

# UNIT - II



## STATES OF MATTER

### Points to be covered in this topic

→ 1. STATES OF MATTER

→ 2. CHANGE IN THE STATE OF MATTER

→ 3. LATENT HEAT, VAPOUR PRESSURE

→ 4. SUBLIMATION, CRITICAL POINT

→ 5. EUTECTIC MIXTURES, GASES, AEROSOLS

→ 6. INHALERS, RELATIVE HUMIDITY

→ 7. LIQUID COMPLEX, GLASSY STATE, SOLIDS

→ 8. REFRACTIVE INDEX, OPTICAL ROTATION

→ 9. DIELECTRIC CONSTANT, DIPOLE MOMENT

→ 10. DISSOCIATION CONSTANT



# STATES OF MATTER

- Matter can be defined as anything that has mass and occupies space.

## STATES OF MATTER

### Physical Classification

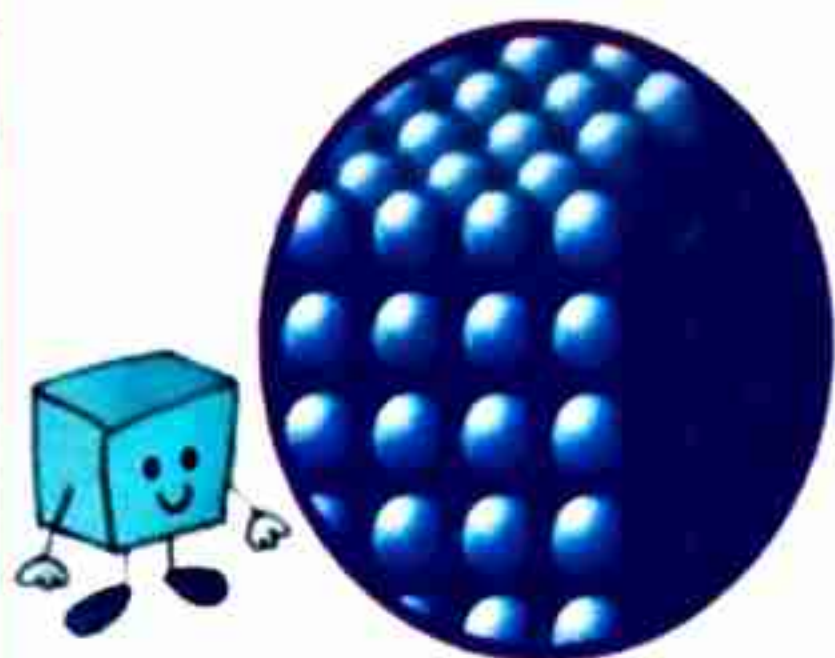
- **Solid** (Ex: Tablet, Capsule)
- **Liquid** (Ex: Oral syrup)
- **Gas** (Ex: Aerosol)
- **Plasma**

### Chemical Classification

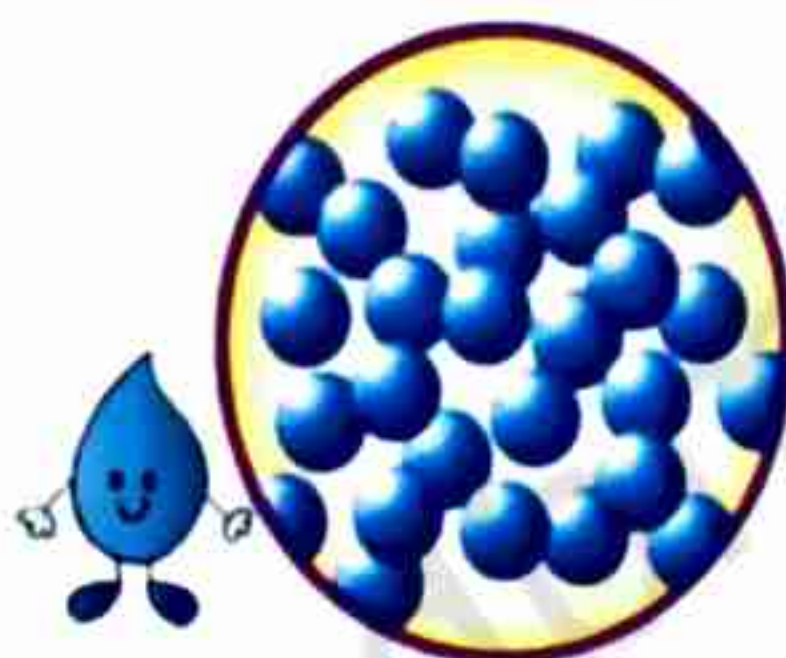
- **Pure Substances** like element and Compound
- **Mixture** like homogeneous and heterogenous

## ❖ Three States of Matter

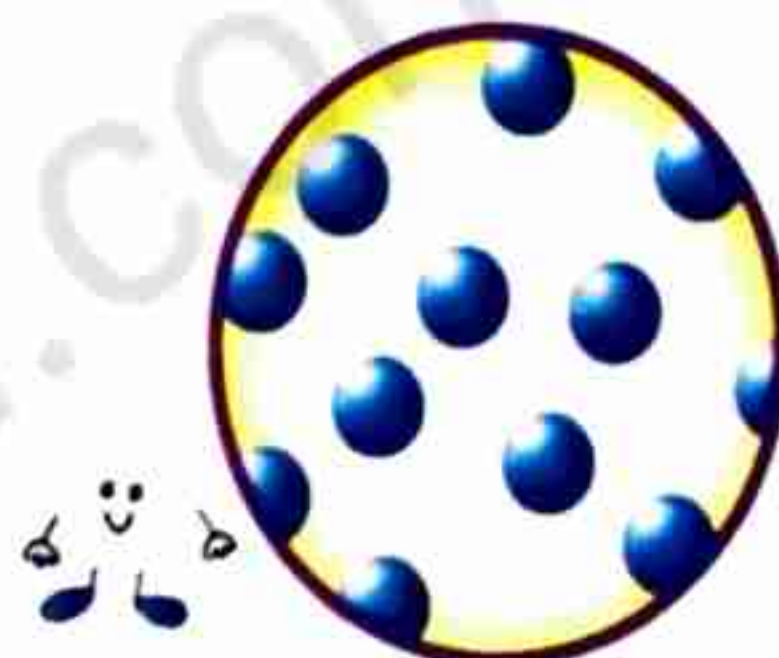
Solid



Liquid



Gas



## Properties of Solid, Liquid and Gaseous State

SOLID	LIQUID	GAS
Retains volume and shape	Assumes the shape of part of the container it occupies	Assumes the shape and volume of container
Particles are rigid and locked into place	Particles can move/slide past one another	Particles (molecules, atoms, ions) can move past one another
A little free space exists between molecules	A little free space exists between molecules	Lots of free space exists between molecules
Do not flow easily	Flows easily	Flows easily
Not easily compressible	Not easily compressible	Easily compressible



## ❖ Pure Substances

- Made of only one kind of matter and has definite properties.
- Every sample of a pure substance is the same.

### ➤ 2 kinds of Pure Substance :

#### 1. Elements

- Atoms – Neon (Ne)
- Molecules – Oxygen ( $O_2$ )

#### 2. Compounds

- Molecules – Water ( $H_2O$ )
- Ions – Sodium Chloride (NaCl)

### 1. Elements

- Elements are pure substance that cannot be broken down into other substances.

### ➤ Composed of atoms - the most basic units of matter.

- ✓ All matter in the universe is composed of atoms.

- Atoms are single units - Neon (Ne)
- Molecules are two atoms of the same kind combined - Oxygen ( $O_2$ )

### 2. Compounds

- A substance made of two or more elements that are chemically combined.
- Have a definite ratio

## ❖ Mixtures

A mixture is a substance which consists of two or more elements or compounds not chemically combined together.

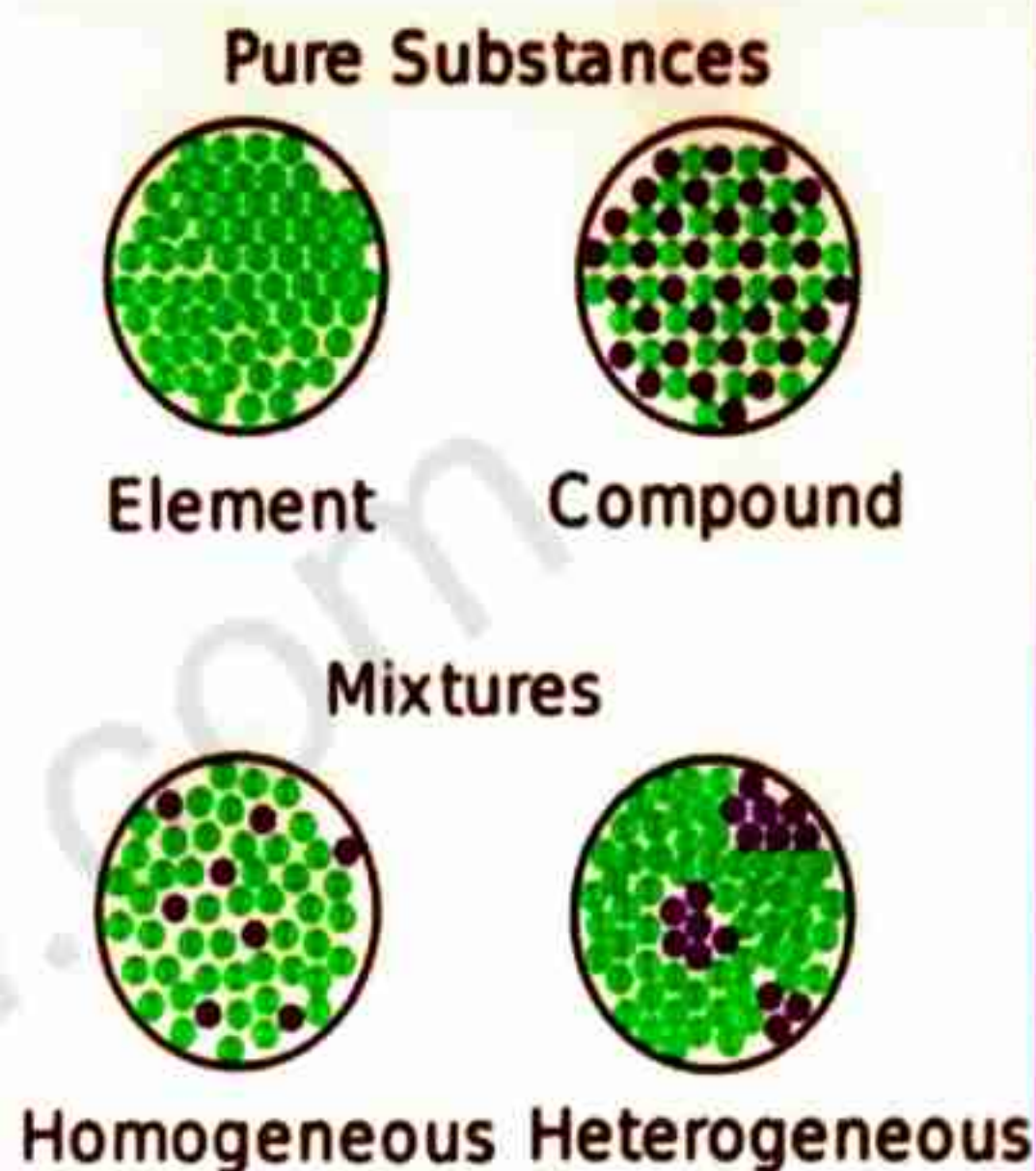
### ➤ Mixtures are of two types :

#### 1. Homogenous Mixture:

In homogenous mixture of solid and liquid the chemical and physical properties of individual components cannot be determined by any single instrumental method of analysis.

