PHYSICAL PHARMACEUTICS-I (Theory), 3rd SEMESTER
Subject Code- BP302T, Syllabus of PCI for Unit-II

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States of Matter and properties of matter: State of matter, changes in the state of matter, latent heats, vapour pressure, sublimation critical point, eutectic mixtures, gases, aerosols– inhalers, relative humidity, liquid complexes, liquid crystals, glassy states, solid crystalline, amorphous & polymorphism.

Physicochemical properties of drug molecules: Refractive index, optical rotation, dielectric constant, dipole moment, dissociation constant, determinations and applications

Unit 2: State of matter

Matter exists in one of the three states-solid liquid or gas. Two factors usually determined the state in which matter exist. One is the intensity of intermolecular force and the other is the temperature. Solid have the strongest intermolecular force and the gases have the weakest.

Matters can be classified into various ways like physical, chemical, and general classifications.

Physical classifications:

- **Solid-Ex: tablet , capsule**
- **Liquid-Ex: oral syrup**
- **Gas-Ex:aerosol**
- **Plasma**

Chemical classifications:

- **Pure substance** like element and compound
- **Mixture** like homogeneous and heterogeneous

Gaseous, liquids and crystalline solids are the three primary state of matter of phases. The molecules atoms and ions in the solid state are held in close proximity by intermolecular, inter atomic or ionic the atoms in the solid can oscillate only about fixed positions. As the temperature increase the atoms in the solid can oscillate only about fixed positions. As the temperature of a solid substance is raised, the atoms acquire sufficient energy to disrupt the ordered arranged of the lattice and pass into the liquid form. Finally when sufficient energy is supplied the atoms or molecules pass into the gaseous state. Solid with high vapour pressure, such as iodine and camphor can pass directly from the solid to the gaseous state without melting at room temperature. This process is known as *sublimation, and the reserve process that is condensation to the solid state, may be referred to as disposition.*

Certain molecules frequently exhibit a 4th phase come more properly termed as mesophase (Greek meso means= middle), which lies between the liquid and crystalline States. This so-called liquid crystalline state is discussed later. Supercritical fluids are also considered as mesophase, in this case is state of matter that exist under high pressure and temperature and has properties that are intermediate between those of liquids and gases supercritical fluids which also be discussed later because of their increased utilization and pharmaceutical agent processing.

The Gaseous State

The physical behaviour of gaseous is independent of chemical nature of the molecules. Therefore almost all gases respond in an identical way to the variations in pressure, temperature and volume. Since the molecules in a gas are always in a state of vigorous and rapid motion, these travel in random parts, collide with one another and with the wall of the container in which they are confined. These tend to occupy completely all the space available in the container and exert a pressure on the wall of the container.

The general behaviour of gases with variation of pressure volume and temperature can be given by the ideal gases equation.

$PV = nRT$ for 'n' moles of ideal gas

Where P is the pressure, v is the volume, n is the number of moles of gas, R is a gas constant and T is the absolute temperature.

From the ideal gas law it is clear that the volume of a gas is directly proportional to the number of moles of the gas and to the absolute temperature and is inverse proportion to the pressure. Real and actual gases usually deviate from ideal behaviour as the molecules tend to attract one another. The deviation from the ideal behavior becomes significant when the pressure becomes very high and the temperature very low. At ordinary temperature and pressure these gases obey the law sufficiently accurately.

The Liquid State

The liquid state may be considered as an intermediate state as matter goes from the solid state to the gaseous state. Liquid can be considered as highly compressed gases or slightly released solids. The molecules of a gas are in a state of constant motion owning to their kinetic energy which is proportional to the absolute temperature of the gas. When the gas is cooled its kinetic energy is gradually reduced. As the temperature is being reduced, a state is reach where the molecules almost lose their kinetic energy and are not able to overcome the force of attraction. As a result the gas molecules come closer and ultimately the gas gets converted into the liquid state. Liquefaction of a gas can also be brought about by increasing the pressure on the gas. However pressure is effective only below a certain temperature. This temperature is called critical temperature and can be defined as the temperature above which a gas cannot be liquefied even if very high pressure is applied. The critical pressure is the pressure required to liquify a gas at its critical temperature. The critical temperature of gas is 374 degree Celsius or 647 degree Kelvin and its critical pressure is 218 atmospheres.

