

# UNIVERSITY SOLVED QUESTION WITH ANSWER

**Year** : 2018-2019

**Subject** : Pharmaceutical Analysis

**Subject Code** : BP-102T

**Subject In-Charge** : Kiranmayee Bhatra



Registration No :

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Total Number of Pages : 01

B.Pharm  
BP102T

1<sup>st</sup> Semester Regular / Back Examination 2018-19

PHARMACEUTICAL ANALYSIS I

BRANCH : B.Pharma

Time : 3 Hours

Max Marks : 75

Q.CODE : E952

Answer Question No.1 (Part-A) and 02 (Part-B) which are compulsory and any TWO from Part-C.

The figures in the right hand margin indicate marks.

**Part- A**

**Q1 Objective Answer Type Questions (Answer All) (2 x 10)**

- Define pharmaceutical analysis and give its scope.
- Define pharmacopoeia. What are different types of pharmacopoeias?
- What is universal indicator? Write its components.
- Give pharmaceutical applications of non-aqueous titrations.
- What is a buffer solution? Give two examples of it.
- Name the indicators used in Fajan's method for titration of halides against silver nitrate.
- What do you mean by Primary and secondary standards in chemical analysis.
- What do you understand by Co-precipitation?
- Write about advantages and disadvantages of diazotization reaction.
- What do you understand by standard hydrogen electrode?

**Part- B**

**Q2 Focused-Short Answer Type Questions- (Answer Any Seven) (5 x 7)**

- Classify errors in pharmaceutical analysis.
- How you will prepare and standardize 0.5 M Sulphuric acid?
- Define limit test. Write in brief about limit test for Sulphate.
- Discuss in brief about Oswald's theory of acid-base indicators.
- Explain the assay procedure of Ephedrine Hydrochloride.
- Differentiate between Mohr's method and Volhard's method.
- State different types of EDTA titration with suitable examples.
- What is gravimetric analysis? Discuss in details about principle involved in it.
- Write the principle and applications of 'Polarography'.

**Part-C**

**Long Answer Type Questions (Answer Any Two)**

**Q3** Discuss in brief about different techniques involved in pharmaceutical analysis. **(10)**

**Q4** Explain non-aqueous titration. Discuss about various types of solvents and indicators used in non-aqueous titrations. **(10)**

**Q5** What are various types of conductivity cells? Why is the platinization of electrodes done? **(10)**

**Q6** Write in brief about basic principle, theory, types and applications of diazotization titration. **(10)**

2018-19

a//

a// pharmaceutical analysis is a branch of pharmaceutical chemistry which deals with identification, determination, quantification and purification of pharmaceutical products by using manual, chemical or instrumental methods.

scope of pharmaceutical analysis -

- Examination of raw material.
- Examination of soil and Rock
- " of Radioactive compound.
- " of various drug substances.
- Food Industry.

b// Pharmacopoeia -

→ pharmacopoeia is derived from 2 greek words "pharmakon" means drug & "poieia" means to 'make'.

- It is legal and official book of standard for drugs issued by recognized authorities appointed by "Government of each country".
- It contains list of pharmaceutical substances formulae along with their description and standards.
- pharmacopoeia is nothing but the collection of monographs.

different type of pharmacopoeia -

- Indian pharmacopoeia.
- British pharmacopoeia.
- United states pharmacopoeia.

c// The universal indicator is a chemical solution used in chemistry to determine the pH of a substance. It changes colour depending on the acidity or alkalinity of the sol<sup>n</sup> it's placed in, allowing scientists to easily identify pH levels.

→ It is a mixture of different types of indicators that exhibits different coloration at different levels.

→ Eg:- methyl red, and phenolphthalein.

of Non aqueous titration is used to know the purity of assays. It is used for the determination of concentration expressions.

→ It is used in the determination of hydrophobic compounds, phenobarbitone, diuretics, steroids.

→ It is used in the determination of the composition of antitubercular drugs and adrenergic drugs.

of A buffer solution resists a change in pH when small amount of acid or alkali are added.

→ An acidic buffer is made by mixing a weak acid with a solution of its salt of a strong alkali.