#### 2. Heterogeneous Mixture:

A heterogeneous mixture is one in which the individual components of the mixture retains their original physicochemical properties.





Composition	Homogeneous mixtures	Heterogeneous mixtures
Composition	Uniform	Non-uniform
Particle distribution	Even	Uneven
Phases	Single	Two or more
Physical separation of phases	No	Yes
Sizes of particles	Smaller	Larger
Stability	More stable	Less stable
Solvation	More solvation	Less solvation
Particles	Not visible	Mostly visible
Physical properties of individual components	Same	Different
Examples	Solution	Suspension

## ❑ CHANGE IN THE STATE OF MATTER

- **Melting:** When solid is converted into Liquid by increasing heat

Eg: Ice cube to water.

- **Vapourisation:** When Liquid is Converted into gas by increasing temp.

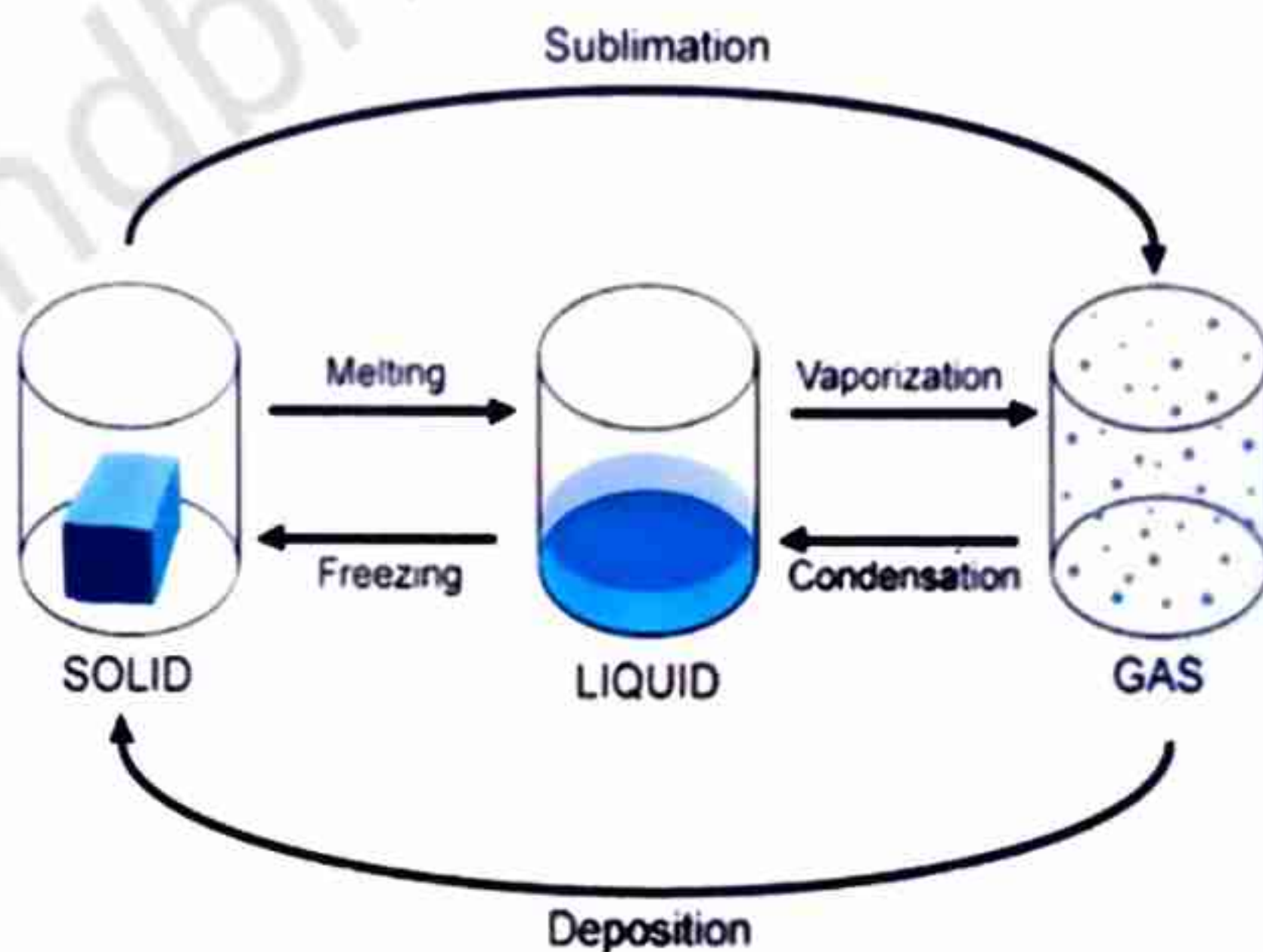
Eg: Water convert into vapours

- **Sublimation:** When solid particles directly convert into gas by increasing temperature or in high temperature.

Eg: On very high temp., ice directly convert into vapours

- **Condensation:** When gas is converted into liquid by decreasing temperature

Eg: Water vapour in the air turn into liquid on colder surface.





- **Freezing** : When liquid is **converted into solid state** by decreasing temperature.

**Eg: Water convert into ice cube in refrigerator**

- **Deposition** : When gas state particles (or vapours) directly convert into solid state **without first becoming a liquid**.

**Eg: At very cold place, water vapour directly converted into ice.**

## **☐ LATENT HEAT**

- The **amount of heat required** to raise the temp. of **1 gram of the solid** is called the **heat capacity**.
- **Temp. of solid continuously** increases until it reaches to its melting point. At melting point the temp. will **hold steady for a while**, heat is added to the solid and hold steady **until the solid completely melts**.
- **The temp. rising** stops because melting requires energy.
- All the energy **added to a crystalline solid** at its melting point goes into **melting and the temp.** of the **solid will begin to increase**.
- This heat is **called the latent heat of melting**.
- **Hence, when a crystalline solid** melt it absorbs a **certain amount of heat, latent heat of melting**, & it undergoes a **change in its heat capacity**.
- Any change like melting, freezing, **boiling or condensation brought** about by heat which has a change in **heat capacity and a latent** heat involved, is **called a first order transition**.
- Any change by heat, which has a **change in heat capacity**, but a latent heat is not involved, is **called a second order transition**.
- **In first order transition melting** is observed with crystalline solid, & in second order **transition glass transition** is **observed with amorphous solid**.



## ☐ 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**.

### FORMULA

$$P_{\text{solution}} = X_{\text{solvent}} P_{\text{solvent}}$$

$P_{\text{solution}}$  = Vapor pressure of the solution

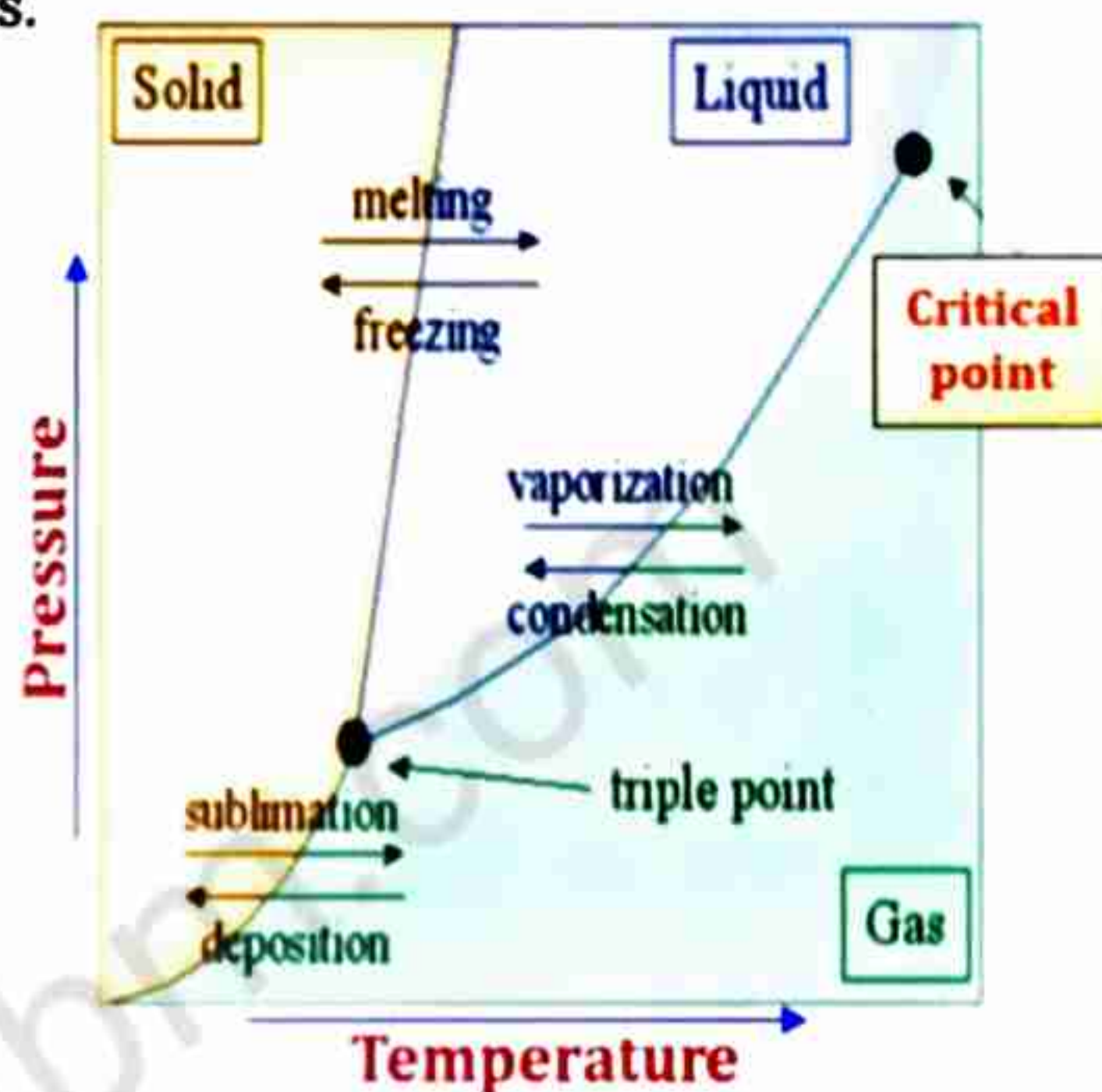
$X_{\text{solvent}}$  = Mole fraction of the solvent

