UNIT II

PART II

PHYSICOCHEMICAL PROPERTIES OF DRUG

Refractive index, Optical rotation, Dielectric constant, Dipole moment, Dissociation constant, Determinations and applications.

2.1 INTRODUCTION:

- For formulation development, knowledge of physical and chemical properties of drug molecule is very important.
- Physical properties of a drug are influenced by the structural constitution of its molecules as well as by the intermolecular forces existing within them. Hence, physical properties help in understanding the relationship between the structure and the mechanism of action of the drug resulting in the development of an effective formulation.

Types of Physical Properties

1. **Additive Properties:**

   Additive property is the property of material which is due to addition of individual property of each atom or individual functional group present in that material.

   Example: Molecular weight or mass of a substance is an additive property which is the sum of the atomic masses of its individual atoms.

2. **Constitutive Properties:**

   Constitutive property of a substance is dependent on the arrangement of atoms and bonds in its structure.

   Example: Optical activity or rotation, surface tension and viscosity.

3. **Additive and Constitutive Properties:**

   The additive and constitutive properties of a substance are due to both, the type of atoms present in it and their intramolecular arrangement.

   Example: Molar refraction, surface tension and viscosity.

4. **Colligative properties:**

Colligative properties are those which depend upon number of basic constituents like atom, molecule or particles present in the solution.

Example: Freezing point depression, boiling point elevation, vapor pressure and osmotic pressure.

- The most important physical properties of a drug molecule which helps in determining its structural configuration include dielectric constant, dipole moment, optical rotation, refractive index, surface tension and viscosity will be discussed in this chapter.

2.2 REFRACTIVE INDEX:

- A Dutch physicist called Willebrord Snell in year 1621 gave relationship between angles when light passes from one medium to another medium.
- A beam of light when allowed to pass from one medium to another, it changes its direction.
- When a beam of light is permitted to pass from a less dense medium like air to denser medium like water the light ray turns towards the normal plane. Similarly, when a beam of light is permitted to pass from a denser medium to a less dense medium, the light ray turns away from the normal plane; this phenomenon in change in direction of light is termed as refraction.

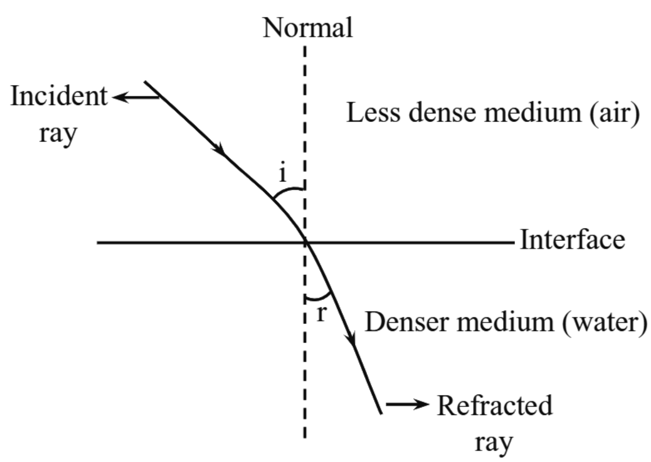


Fig. 1: Refraction of light ray.

Where,

i is angle of incidence

r is angle of refraction

- Refractive index (RI) is defined as ratio of velocity light in any selected medium to the velocity of light in vacuum or air.
- Mathematically it can be represented as follows;

$$n = \frac{\text{Velocity of light in selected material}}{\text{Velocity of light in vacuum or air}} = \frac{c}{v} \quad \text{………… (1)}$$

- Refractive index is a unitless and dimensionless quantity.
- Snell's law can also be used to describe refractive index. This law states that refractive index is ratio of sin of angle of incidence (i) to the sin of angle of refraction (r).

$$n = \frac{\sin i}{\sin r} \quad \text{…………………………..…………… (2)}$$

- Refractive index is a distinctive property of a liquid. Refractive index depends upon wavelength of light used and temperature.
- In general, refractive index is denoted as $[n]_{D}^{20}$.

Where,

20 = Temperature at which refractive index has been determined (℃)

D = Line emission of sodium at 589 nm

- Refractive index of most of substances is more than air; because the majority of material is denser than air hence speed of light in air is more than reference substance. Below table shows refractive index of some of material.

Medium	Refractive index
Air	1
Water	1.330
Ethyl Alcohol	1.36
Acetone	1.36
Diamond	2.417
Glass	1.52

Table 1: Refractive index of some material

2.2.1: MEASUREMENT OF REFRACTIVE INDEX:

- Refractive index can be measured by using instrument called as refractometer. Different types of refractometer like Abbes refractometer, Pulfrich refractometer, and immersion refractometer are used for determination of refractive index.
- The most common, laboratory scale refractometer is Abbes refractometer. Abbes refractometer has several advantages as follows;
    - It is very compact hence require very less space and easy handling.
    - Very small sample is required.
    - Can be used to determine refractive index of large number of material.
    - Ordinary light can also be used for determination of refractive index.