The Solid State

The most important property of the solid state is the high degree of order in which solid substances exist. Their structure may be crystalline and lattice like or non-crystalline such as glass which are not lattice like or only partly lattice like. However even the non-crystalline solids have much more orders than liquid and gases. The molecules of a solid are held together by strong bonds which imparts a high melting point to these substances. In order to their decreasing strengths, these include metallic bonds, ionic bonds, valence bonds and molecular bonds.

There are two types of solid **Crystalline Solid** and **Amorphous Solid**

Crystalline solid:

The crystalline solids are of six types according to bond length and bond angle determined by x-ray crystallography methods.

The structural unit of crystalline solid is arranged in fixed geometric patterns for letters. Crystalline solid generally exhibits a different shape and an orderly arrangement of units. These generally have a sharp melting point. The various crystalline solids have been divided into six distances formed. This includes in the tabular form.

Table 1(Shape and examples of crystalline solid)

Shape	Example
Cubic	NaCl
Tetragonal	Urea
Hexagonal	Iodoform
Rhombic	Iodine
Monoclinic	Sucrose
Triclinic	Boric acid

Amorphous Solid

Unlike crystalline solids, the structural units in amorphous solids are arranged in a random manner. Amorphous solid may be considered as super cooled liquids. Example of solids includes glass wood plastic etc. Amorphous solids do not have a sharp melting point and melt within some narrow range of temperature. These are in general more soluble than crystalline solids

Polymorphism

Many substances may exist in more than one crystalline or amorphous form. *This phenomenon where compounds exist in more than one crystalline and or amorphous form is termed as polymorphism and different crystalline or amorphous forms are known as polymorphs or this is known as modification or polymorphic forms*. The various forms usually arise through packing of the molecules in different arrays within the crystal or by difference in the orientation or conformation of the molecules at lattice sites.

Different polymorphic forms of a substance usually exhibit different melting points, x-ray diffraction patterns, solubilities, dissolution behavior, stability and biological activity. A number ofpharmacologicalactivesubstancessuchaschloramphenicol, novobiocin, sulphonamides, barbiturates, steroids such as cortisone, testosterone, prednisolone etc, have been shown to exhibit a number of polymorphic forms different in their solubility, stability and pharmacological activity. Many organic substances such as tristearin and theobroma oil also exhibit polymorphism. Theobroma oil (cocoa butter) exhibits four different polymorphic forms viz., α, β, β’and γ forms differing in their respective melting points.

Liquid Crystals

In addition to the three States of matter, some asymmetric molecules often exhibit a fourth state known as a liquid crystalline state or mesophase. Liquid crystals possess some of the properties of liquid and some of solids. For example liquid crystal possesses the property of mobility and rotation and thus can be considered to have the flow properties of liquid. On the other hand, these also possess the properties of birefringence, a property of associated with solid crystals. The birefringence, the light passing through a material is divided into two components with different velocities and hence different refractive index.

The two main types of structure of liquid crystal are the smectic (soap or grease like) and nematic (thread like). In the smectic state, the molecules are mobile in two direction and show rotation about one axis. In the nematic state, the molecules are mobile in three dimensions. A third type known as the cholesteric crystals exist but may be considered as a special case of the nematic type.

The liquid crystalline state is found widespread in nature-in nerve, brain tissue and blood vessels. Atherosclerosis thought to result from the desposition of liquid in the liquid crystalline state on the wall of blood vessels. The three components of bile, the cholesterol, the bile salt and water when present in a definite proportion can result in the formation of smectic crystals and these may be involved in the formation of gall stones. Certain smectic crystals are believed to be involved in the stabilization of emulsion and have been used for the solubilization of water in soluble materials.

Glassy state

All the glass is considered to be a non-conducting transparent solid, it is actually a type of solid matter. It can neither be considered as a typical solid nor a typical liquid. The atoms and molecules in most solids are arranged in an orderly manner whereas in Glassy materials these are highly disorder .Glassy materials however, have some short range order as in the case of polymers. Glassy materials also do not have a specific melting point but these slowly and gradually liquefy on heating. Structurally Glassy materials can be considered to be made up of a random selection of polyhedral molecules linked together at their corners. Certain materials can easily be converted to a Glassy state while other pose great difficulty and certain materials cannot be converted at all. Although the theory behind this behaviour is not very clear, it has been shown that material which can be converted to glassy state have a very high viscosity at their melting point which inhibits the formation of an ordered structure

Although the most common materials which can be converted to Glassy state are the metal oxides ,even materials such as Steel can be converted to the Glassy state if it is cooled very quickly. This technique produces glasses since the material solidifies even before it gets chances to develop a crystalline structure.