$P_{\text{solvent}}$  = Vapor pressure of the pure solvent



## ❑ SUBLIMATION

- **Sublimation is another form of phase transitions.** Here solid turns directly into a gas. As a sublimating material changes from a solid to a gas, it never passes **through the liquid state**.
- **Sublimation is just one** of the ways water or another substance can change between its potential phases.
- Substances like water and **carbon dioxide ( $\text{CO}_2$ )** can be plotted on as pressure vs. **temperature to understand** their state of matter (**solid, liquid, or gas**).
- For example, with lower pressures, **liquid water changes** to a gas at temperatures lower **than  $100^\circ\text{C}$** .
- If the pressure is **dropped low enough**, water reaches what's known as a triple point. At pressure and temperature of triple point a **substance can exist** in solid, **liquid, and gaseous forms**



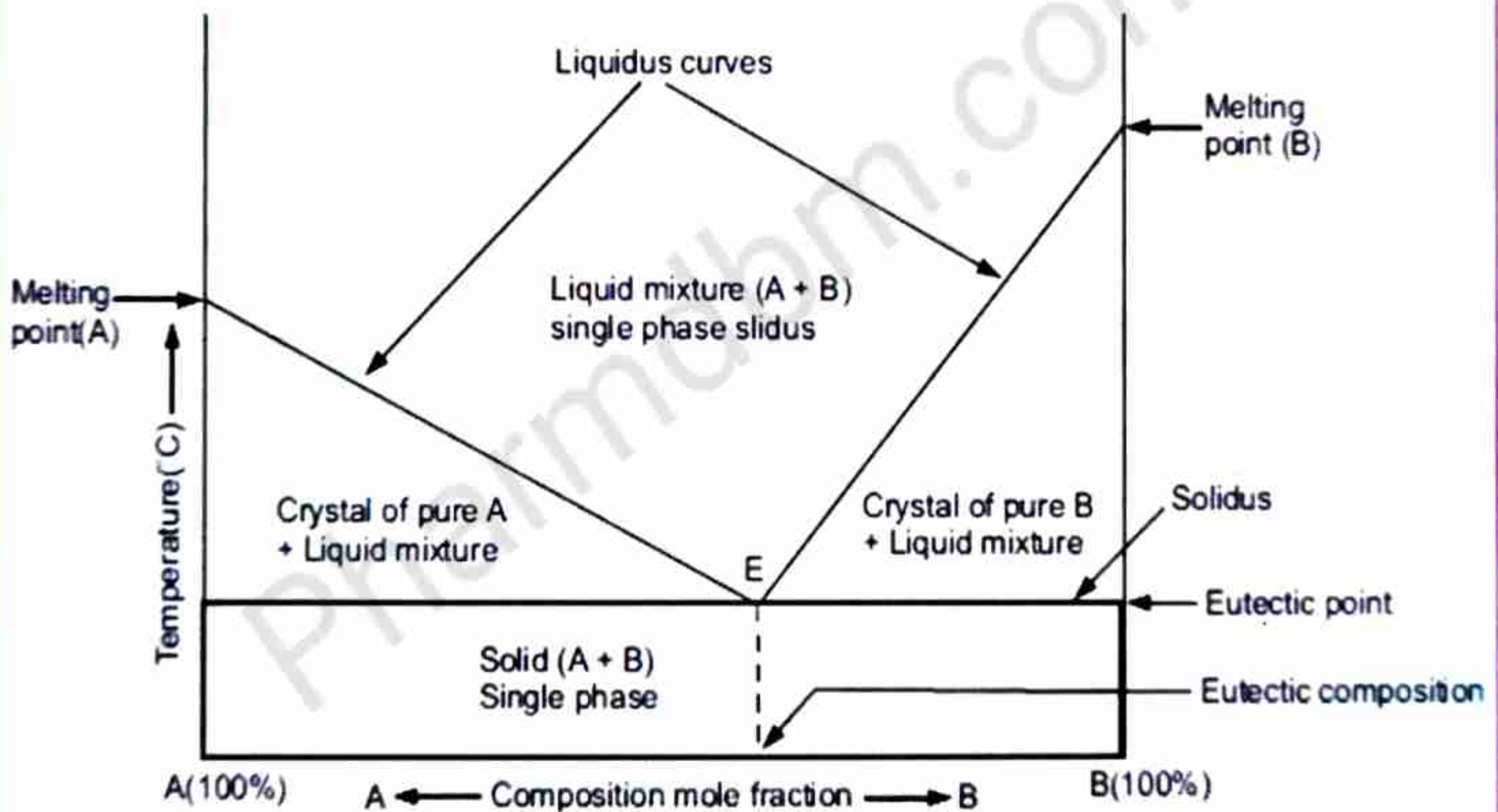
## ❑ CRITICAL POINT

- Gas molecules near to have contact with **each other achieving** more **condensed liquid state**.
- **This state also can be possible** to **achieve by increasing pressure** of the **gas but it has a limitation that pressure is effective** only below specific temperature. This temperature is **called as critical temperature**.
- **At critical temperature**, physical **properties of liquid** and vapour become identical and no **distinction can be made between the two**. **This point is also called as critical point**.



## ☐ EUTECTIC MIXTURES

- A **two-component system** containing a solid and liquid in which the **two components are completely miscible in the liquid states and are completely immiscible in the solid state**. This mixture is **known as eutectic mixture**.
- The **temperature at which** such system exists in **liquid phase is known as eutectic temperature**.
- Above this temperature, the components are liquid and below this **temperature they are solids**. **Physically eutectic systems** are solid dispersions.



- Some examples of this type are **thymol - salol, thymol - camphor, menthol - camphor etc.**
- If salol - thymol combinations is to be dispensed as dry powder, it is necessary that the **ambient temperature** should be **below its eutectic point of 13°C**.
- **Above this temperature**, it exists in liquefied form. At eutectic point their **contribution with respect to composition is 34 % thymol & 66 % salol**.



## ☐ GASES



GAS

- **Gaseous state is the simplest state** amongst the three states of matter.
- Chemical properties of gases vary significantly whereas Physical properties **are simpler to understand**.
- Gaseous state can be described by **considering small scale action** of **individual molecules** or by **large action of the gas**.
- The **model called as kinetic molecular** theory can easily describe the properties.

### ❖ Kinetic Molecular Theory of Ideal Gases:

The kinetic molecular theory is based upon the following postulates :

1. **All matter is composed of tiny particles (molecules or atoms).**
2. **Consist of small particles** (molecules or atoms) that are far apart in comparison to their own size.
3. **Particles are dimensionless points**, which occupy zero volume.
4. Particles are in rapid, **random and constant straight-line** motion. Well-defined and **established laws of motion** can describe this motion.
5. There are no attractive forces between **molecules and the sides** of the **container with which they collide**.
6. **Molecules collide with one** another and the sides of the container.
7. Energy can be transferred in collisions **among molecules**.
8. Energy is **conserved in these collisions**, although one molecule may gain energy at the **expense of the other**.
9. Energy is distributed among the **molecules in a fashion known** as the **Maxwell-Boltzmann Distribution**.
10. **At any instant**, the molecules in each **sample of gas do not at all possess** the same amount of energy. **The average kinetic energy** of all the molecules is **proportional to the absolute temperature**.

### ❖ Characteristics of Gases:

- The volume (V), pressure (P), temperature (T) and the number of moles (n) in the container are measurable characteristic properties of the gas.

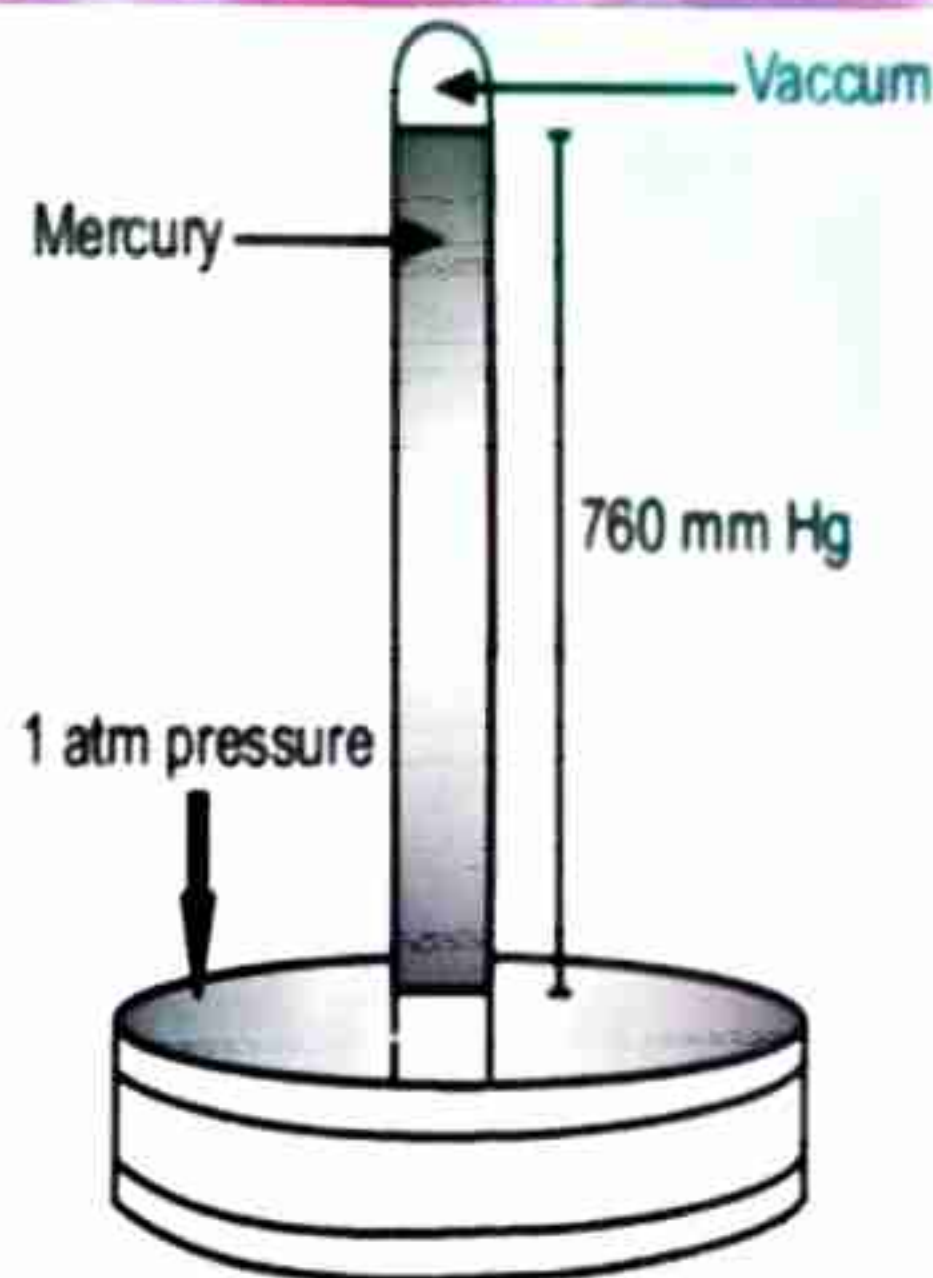


### 1. Volume :

- It is always taken as **volume of the container**.
- **Units = mL or Litres or Cubic centimeters**

