodate ✔
   C. Oxalic acid
   D. EDTA

4. Iodometry is used for the estimation of:
   A. Reducing agents
   B. Oxidizing agents ✔
   C. Weak acids
   D. Weak bases

5. Starch indicator is added:
   A. At the beginning of the titration
   B. Near the endpoint ✔
   C. After the endpoint
   D. Before adding iodine

Multiple Choice Questions (MCQs):

Acid- base Titrations

1. Which theory explains acids as proton donors and bases as proton acceptors?
A. Arrhenius theory
B. Lewis theory
C. Brønsted–Lowry theory
D. Solvent system theory

Answer: C. Brønsted–Lowry theory

2. According to Arrhenius theory, an acid is a substance that:
A. Accepts electrons
B. Produces H^+ ions in aqueous solution
C. Produces OH^- ions
D. Accepts protons

Answer: B. Produces H^+ ions in aqueous solution

3. Which indicator is most suitable for the titration of a strong acid with a strong base?
A. Methyl orange
B. Phenolphthalein
C. Both methyl orange and phenolphthalein
D. Congo red

Answer: C. Both methyl orange and phenolphthalein

4. Phenolphthalein changes color in the pH range:
A. 1.2–2.8
B. 3.1–4.4
C. 6.0–7.6
D. 8.2–10.0

Answer: D. 8.2–10.0

5. Methyl orange changes color from:
A. Yellow to blue
B. Red to yellow
C. Pink to colorless
D. Green to yellow

Answer: B. Red to yellow

6. Which of the following is a strong acid?
A. Acetic acid
B. Oxalic acid
C. Hydrochloric acid
D. Boric acid

Answer: C. Hydrochloric acid

7. Sodium hydroxide is classified as:
A. Weak acid
B. Weak base
C. Strong acid
D. Strong base

Answer: D. Strong base

8. Hydrochloric acid is generally standardized using:

A. Sodium carbonate
B. Sodium chloride
C. Calcium carbonate
D. Sodium bicarbonate

Answer: A. Sodium carbonate

9. Sodium hydroxide solution should be stored in:
A. Copper container
B. Open flask
C. Airtight plastic bottle
D. Iron vessel

Answer: C. Airtight plastic bottle

10. Sodium hydroxide solution absorbs _____ from air.
A. Oxygen
B. Nitrogen
C. Carbon dioxide
D. Hydrogen

Answer: C. Carbon dioxide

11. Which is used as a primary standard for NaOH standardization?
A. Hydrochloric acid
B. Oxalic acid
C. Sulphuric acid
D. Nitric acid

Answer: B. Oxalic acid

12. In a strong acid–strong base titration, the pH at the equivalence point is:
A. 3
B. 5
C. 7
D. 9

Answer: C. 7

13. The equivalence point of a weak acid–strong base titration is:
A. Less than 7
B. Equal to 7
C. Greater than 7
D. Equal to 1

Answer: C. Greater than 7

14. Which indicator is most suitable for a weak acid–strong base titration?
A. Methyl orange
B. Phenolphthalein
C. Methyl red
D. Bromophenol blue

Answer: B. Phenolphthalein

15. A neutralization curve represents:
A. Temperature versus time
B. pH versus volume of titrant added
C. Conductivity versus pressure
D. Volume versus concentration

Answer: B. pH versus volume of titrant added

16. Which acid–base titration shows the sharpest change in pH at the equivalence point?

A. Strong acid–strong base
B. Weak acid–weak base
C. Strong acid–weak base
D. Weak acid–strong base

Answer: A. Strong acid–strong base

17. Ammonium hydroxide is:
A. Strong acid
B. Weak acid
C. Strong base
D. Weak base

Answer: D. Weak base

18. During the assay of ammonium hydroxide, the indicator commonly used is:
A. Phenolphthalein
B. Methyl orange
C. Starch
D. Ferroin

