Name of Unit:	States of Matter and Properties of Matter
Subject/Course name:	B Pharmacy/ Physical Pharmaceutics- I
Course/ Subject Code:	BP302T
Module no.	2
Class:B.Pharm.Semester:	3rd
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Learning Outcome of Module-2

LO	Learning Outcome	Course Outcome Code
LO1	Students will able to learn states of matter along with latent heat, vapour pressure and critical point.	CO2
LO2	They will also able to know the concepts of eutectic mixtures, inhalers, liquid complexes, liquid crystals and glassy state.	CO2
LO3	They will also able to know the concepts of eutectic mixtures, inhalers, liquid complexes, liquid crystals and glassy state.	CO2
LO4	Students will able to learn physiochemical properties of drug molecules.	CO2

Module Contents

No.	Topic
1	State of matter, changes in the state of matter,
2	Latent heats, vapour pressure, sublimation critical point, eutectic mixtures.
3	Gases, aerosols – inhalers, relative humidity, liquid complexes, liquid crystals, glassy states.
4	Solid- crystalline, amorphous and polymorphism.
5	Refractive index, optical rotation, dielectric constant.
6	Dipole moment, dissociation constant, determinations and applications.

STATES OF MATTER

The three states of matter are the three distinct physical forms that matter can take in most environments: solid, liquid, and gas. Solid is the state in which matter maintains a fixed volume and shape; liquid is the state in which matter adapts to the shape of its container but varies only slightly in volume; and gas is the state in which matter expands to occupy the volume and shape of its container. Each of these three classical states of matter can transition directly into either of the other two classical states.

Solids

A solid's particles are packed closely together. The forces between the particles are strong enough that the particles cannot move freely, they can only vibrate. As a result, a solid has a stable, definite shape and a definite volume. Solids can only change shape under force, as when broken or cut.

In crystalline solids, particles are packed in a regularly ordered, repeating pattern. There are many different crystal structures, and the same substance can have more than one structure. For example, iron has a body-centered cubic structure at temperatures below 912 °C and a face- centered cubic structure between 912 and 1394 °C. Ice has fifteen known crystal structures, each of which exists at a different temperature and pressure.

A solid can transform into a liquid through melting, and a liquid can transform into a solid through freezing. A solid can also change directly into a gas through a process called **Sublimation.**

Liquids

A liquid is a fluid that conforms to the shape of its container but that retains a nearly constant volume independent of pressure. The volume is definite (does not change) if the temperature and pressure are constant. When a solid is heated above its melting point, it becomes liquid because the pressure is higher than the **triple point** of the substance. Intermolecular (or interatomic or interionic) forces are still important, but the molecules have enough energy to move around, which makes the structure mobile. This means that a liquid is not definite in shape but rather conforms to the shape of its container. Its volume is usually greater than that of its corresponding solid (water is a well-known exception to this rule). The highest temperature at which a particular liquid can exist is called its **Critical temperature.**

A liquid can be converted to a gas through heating at constant pressure to the substance's boiling point or through reduction of pressure at constant temperature. This process of a liquid changing to a gas is called **Evaporation.**

Gases

Gas molecules have either very weak bonds or no bonds at all, so they can move freely and quickly. Because of this, not only will a gas conform to the shape of its container, it will also expand to completely fill the container. Gas molecules have enough kinetic energy that the effect of intermolecular forces is small (or zero, for an ideal gas), and they are spaced very far apart from each other; the typical distance between neighboring molecules is much greater than the size of the molecules themselves.

A gas at a temperature below its critical temperature can also be called a vapor. A vapor can be liquefied through compression without cooling. It can also exist in equilibrium with a liquid (or solid), in which case the gas pressure equals the vapor pressure of the liquid (or solid).

Supercritical fluid (SCF) is a gas whose temperature and pressure are greater than the critical temperature and critical pressure. In this state, the distinction between liquid and gas disappears. A supercritical fluid has the physical properties of a gas, but its high density lends it the properties of a solvent in some cases.

Latent Heat

The heat required to convert a solid into a liquid or vapour, or a liquid into a vapour, without change of temperature. Latent heat (also known as latent energy, or as Heat of Transformation) is energy released or absorbed, by a body or a thermodynamic system, during a constant- temperature process — usually a first-order phase transition.

Examples of latent heat are latent heat of fusion and latent heat of Vaporization.

