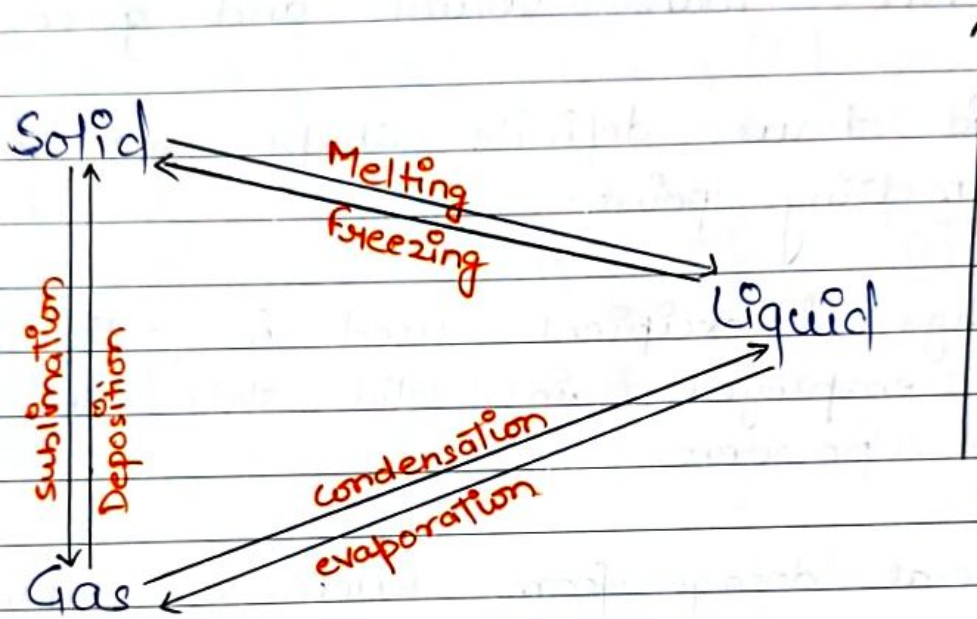
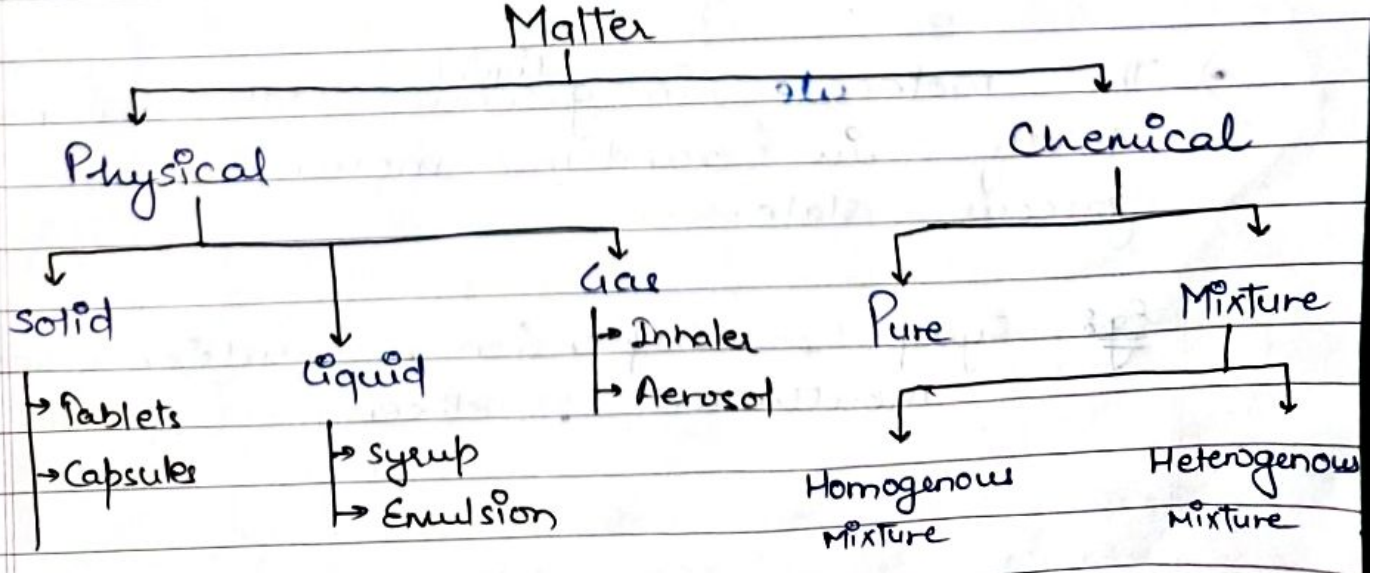
UNIT - II

State Of Matter



* **Matter:** Matter is a substance which occupy space and have a mass.



* Solid :) It consists of ion, atom & molecules which are in fixed position & occupy space & and are closed packed

) Intermolecular force spaces in solid are lesser than liquid and gases.

) solid have definite shape and rigidity, & melting point.

) Drugs & excipient used in solid dosage are employed in solid state as crystals and powders.

) Several dosage form such as tablet, capsule, dry powder injection & dry syrup are exist in solid state.

* Liquid :) The substance which have definite volume but shape & size is not fixed.

) The molecule in liquid state are not totally in random movement as in gaseous state.

Eg: Syrups, suspension, emulsion, solution, mouthwash, elixers.

* Gases :) The substance does not have shape . size & volume.

) Intermolecular space in gaseous molecule are higher.

) Gas molecules have more KE.

Eg: Inhalers , sprays , Nebulizers

* Change In state of Matter :

→ Melting is the physical process in which phase transition change from solid to liquid.