Answer: B. Methyl orange

19. Acid–base titrations are based on the principle of:
A. Oxidation
B. Reduction
C. Neutralization
D. Precipitation

Answer: C. Neutralization

20. Which of the following is NOT an acid–base indicator?
A. Phenolphthalein
B. Methyl orange
C. Starch
D. Methyl red

Answer: C. Starch

Non-Aqueous Titrations

21. The primary purpose of non-aqueous titration is to determine:
A. Strong acids only
B. Strong bases only
C. Weakly acidic and weakly basic substances
D. Neutral salts

Answer: C. Weakly acidic and weakly basic substances

22. Non-aqueous titrations are preferred when:
A. The analyte is highly soluble in water
B. The analyte reacts completely in water
C. The analyte is poorly soluble or weakly ionized in water
D. Water is the best solvent

Answer: C. The analyte is poorly soluble or weakly ionized in water

23. Which of the following is a protogenic solvent?
A. Glacial acetic acid
B. Liquid ammonia
C. Pyridine
D. Benzene

Answer: A. Glacial acetic acid

24. A protophilic solvent is one that:

A. Donates protons
B. Accepts protons
C. Is chemically inert
D. Forms precipitates

Answer: B. Accepts protons

25. Which of the following is a protophilic solvent?
A. Glacial acetic acid
B. Liquid ammonia
C. Formic acid
D. Sulphuric acid

Answer: B. Liquid ammonia

26. Benzene and chloroform are classified as:
A. Amphiprotic solvents
B. Aprotic solvents
C. Protogenic solvents
D. Protophilic solvents

Answer: B. Aprotic solvents

27. Which solvent is most commonly used in non-aqueous acidimetric titrations?
A. Water
B. Glacial acetic acid
C. Ethanol
D. Acetone

Answer: B. Glacial acetic acid

28. The commonly used titrant for non-aqueous acidimetric titration is:
A. Sodium hydroxide
B. Hydrochloric acid
C. Perchloric acid
D. Sulphuric acid

Answer: C. Perchloric acid

29. Perchloric acid used in non-aqueous titration is generally prepared in:
A. Water
B. Glacial acetic acid
C. Ethanol
D. Methanol

Answer: B. Glacial acetic acid

30. Which of the following is commonly used as a basic titrant in non-aqueous titration?
A. Sodium hydroxide
B. Potassium permanganate
C. Sodium methoxide
D. Hydrochloric acid

Answer: C. Sodium methoxide

31. Sodium methoxide solution is prepared in:
A. Water
B. Methanol
C. Acetic acid
D. Benzene

Answer: B. Methanol

32. Crystal violet is commonly used as an indicator in:
A. Redox titrations
B. Non-aqueous acidimetric titrations
C. Complexometric titrations
D. Argentometric titrations

Answer: B. Non-aqueous acidimetric titrations

33. Which acid is standardized using potassium hydrogen phthalate in non-aqueous titration?
A. Nitric acid
B. Sulphuric acid
C. Perchloric acid
D. Hydrochloric acid

Answer: C. Perchloric acid

34. Which of the following drugs can be assayed by non-aqueous titration?
A. Sodium chloride
B. Aspirin
C. Ephedrine hydrochloride
D. Potassium chloride

Answer: C. Ephedrine hydrochloride

35. Sodium benzoate is:
A. Strongly acidic
B. Weakly acidic salt
C. Weakly basic salt
D. Neutral compound

Answer: B. Weakly acidic salt

36. Sodium benzoate is estimated by:
A. Aqueous acid-base titration only
B. Non-aqueous acid-base titration
C. Redox titration
D. Gravimetric analysis

Answer: B. Non-aqueous acid-base titration

37. Which property makes glacial acetic acid suitable for non-aqueous titration?
A. High electrical conductivity
B. Enhances the strength of weak bases
C. Forms precipitates with drugs
D. Neutralizes all acids

Answer: B. Enhances the strength of weak bases

38. Which of the following is an amphiprotic solvent?
A. Water
B. Benzene
C. Chloroform
D. Carbon tetrachloride

Answer: A. Water

39. In non-aqueous titration, the endpoint is detected using:
A. Metal ion indicators
B. Acid-base indicators suitable for non-aqueous media
C. Starch indicator
D. Potassium chromate

Answer: B. Acid-base indicators suitable for non-aqueous media

40. The major advantage of non-aqueous titration is:

A. It is useful only for strong acids.
B. It allows accurate estimation of weak acids and weak bases that cannot be titrated satisfactorily in water.
C. It does not require indicators.
D. It eliminates the need for standardization.

