Non Aqueous Titration

UNIT-II

- **Acid base titration**: Theories of acid base indicators, classification of acid base titrations and theory involved in titrations of strong, weak, and very weak acids and bases, neutralization curves
- **Non aqueous titration**: Solvents, acidimetry and alkalimetry titration and estimation of Sodium benzoate and Ephedrine HCl

Non Aqueous Titration

They use for the titration of weak acid & weak base because we need sharp end point.

The substance which are not soluble in aqueous medium

- Weak acid :- Acid anhydride, Acid halide, COOH, Amino acid
- Weak bases :- N_2 (containing heterocyclics), Quartnery ammonium compound

Factor affecting Non-Aqueous Titration

1. Temperature

- Non-aqueous solvent have more coefficient of expansion then H_2O
- So small different cause significant error
- Standardisation & Titration should be performed at same temperature

$$Vc = V[1+0.0011\ (t_1 - t_2)]$$

Vc = Corrected volume of titrant

V = Volume of titrant measure

t_1= Temperature at which titration was standardized

t_2= Temperature at which titration was carried out

2. Nature of solvent

3. Solubility of substance being titrated

4. Atmosphere CO_2

End point in titration is determined by 2 ways

a) Potentiometric Titration

b) By use of Indicators

- Solvent selection in Non-aqueous titration :-

Solvent :- Soluble of sample

- Nature of sample
- High dielectric constant

Should give sharp end point

- Low toxicity
- Not expensive
- Easily purified

DEPTH OF BIOLOGY

With the help of Indicator we find end point in Non-aqueous

S.No.	Name	Acidic Medium	Basic Medium
1	Crystal violet	Green	Violet
2	Anapthol benzene	Dark blue	Blue
3	Oracet blue	Pink	Blue
4	Quinaldine red	colourless	Magenta or reddish purple

Solvents

These are those substances which are non-aqueous (other than water) in which a solute particles is dissolved.

These are of four types:-

1. Proteogenic
2. Protophilic
3. Aprotic
4. Amphiprotic

1) **Proteogenic Solvents** :- These are those solvents which are acidic in nature. These solvents are used for weak base.

A solvent that can generate proton or that can donate donate proton

is called Proteogenic solvents.

eg:- Sulphuric acid (H_2SO_4), hydrogen fluoride, HNO_3 (nitric acid) etc.

2) Protophilic Solvents :- These are those solvents which are basic in nature and these solvents are used for weak acid.

A solvent that have the capacity to accept a proton is called Protophilic solvent.

They are able to accept a proton, Protophilic solvent is basic in nature.

Eg:- Dimethyl formamide [$(CH_3)_2NCH$], Pyridine (C_5H_5N)

3) Aprotic Solvents:- Those are those solvents which are neither acidic and nor basic, they considered as neutral and used for neutral substances.

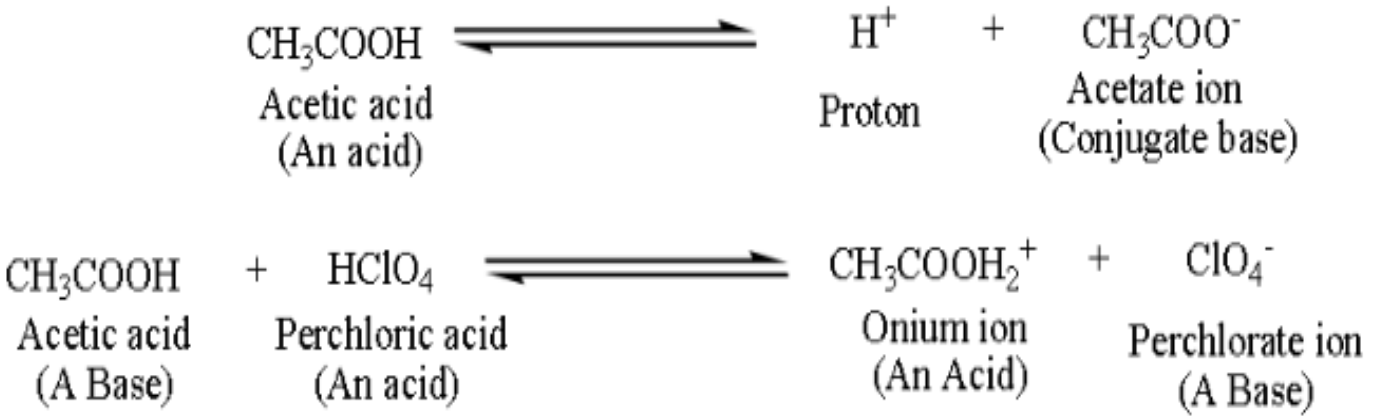
Solvents which are unable to either donate or accept a proton is called Aprotic solvents.