The schematic representation of Abbes refractometer is shown in figure 1.

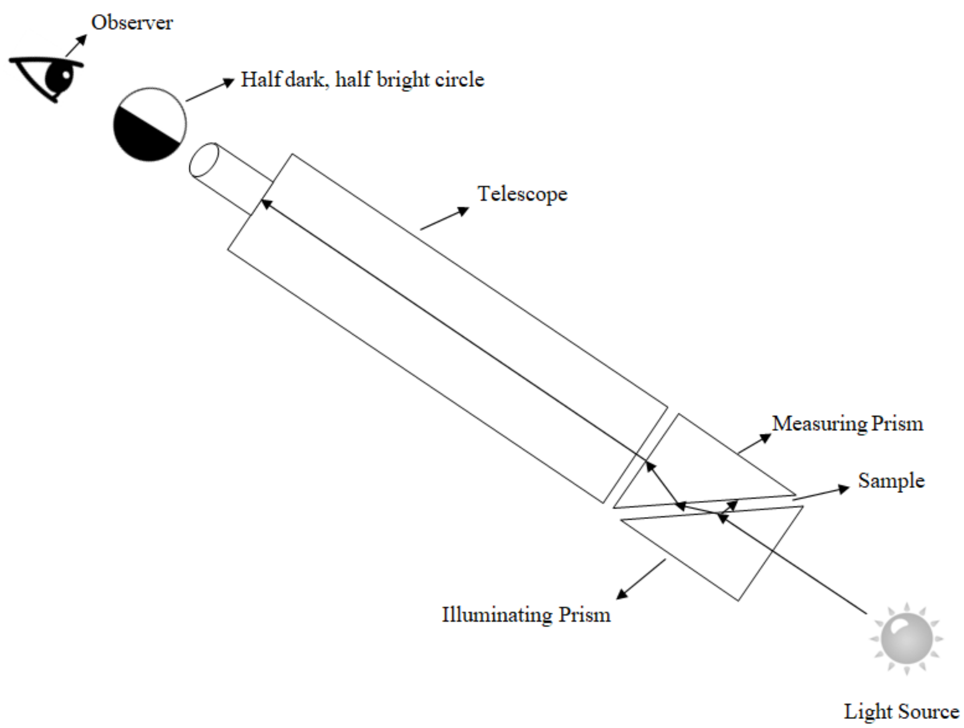


Fig. 1: Schematic representation of Abbes refractometer

2.2.2 CONSTRUCTION OF ABBES REFRACTOMETER:

Abbes refractometer consists of the following parts.

1. Telescope:

Telescope is used to observe changes in the direction of light rays.

2. Prism Assembly

It consists of two prisms mainly illuminating prism and measuring prism. These two prisms are separable to place sample in between them as a very thin film.

3. Scale

Scale is used for calibration of refractometer. Also it is used for measurement of refractive index of sample.

4. Adjusting screw:

Adjusting screw is used for adjusting light such that half black and half bright circle is observed so that accurate reading can be obtained.

2.2.3 WORKING

- The sample whose refractive index is to be measured is placed between the two prisms as a thin film.
- Light is allowed to enter from lower side of refracting prism.
- When viewed through the telescope, either dark band or light band or combination of light and dark band is observed.
- The adjusting screw is then slowly rotated, such that circle becomes half dark and half bright. When half dark and half bright band is observed, reading is recorded.

2.2.4 APPLICATIONS OF REFRACTIVE INDEX

- The major application of refractive index is to determine the purity of sample.
- Measurement of refractive index helps in determining the concentration of the solute present in a solution.
- It helps in identifying a compound.
- It helps to determine the purity of a substance.
- It is used to determine the molar refractions of a compound which in turn provides useful information regarding its structure.
- Refractive index can also be used for determination of molecular weights and structure of organic compounds.
- Refractive index is used to measure refraction characteristics of solid, liquid and gases.

2.3 OPTICAL ROTATION:

- An ordinary light consists of electromagnetic waves having oscillation propagating in all directions called as unpolarized light.

- When such light is passed through polarizer like Nicol prism it gets converted into light which have oscillations propagating in only one direction. Such light is called as plane polarized light.