Answer: B. It allows accurate estimation of weak acids and weak bases that cannot be titrated satisfactorily in water.

Precipitation Titrations and Gravimetry

41. Gravimetric analysis is based on the measurement of:
A. Volume
B. pH
C. Weight (mass)
D. Conductivity

Answer: C. Weight (mass)

42. The first step in gravimetric analysis is:
A. Drying the precipitate
B. Filtration
C. Precipitation of the analyte
D. Ignition

Answer: C. Precipitation of the analyte

43. Which of the following is NOT a step in gravimetric analysis?
A. Precipitation
B. Digestion
C. Filtration
D. Neutralization

Answer: D. Neutralization

44. Digestion of a precipitate is carried out to:
A. Dissolve the precipitate
B. Increase crystal size and purity
C. Change the color of the precipitate
D. Increase acidity

Answer: B. Increase crystal size and purity

45. In gravimetric analysis, washing the precipitate is done to:
A. Increase its weight
B. Remove impurities and adhering electrolytes
C. Dissolve the precipitate
D. Change its composition

Answer: B. Remove impurities and adhering electrolytes

46. Which silver salt is formed during the estimation of chloride by precipitation titration?
A. Silver sulphate
B. Silver nitrate
C. Silver chloride
D. Silver carbonate

Answer: C. Silver chloride

47. Mohr's method is based on:
A. Acid-base reaction
B. Complex formation
C. Precipitation reaction
D. Oxidation-reduction

Answer: C. Precipitation reaction

48. In Mohr's method, the titrant used is:
A. Sodium chloride
B. Silver nitrate
C. Potassium permanganate
D. Sodium thiosulphate

Answer: B. Silver nitrate

49. Which indicator is used in Mohr's method?
A. Starch
B. Potassium chromate
C. Ferroin
D. Eriochrome Black T

Answer: B. Potassium chromate

50. The endpoint in Mohr's method is indicated by the appearance of:
A. Blue color
B. Brick-red precipitate
C. Pink color
D. Yellow solution

Answer: B. Brick-red precipitate

51. Volhard's method is performed in:
A. Neutral medium
B. Alkaline medium
C. Acidic medium
D. Basic medium only

Answer: C. Acidic medium

52. In Volhard's method, the excess silver nitrate is titrated with:
A. Sodium hydroxide
B. Potassium thiocyanate
C. Hydrochloric acid
D. Sodium chloride

Answer: B. Potassium thiocyanate

53. Which indicator is used in Volhard's method?
A. Potassium chromate
B. Ferric ammonium sulphate
C. Starch
D. Phenolphthalein

Answer: B. Ferric ammonium sulphate

54. The endpoint in Volhard's method is indicated by the appearance of:
A. Blue color
B. Permanent red-brown color
C. Green precipitate
D. Yellow solution

Answer: B. Permanent red-brown color

55. In the Modified Volhard's method, chloroform is used to:
A. Dissolve silver nitrate
B. Prevent dissolution of silver chloride by coating the precipitate
C. Increase acidity
D. Act as an indicator

Answer: B. Prevent dissolution of silver chloride by coating the precipitate

56. Fajans method uses:
A. Acid-base indicators
B. Adsorption indicators
C. Metal ion indicators
D. Redox indicators

Answer: B. Adsorption indicators

57. Which of the following is an adsorption indicator used in Fajans method?
A. Fluorescein
B. Starch
C. Ferroin
D. Methyl orange