→ Eg - blood, dissolved acetic acid & sodium acetate.

4// ~~Iron ions are used as indicators in~~ dichlorofluorescein is used as an indicator in fajan's method for titration of halides against silver nitrate.

g// Primary standards -

→ primary standards are reagents with accurately known concentration and very high purity which after dissolving to a known amount of solvent gives primary standard solution.

→ It should be 100% pure.

Secondary standards -

→ secondary standards are those chemical compounds that standardized against a primary standard for use in a specific analysis.

- They basically used in standardization process & for calibrating instrument.
- less pure than primary standard.

by co-precipitation is a kind of precipitation where soluble compounds in a solution are eliminated during the course of precipitation.

- It is the simultaneous precipitation of more than one compound from a sol<sup>n</sup>.

### Disadvantages of microtitration

- Applicable for very less variety of samples.
- Relatively slow compared to other methods.
- Required to maintain temp<sup>n</sup> conditions.
- End point detection is very difficult.

### Advantages

- selective for the all types of sulphonamides.
- sensitive.
- Reproducibility.

### Hydrogen electrode -

- It contains a glass tube with a platinum wire sealed within it.
- platinum foil coated with Pt. black to increase surface area.
- This act as platinum electrode which immersed in 1M HCl to maintain the conc<sup>n</sup> of H<sup>+</sup> ion.
- The hydrogen gas in pure form is continuously bubbled in the acidic sol<sup>n</sup> at 298K and pressure = 1 atm.
- It is attached with another half cell with analyte sol<sup>n</sup>.

## All Errors -

→ Errors are simply defined as "mistake".  
In other words the difference bet<sup>n</sup> true/st -  
- standard value and observed value is called  
error.

$$\text{Error} = \text{standard value} - \text{observed value}$$

### Types of Errors -

Errors are basically divided into 2 category.

- (1) Systemic Errors.
- (2) Random Errors.

#### (1) Systemic Errors -

Systemic errors also known as determinate errors generally occurs by fault in the analytical procedure or in the instrument. Cause of these errors are known to the analyst and can be avoided by preplanning and careful working.

#### Type -

- Personal Errors.
- Instrumental Errors.
- Reagent Error.
- Additive Errors.
- Error in method.

#### Personal Error

These errors arise due to defect personal mistake or carelessness of analyst or due to inability of an individual i.e colour blindness.

#### Instrumental Errors -

These error occurs due to defect in the equipment or use of uncalibrated glasswares apparatus or instruments.

## Reagents Errors -

- These errors depends on the quality of individual reagent.
- many reagents and compounds are not present in pure form & contain impurities.

## Additive Errors -

- sometimes errors are constant throughout the analysis and independent of amount of sample.

## Error in method -

- These type of errors caused due to select<sup>n</sup> of wrong or improper method.

## (2) Indeterminate Errors / Random Error

- Indeterminate errors are also known as Random errors.
- generally Cause of random error is not known, Analyst has no control over it.
- These errors cannot be eliminated, even after using high quality reagents and apparatus.

6/1

Limit test are quantitative or semi-quantitative test designed to identify and control small quantities of impurity that are present in the substance.

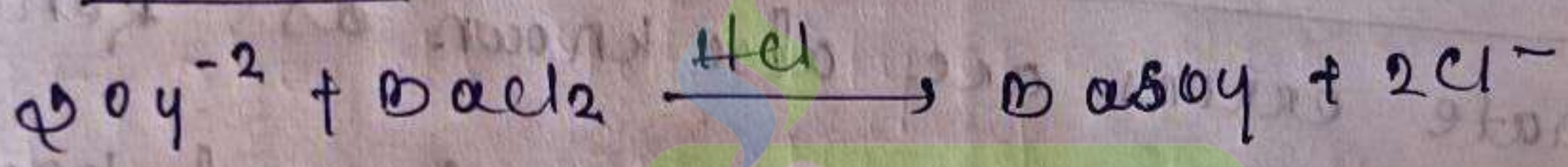
→ It basically involves small comparison of opalescence, turbidity or colour with fixed standards.