Latent heat of fusion: The amount of heat gained by a solid object to convert it into a liquid without any further increase in the temperature is known as latent heat of fusion.

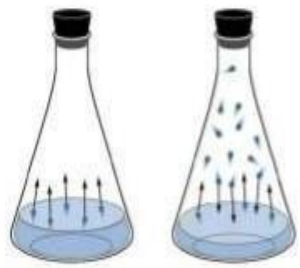
Latent heat of Vapourization: It is defined as amount of energy (enthalpy) that must be added to a liquid substance, to transform a quantity of that substance into a gas. The enthalpy of vaporization is a function of the pressure at which that transformation takes place.

Vapour pressure

It is defined as the pressure exerted by a vapor in thermodynamic equilibrium with its condensed phases (solid or liquid) at a given temperature in a closed system. Vapour pressure is a measure of the tendency of a material to change into the gaseous or vapour state, and it increases with temperature. The temperature at which the vapour pressure at the surface of a liquid becomes equal to the pressure exerted by the surroundings is called the boiling point of the liquid.

Vapour Pressure

- Vapour Pressure – the pressure exerted by a vapor in equilibrium with its liquid state.
- Liquid molecules at the surface escape into the gas phase.
- These gas particles create pressure above the liquid in a closed container.

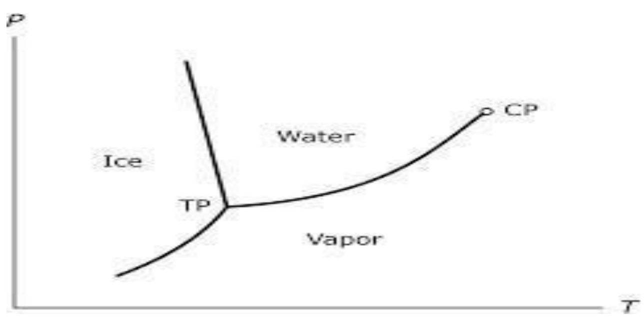


Sublimation

Sublimation critical point refers to the maximum or minimum temperature and pressure beyond which the state of the matter cannot be changed. Sublimation is the process of transition of solid matter directly into gas without it being converted into its liquid form.

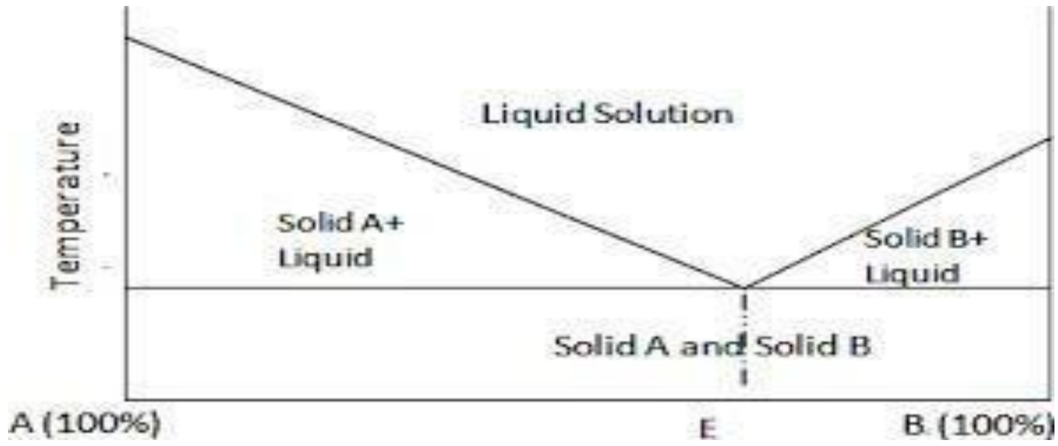
Sublimation is the transition of a substance directly from the solid to the gas state, without passing through the liquid state. Sublimation is an endothermic process that occurs at temperatures and pressures below a substance's **Triple point**.

The **triple point** of a substance is the temperature and pressure at which the three phases (gas, liquid, and solid) of that substance coexist in thermodynamic equilibrium. It is that temperature and pressure at which the sublimation curve, fusion curve and the vaporization curve. Below is the curve, TP in curve stands for triple point.