→ Freezing is the phase transition in which liq. is converted into solid.

→ Evaporation is the phase transition from a liq. to gas.

→ Condensation is the phase transition from gas to liquid.

→ Deposition is a thermodynamic process in which gaseous phase is converted into solid phase without passing through the liquid phase.

→ Sublimation is a transition of substance directly from the solid to gas phase with

* **Latent Heat:** Latent heat is the energy absorbed or released by a substance during a phase transition from one state to another state.

It is denoted by 'L', and its unit is Joule (J) or Cal/mole or unit mass.

Latent heat is of two types:

1) Latent heat of fusion
2) Latent heat of vapourisation / evaporation

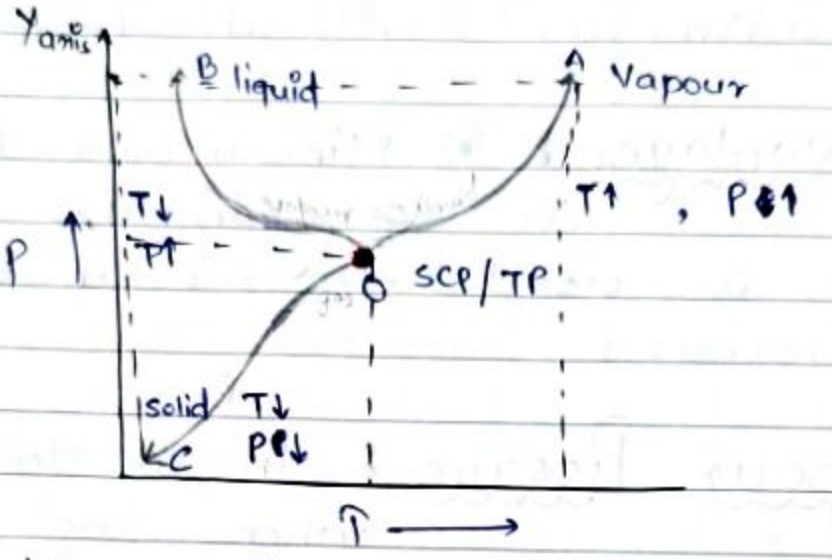
* **Latent heat of fusion:** The heat associated with melting a solid and freezing a liq. is known as latent heat of fusion.

* **Latent Heat of Vapourisation:** Heat associated with vapourising a liq. or condensing a vapour.

* **Sublimation:**

Sublimation is the process of transformation of solid directly into the vapour phase without passing into liquid phase.

* Principle : Sublimation Critical point :-



OA : Vapourizing curve
OB : Melting curve
OC : Sublimation curve

Phase of any matter can be changed by changing temperature & pressure.

'O' is the point where all phases of matter are in equilibrium state.

Line OA represent when we increase the temperature & pressure any solid can change into vapour.

Line OB represent when we increase pressure and decrease temp. then substance is converted into liquid.

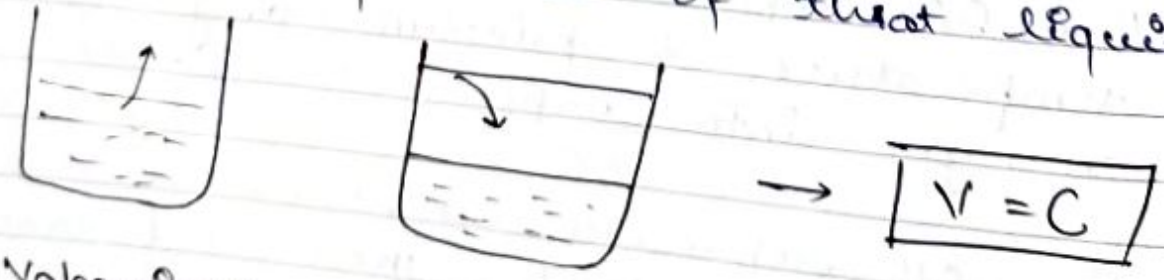
Line OC represent when we decrease temp. & pressure then substance is converted into solid.

→ The point at which this sublimation takes place is known as sublimation critical point (SCP).

* Advantages : • Min. amount of product is loss in this process.
• It is used in the purification process.

* Vapour Pressure : In a closed container when we heat any liquid the liq. gets vapourised & the pressure created by vapours on the inner wall of container is known as vapour pressure.

At the point when the rate of evaporation is equals to the rate of condensation, the pressure created by the vapour is known as vapour pressure of that liquid.



Vapourisation Condensation

* Factors Affecting Vapour Pressure :

- Nature of solvent : Volatile solvents increases the vapour pressure of the system.
- Surface Area : The vapour pressure is independent of the surface area.
- Temperature : The temp. of liq. or solid increases then vapour pressure also increases.
- Intermolecular forces : The liq. having weak intermolecular forces shows higher vapour pressure.

* Eutectic Mixtures :

When two or more solid particles are mixed together in a certain ratio and their melting point reduces and they convert into liq. then the mixture is known as Eutectic mixture.

Eutectic is a greek word which means easy Melting

Mixture tends to liquify due to reduction in its melting point.