### Limit test for sulphate -

#### Principle -

The principle of limit test of sulphate is based on the reaction of soluble sulphate with barium chloride to form barium sulphate in the presence of dil. HCl.

#### Chemical Reaction



#### Test

#### Standard

→ Dissolve specific amount of substance in nessler cylinder as directed in pharmacopoeia.

→ Add 2ml dil HCl.

→ Dilute the sol<sup>n</sup> to 45ml with water.

→ Add 5ml barium sulphate reagent.

→ observe the opalescence.

→ 1ml of 0.1089% w/v sol<sup>n</sup> of  $K_2SO_4$  in nessler cylinder.

→ Add 2ml dil HCl.

→ dil. the sol<sup>n</sup> to 45ml with  $H_2O$ .

→ Add 5ml barium sulphate reagent.

→ observe the opalescence.





## d// Ostwald's theory:-

- According to this theory indicators are generally weak acids or weak bases.
- The change in colour of the indicator is due to their ionisation.
- The unionised form of the indicator has different colour and ionised form has different colour.
- Now there can be two cases:-

### 1) Indicator is weak acid:-

- In case, if the indicator is a weak acid.
- Its ionisation in acid is very low due to common  $H^+$  ions, that means in acids it is unionised form.
- It is fairly ionised in basic or alkaline soln, that means in bases it is in ionised form.

Eg:- phenolphthalein is a weak acid indicator and it is represented by  $HPh$ .

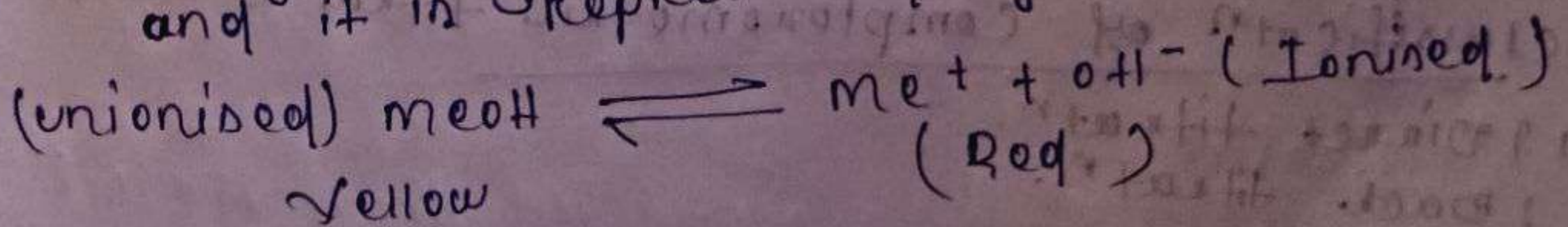


### 2) Indicator is weak base:-

- In case, if the indicator is weak base.
- Its ionisation is very low in bases due to common  $OH^-$  ions, that means in bases it is in unionised form.

- It is fairly ionised in acidic soln by  $H^+$  ions that means in acids it is in ionised form.

Eg:- methy orange is a weak base indicator and it is represented by  $MeOH$ .



## Mohr's method

- (1) It is also known as direct method.
- (2) potassium chromate is used as an indicator.
- (3) A red precipitate of silver chromate forms at the end point.
- (4) Iodides and bromides cannot be titrated.