### 2. Pressure :

- **Atmospheric pressure** is measured using a barometer
- It is the force exerted by gas molecules on unit area of container walls
- Units = atmosphere or **mm Hg or pascals**
- **1 atm = 760 mm Hg =  $1.013 \times 10^5$  pa.**



**Barometer**

### 3. Temperature:

- It is generally measured in **kelvins or absolute degree**.
- **Kelvin = (K) =  $^{\circ}\text{C} + 273$**
- The product of pressure and volume per mole is proportional to the average molecular kinetic energy.
- The average kinetic energy is proportional to the **absolute temperature**.

### 4. Number of Moles of Gas:

The concentration of gas in a **container can be obtained as** ratio of mass 'm' of the gas **sample to the molar mass, M.**

$$\text{Moles of gas} = \frac{\text{Mass (m)}}{\text{Molar mass (M) of the gas}}$$

### ❖ Gas Laws:

- Physical laws describing the behaviour of gas under various conditions of pressures, volumes and temperature is known as gas laws.
- **These laws are described below:**

#### 1. Boyle's Law:

**Robert Boyle, in 1662, formulated a generalization** that the volume of any **definite quantity** of gas at constant **temperature is inversely proportional** to its pressure.



Mathematically it is expressed as;

$$\text{or } V \propto \frac{1}{P}$$
$$V = \frac{k}{P}$$

Where,

V = Volume

P = Pressure of the gas

k = Proportionality constant

- **Boyle's law describes** the behavior of an **ideal gas** and approximates the behaviour of a real gas.
- If in certain condition, pressure and **volume of gas** are  $P_1V_1$  and at any other **condition they are**  $P_2V_2$ , then at constant temperature, this can be expressed as :-

$$P_1V_1 = k = P_2V_2$$

### ❖ Charle's Law:

- **Charles in 1787 investigated** that gases such as hydrogen, carbon dioxide and oxygen **expand to an equal amount** upon heating from  $0^\circ\text{C}$  to  $80^\circ\text{C}$  at **constant pressure**.
- **Charle's law is stated** as the volume of definite quantity of gas at constant pressure is directly proportional to **absolute temperature**.
- **It is expressed as:**

$$V \propto T$$

$$\frac{V_1}{T_1} = \frac{V_2}{T_2}$$

### ❖ Avogadro's Law:

- **It states that** at constant **pressure and temperature** the volume occupied by a gas is **directly proportional** to the number of moles of the gas.
- **Mathematically it is expressed as;**

$$V = n \times \text{constant (When P and T are held fixed)}$$

- If  $V_1$  and  $V_2$  are volumes and  $n_1$  and  $n_2$  are **number of moles of gas** at constant **temperature and pressure, then;**

$$\frac{V_1}{n_1} = \frac{V_2}{n_2}$$



## ❖ Gay Lussac's law:

- **Joseph Gay Lussac observed** that at constant volume, the pressure exerted by a fixed mass of gas is directly **proportional to the absolute temperature**.

$$P \propto T$$

$$\frac{P_1}{T_1} = \frac{P_2}{T_2}$$

## ❖ Ideal Gas Law:

The **ideal gas law** is the equation of state of an ideal gas that **relates pressure, volume, quantity of gas, and absolute temperature**.

$$PV = nRT$$

**P = pressure**

**V = volume**

**n = number of moles of gas**

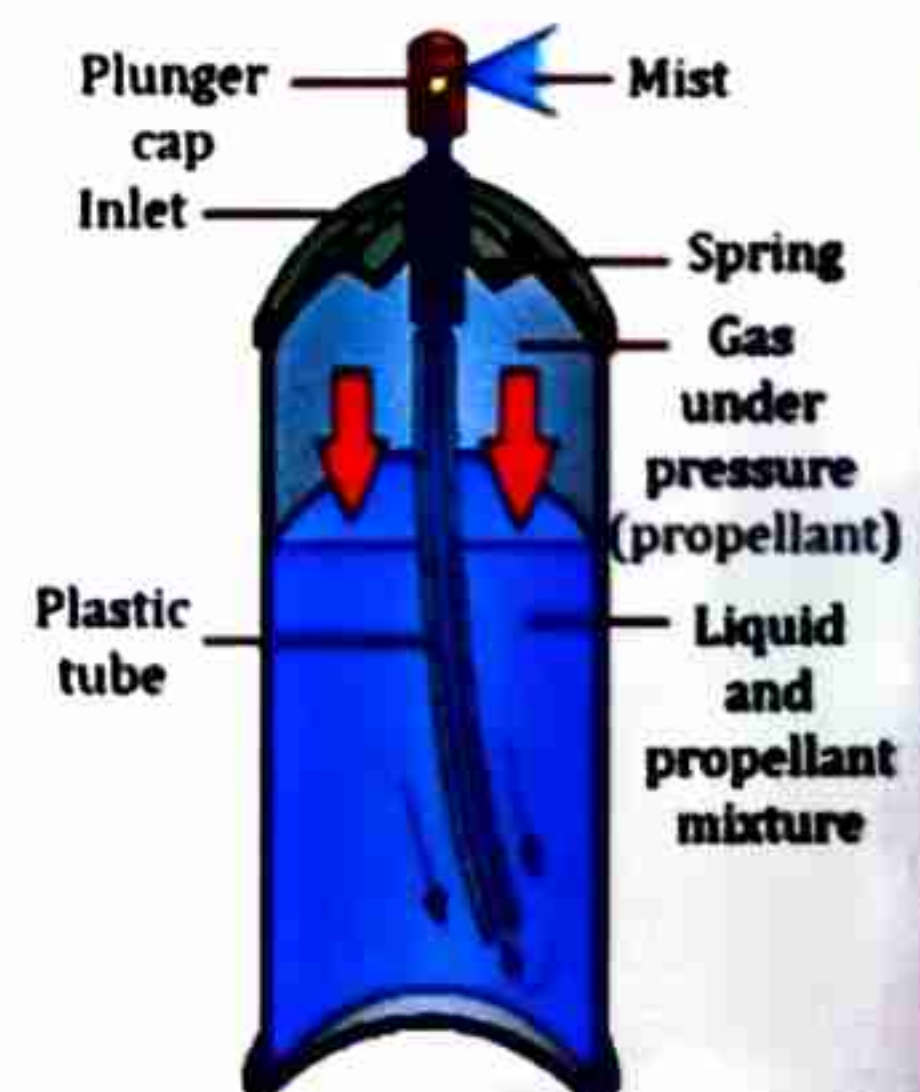
**R = ideal gas constant**

**T = absolute temperature**

R is called as **Molar gas constant** =  $8.314 \times 10^7$  erg/Mol.deg. or **1.987 cal/Mol.deg.** or **0.08205 lit.atm/Mol.deg.**

## ❑ **AEROSOLS**




- **Gases can be liquefied** by **increasing pressure** and **keep the temperature below the critical temperature**.
- **When the pressure is reduced**, the **molecules expand** and the **liquid reverts to a gas**.
- This reversible change of state is the **basic principle involved** in the preparation of **pharmaceutical aerosols**.
- Various drugs which are suitable for this **type of packing** include local anesthetics, **ergotamine, steroids, antiseptics etc.**
- **In such products**, the drug is dissolved or suspended in a '**propellant**', a material that is liquid under the **pressure conditions existing** inside the **container** and **forms** a gas under normal atmospheric conditions.
- **Various propellants** used in the manufacture of aerosols include Hydrocarbons (Propane, Butane etc.), **Chlorofluorocarbon, N, NO<sub>2</sub> etc.**





## ❑ INHALERS

- The delivery of **drugs by inhalation** is a critical issue in obstructive airway diseases such as **bronchial asthma and chronic obstructive** pulmonary disease.
- Ideal device** should be effective, reproducible, **precise, stable,** comfortable, versatile, environmentally **compatible, Affordable.**
- There are three types of Inhalers:**

<b>Metered Dose Inhalers (MDIs)</b>	Largely used for single and combined molecules, and which need a propellant for the dose delivery	
<b>Dry Powder Inhalers (DPIs)</b>	Which do not require any propellant, and are increasingly prescribed for single and combined molecules	
<b>Soft Mist Inhalers (SMIs)</b>	Consisting in only one device for only one molecule (Respimat for Tiotropium bromide)	

- DPIs are available in wide variety of design and represent a substantial **improvement in the inhalation therapy.**
- Mainly they**
  - Eliminate the use of propellants**
  - Simplify the inhalation technique**
  - Improve the patient's compliance to treatment
  - Favor a higher deposition of drugs within the lungs
  - Reduce the variability of the inhaled dose**
  - Reduce the incidence of both local and systemic side effects**

**Classification of DPIs based on their intrinsic resistance with pressure drop across the device**

<b>DPI</b>	<b>Pressure drop across the device</b>	<b>Examples</b>
<b>Low resistance DPIs</b>	<b>&lt; 5 Mbar ½ L/min</b>	<b>Handy Haler, Easy haler and Twishaler</b>
<b>Medium resistance DPIs</b>	<b>5 -10 Mbar ½ L/min</b>	<b>Turbohaler, Accuhaler/Diskus, Ellipta, Novolizer and Genuair</b>
<b>High resistance DPIs</b>	<b>&gt; 10 Mbar ½ L/min</b>	<b>Aerolizer and Breezhaler</b>



## ❑ RELATIVE HUMIDITY

- It is the ratio of the partial pressure of water vapour to the equilibrium vapour pressure of **water at a given temperature**.
- **It depends on temperature and the pressure.**
- Relative humidity is normally expressed as a percentage; a higher percentage means that the air-**water mixture is more humid**.
- **Relative humidity is the ratio of two pressures;**