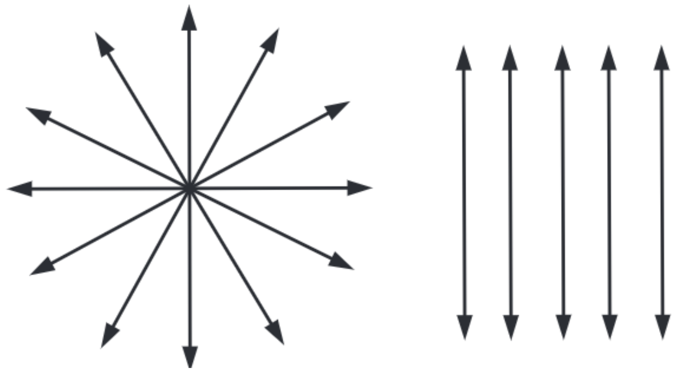
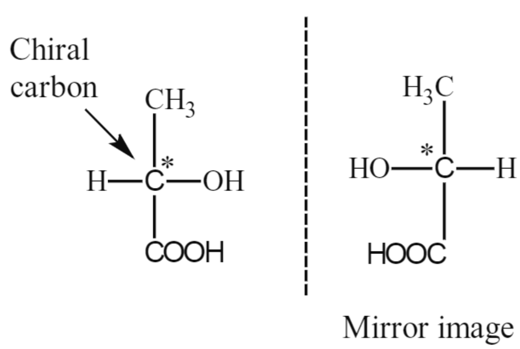


Fig. 2: Ordinary light and polarized light

- When any compound rotates plane polarized light passed through it through some angle, such compound is called as optically active compound.
- This property of optically active substance is called as optical rotation and angle through which light is rotated is called as angle of rotation.
- Optically active compounds are those who has carbon atom in centre attached to four different groups. Such carbon atom is called as chiral carbon.
- Chiral atom is required for a molecule to show optical activity. A chiral molecule is not superimposable on its mirror image and does not have plane of symmetry.
- For example in lactic acid central carbon atom is attached to four different groups like CH_3, H, OH and COOH.



- The two isomers which are not mirror images of each other are termed as enantiomers.
- Based upon which direction plane polarized light is rotated by optically active compound it can be classified into following two types,

- When the substance turns the plane polarized light towards right side or clockwise, it is called dextrorotatory and is denoted by (+) or (*d*).
- When the substance rotates the plane polarized light towards left side or anti-clockwise, it is called levorotatory and is denoted by (–) or (*l*).
- Optical rotation of a substance depends upon the wavelength of light, temperature and density of an optically active substance. It is an intrinsic property of an optically active compound.

2.3.1 SPECIFIC ROTATION:

- Specific rotation is characteristic constant value for given compound. Specific rotation is defined as rotation produced when plane polarized light is passed through one decimeter (10cm) length of sample solution having concentration of 1gm/ml at specific temperature.
- Following formula is used for description of specific optical rotation.

$$\text{Specific rotation} = [\alpha]_{\lambda}^{t} = \frac{\alpha}{l \times c} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (3)$$

Where,

t = Temperature at which optical rotation is measured.

λ = Wavelength of light used

α = Observed rotation

l = Path length

c = Concentration in grams/liter

- Sodium D line is used as source of light in instruments which have wavelength of 589 nm.
- While writing specific optical rotation, solvent and concentration is mentioned in bracket. For example optical rotation of glucose can be written as,

$[\alpha]_{D}^{30}$ = ± 52.7 (water, concentration: 0.5 gm/ml)

- In above example D represent Sodium D lamp as a source, 30 represent temperature 30°C ± 52.7 represent optical rotation of dextro and levo rotatory glucose mixture. Water is a solvent with 0.5 gm/ml concentration of glucose in it.

2.3.2 MEASUREMENT OF OPTICAL ACTIVITY:

- Optical activity of substance is measured by using instrument called as polarimeter.

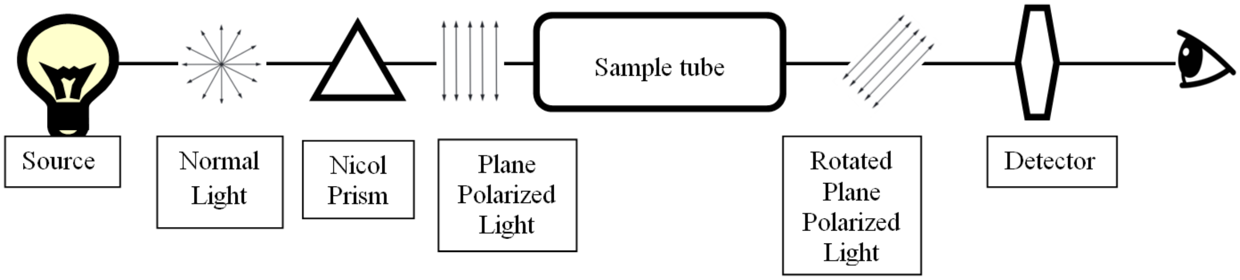


Fig. 3: Schematic presentation of Polarimeter

- A polarimeter consists of the following components.