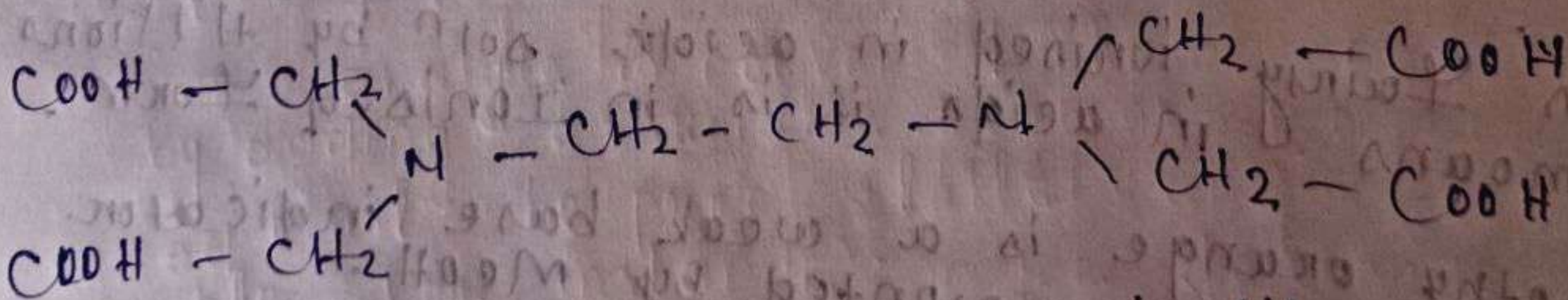
## Volhard's method

- It is also known as indirect titration.
- Ferric ammonium sulphate is used as an indicator.
- A red colour of ferric thiocyanate forms at the end point.
- It can be used to determine iodide, bromide and chloride.

## EDTA

- EDTA stands for ethylene diamine tetraacetic acid.
- It is a multidentate ligand or we can also call them chelates.
- Generally, it is insoluble in water, hence in complexometric titration we used its salt disodium EDTA, which is water soluble.
- It is most widely used as titrant in complexometric titration.

Chemical formula -  $C_{10}H_{16}N_2O_8$



## Classification of complexometric titration

- (1) Direct titration.
- (2) Back titration.
- (3) Replacement titration.
- (4) Alkalimetric titration.

Direct titration  
 → It is the simplest method of complexometric titration.  
 → In this EDTA is mainly used as titrant.  
 → In this end point is simply determined by colour change due to indicator.  
 → It is similar to acid-base titration.  
 → It is not suitable for slow complexometric titration.

Back titration  
 → It is also known as indicator titration.  
 → In this titration is performed by taking excess amount of EDTA.  
 → In this first replacement titration.  
 → This method is used when direct & back titration don't give sharp end point.  
 → In this titration, metal present in the analyte displaces another metal from metal EDTA complex.

Alkalimetric titration  
 → It is used for the determination of anions which generally do not react with EDTA chelate.  
 → In this method, the free  $H^+$  ions get liberated during titration.

Precipitation  
 The analyte is converted into an insoluble precipitate by adding a suitable reagent. The precipitate is filtered, washed, dried, and weighed. The weight of the precipitate is used for the determination of the analyte.

## 4) Gravimetric Analysis:-

- The word gravimetry refers to mass.
- Gravimetric analysis is method of analysis in which we determine the quantity of analyte by measurement of mass.
- In Gravimetric analysis analyte is converted into precipitate.

### Principle of Gravimetric Analysis:-

~~Gravimetric analysis is a method in analytical~~  
precipitation

↓

filtration

↓

washing

↓

drying

↓

weighing

↓

Calculation

### (1) precipitation:-

The analyte is converted into an insoluble precipitate by adding a suitable reagent. The precipitate must be pure, stable, and easily filterable. For instance, in the determination of chloride ion, silver nitrate is added to form silver chloride precipitate.

### (2) Filtration:-

The precipitate is separated from the soln by filtration.

(3) Drying -

The precipitate is dried or ignited to a constant weight. Drying removes moisture content, while ignition might be required to convert the precipitation into a more stable form.

(4) weighing

The dried precipitate is weighed with high precision.

(5) Calculation

The amount of the analyte is calculated using stoichiometric relationships.

(i) polarography

polarography consist of electrolysis of the analyte soln by applying potential difference betn 2 electrodes (a) one that has a fixed and known potential called the reference electrode. and (b) the other that has a variable potential, called the polarizable electrode or an indicator electrode (also called the working electrode). As voltage is applied to the polarizable electrode the resulting change in the current through the soln is monitored and the "current-voltage" curve is traced.

Application

→ polarography is used for determination of oxygen content of fluids including whole body fluids & fermentation liquors & milk for studying the respiration rates of microorganism.

→ several mercury containing antiseptics and insecticides were determined polarographically.

→ several Alkaloids can also be estimated by polarography.