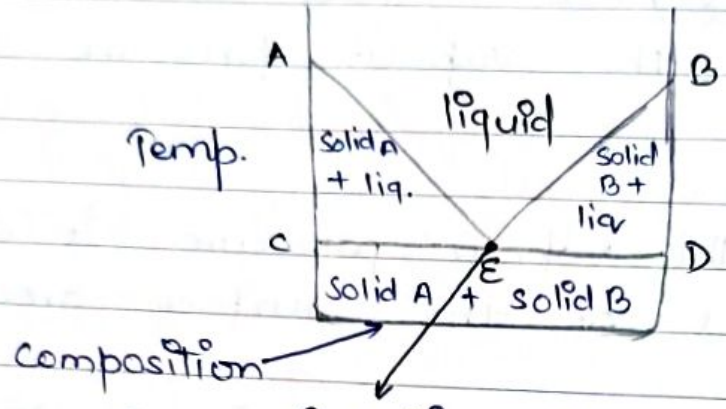
Eg : Ibuprofin M.P → 62°C

Thymol 42°C

Reduced M.P.

37°C

* Principle of Eutectic Mixture :



→ Below the eutectic point, the mixture of 2 substance will exist in a solid state.

→ While above eutectic point, the mixture of 2 substance will convert into a liq. state.

* Gases :

Gas law (P, V, T, n)

Boyle's law - $P \propto \frac{1}{V}$

Charles law - $V \propto T$

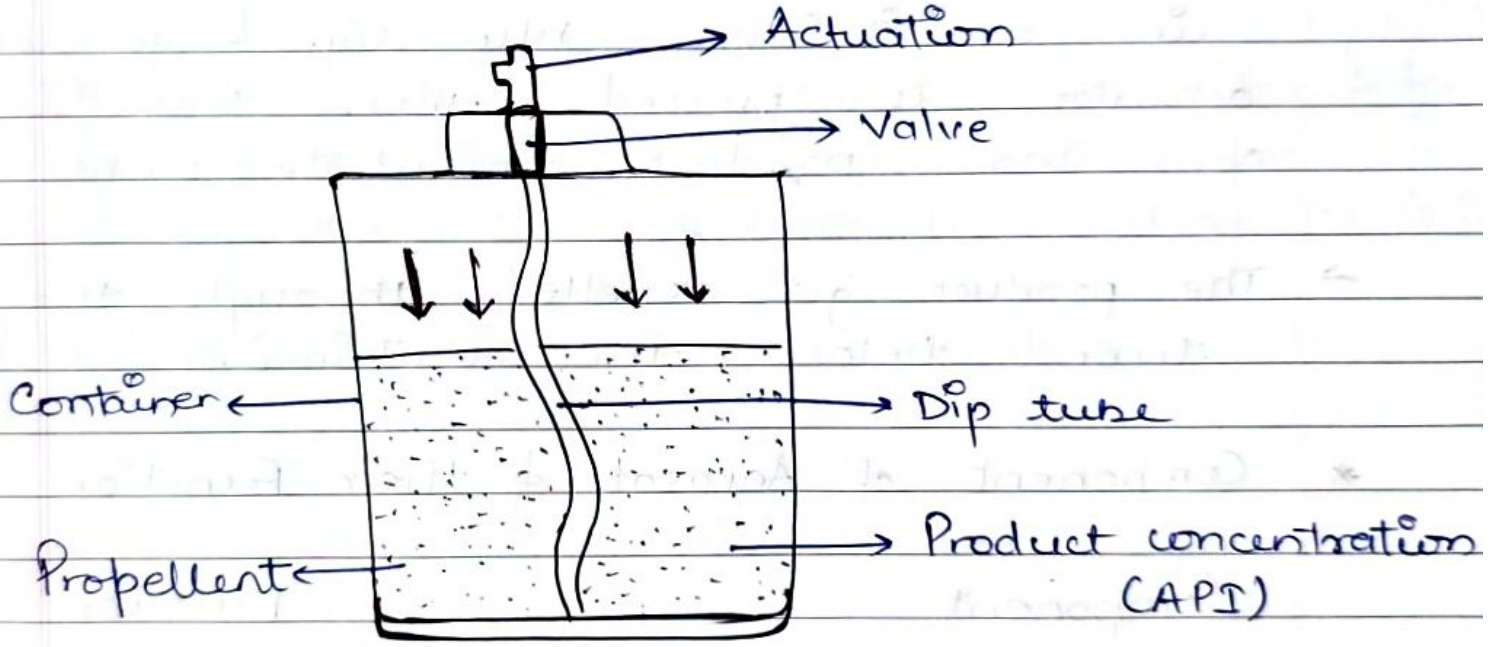
Gay Lussac's law - $P \propto T$

Avagadro's law - $V \propto \frac{1}{n}$

Ideal Gas Equation - $PV = nRT$

* **Aerosols :** Aerosols are pressurized dosage form containing 1 or more therapeutic ingredient which upon actuation emit a fine dispersion of liq. or solid material in the outer environment.

* **Types of Aerosols :**



* **Types of Aerosols :**

- Space Spray
- Surface coating spray
- Foam Spray

* **Function of Aerosols :**

→ The assembly of aerosol are made up of different components such as :-

→ Actualor
→ Valve
→ Dip tube
→ Container
→ Product Concentrate (API)
→ Propellant

→ The product concentrate in container is in equilibrium b/w liq. & gas when actuator is pressed then value is open and product concentrate pushes out

→ The product get expelled through the dip tube below the container.

* Component of Aerosol & their function

Component		function
1. Actuator	:	for opening the value
2. Valve	:	for delievering the
3. Dip Tube	:	Transfer of liq.
4. Container	:	Carry the product
5. Product Concentrate	:	It consists of API & other ingredients.
6. Propellent	:	It develop pressure in the container.

Eg:- Trichloromonofluoromethane, Dichlorofluoromethane

* Advantages : •) Sterility is maintained.

•) Required quantity of medicament can easily withdrawn, without contamination directly to affected part of body.

•) Protected by any chemical & physical degradation.