1. **Source of Light**

   Sodium vapor lamp (D-line source) is used as the source of light.

2. **Polarizer**

   Nicol prism or Polaroid lens is used as a polarizer. It converts ordinary beam of light into plane polarized light.

3. **Sample Tube:**

   It is used for holding the optically active substance whose optical rotation is to be measured. Liquid substance can be directly added to the sample tube. For solids, precisely weighed quantity is initially dissolved in water or other suitable solvent and then filled in the sample tube.

4. **Analyzer/ Detector:**

   It is used for making circle half dark and half bright during the measurement of optical rotation. It can be rotated and is connected to a scale which helps in reading the angle of rotation.

2.3.3 WORKING

- The substance whose optical activity is to be measured is added to the sample tube.
- The optically active compound rotates the plane of polarized light. The extent of rotation is read from the scale, while the direction of rotation is noted.
- Any change in the direction of rotation of plane polarized light with only the solvent is determined and the extent of rotation is read from the scale.
- Difference in the readings obtained with and without sample gives the angle of rotation. This value is substituted in the formula to determine specific rotation of the substance.

2.3.4 APPLICATIONS:

- Specific rotation helps in determining identification of compound.
- It helps in determining the purity of the substance.
- It also helps in quantitative analysis i.e., in determining the concentration of solute in a solute.
- To study rate of reaction in chemical kinetics.
- For determination of adulterants.

2.4 DIELECTRIC CONSTANT:

- Capacitance is dependent upon the type of medium in between the parallel plates called as dielectric medium and distance in between them.

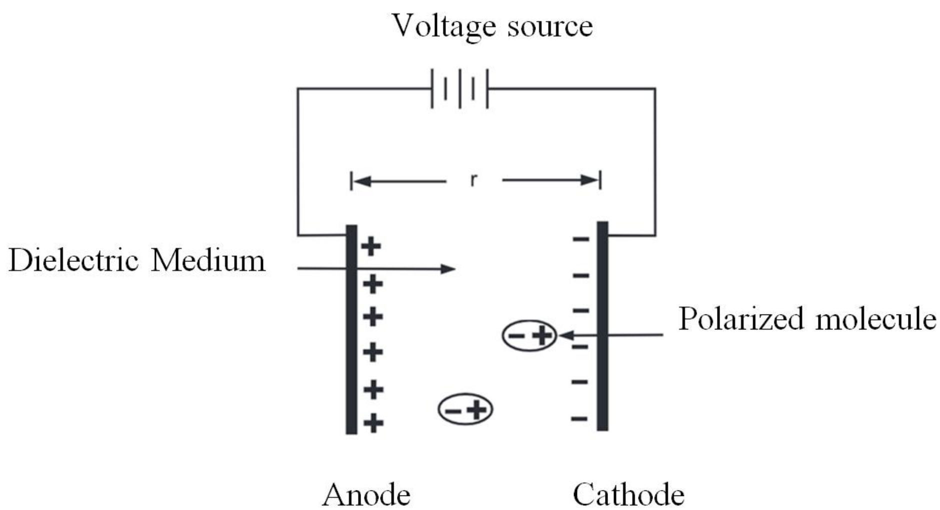


Fig. 4: Parallel plate Condenser

- Ratio between the electric charges on the two parallel plates to the potential difference between the plates is called as Capacitance (C).

$$C = \frac{q}{v} \quad \text{..(4)}$$

Where, C = Capacitance

q = Electric charge

v = Potential difference

- The capacitance of condenser is dependent upon thickness of condenser separating the plates. C_0 is the capacitance of reference medium which is vacuum.

- **Dielectric constant (ε)** is defined as ratio of capacitance of the medium C_x to the capacitance of the vacuum C_o.

$$\varepsilon = \frac{C_x}{C_o} \quad \ldots\ldots(5)$$

- As it is ratio dielectric constant has no unit. Dielectric constant also called as relative permittivity of a solvent is measure of magnitude of charge separation within molecule i.e. polarity.
- Higher dielectric constant of molecule indicates high polarity means high charge separation within the molecule. Dielectric constant affects the solubility of substance. Dielectric constant of some material is given in table.