## part-c

Q3// pharmaceutical analysis involves a variety of techniques to ensure the quality, safety, and efficacy of drugs. These techniques can be broadly categorized into physical, chemical and biological methods. Here are some key techniques commonly used in pharmaceutical analysis.

(1) Chromatography -

High-performance liquid chromatography -

used for the separation, identification, and quantification of components in a mixture. It is highly efficient for analyzing complex mixtures and active pharmaceutical ingredients.

Gas chromatography -

ideal for volatile and semi-volatile compounds. It's widely used in the analysis of raw materials, intermediates and final products.

(2) Spectroscopy -

UV-visible spectroscopy -

measures the absorbance of UV or visible light by a substance. It's commonly used for quantifying drugs & detecting impurities.

Infrared spectroscopy -

utilized for identifying molecular structures by measuring the vibration of bonds. It helps in the identification of functional groups in drug molecules.

Nuclear magnetic resonance spectroscopy -

provides detailed information about the molecular structure, dynamics, and environment of compound.

### (3) Mass Spectrometry

→ often coupled with chromatography for the precise identification & quantification of compounds based on their mass-to-charge ratio.

### (4) Thermal Analysis

• Differential scanning calorimetry - measures heat flow associated with thermal transitions in a sample. It is used to study polymorphism and stability.

### (5) X-ray Diffraction

→ used for characterizing the crystalline structure of solid material. It provides insights into the polymorphic forms of drugs.



(2)

## Non aqueous Titration $\Rightarrow$

$\Rightarrow$  Most of the titration are performed in the aqueous media, means water is used as solvent, but in the case of weak acids & weak bases, use of water don't gives a sharp end.

$\Rightarrow$  Non-Aqueous solvents are those do not contain water.

$\Rightarrow$  Non-Aqueous titration refers to a type of titration in which the analyte is dissolved in a solvent which doesn't contain water.

## Types of non aqueous solvents $\Rightarrow$

There are basically 4 types of solvent used in the non-aqueous titration.

- ① Protophilic solvents
- ② protogenic solvents
- ③ Amphoteric solvents
- ④ Aprotic solvents.

## \* Protophilic solvents $\Rightarrow$

$\Rightarrow$  The word of protophilic stands for 'proton lover'.

$\Rightarrow$  Protophilic solvents are basic in nature.

$\Rightarrow$  They are used to dissolve acidic analytes.

$\Rightarrow$  They possess a high affinity for proton.



$\Rightarrow$   $\epsilon_r$   $\Rightarrow$  pyridine, amine etc.

\* Protogenic solvents  $\Rightarrow$

$\Rightarrow$  The word protogenic stands for 'proton generator.'

$\Rightarrow$  Protogenic solvents are acidic in nature & they can donate proton.

$\Rightarrow$  They are used to dissolve basic analytes.

$\Rightarrow$  They have dielectric const.

$\Rightarrow$   $\epsilon_r$   $\Rightarrow$  Glacial acetic acid, formic acid etc.

\* Amphiprotic solvents  $\Rightarrow$

$\Rightarrow$  They work as both protogenic & protophilic solvent.

$\Rightarrow$  These solvents behave as acid as well as base.

$\Rightarrow$  Amphiprotic solvents can either accept or donate the proton.

$\Rightarrow$   $\epsilon_r$   $\Rightarrow$  Alcohols, methanol, Ethanol etc.

\* Aprotic solvents  $\Rightarrow$

$\Rightarrow$  These solvents are chemically inert.

$\Rightarrow$  They are neither acidic nor basic.

$\Rightarrow$  They do not accept or donate protons.

$\Rightarrow$  They have low dielectric constant.

$\Rightarrow$   $\epsilon_r$   $\Rightarrow$  Benzene, chloroform etc.

Different type of indicators & their uses in non-aqueous titration  $\rightarrow$

1. Potentiometric Indicators  $\rightarrow$

$\Rightarrow$  Glass electrode  $\div$  measures the pH of the sol<sup>n</sup> directly & is often used in nonaqueous titrations where visual indicators are not suitable.

$\Rightarrow$  calomel electrode  $\rightarrow$  used as a reference electrode in potentiometric titration.