Answer: A. Fluorescein

58. Barium is estimated gravimetrically as:
A. Barium chloride
B. Barium sulphate
C. Barium nitrate
D. Barium carbonate

Answer: B. Barium sulphate

59. Barium sulphate is preferred in gravimetric estimation because it is:
A. Highly soluble in water
B. Volatile
C. Highly insoluble and stable
D. Colored

Answer: C. Highly insoluble and stable

60. Which of the following methods is NOT a precipitation titration?
A. Mohr's method
B. Volhard's method
C. Fajans method
D. Cerimetry

Answer: D. Cerimetry

Complexometric Titrations

61. Complexometric titrations are based on the formation of:
A. Precipitates
B. Neutral salts
C. Coordination complexes
D. Oxides

Answer: C. Coordination complexes

62. The most commonly used titrant in complexometric titrations is:
A. Hydrochloric acid
B. Potassium permanganate
C. Disodium EDTA
D. Sodium thiosulphate

Answer: C. Disodium EDTA

63. EDTA stands for:
A. Ethylene Diamine Tetraacetic Acid
B. Ethyl Diamine Triacetic Acid
C. Ethylene Dicarboxylic Acid
D. Ethyl Dinitro Tetraacetic Acid

Answer: A. Ethylene Diamine Tetraacetic Acid

64. EDTA forms complexes with most metal ions in which ratio?
A. 2 : 1
B. 1 : 2
C. 1 : 1
D. 3 : 1

Answer: C. 1 : 1

65. Which of the following is a primary standard used for the standardization of disodium EDTA?
A. Calcium carbonate
B. Sodium chloride
C. Potassium nitrate
D. Oxalic acid

Answer: A. Calcium carbonate

66. The indicator commonly used in the estimation of magnesium by EDTA titration is:
A. Methyl orange
B. Eriochrome Black T
C. Phenolphthalein
D. Starch

Answer: B. Eriochrome Black T

67. Eriochrome Black T gives a _____ color with magnesium ions before the endpoint.
A. Yellow
B. Wine red
C. Blue
D. Green

Answer: B. Wine red

68. At the endpoint of an EDTA titration using Eriochrome Black T, the solution changes from:
A. Blue to red
B. Red to yellow
C. Wine red to blue
D. Green to pink

Answer: C. Wine red to blue

69. The optimum pH for the estimation of magnesium using EDTA is:
A. 2
B. 5
C. 10
D. 13

Answer: C. 10

70. Which buffer is commonly used in magnesium EDTA titration?

A. Acetate buffer
B. Phosphate buffer
C. Ammonia–ammonium chloride buffer
D. Citrate buffer

Answer: C. Ammonia–ammonium chloride buffer

71. A masking agent is used to:
A. Increase the concentration of EDTA
B. Prevent interference from unwanted metal ions
C. Change the color of the indicator
D. Increase acidity

Answer: B. Prevent interference from unwanted metal ions

72. Which of the following is a masking agent?
A. Potassium cyanide
B. Hydrochloric acid
C. Sodium hydroxide
D. Potassium permanganate

Answer: A. Potassium cyanide

73. Demasking is the process of:
A. Destroying the indicator
B. Releasing a masked metal ion for titration
C. Removing EDTA
D. Dissolving the precipitate

Answer: B. Releasing a masked metal ion for titration

74. Which type of indicator is used in complexometric titrations?
A. Adsorption indicator
B. Metal ion indicator
C. Acid-base indicator
D. Redox indicator

Answer: B. Metal ion indicator

75. Which of the following is a metal ion indicator?
A. Starch
B. Eriochrome Black T
C. Methyl orange
D. Potassium chromate

Answer: B. Eriochrome Black T

76. Calcium gluconate is assayed by:
A. Acid-base titration
B. Complexometric titration using EDTA
C. Redox titration
D. Gravimetric analysis

Answer: B. Complexometric titration using EDTA

77. Magnesium sulphate is estimated by:
A. Argentometric titration
B. Complexometric titration
C. Iodometric titration
D. Cerimetric titration

Answer: B. Complexometric titration

78. The endpoint in EDTA titration occurs when:
A. The metal ion is completely precipitated.
B. All metal ions have formed complexes with EDTA.
C. The solution becomes acidic.
D. A gas is evolved.

