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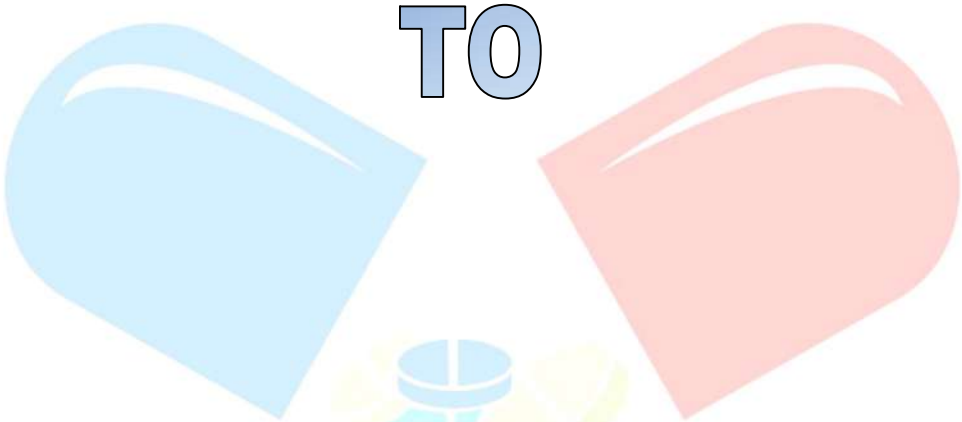

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PHARMACEUTICAL ANALYSIS I

UNIT 2

TOPIC :

- **Non aqueous titration :** Solvents, acidimetry and alkalimetry titration and estimation of Sodium benzoate and Ephedrine HCl

Non – Aqueous titration

→ Titration involving very weak acid or base with the help of non-aqueous solvents to obtain sharp end point are non-aqueous titration.

Principle

★ Organic acids & bases are water insoluable very weak & cannot be analysed via conventional titration method thus non-aqueous titration is used which relies on the principle that non-aqueous solvents are used to dissolve the sample.

Non-Aqueous Solvents

- The nature of solvent is a deciding factor for the behaviour of acid & base. Any solute when dissolved in any given solvent with exhibit acidic or alkaline behaviour
- The Non-aqueous solvents have a characteristic role in non-aqueous titration
  1. The solvent should be non-toxic for its wide use in analysis
  2. It should is liquid at he time of analysis
- These organic solvent are used but it is mainly depents on their properties such as capability of self dissociation dielectric constant & acid base character of solvent

The non-aqueous solvents are classified into

- **Aprotic solvent :**
  - These solvents are considered chemical neutral or inert under specific condition
  - Eg toluene & carbon tetrachloride
  - These solvents have low dielectric constant which restrict the inosiation of solute and there is no reaction between there solvent & acid s and bases

- The Aprotic solvents are widely used as diluting agent for the reaction mixture

- **Protophilic solvents :-** Solvents which have greater tendency to accept proton **Eg :** Water, Alcohol

- **Protogenic solvents :-** These solvents posses acidic character & have high affinity for donating protons **Eg :** Alcohol , Organic acid

- **Amphiprotic solvents :-** In this solvents have the ability to donate as well as accept proton because they caotain both protegenic & protophilic properties. **Eg :** Water , Alcohol , & Organic acid (weak)

Frequently used non-aqueous solvents

★ For the determination of non-aqueous titration there are several solvents available (either organic or inorganic) but only few of them are employed for the purpose
★ The solvent used must be pure,Dry,& best analytical qualities to ensure precise and sharp end point
★ Alcolols : The organic salts of fatty acid can be determined with the help of glycol & alcohol mixture or glycol & hydrocarbon mixture
★ Dimethylformamide : DMF is an excellemt example of protophilic solvent 7 is used for the titration of benzonic acid 7 amide
★ Glacial Acetic Acid : Acetonitrile , Rioxane etc

Advantages of non-aqueous solvents

✓ The acids & bases of organic origin are easily soluable in non-aqueous solvent
✓ Non-aqueous solvent can dissolve two or more acids present in a mixture

- ✓ With the help of a suitable solvent or indicator the selective titrtion of biological ingredients present in a substance can be done whether it is acidic or basic
- ✓ Titration involving non-aqueous are comparatively simple & more accurate than aqueous titration

Indicators in Non-Aqueous Solvents

- A very narrow range of indicator are present which employed in non-aqueous titration
- Methyl Red : A 0.2 % W/V solution of Methyl Red is prepared using dioxane The end point is marked by a change in colour from yellow to red
- Naphthol Benzene :- Nephthol Benzene is used as a solution of 0.2 % W/V in acetic acid. It gives a sharp end point by changing its colour from yellow to green
- Thymol Blue : It is a widely used indicator especially for the substance behaves as acids in solution of DMF
- 0.2 % W/V solution is prepared using methyl alcohol & the end point detected by change in colour from yellow to blue

Application

The application of Non-Aqueous titration are

- Percentage of purity is determined by the assays
- Determination of Hydrophobic compounds
- Determination of the steroids
- Determination of Anti Tubercular drugs
- Determination of phenoburbitone

Types of Non-Aqueous titration

- It is Classify into two types :
  1. Acidimetry
  2. Alkalimetry

1. Acidimetry

→ Acidimetry used to determine the concentration of base substances using standard acid.