Material	Dielectric Constant	Material	Dielectric Constant
Acetone	21.4	Methanol	33.7
Benzene	2.28	Water	80.4
Chloroform	4.8	Phenol	9.7
Octanol	10	Cyclohexane	2
Formaldehyde	22	Hexane	5

Table 2: Dielectric constant of some material

2.4.1 MEASUREMENT OF DIELECTRIC CONSTANT:

- If, in between the plates vacuum is filled as a medium, then the capacitance of the condenser is one and hence the dielectric constant is also one.
- If water or any other polar substance is used as a medium, then there is a rise in the capacitance due to orientation of the polar molecules in the direction of electric field of the condenser. The negative portion of the molecule aligns itself with the positive end of the plate and vice versa. Due to this phenomenon, the rate of flow of electrons increases which increases the capacitance and dielectric constant of the molecule.
- If non-polar medium is placed between the plates, then polarization is induced due to the displacement of electrons and protons from their actual places. In such cases, the value of dielectric constant exceeds one.

2.4.2 APPLICATIONS

- Dielectric constant is used to determine the polarity of solvents.

- Depending upon the values of dielectric constant the solvents can be arranged accordingly which is helpful to choose the appropriate solvent with desired polarity.
- Drug solubility can be increased by choosing suitable solvent or solvent mixture depending upon dielectric constant.

2.5 DIPOLE MOMENT:

- Separation of opposite electric charge from each other by definite distance within a molecule is called as dipole. Positive and negative charges are polarized within molecule due to difference in electronegativity of atoms.
- For example in HCl, chlorine atom is more electronegative than hydrogen atom; hence electron cloud is shifted towards chlorine molecule. Due to this hydrogen atom gains partial positive charge and chlorine atom gains partial negative charge.
- Dipole moment can be defined as product of electric charges (e) and distance (r) between the charges. Greek letter "μ" is used for denoting diploe moment.

$$\mu = e \times r \qquad \text{……………………………………………} (6)$$

- Dipole moment is indicated by using an arrow with cross tail ($+\!\!\!\longrightarrow$). Direction of arrow is towards the more electronegative atom positive tail is towards the electropositive atom.
- For Example dipole moment within HCl molecule can be indicated by as follows;

$$H^{\delta+} \underline{\;+\!\!\!\longrightarrow\;} Cl^{\delta-}$$

- Dipole is vector quantity. It has direction.
- Dipole moment is of two types, Permanent and induced.
- Permanent dipole moment is present in polar molecules which contains electronegative molecule. While induced dipole is created within molecule by external electric field or any other force. Unit of dipole moment is Debye which is defined as net charge present on molecule multiplied by distance between two poles.
- Dipole moment is generally induced in asymmetric molecules. Symmetric molecules do not show dipole moment i.e. total dipole moment is zero.

2.5.1 MEASUREMENT OF DIPOLE MOMENT:

- Various methods are used to determine the dipole moment of a molecule. Some of them have been discussed below,

2.5.1.1 Electric Condenser Method/Vapor Temperature Method:

- A storage battery is charged with the help of two parallel plates of condenser.
- Electric field is applied so that strength is equal to the applied voltage divided by the distance between the two plates.
- Polar molecules act as electric dipoles and their net charge is null. When these polar molecules are placed between the plates they do not move towards either positive or negative plates, but they rotate and orient in such a way that their positive end lie towards the negative plate and vice-versa.
- The orientation or alignment of the molecules is generally in the direction of the electric field.
- Initially plates of the condenser are charged to a certain voltage but after introduction of polar molecule in between the plates voltage is lowered. This lowering of voltage is dependent on the nature of the polar molecule.
- If dielectric constant of medium between the plates is known then dipole moment of molecule can be calculated.

2.5.1.2 By the Use of Rotational Spectra:

- Spectral lines of polar molecule get shifted when it is exposed to strong electric field. This shifting of spectral lines is known as Stark effect.
- The magnitude of the stark effect can be used to determine the exact dipole moment of the molecule.

Molecule	Dipole moment	Molecule	Dipole moment
Ammonia	1.46	Acetonitrile	3.92
Water	1.84	Methanol	1.70
Ethanol	1.69	n-Propanol	1.68
Carbon dioxide	0	Phenobarbital	1.16
Acetic acid	1.4	Sulfanilamide	5.37
Hydrogen bromide	0.78	Acetyl Salicylic acid	2.07

Table 3: Dipole moment of some molecules

2.5.2 APPLICATIONS OF DIPOLE MOMENT:

- Dipole moment can be used for structural elucidation of molecule.
- Differentiation between *cis* and *trans* isomers can be carried out by dipole moment.

- Dipole moment also plays important role in drug - receptor binding.
- Dipole moment helps in understanding biological activity of drug molecules.
- It also helps to identify arrangement of atoms within molecule.
- Nature of bond within the atoms can be predicted by dipole moment.