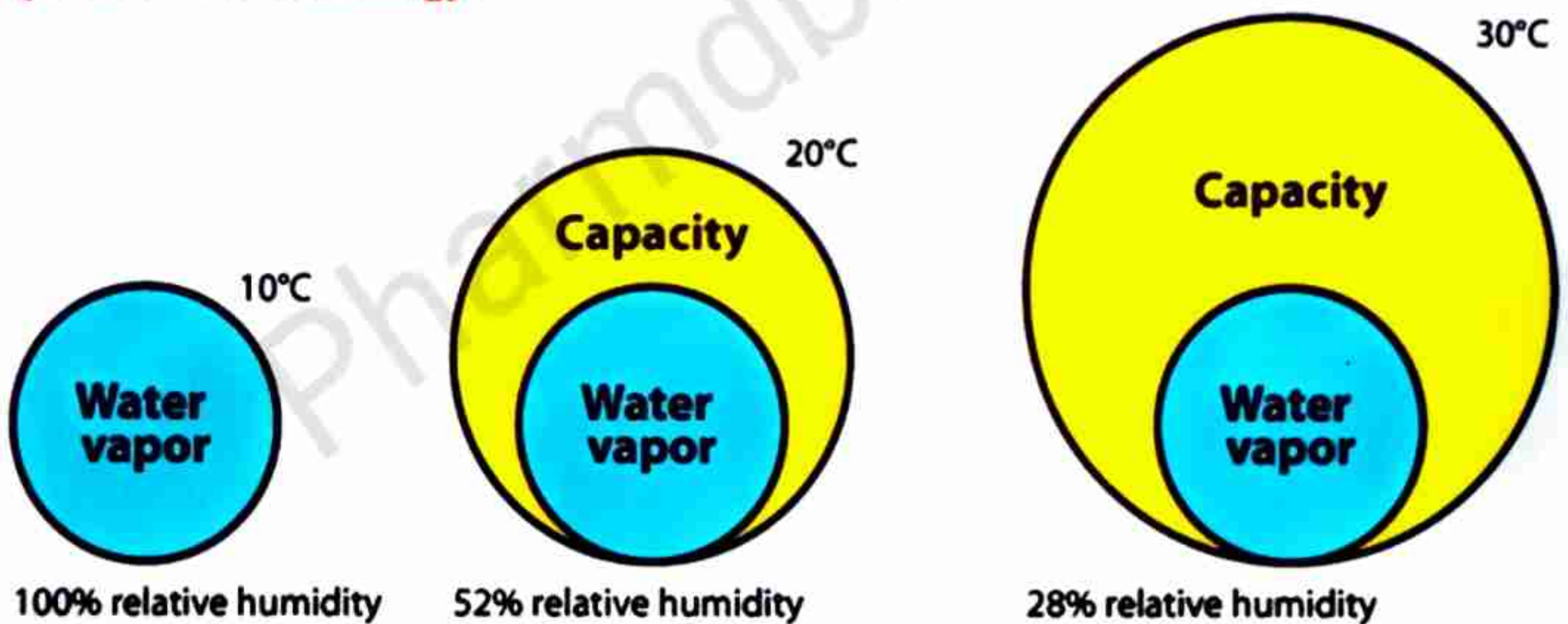
$$\% RH = \frac{P}{P_s} \times 100$$

**Where,**

$P$  = Actual partial pressure of the water vapour present in the ambient

$P_s$  = Saturation pressure of water at the temperature of the ambient

Relative humidity sensors are usually calibrated at normal room temperature **(well above freezing)**.



### ❖ Vapour Concentration (Absolute Humidity)

- The vapour concentration or absolute **humidity of a mixture** of water vapour and dry air is defined as the ratio of the **mass of water vapour ( $M_w$ )** to the volume **( $V$ ) occupied by the mixture**.
- $D_v = M_w / V$ , expressed in grams/ $m^3$  or in grains/cu ft.
- The value of  $D_v$  can be derived from the equation  $PV = n RT$ .



## ❑ LIQUID COMPLEXES

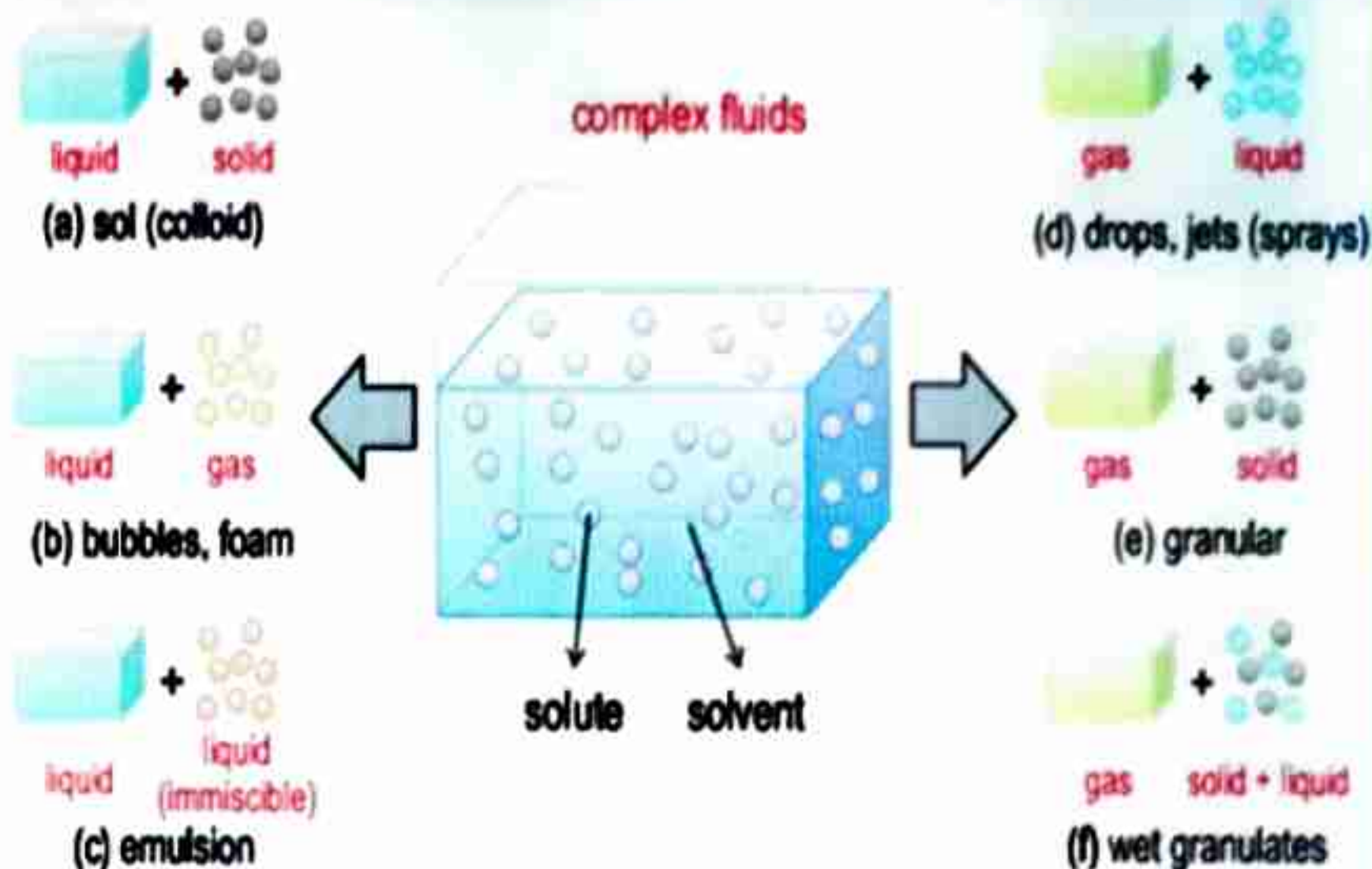
Liquid complexes are binary mixtures that have coexistence between two phases:

### I. Solid-liquid

(suspensions or solutions of macromolecules such as polymers)

### II. Solid-gas (granular)

### III. Liquid-gas (foams) or liquid-liquid (emulsions)



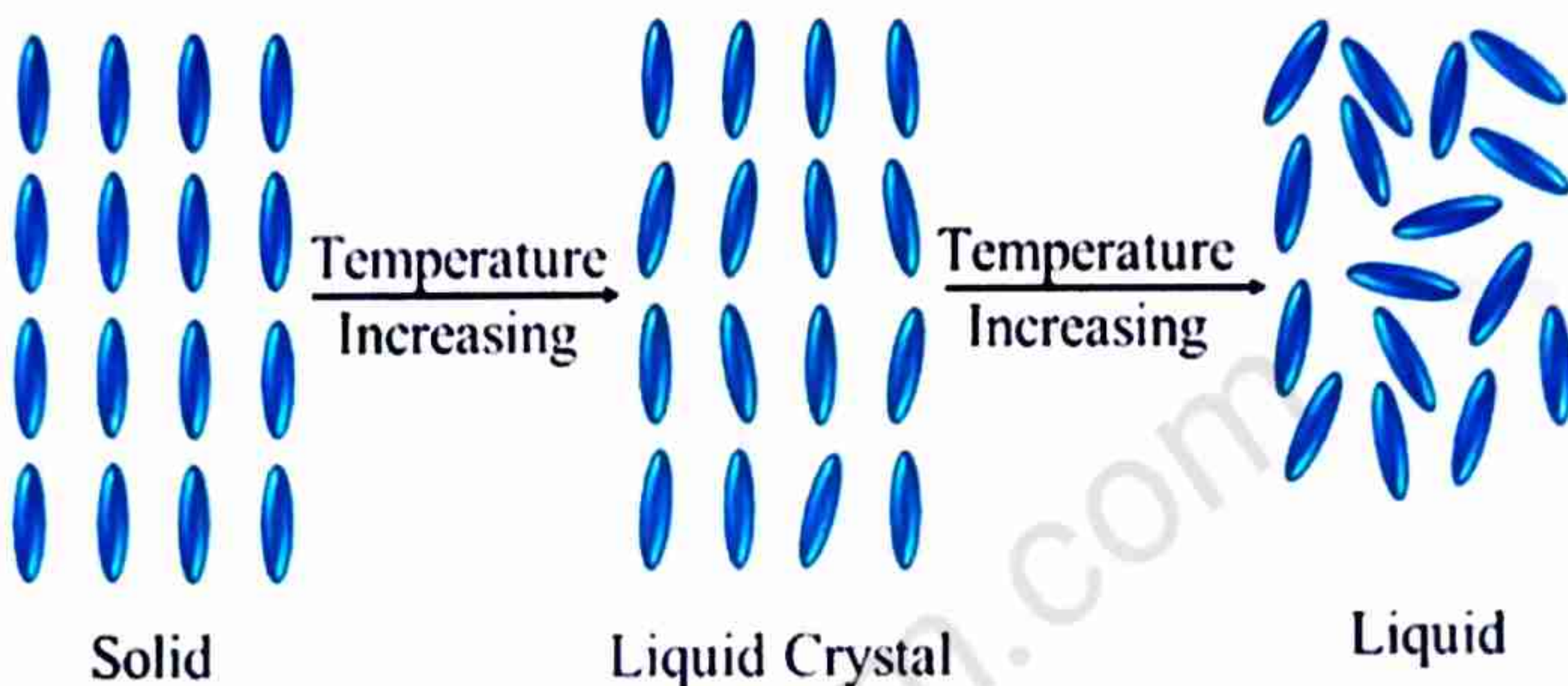
- They exhibit unusual mechanical responses to applied stress or strain **due to the geometrical** constraints that the **phase coexistence imposes**.
- The mechanical response **includes transitions between** solid-like and fluid-like **behavior as well as fluctuations**.
- Their mechanical properties 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.**