→ In acidimetry, a known volume of a base is put into a conical flask. This solution is then titrated against a standard solution of acid taken in a burette till an equivalent quantity of acid is added to base. The point at which the acid and base are added in equivalent amount is termed as the equivalent point.

→ Here in acidimetry

- Acid should be taken in burette
- Base should be taken in conical flask

→ Used to determine the concentration of base using acid

2. Alkalimetry

→ Alkalimetry used to determine the concentration of acid substances using standard base.

→ In alkalimetry a known volume of an acid is put into a conical flask. This solution is then titrated against a standard solution of base taken in a burette till an equivalent quantity of base is added to the acid. The point at which the acid and base are added in equivalent amount is termed as the equivalent point.

→ Here in Alkalimetry

- Acid should be taken in conical flask
- Base should be taken in burette

→ Used to determine the concentration of acid using base

Estimation of Sodium Benzoate

Purpose:

→ To quantitatively estimate the amount of Sodium Benzoate, a weakly acidic salt, using non-aqueous titration (alkalimetry).

Principle:

- Sodium benzoate acts as a weak acid in non-aqueous media.
- It is titrated with a standard solution of sodium methoxide in methanol.
- Thymol blue or azo violet is used as an indicator.
- The reaction is a neutralization between sodium benzoate and sodium methoxide.

Reaction:

$$C_6H_5COONa + CH_3ONa \rightarrow C_6H_5COOCH_3 + NaOH$$

Solvent Used:

- Glacial acetic acid (for solubilizing the sample)
- Sometimes methanol or a mixture of methanol and acetic acid

Titrant:

- Sodium methoxide (0.1 N) in methanol

Indicator:

- Thymol blue
  or
- Azo violet
  (Changes color at the endpoint in non-aqueous medium)

Procedure:

1. Weigh accurately about 0.5–1.0 g of Sodium Benzoate.
2. Dissolve in 25–50 mL of glacial acetic acid.
3. Add 2–3 drops of thymol blue indicator.
4. Titrate against standard sodium methoxide solution.
5. Endpoint: Color change from red to yellow (or purple to green, depending on indicator).

Calculation Formula:

Amount of Sodium Benzoate=V×N×M / 1000

Where:

- **V** = Volume of titrant used (mL)
- **N** = Normality of sodium methoxide
- **M** = Molecular weight of sodium benzoate = **144.11 g/mol**

Applications:

- Quality control of preservatives in pharmaceutical and food industries.
- Standardization of sodium benzoate in bulk drug and dosage forms.
- Used in non-aqueous titration methods for weak acid substances.

Precautions:

- Use dry glassware to avoid reaction with water.
- Store sodium methoxide in airtight containers (it's moisture sensitive).
- Use freshly prepared indicator solution.

Estimation of Ephedrine Hydrochloride

Purpose:

- To quantitatively estimate the amount of Ephedrine HCl, a weakly basic drug, using non-aqueous titration (acidimetry).

Principle:

- Ephedrine HCl is a weak organic base.
- It is titrated in a non-aqueous medium with standard perchloric acid in glacial acetic acid.
- The endpoint is detected using an appropriate non-aqueous indicator like crystal violet.
- The titration is based on acid-base neutralization.

Reaction:

$$\text{Ephedrine} + HClO_4 \rightarrow \text{Ephedrine}.HClO_4$$

A **salt** of ephedrine with perchloric acid is formed.

Solvent Used:

- **Glacial acetic acid**
  (Acts as a solvent and suppresses ionization to allow sharp endpoint)

Titrant:

- 0.1 N Perchloric acid ($HClO_4$) prepared in glacial acetic acid

Indicator:

- Crystal violet (Color changes from violet → blue-green)
- Alternatively: Oracet Blue

Procedure:

1. Accurately weigh about 0.3–0.5 g of Ephedrine HCl.
2. Dissolve it in 25–50 mL of glacial acetic acid.
3. Add 2–3 drops of crystal violet indicator.
4. Titrate with 0.1 N perchloric acid until the violet color changes to blue-green.
5. Record the volume of titrant used.

Calculation Formula:

Amount of Ephedrine HCl=V×N×M / 1000

Where:

- **V** = Volume of perchloric acid used (mL)
- **N** = Normality of perchloric acid
- **M** = Molecular weight of Ephedrine HCl = **201.7 g/mol**

Applications:

- Used for assaying Ephedrine HCl in bulk and tablet dosage forms.
- Helps in quality control and standardization of basic drug substances.
- Suitable for drugs that are not easily titratable in aqueous media.

Precautions:

- Use dry glassware to avoid moisture interference.
- Perchloric acid should be handled with care (strong oxidizer).
- The titrant and indicator should be freshly prepared.
- Avoid exposure to moisture, as glacial acetic acid is hygroscopic.