•) Through inhalation (oral) it is suitable for bronchial disease as fine dispersion directly ~~dis~~ delivers to bronchi avoiding the GIT.

* Disadvantages : •) Most propellant is toxic in nature.

•) This system is difficult in design

•) Expensive in cost.

* Inhalers : It is a medical device used for delivering medication into the body ~~via~~ via. lungs.

Eg: Inhalers used to treat COPD (Chronic obstructive Pulmonary Disease) & also used by asthama patient.

* Types of Inhalers :

1) Pressurized metered Dose Inhaler
2) Dry Powder Inhaler.
3) Nebulizer
4) Nasal Inhaler

* **Relative Humidity**: It is defined as the ratio of actual partial pressure of water pressure in the moist air to the saturated.

Partial pressure of water ~~pressure produced~~ vapour corresponding to the temp. is relative humidity

OR

It may be defined as ratio of amount of ~~water~~ vapour in the air at specific temp. to the max. amount of water vapour that air can hold at that temp.

→ It is expressed in percentage.

$$\text{Relative humidity} = \frac{\text{Actual water VP}}{\text{saturated water VP}} \times 100$$

$$\%\,RH = \frac{\text{Actual water in air}}{\text{Max. water air can hold}} \times 100$$

* Liquid Complex :

→ liquid complex are binary system or mixtures that have co-existence b/w the two phases i.e. solid ÷ liquid (suspension), liquid - liquid (emulsion), solid - gas (granular), liquid - gas (-foams).

→ They exibit unusual mechanical responses to apply stress or strain due to the geometrical arrangement.

* Liquid Crystal :

→ They have long rod like molecules. They do not melt to give the liquid substance directly.

→ They passed through an intermediate state b/w solid state & liquid state. It is known as liquid crystal.

$$\text{Solid state} \xrightarrow[\text{state}]{\text{Intermediate}} \text{liquid state}$$

Eg: Cholestrol, Benzoate (145°C to 178°C)

* Glassy state : Glass is a non-equilibrium non-crystalline state of matter that appear on solid on a short scale but continuously relax towards the liquid state.

Glass is a transparent, brittle, does not have a proper structure & have solid appearance.

* Materials Used in Preparation of Glass:

•) Formers : Any compound that can be melted & cooled into a glass

Eg : Anhydrous boric acid
Anhydrous phosphoric acid

•) Fluxes : Fluxes are used to reduce melting point of formers at lower temperature.

Eg : Silica or sand (which melt at / upto 2000°C)

•) Stabilizers : Fluxes makes the glass unstable chemically therefore, stabilizers such as limestone, alumina, zinc oxide are used to stabilize the glass.

* Glass Transition Temperature :

• Temperature below which a polymer is hard, brittle & above which it is soft is known a glass transition temperature.

• The hard & brittle state is glass state while soft & flexible state is rubber state.

* Difference between

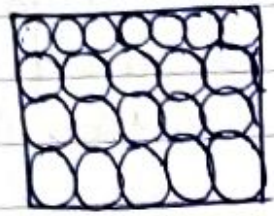
* Solid : Solid consists of ion, atom & molecule which are held in fixed positions and closely packed.

The interparticle attraction in solid are stronger than liquids hence solid have following characteristics such as :- definite shape, volume & melting point. and mass.

* Types of solid :

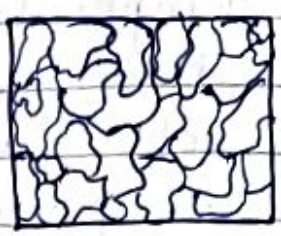
- Crystalline
- Amorphous

Crystalline



- The atom & molecule are arranged in definite pattern.
- On cutting crystalline solid plane & smooth edges are formed
- Crystalline solid have sharp melting & boiling point.
- Shows poor water solubility because more energy is required by orderly arranged molecule. for dissolution
- When crystalline solid is heated at constant rate the temp. increases
- Crystalline solid have less absorption rate therefore, less ~~bioabai-~~ ~~bili~~ bioavailability

Amorphous



- The atom & molecule are non-arranged in definite pattern
- On cutting amorphous solid rough edges are formed.
- Amorphous solid have low melting and boiling point.
- Shows good water solubility because less energy is required by randomly arranged molecule for dissolution.
- When amorphous solid is heated at a constant rate the temp. increases & at different rate.
- Amorphous solid have more absorption rate therefore, more bioavailability.

• It is partially incompressible • Higher energy is required for molecules to escape from crystal form • These solids are stable than amorphous solid. • Handling quality of crystalline material is poor.	• It is practically compressible. • less energy is required for molecule to escape from amorphous form. • These solids are less stable than crystalline solid. • Handling quality of amorphous material is better.

* **Polymorphism** : It is the ability of a molecule to crystallize into more than one different crystal structure.

→ The term polymorph means the substance have same molecular composition but have different crystalline forms.

→ Substance in 2 different form is known as dimorphic while in 3-different form is known as trimorphic.

→ Polymorphs are ~~capably~~ chemically same but are different with respect to physicochemical properties.

→ The different forms have different thermodynamic properties such as melting point, lattice energy, vapour pressure, solubility & bioavailability.

* Types of Polymorphs:

→ Monotrophic: When polymorphic changes is non reversible then it is called monotrophic

→ Enantiotrophic: If the changes from 1 - polymorph to another is reversible is known as

* Example of Polymorphism:

1) Chloramphenicol Palmitate: Form A, Form B

2) Phenoparbital: form I, form II, form III

* Physiochemical properties of drug Molecules:

Physicochemical properties involve the specific interaction b/w the molecule & these are determined with at the use of animal & isolated organ.