Eutectic mixtures

A eutectic system is obtained from the Greek word which means easy melting) is a homogeneous mixture of substances that melts or solidifies at a single temperature that is lower than the melting point of any of the constituents. Upon heating any other mixture ratio and reaching the eutectic temperature, one component's lattice will melt first, while the temperature of the mixture has to further increase for (all) the other component lattice(s) to melt. Conversely, as a non- eutectic mixture cools down, each mixture's component will solidify (form its lattice) at a distinct temperature, until all material is solid.



1. Below the eutectic temperature the mixture of two substances will exist as solid while above its point the mixture will convert into liquid.
2. The phenomenon of eutectic mixture has been used in pharmaceutical practices to improve dissolution behavior of drugs.
3. Eutectic mixture of aspirin (37%) and acetaminophen (63%), urea (46%) and acetaminophen (54%) will dissolve more rapidly than the alone drug.

Aerosols – Inhalers

Inhaler aerosols are pressurized systems intended for local action in the respiratory tract. Various types of inhalers such as nebulizers, metered dose inhalers (MDIs) and dry powder inhalers (DPIs) are available. Inhalers are designed to deliver medication directly to the lungs through a person's own breathing. This may benefit a patient by providing medicines directly to areas of disease, allowing medication to take a greater effect on its intended target, and limit side effects of medications due to localized treatment. Inhalers are used in a variety of different medical conditions with diseases of the lungs and respiratory system being among the most common. These conditions utilize medications designed to decrease airway inflammation and obstruction to allow for easier and less strained breathing. Antibiotic medications have even been developed for inhalers to allow for direct delivery to areas of infection within the lungs. Two of the most common conditions that warrant inhaler therapy are asthma and chronic obstructive pulmonary disease.

Types of inhalers

1. **Meter- dose inhaler:** The most common type of inhaler is the pressurized metered-dose inhaler (MDI) which is made up of 3 standard components- a metal canister, plastic actuator, and a metering valve. The medication is typically stored in solution in a pressurized canister that contains a propellant or suspension. The MDI canister is attached to a plastic, hand-operated actuator. On activation, the metered-dose inhaler releases a fixed dose of medication in aerosol form through the actuator and into a patient's lungs. These devices require significant coordination as a person must discharge the medication at or near the same time that they inhale in order for the medication to be effective.
2. **Dry powder inhaler:** Dry powder inhalers release a metered or device-measured dose of powdered medication that is inhaled through a DPI device. This device usually contains a chamber in which the powdered medication is deposited prior to each dosage. The powder can then be inhaled with a quick breath. This allows for medication to be delivered to the lungs without the need for use of propellant/suspension.
3. **Soft- mist inhaler:** Soft mist inhalers release a light mist containing medication without the need for a propellant/suspension. Upon pressing a button, the inhaler creates a mist of medication, allowing for inhalation into the lungs. SMIs suspend inhaled medications for roughly 1.2 seconds, which is longer than the average MDI inhaler suspension time period. This requires less coordination when using and may be helpful for young patients or patients that find the MDI inhalers difficult to use.
4. **Nebulizer:** Nebulizers are designed to deliver medications over an extended period of time over multiple breaths through a mouthpiece or face mask. They generate a continuous mist with aerosolized medication, allowing a patient to breath normally and receive medications. They are commonly used in infants and toddlers requiring inhaled medications or in patients in the hospital who require inhaled medication.

Relative humidity

Relative humidity (RH) is the ratio of the partial pressure of water vapor to the equilibrium vapor pressure of water at a given temperature. Relative humidity depends on temperature and the pressure of the system of interest. The same amount of water vapor results in higher relative humidity in cool air than warm air. A related parameter is the dew point.

Liquid Complexes

Liquid crystals (LCs) are a state of matter which has properties between those of conventional liquids and those of solid crystals. For instance, a liquid crystal may flow like a liquid, but its molecules may be oriented in a crystal-like way. Liquid crystals can be divided into thermotropic, lyotropic and metallotropic phases. In addition to three states of matter some asymmetrical molecules exhibit fourth state which is known as liquid crystals that possess some properties of liquid and some properties of solids. For example liquid crystals possess property of mobility and rotation so can be considered as flow properties of liquid and on the other hand they also possess property of birefringence which is considered to be flow properties of solid.

Uses of liquid crystals

1. It is used in stability of emulsion.
2. They are also used for solubilization of water in soluble material.

Glassy State

Glass is considered to be non-conducting transparent solid which can neither be considered as typical solid nor a typical liquid, so the atoms and molecules in the glassy state are highly disordered. They do not have specific melting point but on heating they slowly gets converted into liquid form. For example metals, oxides and steel which can be converted into glassy state if it is cooled very quickly.