2.6 DISSOCIATION CONSTANT

- Dissociation is a process by which chemical compound break down into smaller constituents.
- Most of the drugs are either weak acidic or weak basic. These drugs may undergo process of dissociation. Dissociation may occur in solid, liquid or gaseous state.
- Dissociation of a drug molecule A_xB_y undergoing can be given as follows;

$$A_xB_y \rightleftharpoons xA + yB$$

Hence Dissociation constant (pK_a) can be written as

$$pK_a = \frac{[A]^x[B]^y}{[A_xB_y]} \quad \text{.......................................(7)}$$

Where,

[A] is molar concentration of A

[B] is molar concentration of B

$[A_xB_y]$ is molar concentration of A_xB_y.

- Dissociation constant is defined as tendency of particular substance in solution to be dissociated into ions. It is equal to the product of respective ion concentration divided by the concentration of non-ionic molecule. Numerically, ionization ability of a drug is given by ionization/dissociation constant which represents the relative proton transferred or donated by that compound.
- Degree of dissociation determines the relative amounts of ionized and unionized forms of the drug and influences the distribution of mainly weakly acidic or weakly basic drugs.
- The ratio of ionized and unionized drugs is given by Henderson-Hasselbalch equation.

$$pH = pK_a + \log \frac{[\text{Unionized form}]}{[\text{ionized form}]} \quad \text{..(8)}$$

- The above Henderson - Hasselbalch equation aids in calculating the ionization constant of compounds at a particular pH.

Percentage ionization:

- Percentage of ionization is defined at particular concentration of weak acid that exits as ions. Percentage of ionization can be calculated by using following formula;

$$\% \text{ ionization} = \frac{(I)}{(I+U)} \times 100 \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (9)$$

Where,

I = Concentration of ionic form

U = Concentration of undissociated form

2.6.1METHODS FOR DETERMINATION OF DISSOCIATION CONSTANT:

Determination of dissociation constant for a drug capable of ionization within a pH range of 1 to 10 is important since solubility and consequently absorption, can be altered by orders of magnitude with changing pH. The dissociation constant value (pKa), are essential for understanding many fundamental reactions in chemistry. Dissociation constant is measured by using following methods;

2.6.1.1 Potentiometric titration

Dissociation of a week acid represents one of the proton exchange reaction; they are also called as acid-base reactions. According to the Bronsted-Lowry classification, an acid is a proton donor (protogenic substance) and a base is a proton acceptor (protofilic substance). In a potentiometric titration, a sample is titrated with acid or base using a pH electrode to monitor the course of titration. The pKa value is calculated from the change in shape of the titration curve compared with that of blank titration without a sample present. Potentiometric titration is based on the quantitative relationship of the E.M.F. of a cell as given by the following equation.

$$E_{Cell} = E_{ref} + E_{indicator} + E_{junction} \ldots\ldots\ldots\ldots\ldots (10)$$

2.6.1.2 Spectrophotometric method

UV-Visible spectroscopy is based on the principle of the absorption of electromagnetic radiation from the 200–800 nm range and following excitation of electrons to higher energy states. UV–VIS spectrophotometry handles compounds with lower solubility and lower sample concentrations. A number of aromatic molecules are easily determined by UV spectroscopy. The λmax of two different form of drug must be different. There are various UV spectroscopic methods such as Simultaneous equation method, 96 well microtiter plates method , Multipeaks

Gaussian fitting method, Molar ratio method, Least squares nonlinear regression of Multi-wavelength spectroscopic method, Second derivative method, Orthogonal method, are used to dissociation constant.

2.6.1.3 Calorimetry Method

All calorimetric methods work by the same principle of measurement of the amount of heat evolved as a physical or chemical process takes place in a sample. For the measurement of pKa values, in Isothermal Titration Calorimetry [ITC], a regular acid-base titration is carried inside the calorimeter while the energy required to keep the temperature constant is measured. This method also calculates the pKa indirectly from a measured enthalpy change ΔH. By plotting the minima or maxima versus pH, a sigmoid curve is obtained from which the pKa can be determined from the inflection point.

2.6.1.4 Liquid Chromatography

The different retention behavior of the protonized and the nonprotonized form of the test material serves the base for liquid chromatography method. The retention time is determined in relationship to the pH-value of the mobile phase by reversed - phase HPLC. The high performance liquid chromatography method is advantageous to determine pKa value of low water soluble drug with low sample consumption, rapid sample analysis, high sensitivity and precision. The most important feature is the excellent resolution that can be achieved under a wide range of conditions for very closely related molecules, as well as structurally relatively distinct molecules. Dissociation constant is greatly affected by changing in pH, ionic strength, and temperature. The pH of the mobile phase affects retention of acidic and basic drug. A general equation which relates the observed retention factor to the pH of the mobile phase, the dissociation constants, and the retention factors of the different ionic species has been used to determine dissociation constant of polyprotic weak acid and base. It is written as:

$$K_D = K_o + \frac{\sum_{r=1}^{n} K_r \, . \, K_a.[r]e^{rx}}{1+\sum_{r=1}^{n} K_a.[r]e^{rx}} \quad \ldots\ldots\ldots\ldots\ldots\ldots (11)$$