Eg:- Hexane (C_6H_{14}), Carbon tetrachloride [CC_{l4}]

4) Amphiprotic Solvents:- These are those solvents which are acidic as well as basic in nature.

They contain both proteogenic and Protophilic properties

Eg:- water (H_2O), Ethanol [C_2H_5OH] etc.



Levelling Effect

- The weak acids in presence of strong Protophilic solvents

or

- weak base in presence of strong proteogenic solvents enhances the acid character of weak acid or basic character of weak base.
- This is known as Levelling effect.

Advantages of non-aqueous solvents

- Water insoluble drugs are easily soluble
- Helps in titration of weak acids and bases
- To provide sharp end point

Levelling Effect

Common Solvents in non-aqueous titrations

- Glacial acetic acid
- Dimethylformamide
- Acetonitrile
- Dioxan
- Alcohol

Glacial acetic acid

- Glacial acetic 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%.
- A small amount of acetic anhydride may be added to solvent to convert water into acetic acid.

Dimethylformamide

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

Acetonitrile

- Acetonitrile (Methyl cyanide, Cyanmethane) is frequently used with other solvents such as chloroform and phenol and especially with acetic acid.
- It enables very sharp end points to be obtained in the titration of metal ethanoates when titrated with perchloric acid.

Dioxan

1. Dioxan is another popular solvent, which is often used in place of glacial acetic acid when mixtures of substances are to be quantified.
2. Unlike acetic acid, dioxin is not a leveling solvent.

Alcohol

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

Indicators in Non-Aqueous Titrations

Two methods can be employed for end-point detection in non-aqueous titration

1. potentiometric end-point determination
2. visible end-point determination.

The visible end-point determination can be achieved by the use of indicators.

DEPTH OF BIOLOGY

S.No.	Name of Indicator	Concentration	Color change		
			Acidic	Neutral	Alkaline
1	Crystal violet	0.5% w/v in Glacial acetic acid	Yellowish green	Blue green	Violet
2	Methyl red	0.2% w/v in Dioxan	Red	-	Yellow
3	1-Napthol benzoin	0.2% w/v in Glacial acetic acid	Dark green	Orange	Blue or blue green
4	Quinaldine red	0.1% w/v in Ethanol	Almost colorless	-	Magenta
5	Thymol red	0.2% w/v in Methanol	Yellow	-	Blue
6	Oracet Blue B	0.5% w/v in Glacial acetic	Pink	Purple	Blue

ACIDIMETRY

- It is determination of unknown concentration of basic/alkaline solution by using standard acidic solution.
- In non-aqueous, concentration of weak base is determined by using strong acidic solution.
- In this, samples are ephedrine, morphine, adrenaline, caffeine etc…
- Proteogenic solvents (acids) are used