* Application of Physicochemical Properties:

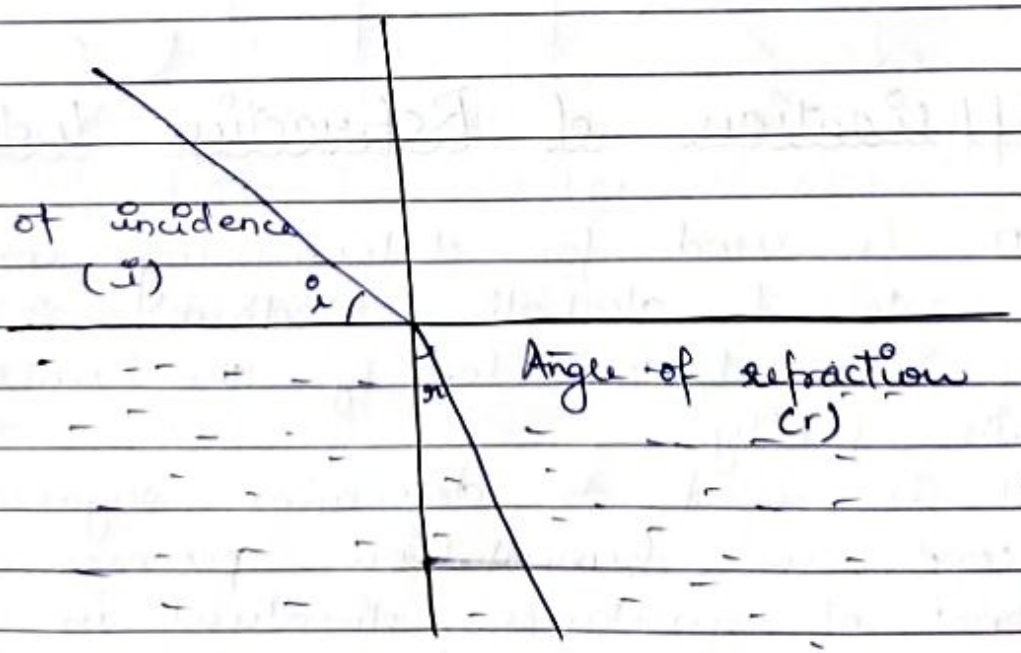
→ Identification of drug molecules
→ Determination of % composition of drug
→ It is used in drug synthesis.
→ Analysis of the structure of molecule.
→ formulation of dosage form.

* Refractive Index : Refractive index is the ratio velocity of light in empty space / air / vacuum to the velocity in the selected medium.

$$\eta = \frac{c}{v}$$

where,

η = Refractive index
c = velocity of empty space / air
v = velocity of dense medium



→ When a ray of light passes from one medium to other medium it shows refraction i.e., change in direction & change in direction of ray is known as Refraction.

→ If the light rays from less dense medium (air) to the denser medium (water). It reflects towards the normal.

* **Snell's law:** It states the refractive index is the ratio of sin of angle of incidence to the sin of angle of refraction:

$$\eta = \frac{\sin i}{\sin r}$$

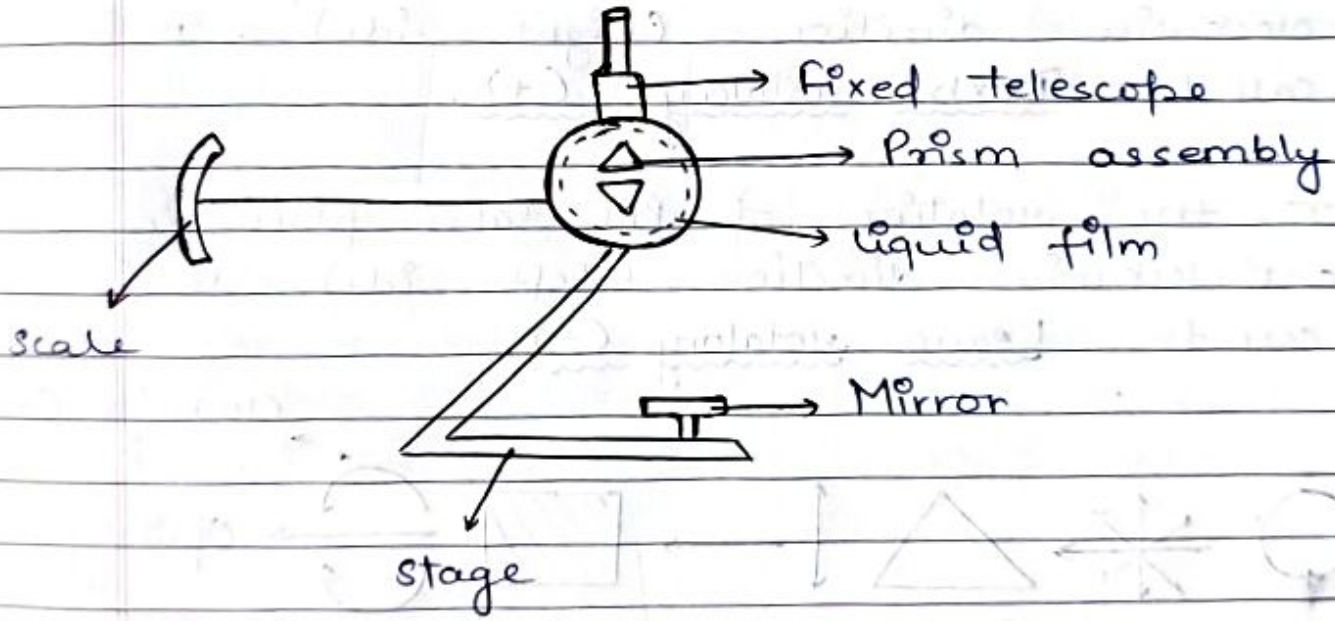
* **Application of Refractive Index:**

→ It is used for determining concn of water & alcoholic medium.
→ It is used to identify the substance & its purity.
→ It is used to determine sugar & alcohol concn in fermentation process.
→ Concn of substance dissolved in liquid can be identified.
→ It is used for determining the isotropic nature of compound.