Answer: B. All metal ions have formed complexes with EDTA.

79. Which statement about EDTA is correct?
A. It reacts only with calcium ions.
B. It forms stable complexes with many metal ions.
C. It is used only in acid-base titrations.
D. It acts as an oxidation indicator.
Answer: B. It forms stable complexes with many metal ions.

80. Which of the following is NOT used in complexometric titration?
A. Disodium EDTA
B. Eriochrome Black T
C. Ammonia buffer
D. Potassium permanganate

Answer: D. Potassium permanganate

Redox Titrations

81. Oxidation is defined as:
A. Gain of electrons
B. Loss of electrons
C. Gain of hydrogen
D. Loss of oxygen

Answer: B. Loss of electrons

82. Reduction is the process involving:
A. Loss of electrons
B. Gain of electrons
C. Gain of oxygen
D. Loss of hydrogen

Answer: B. Gain of electrons

83. A substance that accepts electrons and undergoes reduction is called:
A. Reducing agent
B. Oxidizing agent
C. Catalyst
D. Indicator

Answer: B. Oxidizing agent

84. Which of the following is a strong oxidizing agent commonly used in redox titrations?
A. Sodium hydroxide
B. Potassium permanganate
C. Sodium chloride
D. Oxalic acid

Answer: B. Potassium permanganate

85. Permanganometric titrations use:
A. Potassium dichromate
B. Potassium permanganate
C. Sodium thiosulphate
D. Ceric sulphate

Answer: B. Potassium permanganate

86. Potassium permanganate acts as:

A. A self-indicator
B. An adsorption indicator
C. A metal ion indicator
D. A fluorescent indicator

Answer: A. A self-indicator

87. The end point in permanganometric titration is indicated by the appearance of:
A. Blue color
B. Green color
C. Permanent pale pink color
D. Yellow color

Answer: C. Permanent pale pink color

88. Potassium permanganate solutions are standardized using:
A. Sodium chloride
B. Oxalic acid
C. Hydrochloric acid
D. Potassium iodide

Answer: B. Oxalic acid

89. Permanganometric titrations are generally carried out in the presence of:
A. Hydrochloric acid
B. Nitric acid
C. Dilute sulphuric acid
D. Acetic acid

Answer: C. Dilute sulphuric acid

90. Cerimetry involves the use of:
A. Ceric ammonium sulphate
B. Potassium permanganate
C. Sodium thiosulphate
D. Potassium iodide

Answer: A. Ceric ammonium sulphate

91. The oxidation state of cerium in cerimetry is:
A. +2
B. +3
C. +4
D. +6

Answer: C. +4

92. Which indicator is commonly used in cerimetry?
A. Starch
B. Ferroin
C. Methyl orange
D. Phenolphthalein

Answer: B. Ferroin

93. Iodimetry is a titration in which:
A. Iodine acts as the oxidizing agent.
B. Sodium thiosulphate is the oxidizing agent.
C. Potassium permanganate is reduced.
D. Ceric ions are reduced.

Answer: A. Iodine acts as the oxidizing agent.

94. Iodometry is based on the titration of liberated iodine with:
A. Sodium hydroxide
B. Hydrochloric acid
C. Sodium thiosulphate
D. Potassium permanganate

Answer: C. Sodium thiosulphate

95. Which indicator is used in iodometric titrations?
A. Methyl red
B. Phenolphthalein
C. Starch
D. Eriochrome Black T

Answer: C. Starch

96. Starch indicator is added:
A. At the beginning of every iodometric titration
B. Near the end point
C. Before adding iodine
D. After completion of the titration

Answer: B. Near the end point

97. The blue color in iodometric titration is due to the formation of:
A. Iodine–starch complex
B. Sodium iodide
C. Potassium iodide
D. Cerium complex