Where,

Ko retention factor of undissociated species

Kr value is the retention factor of dissociated species

Ka[r], product of the first r- dissociation constants

n is the ionisation constant

X is related to pH of the mobile phase: x=2.303.pH

2.6.1.5 Capillary Zone electrophoresis

Capillary zone electrophoresis [CZE] serves as a useful tool for determination of pKa values with several advantages over potentiometric and spectroscopic methods. Since the pH influences the electrophoretic behavior of the substances, a relation can be established between pH, pKa and the electrophoretic mobility of compounds. The electrophoretic mobilities were calculated using the following formula:

$$\mu_{ep} = \mu_{app} - \mu_{eof} = \frac{L_d - L_t}{V}\left[\frac{1}{t_m} - \frac{1}{t_o}\right] \quad \text{......} (12)$$

Where,

μ_{ep} is the electrophoretic mobility of compounds in cm^2/Vs

μ_{app} is the apparent electrophoretic mobility of the solute in cm^2/Vs.

μ_{eof} is the electroosmotic mobility of a neutral marker in cm^2/Vs.

Ld is the distance from the injection point to the detector [cm]

Lt is the total length of capillary [cm]

V is the applied voltage [volt]

t_m and t_o are the migration times [s] of the analyte and neutral marker, respectively.

2.6.2 APPLICATIONS OF DISSOCIATION CONSTANT:

- Dissociation constant is useful in determination of bioavailability of drug and distribution of drug inside body in tissues.
- Dissociation of drug also affects its solubility and permeation.
- Dissociation constant is also useful in pH indicators.
- Buffer design also depends upon dissociation constant.

2.7 POINTS TO REMEMBER

- For formulation development, knowledge of physical and chemical properties of drug molecule is very important.

- There are four types of physical properties of additive property, constitutive property, additive and constitutive property and colligative property.
- Refractive index (RI) is defined as ratio of velocity light in any selected medium to the velocity of light in vacuum or air.
- Mathematically refractive index can be represented as follows;

$$n = \frac{\text{Velocity of light in selected material}}{\text{Velocity of light in vacuum or air}} = \frac{\text{c}}{\text{v}}$$

- Snell's law states that refractive index is ratio of sin of angle of incidence (i) to the sin of angle of refraction (r).

$$n = \frac{\sin \text{i}}{\sin \text{r}}$$

- Abbes refractometer is used for determination of refractive index. It contains telescope, prism, scale and adjusting screw.
- Refractive index is used for determination of Identity, purity, concentration and molecular weight of sample.
- When any compound rotates plane polarized light passed through it through some angle, such compound is called as optically active compound. This property of optically active substance is called as optical rotation and angle through which light is rotated is called as angle of rotation.
- When the substance turns the plane polarized light towards right side or clockwise, it is called dextrorotatory and is denoted by (+) or (*d*).
- When the substance rotates the plane polarized light towards left side or anti-clockwise, it is called levorotatory and is denoted by (–) or (*l*).
- Specific rotation is characteristic constant value for given compound. Specific rotation is defined as rotation produced when plane polarized light is passed through one decimeter (10 cm) length of sample solution having concentration of 1 gm / ml at specific temperature.
- Polarimeter is used for measurement of optical rotation. It consists of light source, monochromator, sample tube and detector.
- Optical rotation is used for identification and determination of purity of compound, chemical kinetics of reaction.

- Dielectric constant (ε) is defined as ratio of capacitance of the medium C_X to the capacitance of the vacuum.

$$\varepsilon = \frac{C_x}{C_o}$$

- Dielectric constant is used for determination of polarity of solvent, depending upon which suitable solvent can be identified.
- Dipole moment can be defined as product of electric charges (e) and distance (r) between the charges. Greek letter "μ" is used for denoting dipole moment.

$$\mu = e\ r$$

- Permanent dipole moment is present in polar molecules which contains electronegative molecule. While induced dipole is created within molecule by external electric field or any other force. Unit of dipole moment is Debye which is defined as net charge present on molecule multiplied by distance between two poles.
- Dipole moment is used for structural elucidation of compound, to differentiate between cis and trans isomers, to study drug receptor binding.
- Dissociation constant is defined as tendency of particular substance in solution to be dissociated into ions. It is equal to the product of respective ion concentration divided by the concentration of non-ionic molecule.
- Dissociation of a drug molecule A_xB_y undergoing can be given as follows;

$$A_xB_y \rightleftharpoons xA + yB$$

Hence Dissociation constant can be written as

$$\text{Dissociation constant } (pK_a) = \frac{[A]^x[B]^y}{[A_xB_y]}$$

- Dissociation constant is useful in determination of bioavailability of drug and distribution of drug inside body in tissue; it also affects its solubility and permeation of drug molecule.