## ❑ LIQUID CRYSTALS

- Three states of matter, gas, **liquid and solid**, have been discussed.
- A fourth state of matter is the **liquid crystal state or mesophase**.
- The liquid crystal state is a distinct state of **matter observed between** the **crystalline solid and liquid states**.
- **In the crystalline solid state**, **arrangement of molecules is regular**.
- The molecules are held in fixed positions by **intermolecular forces**.
- **As the temperature** of a substance increases, its molecules vibrate and eventually these vibrations overcome the **forces that hold the molecules** in place and the **molecules start to move**.
- **In the liquid state**, this motion overcomes the **intermolecular forces** and the molecules move into random positions.
- **In the liquid crystal state**, the increased molecular motion overcomes **the weaker forces**, but molecules remain **bound by the stronger forces**.



- **This produces a molecular arrangement** where molecules are in layers, but within each layer, molecules are **arranged in random positions**, more or less **parallel to each other**.
- The molecules can slide **around each other and the layers** can slide over one another.
- **This molecular mobility** produces the **fluidity in liquid crystal state**.



TYPES OF LIQUID CRYSTALS	
<b>Thermotropic Liquid Crystals</b>	Liquid crystals are said to be thermotropic if liquid crystalline properties depend on the temperature.
<b>Nematic Liquid Crystals</b>	Here the molecules (mesogens) have no positional order, but they have long-range orientational order
<b>Smectic Liquid Crystals</b>	In this, the mesogens have both positional order and orientational order.
<b>Cholesteric liquid Crystals</b>	The cholesteric phase can be defined as a special type of nematic liquid crystals in which thin layers of the parallel mesogens have their longitudinal axes rotated in adjacent layers at certain angle.
<b>Lyotropic Liquid Crystals</b>	Liquid crystals which are prepared by mixing two or more substances, of which one is a polar molecule, are known as lyotropic liquid crystals.



## □ GLASSY STATE

- The glassy state of **materials refers to non equilibrium**, solid state, such as is typical of inorganic glasses, synthetic non **crystalline polymers and food components**.
- **Characteristics of the glassy state** include transparency, solid appearance and brittleness.
- In such systems, molecules have **no ordered structure** and the volume of the system is **larger than that of crystalline systems** with the same composition.
- These systems are often referred to as amorphous (i.e., disordered) solids (e.g., glass) or super cooled liquids (**e.g., rubber, leather, syrup**).
- All the glass is considered to be a non-conducting transparent solid, it is **actually a type of solid matter**.
- The atoms and molecules in most solids are arranged in an orderly manner whereas in **Glassy materials** these are highly disorder.
- Glassy materials also do not have a **specific melting point** but these slowly and **gradually liquefy on heating**.

### TYPES OF GLASSY STATES

<b>The first type</b>	It is characterized by the cessation of the vibratory movement of rotation of the molecules in a defined (critical) temperature region. This results in stabilization of the chain structures of rigidly <b>associated polar molecules (by means of dipoles)</b> .
<b>The second type</b>	It is consists of organic glassy polymerization products. These glass in the stabilized state have fibrous structure of rigid valence bonded carbon atoms with small lateral branches in the form of <b>hydrogen atoms or more complex radicals</b> .
<b>The Third type</b>	The third most extensive type of glassy state consists of refractory inorganic compounds of multivalent elements. These glasses in the stabilized state have the most thermostable chemical structure in the form of a three <b>dimensional rigid atomic valency-bonded spatial network</b> .

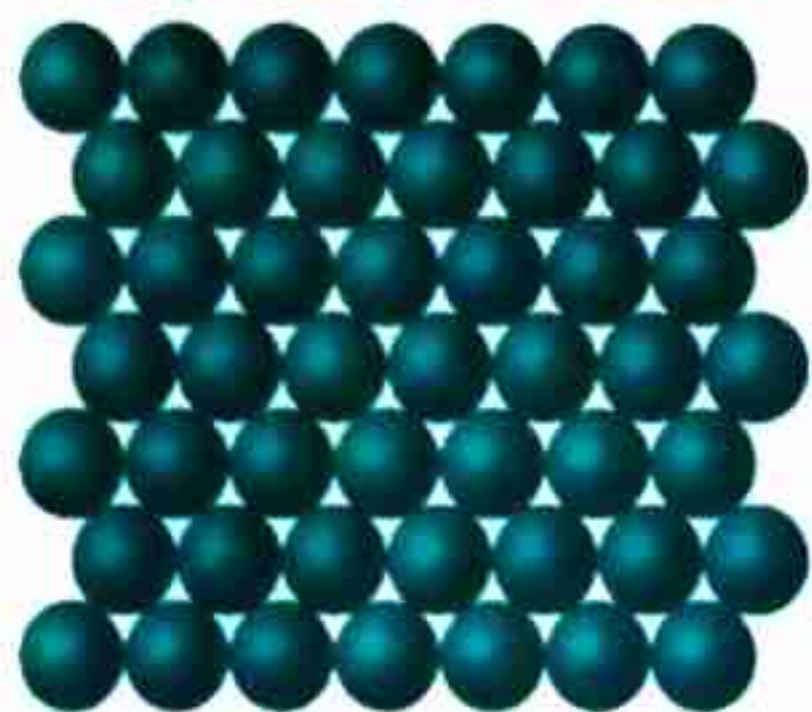


## ☐ SOLIDS

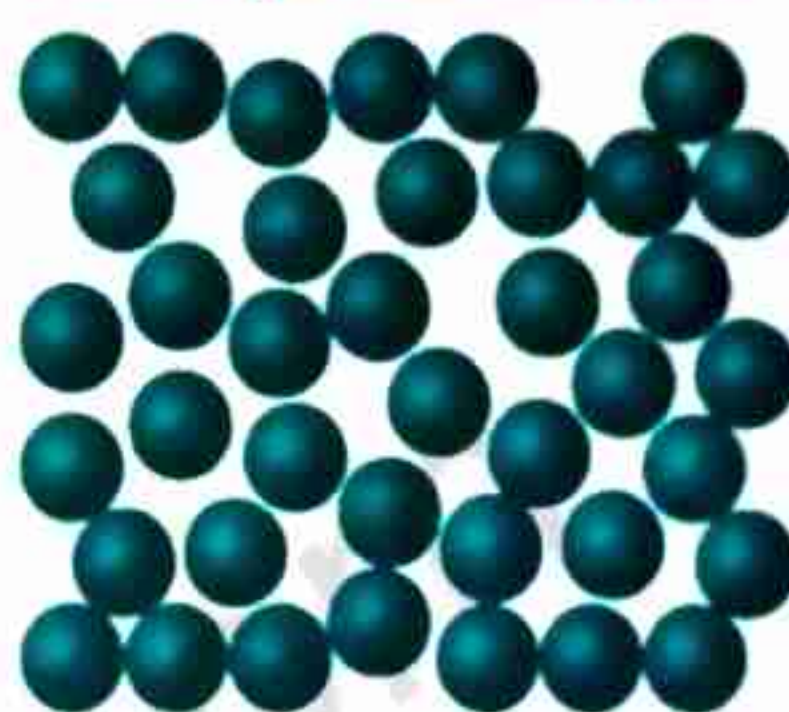
- The state, in which a substance has no tendency to flow under stress, resists **forces that tend to deform** it, and remain in definite size and shape is called as solid state

### ➤ Two types of solids

#### Crystalline solids



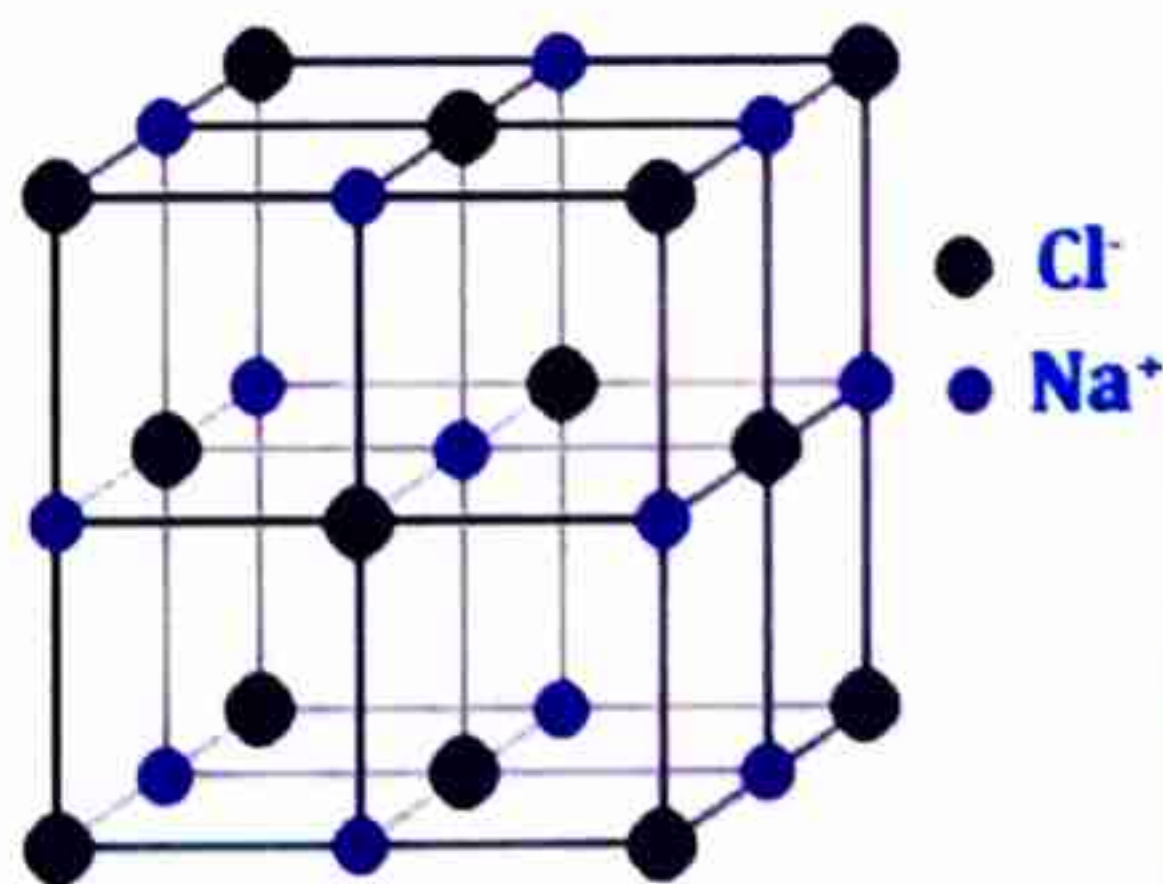
#### Amorphous solids



### ❖ Crystalline Solids

- These are characterized by definite **geometric shape**. The atoms, molecules or ions have regular, repeating **crystal arrangement**.
- The structural units of crystalline solids, **such as ice**, sodium chloride, and menthol, are arranged in fixed geometric patterns or lattices.
- They **have definite melting points** and so they pass sharply from solid to liquid state.