Answer: A. Iodine–starch complex

98. Potassium iodate is a:
A. Reducing agent
B. Weak acid
C. Primary standard oxidizing agent
D. Complexing agent

Answer: C. Primary standard oxidizing agent

99. Which of the following is NOT a type of redox titration?
A. Permanganometry
B. Cerimetry
C. Iodometry
D. Complexometric

Answer: D. Complexometric

100. The main principle of redox titration is:

A. Formation of precipitate
B. Neutralization reaction
C. Electron transfer between oxidizing and reducing agents
D. Formation of a colored complex

Answer: C. Electron transfer between oxidizing and reducing agents

Short Answer Type Questions (Objective type questions):

1. Define acid-base titration.
2. List the theories of acid-base indicators.
3. Define neutralization curve.
4. Name the primary standard used for standardization of hydrochloric acid.
5. Name the primary standard used for standardization of sodium hydroxide.
6. Define non-aqueous titration.
7. List the types of solvents used in non-aqueous titrations.
8. Define gravimetric analysis.
9. List the steps involved in gravimetric analysis.
10. Define adsorption indicator with one example.
11. Define complexometric titration.
12. Classify complexometric titrations.
13. Define oxidation and reduction.
14. List the different types of redox titrations.
15. Name the indicator used in iodometric titrations.

16. Classify acid-base titrations with suitable examples.
17. Explain why different indicators are selected for strong acid–strong base and weak acid–strong base titrations.
18. Explain the principle of standardization of hydrochloric acid.
19. Why are non-aqueous titrations preferred for weak acidic and weak basic substances?
20. Explain the principle of estimation of sodium benzoate by non-aqueous titration.
21. Explain the principle of Mohr's method.
22. Describe the role of potassium chromate in Mohr's method.
23. Explain masking and demasking reagents with one example each.
24. Why is EDTA known as a universal complexing agent?
25. Explain the principle involved in the estimation of calcium gluconate by EDTA titration.
26. Explain the principle of permanganometry.
27. Describe the role of potassium iodate in redox titrations.
28. Explain the principle of cerimetry.

Long Answer Type Questions

1. Discuss the theories of acid-base indicators with suitable examples.

2. Explain the preparation, standardization, and pharmaceutical applications of hydrochloric acid and sodium hydroxide as titrants.

3. Explain the principles of non-aqueous titrations and discuss the different types of solvents with suitable examples.
4. Describe the preparation and standardization of acidic and basic non-aqueous titrants.
5. Explain the principle, procedure, and estimation of sodium benzoate by non-aqueous titration.
6. Discuss the principle and various steps involved in gravimetric analysis. Explain the estimation of barium sulphate by gravimetry.
7. Describe the classification of complexometric titrations. Explain the role of metal ion indicators, masking agents, and demasking agents.
8. Explain the preparation and standardization of disodium EDTA and discuss its pharmaceutical applications.
9. Discuss the concepts of oxidation and reduction. Explain the principles and applications of permanganometry and cerimetry.

10. Explain the principles, reactions, and pharmaceutical applications of iodimetry, iodometry, and potassium iodate titrations.

11. Explain the assay of ammonium hydroxide with principle, reaction, calculations, and precautions.

12. Explain the estimation of magnesium sulphate by complexometric titration with principle, reaction, calculations, and precautions.

13. Explain the estimation of calcium gluconate by complexometric titration with principle, reaction, calculations, and precautions.

14. Explain the theory of acid-base titrations with suitable neutralization curves for strong acid–strong base, weak acid–strong base, weak base–strong acid, and weak acid–weak base titrations.

15. Compare acid-base, non-aqueous, precipitation, complexometric, and redox titrations with respect to principle, titrant, indicator, end-point detection, advantages, limitations, and pharmaceutical applications.