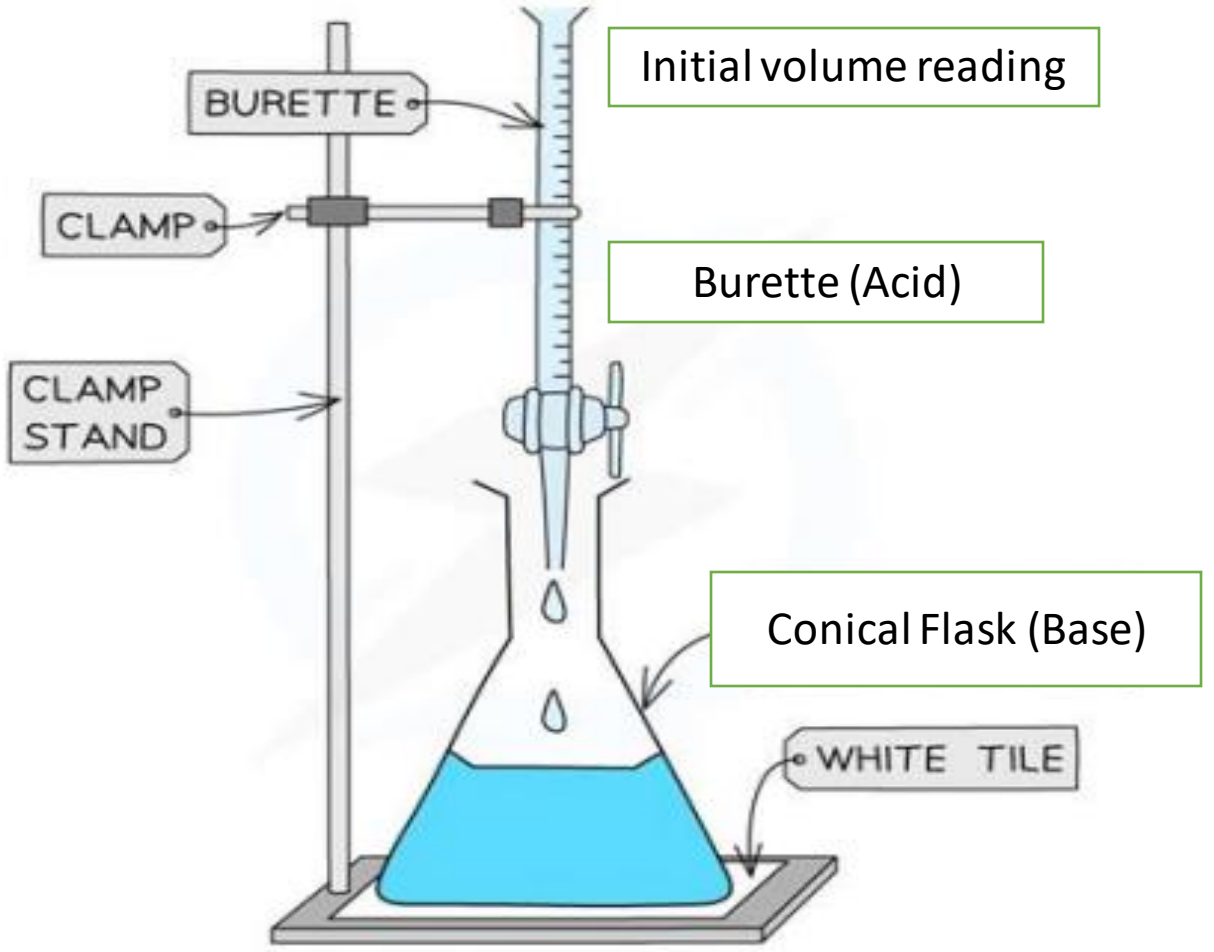
E.g. :- Nitric acid, glacial acetic acids.

ACIDIMETRY

- Titrant used are strong acid

E.g. :- Perchloric acid ($HClO_4$)

Indicator used in this titration is crystal violet, which changes from violet to light green.



ALKALIMETRY

- It is determination of unknown concentration of acidic solution by using standard basic solution.
- In non-aqueous, concentration of weak acid is determined by using strong basic solution.
- In this, samples are Acetazolamide, Nalidixic acid etc.