Boiling point

The temperature at which vapour pressure of liquid equals to external or atmospheric pressure is called boiling point.

Melting point

The temperature at which solids passed into liquid state under an atmospheric pressure is called melting point.

Crystalline solids

They are arranged in fixed geometric pattern and they exhibit definite shape and orderly arrangements of solids. The various crystalline solids have been divided into seven forms:

1. Cubic form (Sodium chloride)
2. Tetragonal form (iodoform)

3. Hexagonal form (iodine)
4. Orthorhombic (urea)
5. Monoclinic (sucrose)
6. Trigonal (calamine)
7. Triclinic (boric acid)

Amorphous solids

The structural units in the amorphous solid are arranged in random manner and they may be considered as super cooled liquids. They do not have sharp melting point and melt within some narrow ranges of temperature.

Supercooled liquids: It is a process of lowering the temperature of liquid or gases below its freezing point without gets converted into solid form.

Polymorphism

Many substances may exist in more than one crystalline or amorphous form so the phenomenon where compounds exist in more than one form is called polymorphism and different crystalline and amorphous forms are known as polymorphic forms.

Properties:

1. Different polymorphic forms exhibit different melting points, X-ray diffraction pattern, different solubility and different biological activity.
2. Polymorphism can affect mechanical properties of drug particles which

3. may directly affect the dosage form.
4. Many organic substances such as Theobroma oil exhibit four different polymorphic forms such as α, β,γ and β is considered as most stable form.

Physiochemical Properties of Drug Molecules

Physiochemical is defined as study of both physical and chemical property along with characteristics.

Optical rotation

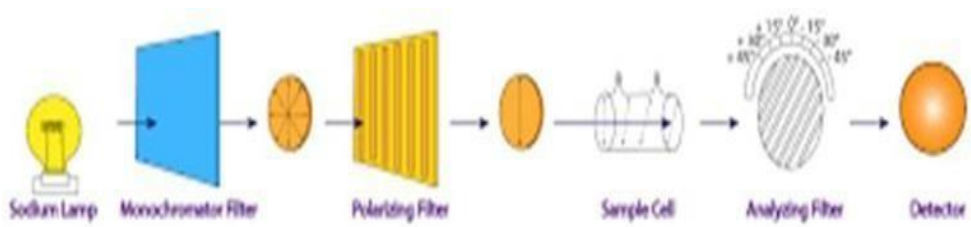
It is defined as angle at which plane of polarization is rotated when polarized light passes through a layer of liquid. The optically active substances are of two types.

1. Dextrorotatory: The substances which rotate plane of polarization of light towards right or clockwise direction. It is denoted by symbol (+).
2. Levorotatory: The substances which rotate plane of polarization towards left or in an anticlockwise direction. It is denoted by symbol (-).

Measurement of optical rotation

Polarimeters are used for measurement of optical rotation. A polarimeter consists of:

1. Polarised light source
2. Polarizer
3. Analyzer
4. Sample tube
5. Detector



When a light is passed through polarizer only light oscillating in one plane will leave the polarizer than PPL is introduced into a tube containing a solution with substance to be measured. If the substance is optically inactive the PPL will not change its orientation and if the substance is optically active the PPL either moves towards left or right.

Applications of optical rotation

1. It is used for identification and determination of optically active compounds.
2. It is also used in sugar industries to determine quality of juice from sugarcane and refined sucrose.
3. It is also used in chemical industries to determine specific rotation of chemicals.