Question Bank
Acid–Base Titrations

Short Answer Questions (2 Marks)

1. Define acid–base titration.
2. State Ostwald's theory of acid–base indicators.
3. What is the Quinonoid theory of indicators?
4. Classify acid–base titrations with examples.
5. Why is hydrochloric acid not a primary standard?
6. Why is sodium hydroxide stored in a polyethylene bottle?
7. Name two indicators used in acid–base titrations.
8. What is the difference between endpoint and equivalence point?
9. Which indicator is suitable for strong acid–weak base titration? Justify your answer.
10. Why is phenolphthalein not suitable for strong acid–weak base titration?
11. State the principle of ammonium hydroxide assay.
12. What is meant by a neutralization curve?
13. Predict the pH at the equivalence point of a strong acid–strong base titration.
14. Why are neutralization curves useful in analytical chemistry?
15. Write one application of acid–base titration.

Long Answer Questions (5 Marks)

1. Explain Ostwald's and Quinonoid theories of acid–base indicators with suitable examples.
2. Discuss the classification of acid–base titrations with appropriate examples.
3. Describe the preparation and standardization of hydrochloric acid.
4. Explain the preparation and standardization of sodium hydroxide solution.
5. Compare strong acid–strong base and weak acid–strong base titrations with suitable neutralization curves.
6. Explain the theory involved in the titration of strong, weak, and very weak acids and bases.
7. Discuss the factors affecting the selection of acid–base indicators.
8. Explain the assay of ammonium hydroxide with principle, reactions, procedure, and calculations.

Very Long Answer Questions (10 Marks)

1. Explain acid–base indicators in detail, including theories, properties, pH range, and applications.
2. Discuss the classification of acid–base titrations, theory of titrations, neutralization curves, and indicators used.
3. Describe the preparation, standardization, precautions, calculations, and applications of hydrochloric acid and sodium hydroxide titrants.
4. Explain the assay of ammonium hydroxide with principle, reactions, procedure, calculations, precautions, and applications.

Non-Aqueous Titrations

Short Answer Questions (2 Marks)

1. Define non-aqueous titration.
2. Why are non-aqueous titrations required?
3. Define proteogenic solvent with one example.
4. Define protophilic solvent with one example.
5. Define amphiprotic solvent.
6. What is an aprotic solvent?
7. Name two non-aqueous indicators.
8. Why is glacial acetic acid commonly used?
9. What is acidimetric non-aqueous titration?
10. What is alkalimetric non-aqueous titration?
11. Why is sodium benzoate estimated by non-aqueous titration?
12. Name the titrant used for weak acids.
13. Name the titrant used for weak bases.
14. Mention one limitation of aqueous titration.
15. State one pharmaceutical application of non-aqueous titration.

Long Answer Questions (5 Marks)

1. Explain the principle of non-aqueous titration.
2. Classify non-aqueous solvents with suitable examples.
3. Describe acidimetric and alkalimetric non-aqueous titrations.
4. Explain the preparation and standardization of perchloric acid.
5. Describe the preparation and standardization of sodium methoxide.
6. Explain the estimation of sodium benzoate.
7. Compare aqueous and non-aqueous titrations.

Very Long Answer Questions (10 Marks)

1. Explain non-aqueous titrations in detail, including principle, solvent classification, indicators, titrants, advantages, limitations, and applications.
2. Describe the preparation, standardization, and pharmaceutical applications of acidic and basic non-aqueous titrants.
3. Explain the estimation of weakly acidic and weakly basic substances by non-aqueous titration.

Precipitation Titrations and Gravimetry

Short Answer Questions (2 Marks)

1. Define gravimetric analysis.
2. List the steps involved in gravimetric analysis.
3. What is digestion?
4. Define supersaturation.
5. Define nucleation.
6. State the principle of Mohr's method.
7. Why should Mohr's titration be carried out in neutral medium?
8. What is the indicator used in Volhard's method?
9. Why is chloroform added in modified Volhard's method?
10. What is an adsorption indicator?
11. Name the indicator used in Fajans method.
12. State one application of gravimetry.
13. Why is barium sulphate suitable for gravimetric estimation?
14. Differentiate between direct and back titration.
15. Mention one advantage of Fajans method.