ALKALIMETRY

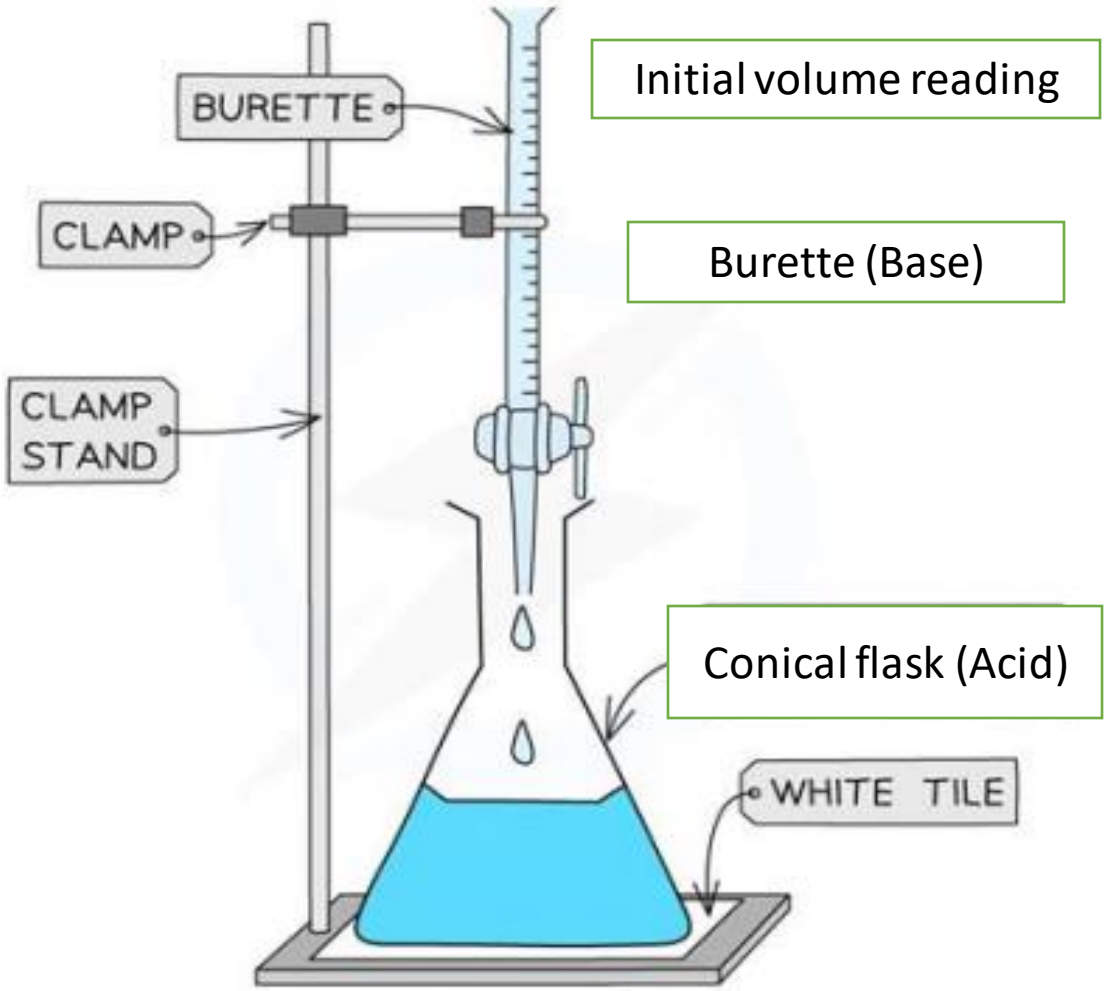
- Protophilic solvents (base) are used

E.g. Dimethylformamide (DMF), Pyridine (C_5H_5N)

- Titrant used are strong base.

E.g. Sodium Methoxide (CH_3ONa)

- Indicator used in this titration is thymol blue, which changes from pink to blue colour.