4. Polarimeters are also used in remote sensing applications.

Refractive Index

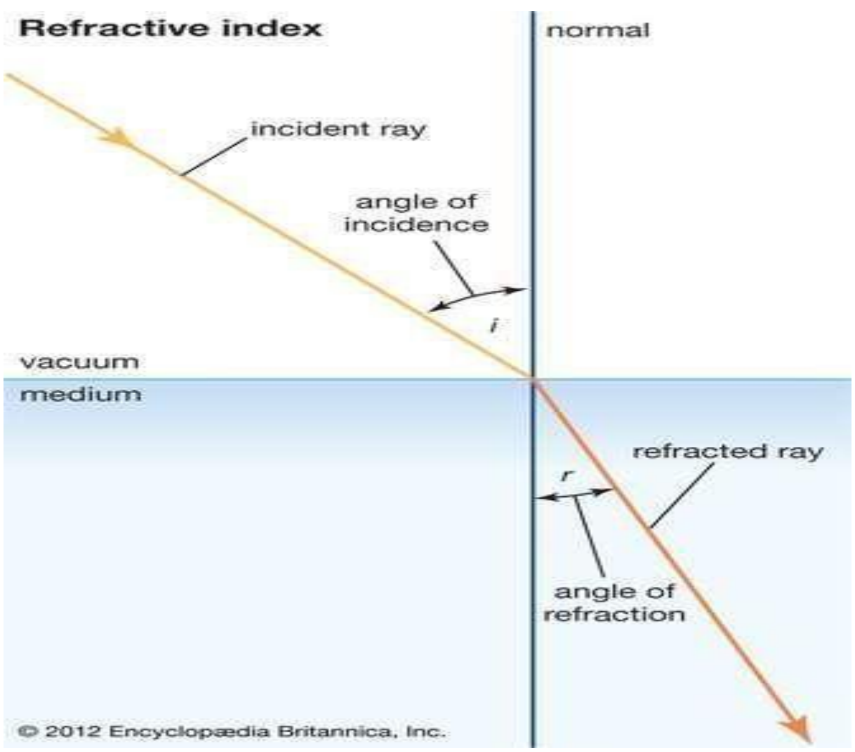
In optics, the refractive index (also known as refraction index or index of refraction) of a material is a dimensionless number that describes how fast light travels through the material.

It is defined as

$$\eta = c/v$$

Where c is the speed of light in vacuum and v is the phase velocity of light in the medium. For example, the refractive index of water is 1.333, meaning that light travels 1.333 times as fast in vaccum as in water. Increasing refractive index corresponds to decreasing speed of light in the material.

A ray of light when passing from one medium into another. If i is the angle of incidence of a ray in vacuum (angle between the incoming ray and the perpendicular to the surface of a medium, called the normal) and r is the angle of refraction (angle between the ray in the medium and the normal), the refractive index n is defined as the ratio of the sine of the angle of incidence to the sine of the angle of refraction; i.e., n = sin i / sin r. Refractive index is also equal to the velocity of light c of a given wavelength in empty space divided by its velocity v in a substance.



Measurement of Refractive Index

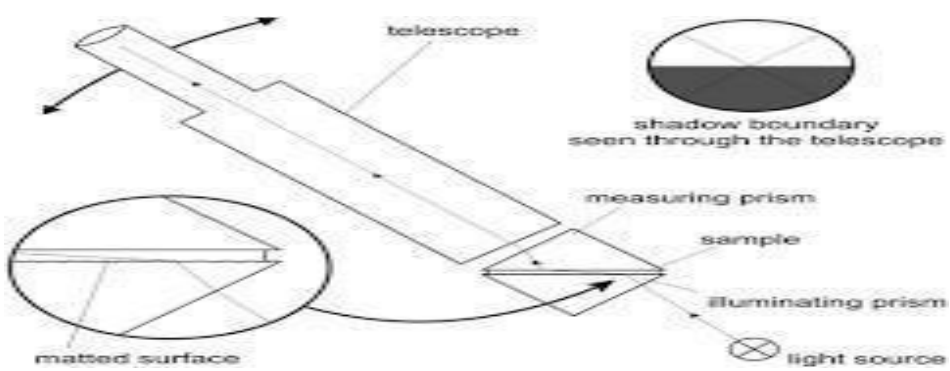
The refractive index of different substrates is measured with refractometers. There are different types of refractometer.

1. Abbe's refractometer
2. Pulfrich refractometer
3. Immersion refractometer
4. V-blockrefractometer

1. Abbe's Refractometer

The Abbe refractometer, named after its inventor Ernst Abbe (1840-1905), was the first laboratory instrument for the precise determination of the refractive index of liquids. The measuring principle of an Abbe refractometer is based on the principle of total reflection.