2. Redox indicators  $\rightarrow$

\* Ferric  $\div$

used in nonaqueous redox titrations, changes from red to pale blue when oxidized.

\* Diphenylamine  $\div$  Another redox indicator that changes

from colorless to blue.



(B3)

conductivity cells  $\Rightarrow$

$\Rightarrow$  It is made up with glass vessels in which 2 electrodes are presents at a definite distance i.e. 1cm, & these electrodes are used to measure conductance.

$\Rightarrow$  Electrodes are made up of pt & are coated with platinum black to avoid polarisation & to increase surface area.

$\Rightarrow$  surface area of electrode is  $1\text{cm}^2$  & distance bet<sup>n</sup> two electrodes is 1cm.

It is of three types  $\Rightarrow$

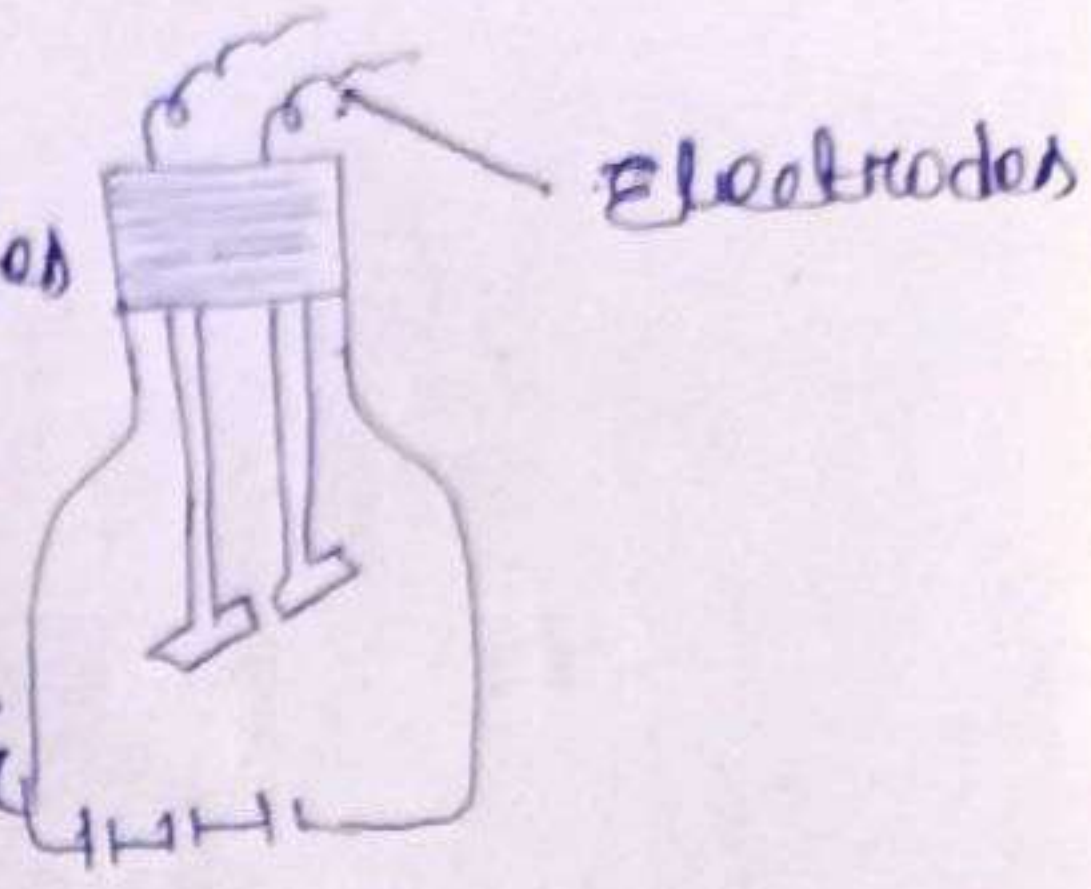