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



**Crystal lattice of sodium chloride**



## ❖ Amorphous Solids

- The solids in **which the particles** are not arranged **in any specific order** or the solids that lack the overall order of a crystal lattice are called **amorphous solids**.
- Amorphous solid may be **considered as super cooled liquids**.
- The common examples of amorphous solids **are glass and plastics**.
- **The examples of amorphous** drugs are accupril/accuretic used to treat high blood pressure and **itraconazole used as an acne medication**.

### Difference between Crystalline and Amorphous Solids

CRYSTALLINE SOLIDS	AMORPHOUS SOLIDS
They are arranged in neat and orderly fashion as fixed 3D crystal lattice or geometric patterns.	They are just strewn in any old fashion with random unoriented molecules.
<b>Practically incompressible.</b>	<b>Practically compressible.</b>
Show definite melting point	Do not show definite melting point
Higher energy is required for molecule to escape from a crystal form.	Low energy is required for molecule to escape from an amorphous form.
<b>Handling quality is poor.</b>	<b>Handling quality is better.</b>
Shows poor aqueous solubility because more energy required.	Shows good aqueous solubility because minimal energy required.
Melting happens.	Glass transition happens.
When crystalline solid is heated at a constant rate, the temperature increases at a constant rate.	When crystalline solid is heated at a constant rate, the temperature increases at different rates.
Poor absorption and low bioavailability.	Rapidly absorbed and show higher bioavailability.
<b>Stable than amorphous solids.</b>	<b>Less stable than crystalline solids.</b>
Examples are ice, methanol, penicillin G and sodium chloride.	Examples are glass, plastic, penicillin G, and novobiocin.



## ❖ Polymorphism

- Many substances due to **differences in their intermolecular** forces exist in more than one **crystalline or amorphous form**.
- These forms are called as polymorphs and **substances are called polymorphic**.
- **Allotropy is synonymous to polymorphism**.
- Elements like carbon, sulfur and **phosphorus etc. show allotropy**.
- Substance in two **different forms** is called **dimorphic** while in three forms called trimorphic.
- The different **forms have different thermodynamic** properties such as **lattice energy, melting point**, and x-ray diffraction pattern; vapour pressure, intrinsic solubility, **and the biological activity**.
- Many drugs such as steroids (**Cortisone, Testosterone, and Prednisolone**), **barbiturates and Sulphonamides** show property of polymorphism.
- Many organic substances **such as tristearin and Theobroma** oil also exhibit polymorphism.
- **Theobroma oil exhibits four different polymorphic** forms viz.,  $\alpha$ ,  $\beta$ ,  $\beta'$  and  $\gamma$  forms differing in **their respective melting points**.

### ➤ Types of Polymorphs:

1. **Monotropic** : When polymorphic change is not reversible the system is **called monotropic**.
2. **Enantiotropic** : If the change from one polymorph to another is reversible, the **system is called enantiotropic**



# PHYSICOCHEMICAL PROPERTIES OF DRUG MOLECULES

## ❑ Refractive index :

- If the light enters the denser substance at an angle, one part of the wave slows down more quickly as it passes the interface, and this produces a bending of the wave toward the interface. This phenomenon is called refraction.
- The relative value of this effect between two substance is given by the refractive index or Snell's laws.

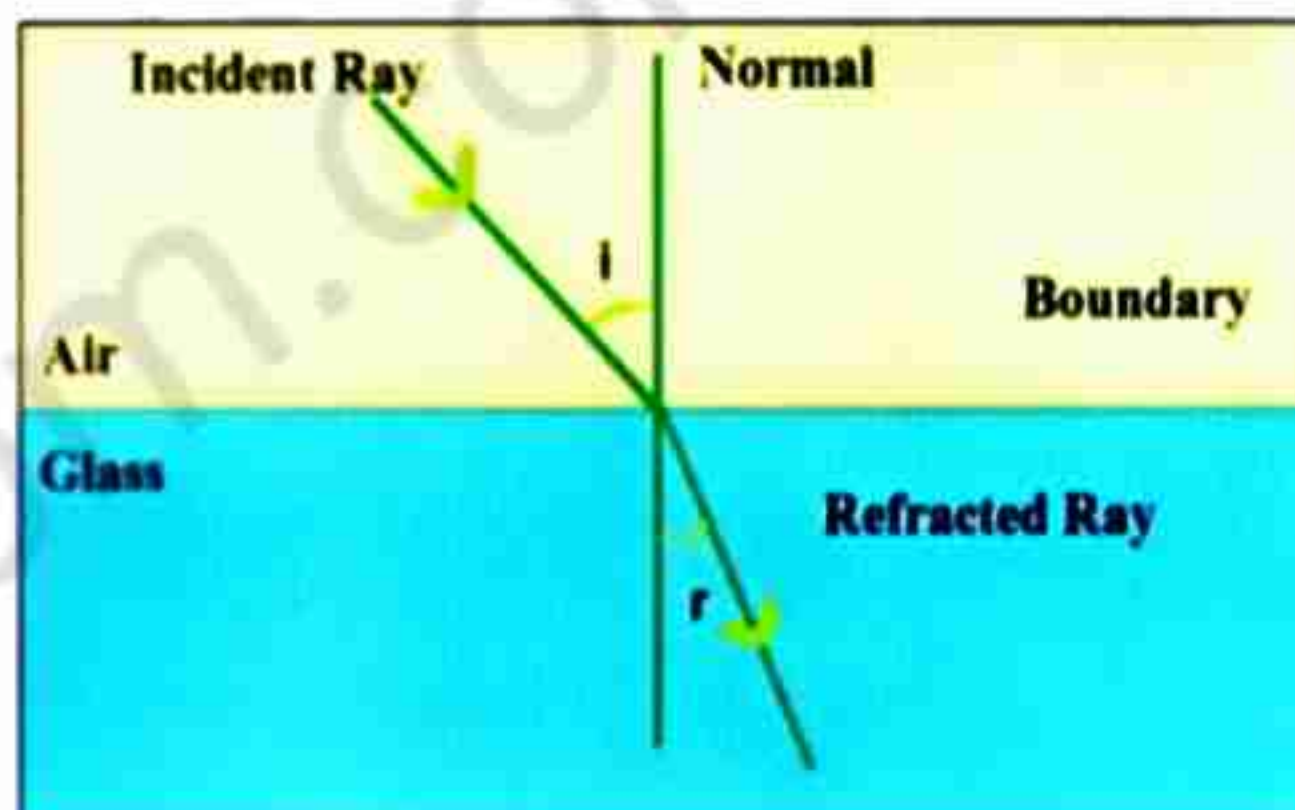
$$n = \frac{\sin i}{\sin r}$$

OR

$$n = \frac{\text{Velocity of light in substance}}{\text{Velocity of light in vacuum or air}}$$

Where

- $\sin i$  = sine of the angle of the incident ray of light
- $\sin r$  = sine of the angle of the refracted ray



- The refractive index is greater than 1 for substance denser than air.
- The refractive index varies with the wavelength of light and the temperature because both alter the energy of interaction.

### Refractive Indices of Some

Material	RI value	Material	RI value	Material	RI value
Air	1.00029	Crystal	2.00	Alcohol	1.329
Water	1.330	Ice	1.309	NaCl	1.544
Glass	1.510	Acetone	1.36	Iodine Crystal	3.34

- ❖ **Molar Refraction( $R_m$ ):** It is related to both the refractive index and the molecular properties of a compound being tested. It is expressed as