Change in the state of matter

The molecules, atoms or ions in a solid are strongly held in close proximity by intermolecular, interatomic or ionic forces respectively. The particles of the solid can oxalate only about fixed position. As the temperature of a solid substance is raised the particles acquire sufficient energy to disrupt the order arrangement and pass into the liquid state. On further increasing the temperature the molecules pass into the gaseous state. In gaseous state the intermolecular forces are reduced to almost negligible. Sometimes a change of state occurs directly from solid state to the gaseous state and this is termed as sublimation.

As solid changes to a liquid state and then to gaseous state common heat is absorbed and the at enthalpy heat content of the material increases. Does the enthalpy of a liquid is greater than that of a solid and the enthalpy of a gas is greater than that of this liquid. The entropy (degree of molecular randomness) of the material also increases as it goes from a solid to a liquid and to gas.

Latent heat

When is change in the state of a material occurs, the temperature usually remains constant but heat is absorbed. This heat which results in the change of matter without increasing the temperature is called the latent heat. When this heat results in the change of state from a solid to liquid it is known as the latent heat of fusion. For example the heat required to change ice to water at 0^0C is the latent heat of fusion. Likewise the latent heat of vaporization is the quantity of heat absorbed when a change of state from liquid to vapour occurs at its boiling point without changing the temperature of the material. For example the heat required to change water to vapour at $100\,^0$ C is the latent heat of vaporization.

Vapour pressure

When a liquid is kept in a closed evacuated container, molecules from its surface continuously leave and go into the free space above it. This is known as the process of vaporization. Some molecules however return to the surface depending on their concentration in the vapour (the process of condensation). Eventually a condition of equilibrium gets established when the rate of escape of molecules becomes equal to the rate of return. The vapour is then said to be saturated and the pressure exerted by vapour at equilibrium is known as the vapour pressure

The vapour pressure of a liquid depends on the temperature and not on amount of liquid or vapour as long as both liquid and vapour are present and equilibrium is maintained. As the temperature is raised, more of the liquid goes into the vapour state and the vapour pressure increases. As the temperature is raised further, the density of the vapour increases while that of liquid decreases. Eventually, the densities of both the phases become equal and the two phases cannot be distinguished. The temperature at which this happens is known as the critical temperature and above this the temperature; there is no liquid-phase.

Boiling point

When a liquid is heated in an open vessel, the vapour pressure above it increases. On further heating, its vapour pressure becomes equal to the atmospheric pressure. The temperature at which the vapour pressure of a liquid equals the external or atmospheric pressure is known as its boiling point. At the boiling point all the absorbed it is used to change the liquid to the vapour state and there is no rise in the temperature of the liquid until it is completely vaporized. Different liquids have different boiling point.

If the external pressure above the surface of a liquid is decrease or increase the boiling point of the liquid is also decreased or increased.

Melting point and freezing point

The temperature at which a solid passes into liquid state under atmospheric pressure is known as its melting point. The melting point is referred to as freezing point if the liquid passes into the solid-state. The melting or freezing point of a crystalline substance is actually the temperature at which the pure liquid and solid coexist in equilibrium. In practice this point is taken as the temperature of the equilibrium mixture at an external pressure of 1atm.

Vapour pressure of a mixture of liquids

In the case of miscible liquids (solution of a liquid in liquid), the partial vapour pressure exerted by each components is proportional to its molar concentration in the mixture solution. The total vapour pressure P is given by :

$P=P_A+P_B=Po_AX_A+Po_BX_B$

When X_A and X_B are mole fraction of components A and B respectively

Po_A & Po_B are the vapour pressure exerted by the pure components A and B respectively.

P_A and P_B are the partial vapour pressure exerted by A and B respectively in the liquid mixture in the case of a mixture containing two miscible liquids each liquid exerts it own vapour pressure independently of the others. The total vapour pressure P is then given by:

$P=Po_A+Po_B$

Sublimation

Sublimation is defined as the process of transformation of solids directly into the vapour phase without passing into the intermediate liquid-phase. A number of substances including camphor, menthol, naphthalene, etc., exhibit the phenomenon of sublimation. Other substances such as ices can also be forced to exhibit the phenomenon of sublimation by varying the temperature and pressure; the process being adopted during freeze drying of heat labile substances