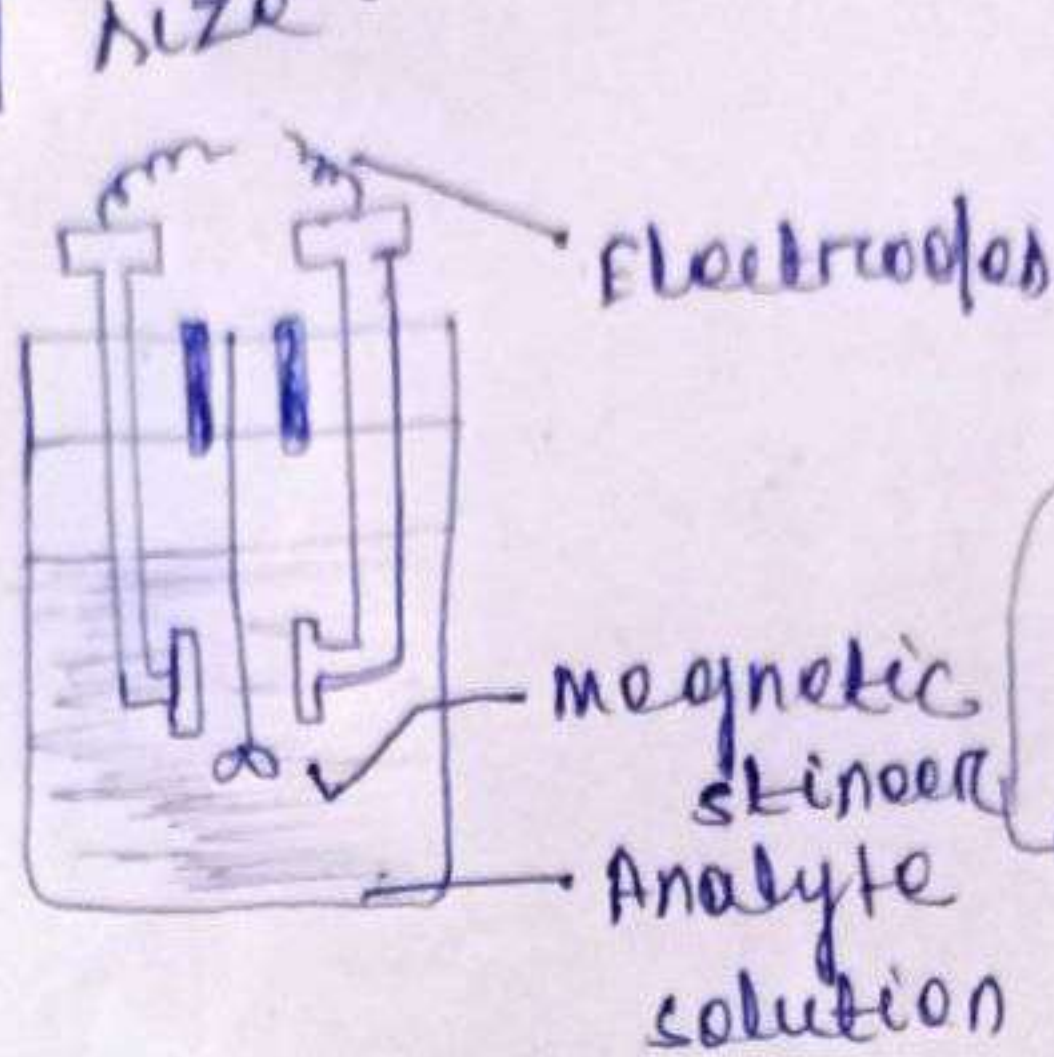
(i) low concentration  $\Rightarrow$

It consists a few in which two electrodes are dipped in solution & electrodes are made up of platinum.

(ii) precipitate type  $\Rightarrow$

It is used those which contain precipitate sol<sup>n</sup>. It contains magnetic stirrer. due to this precipitate does not stick on surface of electrodes.

(iii) Dipped type  $\Rightarrow$  completely dipped in sol<sup>n</sup> due to its compressed size.



① low conc<sup>n</sup> type

② precipitation type

(iii) dipped type

### CONDUCTOMETRIC TITRATION $\Rightarrow$

It is the determination of end point of a titration by means of conductivity measurement is known as conductometric titration.