Long Answer Questions (5 Marks)

1. Explain the principle and steps involved in gravimetric analysis.
2. Describe Mohr's method with reactions and applications.
3. Explain Volhard's method in detail.
4. Discuss the modified Volhard's method.
5. Explain the principle and procedure of Fajans method.
6. Compare Mohr's, Volhard's, and Fajans methods.
7. Explain the estimation of barium sulphate by gravimetry.

Very Long Answer Questions (10 Marks)

1. Explain gravimetric analysis in detail with principle, procedure, factors affecting precipitation, advantages, limitations, and applications.
2. Discuss precipitation titrations in detail with Mohr's, Volhard's, Modified Volhard's, and Fajans methods, including reactions, procedures, advantages, limitations, and applications.
3. Explain the estimation of barium sulphate by gravimetric analysis with calculations and precautions.

Complexometric Titrations

Short Answer Questions (2 Marks)

1. Define complexometric titration.
2. What is EDTA?
3. Why is EDTA called a hexadentate ligand?
4. Define masking agent.
5. Define demasking agent.
6. Name two masking agents.
7. Name two metal ion indicators.
8. What is the role of ammonia buffer?
9. Why is pH important in complexometric titration?
10. What is the colour change of Eriochrome Black T?
11. Why is EDTA not a primary standard?
12. State one application of EDTA titration.
13. Which indicator is used for calcium estimation?
14. Which indicator is used for magnesium estimation?
15. State one advantage of complexometric titration.

Long Answer Questions (5 Marks)

1. Explain the principle and classification of complexometric titrations.
2. Discuss metal ion indicators with suitable examples.
3. Explain masking and demasking reagents with examples.
4. Describe the preparation and standardization of disodium EDTA.
5. Explain the estimation of magnesium sulphate.
6. Explain the estimation of calcium gluconate.
7. Compare Eriochrome Black T and Murexide indicators.

Very Long Answer Questions (10 Marks)

1. Explain complexometric titrations in detail with principle, classification, indicators, masking and demasking agents, advantages, limitations, and applications.
2. Describe the preparation, standardization, and pharmaceutical applications of disodium EDTA.
3. Explain the estimation of magnesium sulphate and calcium gluconate with reactions, procedures, calculations, and precautions.

Redox Titrations

Short Answer Questions (2 Marks)

1. Define oxidation and reduction.
2. Differentiate between oxidizing and reducing agents.
3. Classify redox titrations.
4. Why is potassium permanganate called a self-indicator?
5. Why is sulphuric acid preferred in permanganometry?
6. Why is hydrochloric acid not used in permanganometry?
7. Define cerimetry.
8. Name one indicator used in cerimetry.
9. Differentiate between iodimetry and iodometry.
10. Why is starch added near the endpoint in iodometry?
11. Why is sodium thiosulphate not a primary standard?
12. Why is potassium iodate considered a primary standard?
13. Name two primary standards used for sodium thiosulphate standardization.
14. State one application of potassium iodate titration.
15. Why is oxalic acid heated during permanganate titration?

Long Answer Questions (5 Marks)

1. Explain the concepts of oxidation and reduction with suitable examples.
2. Describe permanganometry with principle, reactions, procedure, and applications.
3. Explain cerimetry in detail.
4. Differentiate between iodimetry and iodometry.
5. Explain the standardization of sodium thiosulphate using potassium iodate.
6. Explain potassium iodate titrations with principle and reactions.
7. Compare permanganometry and cerimetry.

Very Long Answer Questions (10 Marks)

1. Explain redox titrations in detail, including the concepts of oxidation and reduction and the classification of redox titrations.
2. Describe permanganometry, cerimetry with principles, reactions, procedures, indicators, advantages, limitations, and applications.
3. Explain potassium iodate titrations and the standardization of sodium thiosulphate using potassium iodate with reactions, calculations, precautions, and pharmaceutical applications.