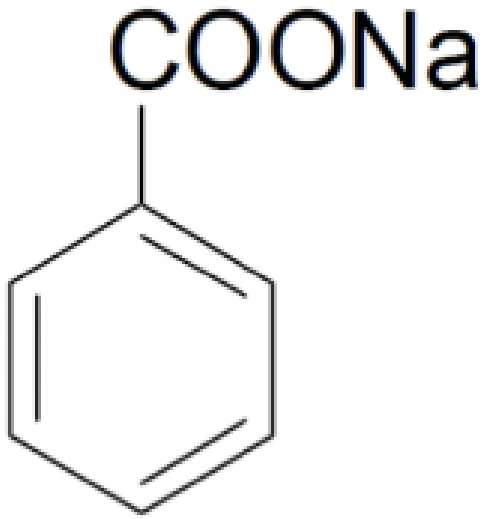
Estimation of Sodium Benzoate

Formula : $C_7H_5NaO_2$

Mol. Wt. 144.1 Sodium

Sodium Benzoate contains not less than 99.0% and not more than 100.5% of $C_7H_5NaO_2$, calculated on the dried basis.

Description: A white, crystalline or granular powder or flakes; odourless or with a faint odour; hygroscopic.



Preparation of 0.1N 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 hour.
- Acetic anhydride absorbs 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.

Standardisation 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 $HClO_4$. The colour changes from blue to blue green.

Assay Procedure

- Weigh accurately about 0.25 g of Sodium Benzoate, dissolve in 20 ml of anhydrous glacial acetic acid, warming to 50º if necessary, cool.
- Titrate with 0.1 M perchloric acid, using 0.05 ml of 1-naphtholbenzein solution as indicator. Carry out a blank titration.

Equivalent or I.P factor

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

$$\% \text{ Sodium Benzoate} = \frac{X \text{ ml} \times \text{Normality (Calculated)} \times 0.01441 \times 100}{N \text{ (Given)} \times \text{Wt. of sample(in gm)}}$$

X ml = Volume of titrant consumed at end point

Normality Calculated = Normality of Perchloric acid

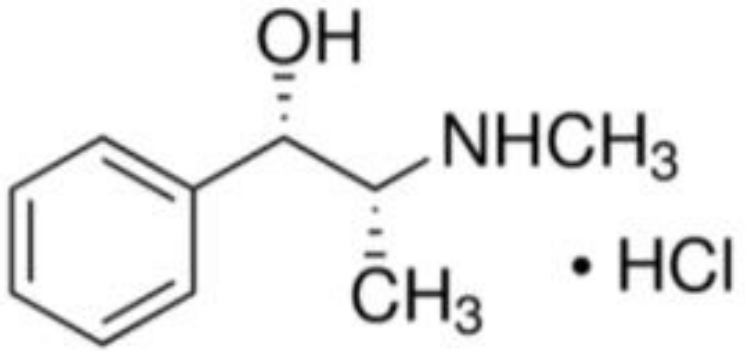
after standardization Normality Given = 0.1 N

(theoretically)

DEPTH OF BIOLOGY

Estimation of Ephedrine Hydrochloride

- **Formula** : $C_{10}H_{15}NO,HCl$
- **Mol. Wt.** 201.7
- Ephedrine Hydrochloride contains not less than 99.0 per cent and not more than 101.0 per cent of
- $C_{10}H_{15}NO,HCl$ calculated on the dried basis.



Description

- Colourless crystals or a white, crystalline powder;
- odourless. It is affected by light.

Preparation of 0.1N solution of $HClO_4$ and its standardization

1. 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 hour.
2. Acetic anhydride absorbed all the water from $HClO_4$ and glacial acetic acid and renders the solution virtually anhydrous.
3. $HClO_4$ must be well diluted with glacial acetic acid before adding acetic anhydride because reaction between $HClO_4$ and acetic anhydride is explosive.

Standardisation 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 $HClO_4$.
- The colour changes from blue to blue green.

Assay Procedure

- Weigh accurately about 0.17 g of Ephedrine Hydrochloride, 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.

Equivalent or I.P factor

1 ml of 0.1 M perchloric acid is equivalent to 0.02017 g of $C_{10}H_{15}NO,HCl$.

$$\% \text{ Ephedrine Hydrochloride} = \frac{X \text{ ml} \times \text{Normality (Calculated)} \times 0.02017 \times 100}{N \text{ (Given)} \times \text{Wt. of sample(in gm)}}$$

X ml = Volume of titrant consumed at end point

Normality Calculated = Normality of Perchloric acid after standardization

Normality Given = 0.1 N (theoretically)