→ It is used to calculate focusing power of lenses.
→ Dielectric constant can also be determined.

* Determination of Refractive Index :

Abbe's Refractrometer is a quick & convinient instrument for determining the refractive index.



* Eg. of Refractive Index of Chemicals :

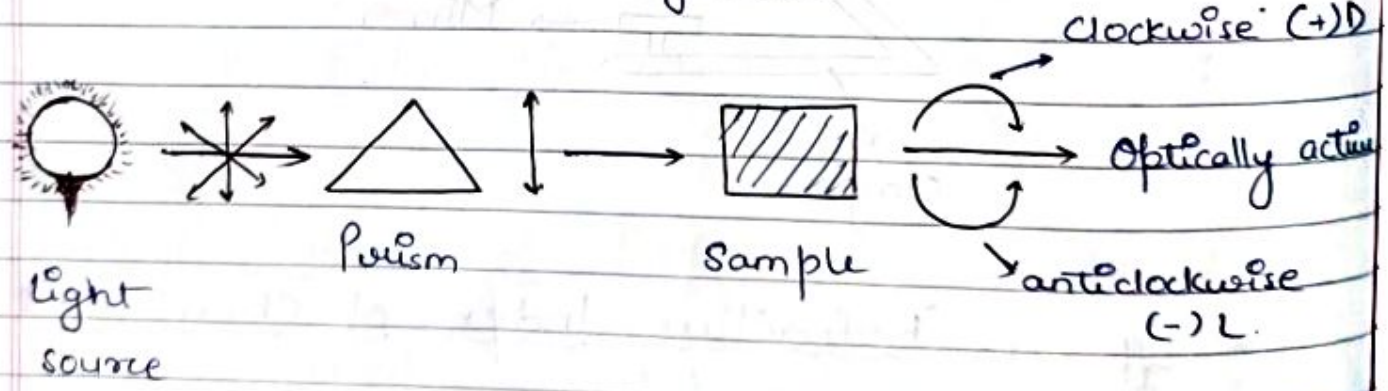
1) Methyl Acetate : 1.3615 - 1.3625
2) Nitro Benzene : 1.380.

* **Optical Rotation:** Optical activity is the ability of certain substance to rotate the plane of polarised light (PPL)

→ Optically active substance are the substance which can rotate the light either in to right side or to left side.

→ If the rotation of PPL takes place in clockwise direction (Right side). It is called Dextro rotatory (+).

→ If the rotation of PPL takes place in anticlockwise direction (Left side). It is called Leavo rotatory (-).



* **Application of Optical Rotation:**

→ It is used to identify whether the substance is optically active or not

→ Purity of substance is determined.

→ The concentration of substance dissolved in

solvent can be determined.

→ Optically activity is used in study of structure of Anerobopic material.

→ Adultration in the optically active substance can be determined from the optical rotation.

→ Polarimetry is used in analysis of various drugs & pharmaceutical formulations.

* Dielectric Constant :

→ A polar molecule can sustain a separation of electric charges either through the induction by an external electric field or by a permanent charge separation within a molecule.

→ The seperation of charges can be better understood by the concept which is k/a dielectric constant.

→ Dielectric constant is the ratio b/w the permitivity of the medium to the permitivity of free space.

$$\varepsilon_r = \frac{\varepsilon_m}{\varepsilon_0}$$

→ The characteristics of dielectric medium can be determined by dielectric constant.

→ It has no unit.

→ Dielectrics are the material having electric dipole moment. Dipole is an entity in which equal positive & negative charges are separated by a small distance.

Eg: Dielectric constant of few liquid.

Water - 78.50	Methanol - 32.60
Benzene - 2.27	Ethanol - 24.60

* Determination of Dielectric Constant:

→ The dielectric constant of a solvent is measured by

↓

determining conductance b/w two plates by keeping test solution in between

↓

After that measure the conductance by maintaining vaccum b/w plates.

↓

Ratio of first conductance and second

Conductance gives dielectric constant.

* Applications of Dielectric Constant :

It can be used in formulation design such as crystalization.

It is an index polarity of solvent which governs the solubility of drug.