2.8 EXERCISE:

A) MULTIPLE CHOICE QUESTIONS:

1. **Colligative property depends upon**
   a) Number of basic units present in substance
   b) Addition of properties of individual functional group

c) Arrangement of atoms and bond structure.

d) All of above

Ans: (a) Number of basic units present in substance

2. Refractive index (RI) is defined as ratio of velocity light in any selected medium to the velocity of light in ………..

a) Vacuum

b) Glass

c) Water

d) None of above

Ans: (a) Vacuum

3. Which is correct Snell's law?

a) $n = \frac{\sin r}{\sin i}$

b) $n = \frac{\sin i}{\sin r}$

c) $n = \frac{\sin i}{\cos r}$

d) None of above

Ans: (b) $n = \frac{\sin i}{\sin r}$

4. Refractive index is denoted as $[n]_D^{20}$, where 20 is?

a) Melting point

b) Temperature in ^{o}F

c) Molecular weight

d) Temperature in ^{o}C

Ans: (d) Temperature in ^{o}C

5. Which types of prism are present in Abbes refractometer?

a) Illuminating .

b) Measuring

c) Both a and b

d) None of above

Ans: (c) Both a and b

6. **When the substance turns the plane polarized light towards right side or clockwise, it is called,**
    a) Levo as well as dextro
    b) Dextro
    c) Levo
    d) None of above

    Ans: (b) Dextro

7. **What are types of dipole moment?**
    a) Permanent dipole moment
    b) Induced dipole moment
    c) Both
    d) None

    Ans: (c) Both

8. **Dissociation constant can be used for,**
    a) Determination of solubility of drug
    b) Designing of buffer systems
    c) To study distribution pattern of drug inside body
    d) All of above

    Ans: (d) All of above

B) TRUE OR FALSE:

1) **By using refractometer, optical rotation of compound can be measured.**
   Ans: False
2) **Refractive index can be used for purity determination of compound**
   Ans: True
3) **If chiral atom is present in molecule it will not show optical activity.**
   Ans: False
4) **If plane polarized light is rotated towards left side or anti-clockwise then it is called levorotatory**
   Ans: True
5) **Temperature does not affect refractive index.**

Ans: False

6) **Refractive index (RI) is defined as ratio of velocity light in any selected medium to the velocity of light in water.**

Ans: False

7) **Symmetric molecules show dipole moment.**

Ans: False

8) **Dipole moment is vector quantity.**

Ans: True

9) **A beam of light when allowed to pass from one medium to another, it does not change its direction.**

Ans: False

C) FILL IN THE BLANKS:

1) **Freezing point depression is ………………….. property of substance.**

Ans: Colligative

2) **Refractive index (RI) is defined as ratio of velocity light in any selected medium to the velocity of light in…………………**

Ans: Vacuum

3) **When ordinary light is passed through Nicol prism it gets converted into ………………………….**

Ans: Plane polarized light.

4) **Molecule having carbon atom in centre attached to four different groups is called as ………………**

Ans: Chiral

5) **Dielectric constant is defined as ratio of capacitance of the………….. to the capacitance of the ……………………..**

Ans: Medium, Vacuum

6) **Electronegative atom present in molecule causes………………….dipole moment.**

Ans: Permanent

7) **…………………..compound rotates plane polarized light towards right side/clockwise**

Ans: Dextrorotatory

D) VERY SHORT ANSWER QUESTION:

1) Define - Colligative properties
   - Constitutive Property
   - Additive Property
2) Define - Refractive index
   - Refractive index
   - Optical rotation
   - Dipole moment
   - Dissociation constant
3) Give equation of Snell's law.
4) Refractive index is denoted as $[n]_{D}^{20}$. What is 20 and D?
5) Give advantages of Abbes refractometer.
6) Give name of parts of refractometer.
7) What is plane polarized light?
8) What is chiral atom?
9) Define specific rotation.
10) Enlist parts of polarimeter.
11) Where sample is placed in refractometer?

12) Define electronegativity.
13) Indicate dipole moment of molecule HNO_3.

E) SHORT ANSWER TYPE QUESTIONS:

1) Explain different types of properties of substance.
2) Define refractive index, how it is measure and give its application.

3) Define optical rotation, how it is measured and give its application.
4) Define Dielectric constant, how it is measured and give its application.
5) Explain construction and working of Abbes refractometer and polarimeter