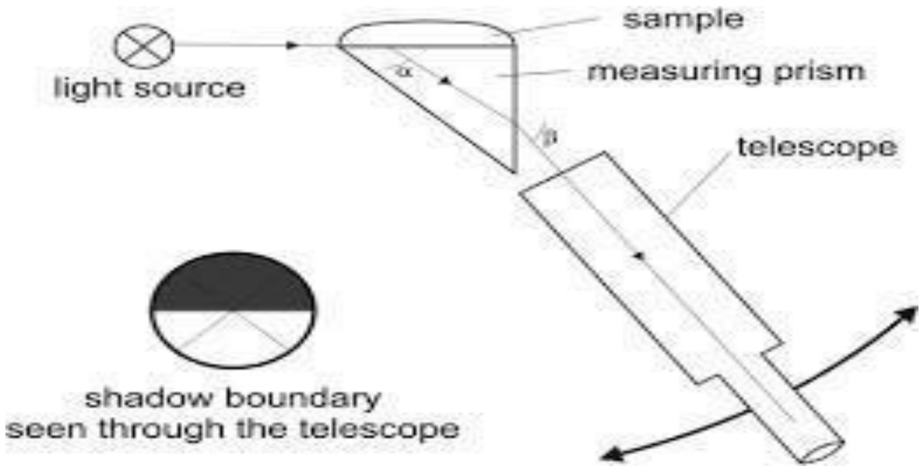
Abbé refractometer working principle is based on critical angle. Sample is put between two prisms - measuring and illuminating. Light enters sample from the illuminating prism, gets refracted at critical angle at the bottom surface of measuring prism, and then the telescope is used to measure position of the border between bright and light areas. Telescope reverts the image, so the dark area is at the bottom, even if we expect it to be in the upper part of the field of view. Knowing the angle and refractive index of the measuring prism it is not difficult to calculate refractive index of the sample. Surface of the illuminating prism is matted, so that the light enters the sample at all possible angles, including those almost parallel to the surface. Refractive index of a substance is a function of a wavelength. If the light source is not monochromatic (and in simple devices it rarely is) light gets



Dispersed and Shadow boundary is not well defined, instead of seeing sharp edge between white and black, you will see a blurred blue or red border.

2.Pulfrich Refractometer

Pulfrich refractometer is used to measure the refractive index of solids and liquid. It consist of right angled prism. A having its two faces perfectly plane. The solid B whose refractive index is to be determined is taken having two faces cut perpendicular to one another.

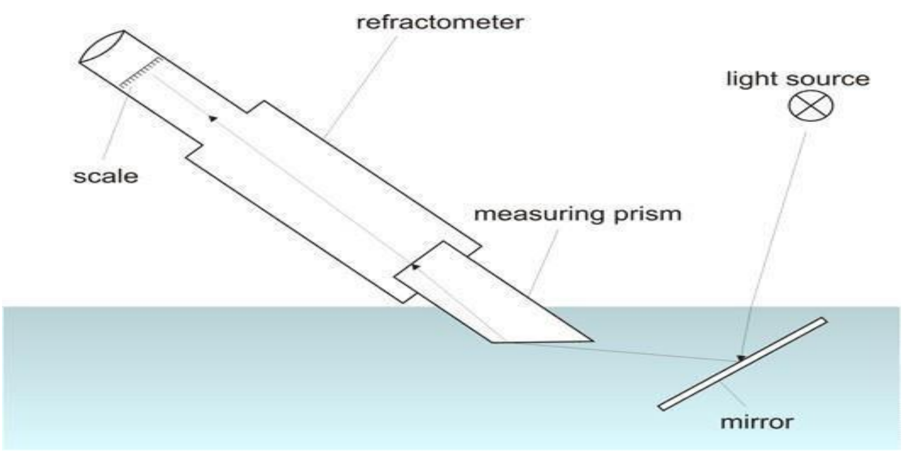


A glass prism of high refractive index has two plane polished faces, which are perpendicular to one another, and is so placed that one of these is vertical and the other horizontal. The substance whose refractive index is required is placed upon the horizontal surface, and in the case of a liquid is contained in a glass cell cemented to the prism so as to contain that face. A beam of monochromatic light is directed almost horizontally through the substance so that it meets the prism face at grazing incidence. the emergent beam is bounded sharply by the ray which actually grazes the prism surface, and the sharp boundary is observed with a telescope attached to a divided circle. On this circle, whose axis of rotation is horizontal, the angle of emergence of the beam from the vertical prism face can be read to one minute, with the aid of a vernier. For making measurements of dispersion a clam and a micrometer are provided, the smallest division on the drumhead of the micrometer screw corresponding to 6 seconds of arc. A condensing lens and supporting rod for vacuum tube form part of the apparatus. A small reflecting prism us also provided so that another source of light, e.g., a sodium flame, is easily interchangeable with the vacuum tube.
A special feature of the instrument is the increased effectiveness in the temperature control as compared with that to be found in previous designs. the hollow metal water jacket surrounding the prism is provided with a top cover with is itself of hollow metal. These two are connected in train with the thermometer jacket which dips into the cell for liquids. The prism and the substance experimented upon are thus completely jacketed with the exception of the vertical prism face from which the light

emerges, and a small rectangular aperture by which the light enters the prism. The temperature can thus be maintained very constant by pumping a stream of water at constant temperature through the system described.