Eg : Dielectric Constant of Drug

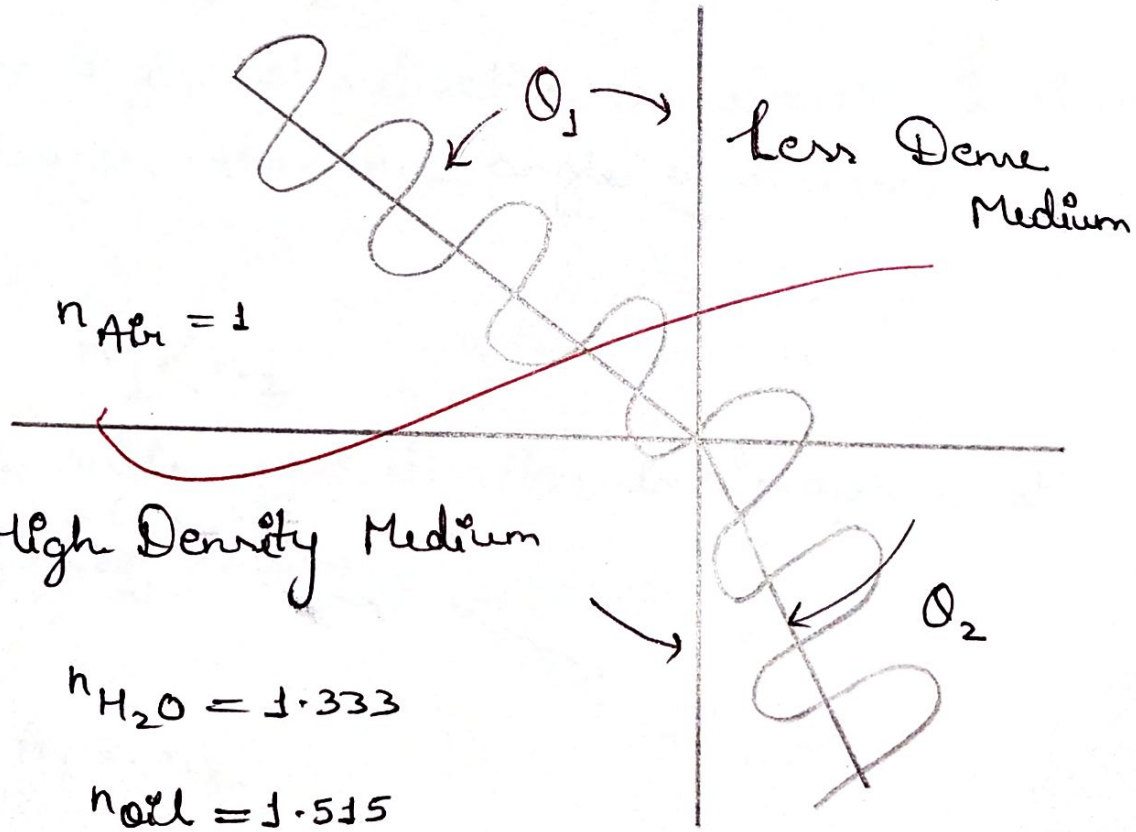
Caffeine : 40-43

Phenobarbital : 27-30

PHYSICOCHEMICAL PROPERTIES OF DRUG MOLECULES :-

Refractive Index :-

Refractive Index (Index of Refraction) is a value calculated from the ratio of the speed of light in a vaccum to that in a second medium of greater density. The refractive index variable is most commonly symbolized by the letter n or n' in descriptive text & mathematical equations.



Refraction of light

As presented in the figure above, a wavefront incident upon a plane surface separating two media is refracted upon entering the second medium if the incident wave is oblique to the surface. The incident angle (θ_1) is ~~refr~~ related to the refraction angle (θ_2) by the simple relationship known as "Snell's law".

$$n_1 \times \sin(\theta_1) = n_2 \times \sin(\theta_2)$$

where,

n = Refractive index of material (1) & (2)

θ = Angles of light travelling through there materials with respect to the normal.

If,

$$n_1 > n_2$$

then, the angle of refractive or refraction is always larger than the angle of incidence.

If,

$$n_1 < n_2$$

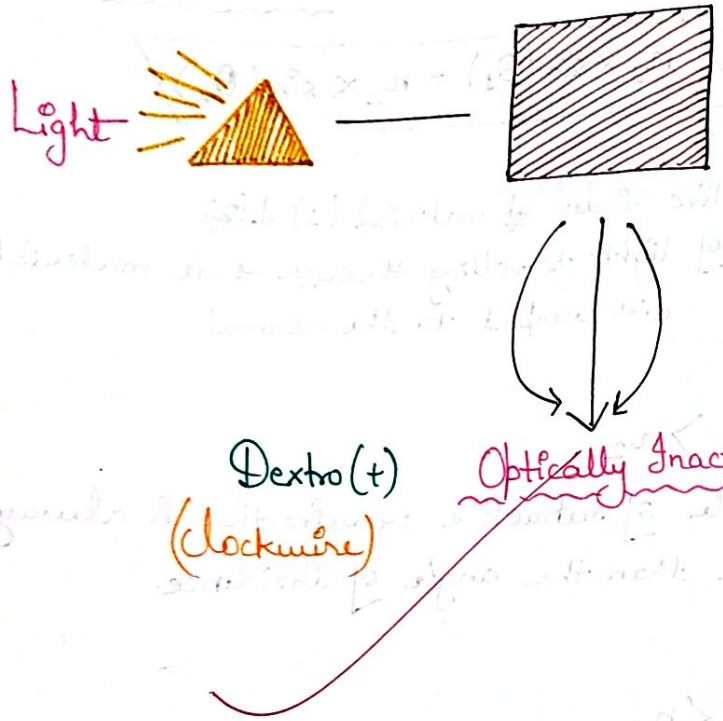
then, the angle of refraction is always smaller than the angle of incidence.

If,

$$n_1 = n_2$$

then, the light is passed through without any type of refraction.

OPTICAL ROTATION



Optical Rotation :—

→ The optical Rotation is the angle through which the plane of polarization is rotated when polarised light passes through a layer of liquid.

→ Optical activity is the ability of a compound to rotate the plane of polarized light.

→ The property of rotating rises from an interaction of the electromagnetic radiation of polarized light with the unsymmetric electric fields generated by the electrons in a chiral molecule.

→ A compound is said to be optically active when the linearly polarised light is being rotated when it is paring through it.