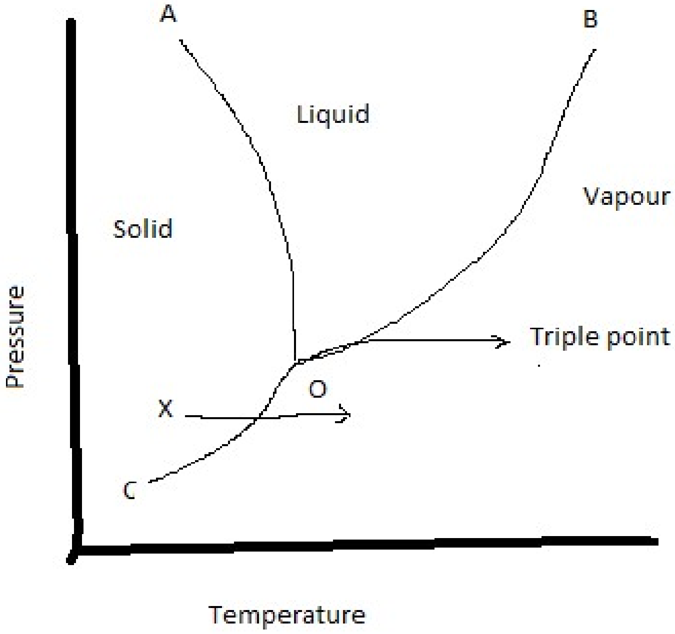

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Fig. 1: Phase diagram illustrating the principle of sublimation

Principle:

Latest considered the phase diagram for a substance as shown in fig .1

The curves AO represent the melting point of the solid phase of the substance at different pressure. Along the curve AO, the solid exists in equilibrium with its liquid phase. To the left of the curve the substance exist in the solid state while to the right; it is in the liquid state. BO represents the vapour pressure of the liquid form of the substance at various temperatures. This curve is known as the vapour pressure of the liquid. Above this curve, the materials exist in the form of liquid while below it, only the vapour from exists. The curve CO represents the vapour pressure of the solid at various temperatures and is also known as the Sublimation curve. To the left of the curve, only solid exists while to the right, only the vapour form is stable. However there exists one point (O) where all the three phases of the material are in equilibrium with each other and this is known as **the triple point**. For pure water this corresponds to a pressure of 610 N/m² and a temperature of 0.0075°C

Now let us consider a point 'X' below the triple point where the substance is present in the form of a solid. If heat is applied to the substance at this point it will pass directly into the vapour phase without passing through the liquid state. This is the process of sublimation.

Eutectic mixture

Certain substances such as menthol, thymol, camphor, phenol, salol etc, when mixed in a particular portion tend to liquify due to reduction in their respective melting points. Mixtures of such substances are known as eutectic mixture. (Greek meaning:; Eutectic-easy melting)

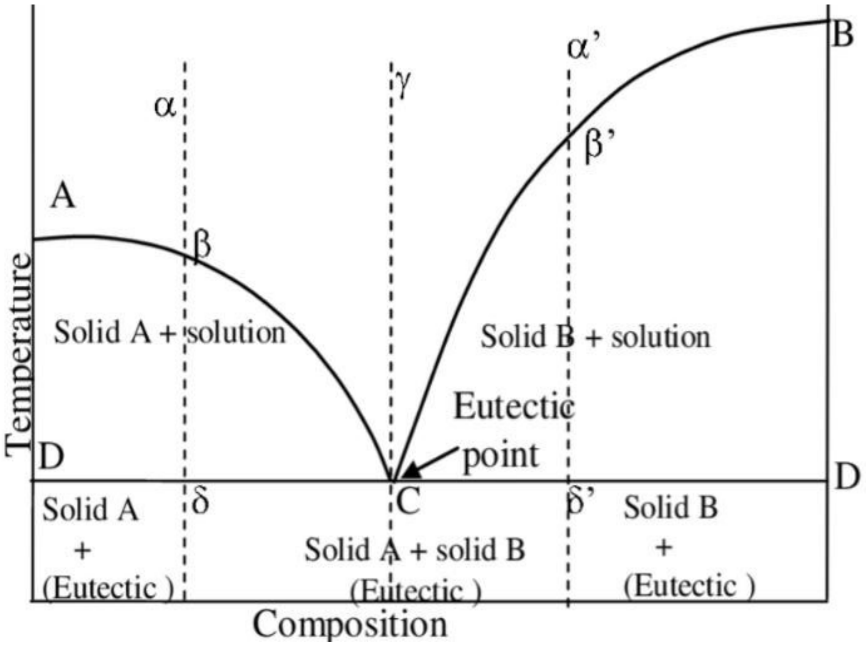


Fig 2 phase diagram showing a eutectic system

Principle*:*

Let us consider two substances A and B. In fig 2, the point A and B represent the melting point of the two components. As increasing quantities of B are added to A, the freezing point of A falls along the curve AC. Similarly, as increasing quantities of A are added to B, the freezing point of B falls along the curve BC. At a particular composition C, known as a eutectic point, the mixture of the two substances has the lowest melting point. This composition of the two substances is known as the eutectic mixture. Below the eutectic temperature the mixture of the two substances will exist as solid while above it, the mixture will convert into a liquid.