3. Dip or Immersion Refractometer

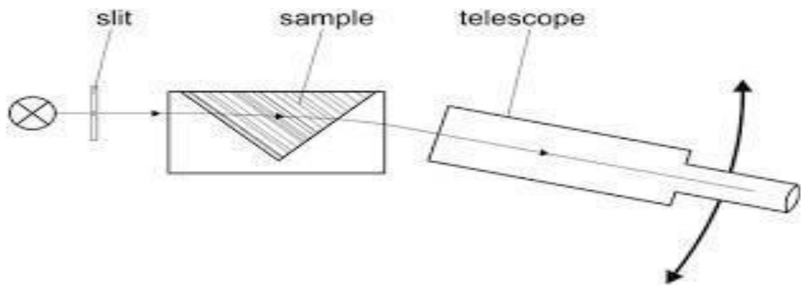
Dip, or immersion refractometer is designed to allow quick measurement of the refractive index of the liquid directly in the vat, without a need of taking samples. Simplest design is a refractometer that you just immerse partially into solution to make a measurement. In most cases dip refractometer is just a liquid proof Abbé refractometer (critical angle refractometer) mounted in a tube, with an additional immersible light source, or mirror that helps direct natural light on the measuring prism surface. If the light is directed at almost grazing angle, illuminating prism in not necessary.



First immersion refractometer was designed by Pulfrich and introduced by Carl-Zeiss in 1899, soon to be followed by an improved model in 1902. The refractometer didn't have an illuminating prism and a movable telescope - refractive index was read directly from the linear 1- 100 scale. The measuring prism was sticking out from the tube and was the only element of the refractometer that was in the contact with the solution, which helped keep the device corrosion free even in highly acidic solutions. Lack of the movable telescope meant the device had a very narrow working range, and required calibration, but it could also yield very high accuracy. Later instruments had interchangeable measuring prisms, which allowed measurements in a wider range of refractive indexes.

4. V- Block Refractometer

V block refractometer was initially designed by J.V. Angle at which light exits the refractometer block is a function of refractive index of the sample and of the glass (note additional refraction of the beam leaving the glass; incident beam enters the refractometer at zero angle.



The most important part of the v block refractometer is the v-shaped cell, cut in the rectangular block of glass (in practice it is much easier to build the refractometer cell gluing two prisms, butit is shape - not the method of getting it - that matters). Cell walls are perpendicular. Cell is filled with the liquid. Beam of light enters the sample and gets refracted twice at two perpendicular cell walls. Angle at which light exits the refractometer block is a function of refractive index of the sample and of the glass (note additional refraction of the beam leaving the glass; incident beam enters the refractometer at zero angle, so it doesn't get refracted). Knowing the exit angle and the refractive index of the glass we can easily calculate refractive index of the sample.

Applications of Refractive Index

1. It is mainly used to identify particular substance, confirm its purity or measure its concentration.
2. It is used to calculate the focal power of lenses and dispersive power of prisms.
3. It also applies to estimate thermophysical properties of hydrocarbon and petroleum mixtures.
4. It is used in the estimation of organic compounds, solutions and food products.
5. In veterinary medicines, refractometer is used to measure total plasma protein in bloodsample.

Dielectric Constant

Dielectric constant (ϵr) is defined as the ratio of the electric permeability of the material to the electric permeability of free space (i.e., vacuum) and its value can derived from a simplified capacitor model**.**

The dielectric constant is generally defined to be κ=E0E or the ratio of the electric field in a vacuum to that in the dielectric material, and is intimately related to the polarizability of the material.