#### Principle $\Rightarrow$

$\Rightarrow$  It is based on the principle that, during titration ion is replaced by other, which differ in ionic conductance.

$\Rightarrow$  Due to this, graph occurs bet<sup>n</sup> changes in conductance & volume of titrant had sharp changes which helps in detection of end point.

$\Rightarrow$  The platinization of electrodes are used to increase the surface area of the conductivity cell.

06//

## Diazotisation Titration $\Rightarrow$

$\Rightarrow$  Diazotisation titration is a method used for determination of primary aromatic amine compounds.

$\Rightarrow$  The diazotisation titration ~~and~~ is nothing but simply the conversion of primary aromatic amine to a diazonium compound.

$\Rightarrow$  The process was 1st discovered by Peter Griess in 1853.

$\Rightarrow$  The method is mainly used for determination of dyes.

## Principle of diazotisation titration $\Rightarrow$

\* Primary aromatic amines in the presence of HCl reacts with sodium nitrite ( $\text{NaNO}_2$ ) & form diazonium salt.

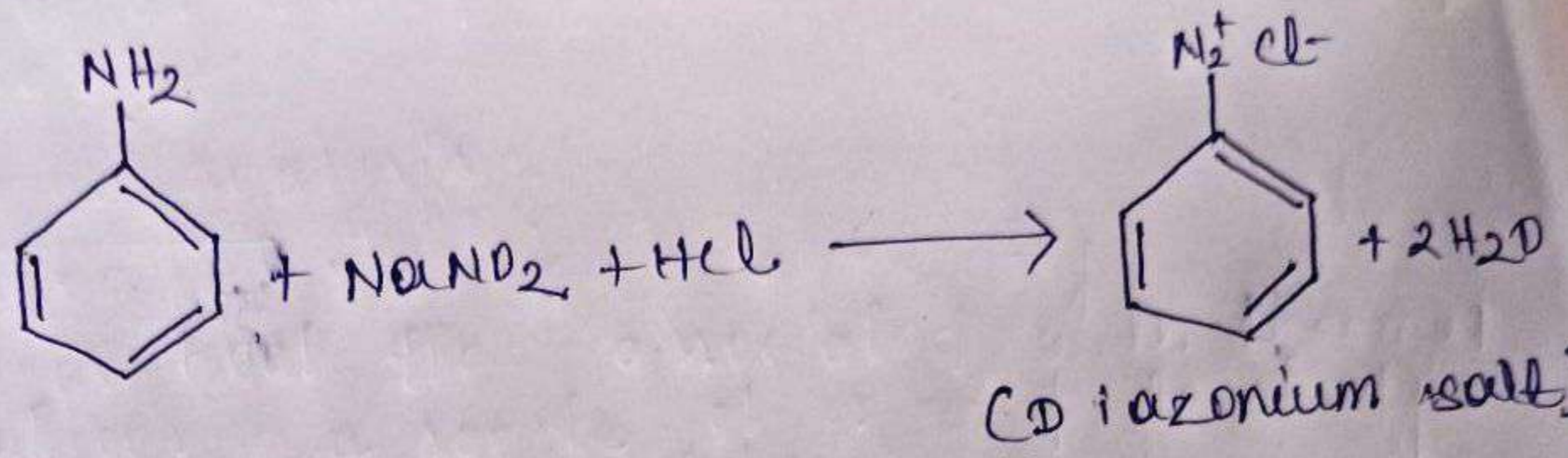
\* The reaction completed in two steps.

STEP-I



Sodium Nitrite ( $\text{NaNO}_2$ ) react with  $\text{HCl}$  & form Nitrous acid ( $\text{HNO}_2$ ) & sodium chloride ( $\text{NaCl}$ ).

Step - II



The obtained nitrous acid react with primary aromatic amine to form Diazonium salt.

Applications of Diazotisation Titration  $\Rightarrow$

- \* used in the determination of sulphanamidol
- \* " " " " " chlorophenol
- \* " " " " " procaine
- \* " " " " " ofopamine
- \* " " " " " ephedrine
- \* " " " " "