In pharmaceutical practice, eutectic mixtures are difficult to dispense in the form of a powder. In order to incorporate such materials in a powder, it is essential to first mix each ingredient separately with an inert diluent such as light magnesium oxide, magnesium carbonate, starch, kaolin etc. followed by gentle blending of the different positions. Alternative the eutectic materials can first be triturated together in order to force them to liquify. The liquid can then be adsorbed on an inert diluents.

The phenomenon of eutectic formation has also been used in pharmaceutical practice to improve the dissolution behaviour of certain drugs. For example eutectic mixture of Aspirin - acetaminophen (37% and 63% respectively), urea – acetaminophen (46% and 54% respectively) and griseofulvin-succinic acid (55% and 45% respectively) dissolve rapidly than the drugs alone or their simple mixtures.

Aerosols

Liquefaction of a gas can be achieved by applying pressure on it and keep the temperature below the critical temperature. When the pressure is reduced, the molecules expand and the liquid reverts back to the gaseous state. Aerosols are based on the principle of reversible change of state on the application and release of pressure. In pharmaceutical aerosols, a drug is dissolved or suspended in a propellant, a material which exists as a liquid under the pressure conditions prevalent inside the container but gets converted to a gas under normal atmospheric conditions. The container is designed in such a manner that on depressing a valve, some of the drug-propellant mixture is expelled out due to the excess pressure inside the container. The propellant used in such a products are generally fluorinated hydrocarbons although gases such as nitrogen and carbon dioxide and also being used.

The aerosol containers are filled either by cooling the propellant and drug to a low temperature within the container which is then sealed with the valve. Alternatively, the drug is sealed in the container at room temperature and the required quantity of propellant is forced into the container under pressure. In both the cases, when the container is at room temperature, part of the propellant is in the gaseous state and exerts pressure necessary to extrude the drug while the remaining is in the liquid state and provides a solution or suspension vehicle for the drug.

Inhalers

An inhaler is a device holding a medicine that you take by breathing in(inhaling). Inhalers are often used to treat chronic obstructive pulmonary disease (COPD).There are three types of Inhalers:

- Metered -dose inhalers

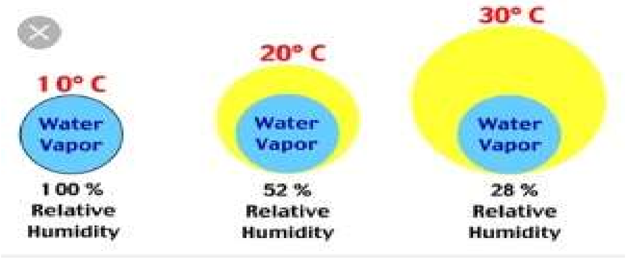
- Dry powder inhaler

- Nebulizers

Relative humidity:

It is a ratio, expressed in percent, the amount of atmospheric moisture present relative to the amount that would be present if the air is saturated.

Since the later amount is dependent on temperature. Relative humidity is a function of both moisture content and temperature. Relative humidity is derived from the associated temperature and dew point for the indicator hour



Liquid complexes*:*

Complex fluids are binary mixtures that have coexistence between two phases: Solid- liquid (suspension and solution of macromolecules such as polymers) solid-gas (granular), liquid-gas (foams) or liquid-liquid (emulsions). They exhibit usual mechanical responses to applied stress or strain due to the geometrical constraints that the phases coexistence imposes. The mechanical response includes transitions between solid like and fluid like behavior as well as fluctuations. Their mechanical properties can be attributed to characteristics such as high disorder, caging and clustering on multiple length scales.

Shaving cream is an example of a complex fluid. Without stress the foam appears to be a solid: it does not flow and can support (very) light loads. However, when adequate stress is applied, shaving cream flows easily like a fluid. On the level of individual bubbles the flow is due to the rearrangement of small collections of bubbles. On this scale the flow is not smooth, but instead consists of fluctuations due to rearrangement of the bubbles and release of stress.