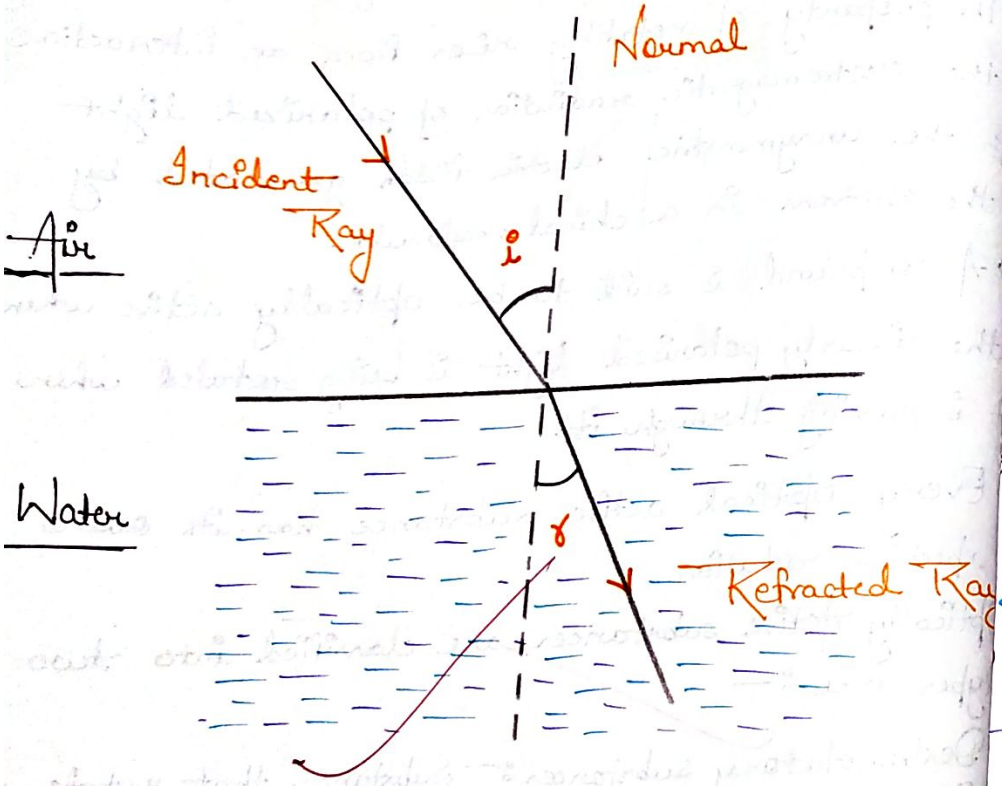
→ Every optical active substance has its own specific rotation.

Optically Active substances are clasified into two types are :—

1) Dextrorotatory substances :— Substances that rotate the plane of polarization of the light towards the right are known as right handed or Dextrorotatory.

2) Laevorotatory substances :— Substances which rotate the plane of polarisation of the light toward the left are known as Left handed.

SNELL's Law :—



6) Dielectric Constant :—

It is the ratio of permitivity of medium (ε) upon permitivity of free space (ε_0).

$$\text{Dielectric Constant} = \frac{\varepsilon}{\varepsilon_0}$$

Measurement :—

1) Co-axial problem method.
2) free space method.
3) Resonant cavity Method.
4) Parallel-plate Capacitor method.

Applications :—

1) Dielectrics are used to manfacture capacitor.
2) Used to manufacture transformer.
3) They are used in measuring & heating process.

SNELL's Law :—

It gives the relation between the angle of incidence & angle of refraction.

$$\eta = \frac{\sin i}{\sin r}$$

where,

i = Angle of incidence

r = Angle of refraction.

1) Dipole Moment :—

→ The mathematical product of the charge into distance.

$$\mu = q \cdot \gamma$$

where,

μ = dipole moment

q = charger product

γ = distance present between the two charger.

→ The measurement of net molecular polarity, which is the magnitude of the charge Q at either end of the molecular dipole times the distance γ between the two charger.

→ The SI unit for electric dipole moment is the Coulomb–meter (C·m)

Is Dipole moment a force?

→ Whenever two equal & opposite charger are brought together there will be either some attraction or repulsion force between them.

1) DISSOCIATION CONSTANT:-

1) The dissociation constant is an immediate consequence of the law of mass action which describes equilibria in a more general way.

1) The dissociation constant is also sometimes called Ionisation Constant when applied to salts.

1) The inverse of the dissociation constant is called "Association constant".

1) The dissociation constant is usually written as a quotient of the equilibrium concentration (in mol/l).

$$H_2O \rightleftharpoons H^+ + OH^-$$

According to law of mass Action:-

$$\text{Rate of Reaction} \propto \frac{[H^+][OH^-]}{[H_2O]}$$

$$\frac{dx}{dt} = \frac{K_a [H^+][OH^-]}{[H_2O]}$$

$$\boxed{K_a = \frac{[H_2O]}{[H^+][OH^-]} \cdot \frac{dx}{dt}}$$

IONIZATION OF WEAK BASES: The ionization of a weak base (ammonium hydroxide), in water can be written as

$$NH_4OH + H_2O \rightleftharpoons NH_4^+ + OH^-$$

1. The ionization constant or the dissociation constant or basicity constant of ammonium hydroxide is given by the below equation.

$$K_b = \frac{[NH_4^+][OH]}{[NH_4OH]}$$

2. K_b values can be used to compare strength of weak bases. If K_b is more the base is stronger than the other.

3. Negative logarithm of K_b is called pK_b. If pK_b of a base is less, it is strong base.

4. pK_b can be found by half neutralization method. In this method, the base is half neutralized and the pH will be equal to the pK_b of the base.