Measurement of Dielectric Constant

It is measured by the effect of measuring the inverting solvent on the electric field between two opposite charged particles. The capacitance between two plate for holding the test solution between the plate is measured. After that, measure the capacitance by maintaining the vaccum between the plates. Then the dielectric constant between the plate is obtained which is ratio of capacitance (C) of a capacitor completely filled with the dielectric to the capacitance (C0) of the capacitor filled with space or vaccum. It has no dimensions.

$$\varepsilon = c/co \text{ and } CO = \varepsilon O\ A/t$$

Where, C is capacitance using the material as the dielectric in the capacitor CO is the capacitance using vaccum as the dielectric εo permittivity of free space.s A is area of plate or cross section areaT is thickness of the sample

Applications of Dielectric Constant

1. These are used for energy storage in capacitors.
2. To enhance the performance of a semiconductor device, high permittivity dielectric materials are used.
3. Dielectrics are used in Liquid Crystal Displays.
4. Ceramic dielectric is used in Dielectric Resonator Oscillator.
5. Barium Strontium Titanate thin films are dielectric which are used in microwave tunabledevices providing high tunability and low leakage current.
6. Parylene is used in industrial coatings acts as a barrier between the substrate and theexternal environment.
7. In electrical transformers, mineral oils are used as a liquid dielectric and they assist in thecooling process.
8. Castor oil is used in high-voltage capacitors to increase its capacitance value.
9. Electrets, a specially processed dielectric material acts as electrostatic equivalent to magnets.

Dipole Moment

A dipole moment arises in any system in which there is a separation of charge. They can, therefore, arise in ionic bonds as well as in covalent bonds. Dipole moments occur due to the difference in electronegativity between two chemically bonded atoms. A bond dipole moment isa measure of the polarity of a chemical bond between two atoms in a molecule. It involves the concept of electric dipole moment, which is a measure of the separation of negative and positive charges in a system.

1. The dipole moment of a single bond in a polyatomic molecule is known as the bond dipole moment and it is different from the dipole moment of the molecule as a whole.
2. It is a vector quantity, i.e. it has magnitude as well as definite directions.
3. Being a vector quantity, it can also be zero as the two oppositely acting bond
4. dipoles can cancel each other.
5. By convention, it is denoted by a small arrow with its tail on the negative center and itshead on the positive center.
6. In chemistry, the dipole moment is represented by a slight variation of the arrow symbol.
7. It is denoted by a cross on the positive center and arrowhead on the negative center. Thisarrow symbolizes the shift of electron density in the molecule.
8. In the case of a polyatomic molecule, the dipole moment of the molecule is the vectorsum of the all present bond dipoles in the molecule.

$$\text{Dipole momet } (\mu) = q * r$$

Greater is the charge, larger will be dipole moment, and smaller is the distance, larger will be dipole moment.

Dissociation Constant

An acid dissociation constant, Ka, (also known as acidity constant, or acid-ionization constant) isa quantitative measure of the strength of an acid in solution. It is the equilibrium constant for a chemical reaction which is known as dissociation in the context of acid–base reactions.

Important key points of Module

1. Matter can exist in one of three main states: solid, liquid, or gas.
2. Solid matter is composed of tightly packed particles. A solid will retain its shape; the particles are not free to move around.
3. Liquid matter is made of more loosely packed particles. It will take the shape of its container. Particles can move about within a liquid, but they are packed densely enough that volume is maintained.
4. Gaseous matter is composed of particles packed so loosely that it has neither a defined shape nor a defined volume. A gas can be compressed.
5. Four types of refractometers are used to determine refractive index.

6. The substances which are used to rotate plane polarized light towards right are called dextrorotatory and which rotate towards left are called levorotatory.
7. The dipole moment of a single bond in a polyatomic molecule is known as the bond dipole moment and it is different from the dipole moment of the molecule as a whole.

Important Questions

2 Marks

1. Define dipole moment.
2. What is solubility?
3. Define process of solute and solvent interaction.
4. Define latent heat.
5. What are eutectic mixtures.
6. Define vapour pressure.
7. What is relative humidity?
8. Define glassy state and liquid crystals.
9. What is triple point?
10. What is critical point in sublimation.

5 Marks

1. Explain the process of sublimation.
2. Write a note on aerosols and inhalers.
3. Write a note on different forms of matter.
4. Differentiate between crystalline and amorphous forms.
5. Explain polymorphism.

10 Marks

1. Explain the different types of refractometers used in determination of refractive index.
2. Write a note on optical rotation.
3. Explain dipole moment and dissociation constant along with its applications.
4. Explain the applications of refractive index.