Physico chemical property of drug molecules:

A study of physical property of drug molecules is very important for product formulation and it often leads to better understanding of interrelationship between molecular structure and drug action.

Significance

- Arrangement of an atom in the drug molecules can be obtained.
- By studying the physical and chemical properties the structure of the drug molecules can be determined.
- Solubility of a compound can be determined.
- It gives an idea how a compound can be measures qualitatively and quantitatively.

Classifications

The physical properties can be classified as:

1. Additive property
2. Constitutive property
3. Colligative property

Additive property: They are derived from the sum of the properties of the individual atoms or the functional groups within the molecules.

Example. Molecular weight

Constitutive properties: The constitutive property depends on the structural arrangement within the molecules.

Example. Optical rotation

Colligative properties: The colligative property depends on the number of particles.

Example.1.Lowering of volatile point.
2. Elevation of boiling point.3.Depression of freezing point.
The various physical properties of drug to be studied in this chapter are.

- Refractive index
- Optical rotation
- Dielectric constant
- Dipole moment
- Dissociation constant

Refractive index

If the light enters the denser substance at an angle 1 part of the wave shows down more quickly as if pass the interface and this produces a bending of the wave towards the interphase. This phenomenon is called refraction. If light enters a less dense substance, it is refracted away from the interface rather than towards it. The relative value of this effect between two substance is given by the refractive index or Snell’s laws.

Snell's law

Refractive index of a medium is given by the Snell’s law.

n= sini/sinr=velocity of light in air (vacuum)/velocity of light in medium

Where *i* angle of incidence when light travels through air

r =angle of refraction

Refractive index varies with the wavelength of light and temperature. Usually the velocity of the light in air is also higher.

Refractive index of the liquid at 25°C

Substances.	***RI value***
Carbon tetrachloride.	*1.4603*
Toluene	*1.4969*
A-methyl naphthalene.	*1.6176*
Water.	*1.3325*

Abbes refractometer is commonly used for the determination of refractive index. Liquids and mixtures of liquids possesses a characteristic refractive index

For example, carbon tetrachloride has a lower refractive index and benzene has a high refractive index. When benzene as added for carbon tetrachloride the refractive index of carbon tetrachloride increases. And the proportion of benzene increasing refractive index also increases linearly.

The principle is used to find the percent composition of benzene in carbon tetrachloride. Refractive index of the unknown mixture can be determined experimentally

Applications

Refractive index can be used to identify a substance, to measure its purity and to determine the concentration of one substance dissolved in another.

Optical rotation

Polychromatic light

The light which contains rays of different wavelength**.**

Monochromatic light.

The light which contains rays of only wavelengths.

Polarized light.

When a ray of light is passed through a Nichols prism, that emerges out has vibration restricted to one plane and is called as polarized ray and the light in which vibration are restricted to one plane is called plane polarized light

Optical activity

When a monochromatic polarized beam of light is passed through a solution of a substance in the plane of the polarized light is turned through a certain angle, such substance is said to be optical active and the phenomenon is called as optical activity.

If the plan of polarized light is turned to the right of the substance is called dextrorotatory and if it is done to the left it is called levo-rotary. The d and l form are non super imposable and are mirror image of each other. The optical activity is due to a symmetric carbon atoms or chiral carbon. They are called enantiomers. If equal amount off d and l are mixed, then the solution is racemic mixture and it is optically inactive.

Example: *Tartaric acid.* The d and l form are enantiomorphs and meso form is optically inactive.

A polarimeter is used to measure optical activity.

EXPLANATION:

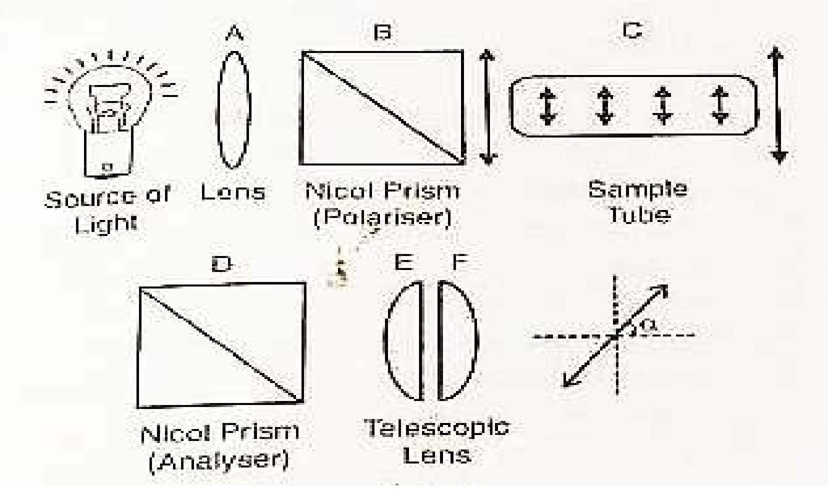


Fig.3.Polarimeter

Light passes through lens A which makes the light rays parallel and enter the Nichol prism B. The light emerges out as the plane polarised light and then passed through the sample and then the analyzer D, E and F are the telescopic lenses which shows the field as two unequal illuminated halves. The analyzer is rotated to a point when the two halves appear uniformly dark.

The reading can be taken at this point. The direct reading gives the optical rotation. This method is also called as the half shadow measurement.

Specific rotation

Specific rotation is the angle of rotation of the plane of polarised light caused by 1 decimeter columns of solution containing 1 gram of the substance per cubic centimeter.

$$[\alpha]_{\lambda}^{t} = \frac{100a}{lc},$$

Where α-specific rotation

a -angle of rotation

l –length of column

C- Concentration of solution

Applications

The value of specific rotation can be used to identify the compound

Example: lactic acid can exist as dextro and levo form. The specific rotation at 25^{O}C using sodium light is $+3.8^{O}$ dextro isomer and -3.8^{O} for Levo isomer.

Optical rotation changes as a function of the wavelength of light. By varying the wavelength of light, the specific rotation for an optical active substance will change. A graph of specific rotation versus wavelength shows an inflection and then passed through zero at the wavelength of maximum absorption of polarised light. This change is specific rotation is known as a cotton effect. Compounds whose specific rotation show maximum before passing through zero as the wavelength of polarized light becomes smaller are said to be show a positive cotton effect. Whereas if α show a maximum after passing through zero of approaching shorter wavelength the compound shows a negative cotton effect . Enantiomers can be characterized by the cotton effect. This is used for the structural examination of organic compounds. For example it is possible to distinguish between two standards with keto groups at position 3 and 17 using rotary discretion curves

Dielectric constant:

The capacitance of the answer filled with some materials C_X divided by the reference standard C_o is referred as the dielectric constant (ε)

$\varepsilon = C_X / C_o$

Derivation

Considered two parallel plate separated by some medium across a distance of the and connected to a battery electric city will flow from the light plate to the right until the potential differences of the plates is usually to that of the battery supplying the initial potential differences. The Capacitance of the condenser (c) in Farads is then equal to the quantity of electric charges q in coulombs stored on the plates divided by the potential differences V between the plates

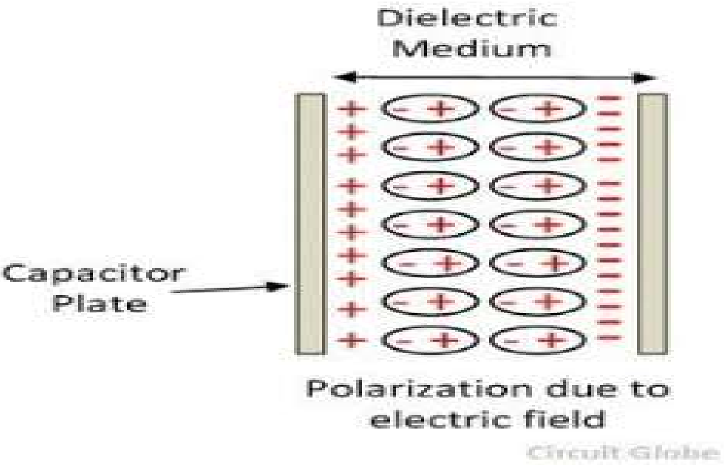


Fig.4.Measurement of dielectric constant

$$C = q/V$$

If water fills the space, the capacity C_X is given by:

$\varepsilon = qx / Vx$

When water fills the space capacitance Cx is given by;

$Cx = qx/Vx$

When water fills the space the capacitance is increased; the capacitance for water or any other liquid fuels on the space and the capacitance when vacuum feels the space gives the dielectric constant of water or for any other liquid.

$\varepsilon = C_X/C_o$

Dielectric constant of the liquid at 25°

Substance.	**Dielectric constant**
Formamide.	110.00
Water.	78.50
Methanol.	32.60
Carbon Tetrachloride.	2.23

Dielectric constant can be determined by Oscillometry in which the frequency of a signal is kept constant by electrical changing the capacitance between the parallel plates. The liquid whose dielectric constant is being measured is placed in glass container between the two plates during the experiment. The dielectric constant of solvent mixture can be related to drug solubility Dielectric constant of drug molecules can be related to drug plate's concentration.

Application

1. The ease of solution of salt soluble like water & glycerin bi explain based on high dielectric constant.
2. More polar is the solvent higher the dielectric constant.
3. Dielectric constants are related dipole-dipole interactions and full induced dipole-dipole interaction.
4. Solvents with large dipole moment will have large dielectric constant.
5. As the temperature increases the dielectric constant of dipolar solvent will tend to decrease.

Dipole moment

An electric dipole is a system of positive and negative charge separated by a finite distance. If positive and negative charges are + Q and -Q are separated by a distance 1 then the dipole moment is given as: $\mu = QI$

Debye is the unit of dipole moment=10^{-18} esu x cm

Where esu indicates electrostatic unit of charge

Applications

1. To confirm the structure of the molecule.

Examples:

a) Benzene and carbon tetrachloride are symmetrical molecules and the dipole moment is zero.

b) Water molecule has a dipole moment of 1.85 D. So there is an angle of 108^{O} between the OH bonds of the water molecules.

c) Dipole moment of carbon dioxide is zero and this shows that it is a linear molecule. [O=C=O]

d) The dipole moment of Para dichlorobenzene is zero and of meta dichlorobenzene is 2.6D.

2. Dipole moment can be used to distinguish between the cis and trans forms.
    a) Trans dichloroethylene has dipole moment of zero and cis has 2.95D.
3. The insecticidal activity can be measured from dipole moment. Lower the value greater will be lipoidal solubility and greater will be the toxicity.

Example: DDT (Para isomer) has a dipole moment of 1.1 D

The para isomer of DDT has a smallest dipole moment of 1.10 whereas the meta isomer has a dipole moment of 1.55 and ortho isomer 1.90. Because of the smallest dipole moment the para form shows greater activity. It can easily penetrate into the lipoidal membrane of the insect and attack the enzyme present in the insect lower dipole moment means greater insecticidal action

4. Dipole moment can be used to determine the percentage ion character of a covalent bond.

Examples In case of HCl, dipole moment is 6.1D, if it is fully ionic. But the practical value is 1.0 4D

Dissociation constant

Acid and bases can ionize in water to give their respective conjugate base and conjugate acid. According to law of mass action a ratio of ionized molecule to unionized molecule can be given. This ratio is called as ionization constant or dissociation constant.

For an acid

$HA + H_2O <=====> A^{--} + H_3O^+$

K_a =acidity constant= $[A^-][H_3O^+]/[HA]$

For a base

$B + H_2O <==> BH^+ + OH^{--}$

K_b = basicity constant = $[OH^-](BH^+)/[B]$

Ionization of water

$H_2O + H_2O <====> H_3O^+ + OH^{--}$

$K_w = [H_3O^+][OH^{--}]/[H_2O]$

$K_w = K_b x Ka$

It is also called as ionic product of water.

Dissociation constant of the liquid

Substance.	Dissociation constant
Acetic acid	$1.75 \times 10^{--5}$
Boric acid	$5.8 \times 10^{--10}$
Ammonia	$1.74 \times 10^{--5}$
Caffeine	$4.1 \times 10^{--14}$

Determination of dissociation constant

There are various methods like conductivity method, visible or UV absorption spectrometer, potentiometer etc.Potentiometeric pH is most widely used

Dissociation constant of acid

$K_a= [H_3O^+] [A^{--}]/ [HA]$

When equimolar concentration of salt A^- and an acid [HA] are present, the K_a--- dissociation constant is numerically equal to the hydronium ion concentration.

$Ka= [H_3O^+]$ when $[A^-] = [HA]$

Method

PH of the solution containing equimolar concentration of the acid and a strong base salt of the acid may measured. At one concentration equal to pKa. From pKa , ka may calculated. pKa is the negative logarithm of dissociation constant.

Applications

Dissociation constant are related to physiological and pharmaceutical activities, solubility, rate of the solution, side of binding (protein binding) and rate absorption of the drug.

Example: Rate and extent absorption of weakly acidic drugs take place from the stomach region as the amount of unionized drug available is more from stomach. Similarly the absorption of the weak bases is better from the intestine

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