$$R_m = \frac{n^2 - 1}{n^2 + 2} \left( \frac{M}{\rho} \right)$$

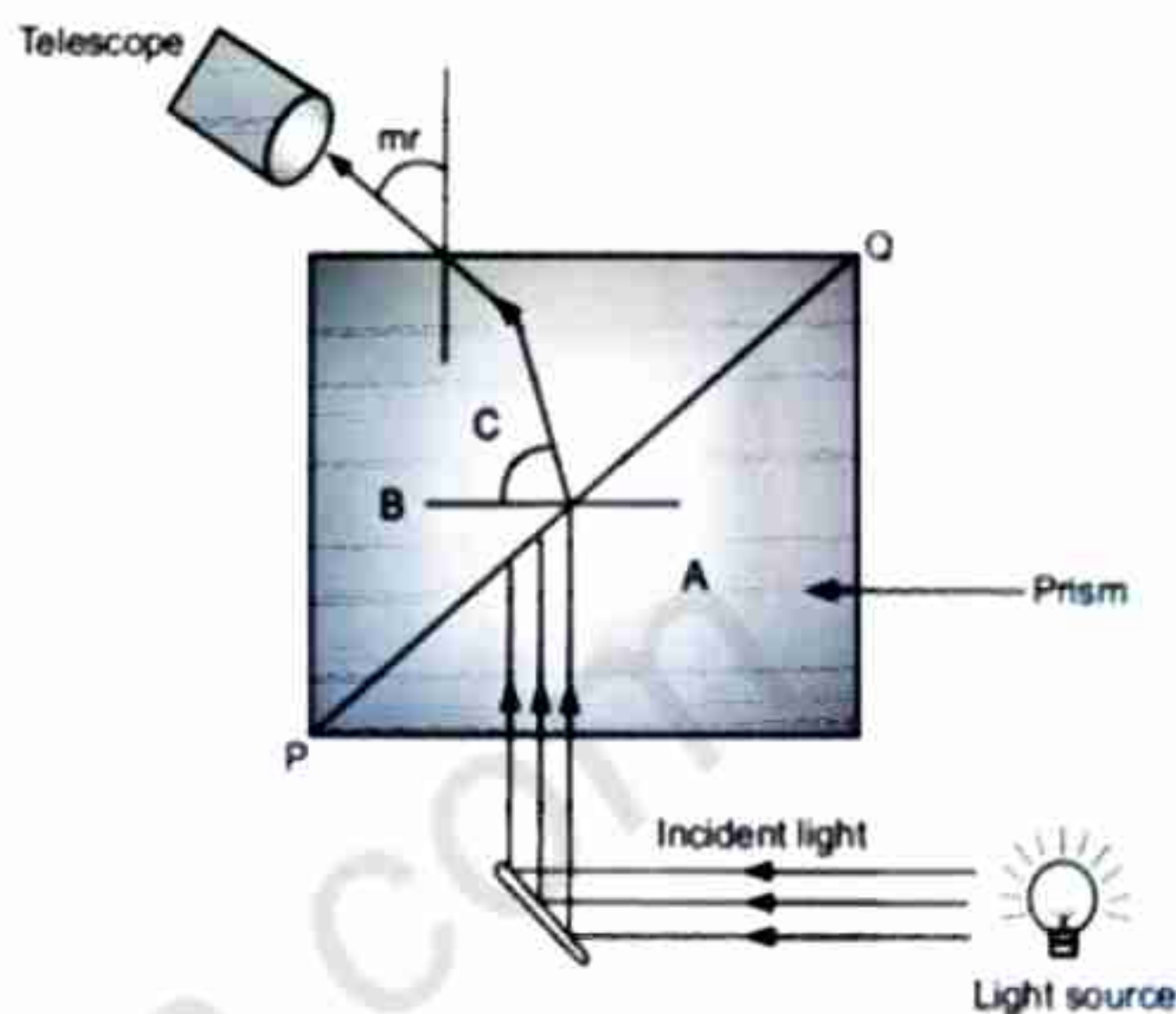
Where,

**M** = Molecular weight  
 **$\rho$**  = Density  
**n** = Refractive index



## ❖ Measurement of Refractive Index:

- Refractive index is determined by **using instrument called refractometer**. **Abbes refractometer**, immersion refractometer and **Pulfrich refractometer** are used for this purpose.
- **Abbes refractometer** is commonly used at laboratory scale because of its advantages over **other refractometers**.
- It is **most convenient**, reliable and **simple instrument** with small sample size requirement suitable for **range of substances**.
- **Ordinary light source**, easy maintenance and economy and **easy determinations** are some of the other advantages of this instrument.
- **The components** of **Abbes refractometers** include light reflection mirror, dispersion compensator, telescope, **and index arm and prism box**.



## ❖ Applications:

- Since **refractive index** is a **fundamental physical property** of a substance it is often used to analyze and identify a particular substance, confirm its purity, or **measure its concentration**.
- **Refractive index** values are useful in **determination of molecular weights** and structures of organic compounds from their **molar refraction values**.
- **Refractive index** is used to measure refraction characteristics of solids, liquids, and gases. Most commonly it is used to **measure the concentration** of a solute in an **aqueous solution**.
- For a solution of sugar, the **refractive index** can be used to determine the sugar content.
- **Alcohol content in bioproduction** is determined **from refractometry**.



## ❑ Optical Rotation :

- Ordinary light **consists of vibrations**, which are evenly distributed in all directions in a **plane perpendicular** to the direction of propagation, **called as unpolarized light**.
- When the **vibrations of light are restricted** to only one plane, the light is said to be **polarized light**
- Some substances rotates the plane of polarized light are called as **optically active substances**.
- This **property of optically active** substance is measured as angle of rotation.
- The property in which **rotation of plane polarized light is observed** is **known as optical activity**.
- Based on the direction of rotation the compounds can be either dextrorotatory (**rotation in clock wise direction**) or **levorotatory (rotation in anticlock wise direction)**.
- Example: Tartaric acid. The d and l form are **enantiomorphs** and **meso form** is **optically inactive**.
- Polarimeter is used in **measurement of optical activity**.



unpolarized  
light



polarizer



plane  
polarized  
light

### ❖ Specific Rotation:

The **specific rotation**,  $\{\alpha^t_\lambda\}$  at a specified **temperature t** and **wavelength  $\lambda$**  (**usually the D line of sodium**), is characteristic for a pure, optically active substance. **It is given by the equation**

$$\{\alpha^t_\lambda\} = \frac{\alpha v}{l g}$$

**Where,**

**$l$  = length in decimeters of the light path through the sample**

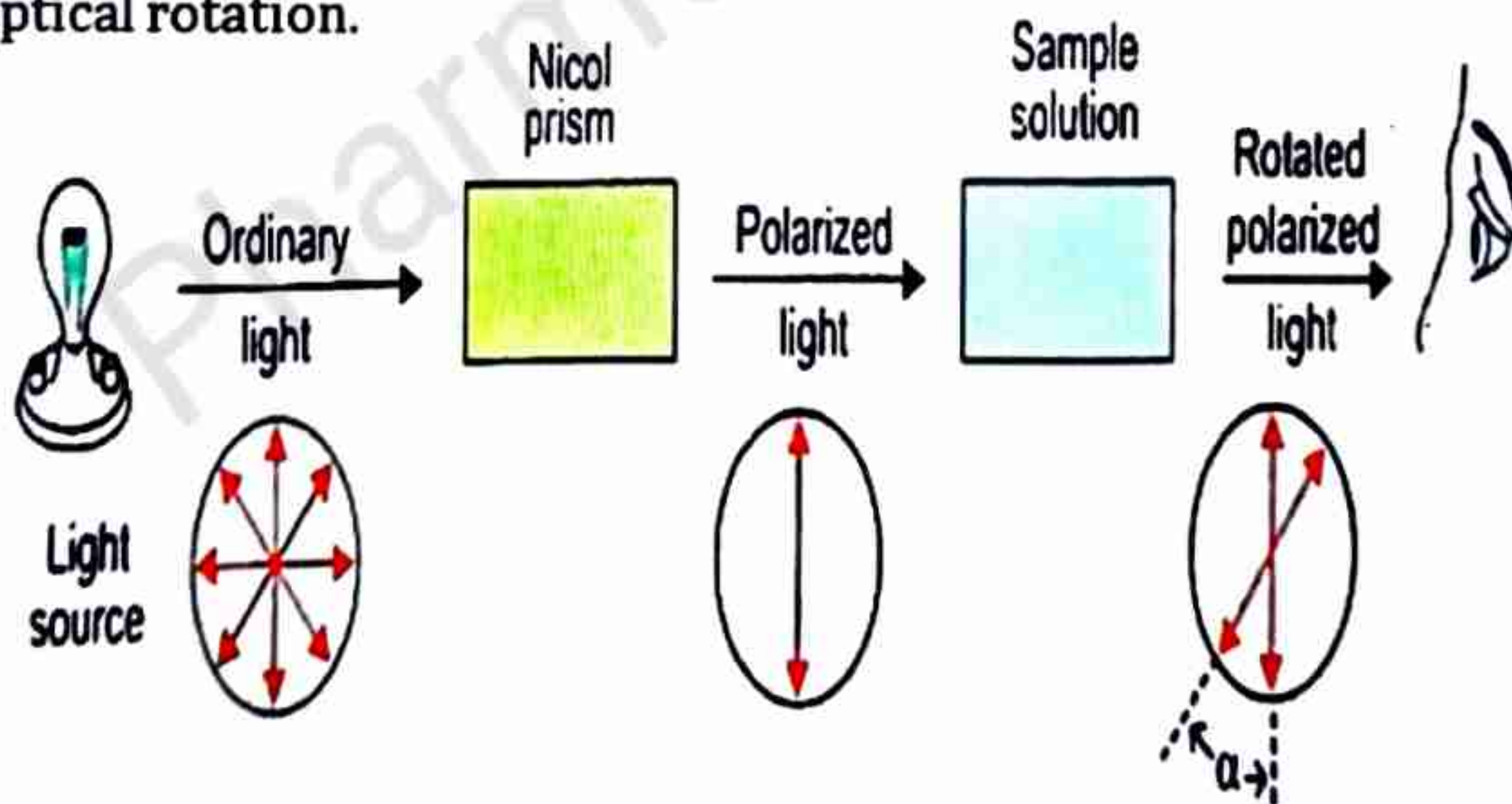
**$g$  = number of grams of optically active substance**

**$V$  = milliliter of volume**



## ❖ Measurement of Optical Activity:

- **Measurement of orientation of plane** polarized light is called polarimetry, and the instrument **used is called a polarimeter.**
- The simplest polarimeter consists of monochromatic light source, a polarizer, a sample cell, a **second polarizer** which is called the **analyzer** and a light detector.
- **Polarizer and analyzer are made up of Nicol prisms.**
- When analyzer is **oriented  $90^\circ$  to the polarizer** no light reaches to the detector.
- **The polarizer is placed near** to the light source while analyzer is placed **between sample cell and the detector.**
- The sample cell of suitable size and capacity with outward projection at the centre, to trap the air **bubble is usually used.**
- **When an optically active** substance is placed in the sample cell and beam of light is passed through, it rotates the **polarization of the light reaching the analyzer so that there is a component** that reaches the detector.
- The **angle that the analyzer** must be rotated from the original position is the optical rotation.



## ❖ Applications:

- The value of specific rotation can be **used to identify the compound**
- **Polarimetry is used** in the analysis of various drugs and pharmaceutical formulations such as **Adrenaline Bitartrate**, **anticoagulant Citrate Dextrose Solution**, **Dextran 40 Injection**, **Dextrose Injection**, **Sodium Chloride** and **Dextrose injection etc.**



## □ Dielectric Constant :

- It is denoted by  $\epsilon$  (epsilon).
- It is defined as the property of a substance to weaken the force of attraction between the **two parallel conducting plates**, such as the **plate of electric condenser**; when dipped in the **solvent under study**.
- The ease with which a molecule is polarized by any external force (electric field, light or any other molecule) is **known as polarizability**.
- The **Dielectric Constant** can be **determined by Oscillometry**.

Where,

$$\epsilon = C_m / C_o$$

$C_m$  = Capacitance of medium under study

$C_o$  = Capacitance, when the space is filled with vacuum

**Note:** The value of  $C_o$  is equal to one.

### Dielectric Constants of Some Liquid at 20 °C

Liquids	Dielectric constants	Liquids	Dielectric constants
Acetone	21.4	Formaldehyde	22.0
Benzene	2.28	Glycols	50.0
$\text{CCl}_4$	2.24	N-Methyl formamide	190
Fixed oil	0	Ether petroleum	4.35
Ethanol	25.7	Water	80.4

- The relation between concentration, dielectric constant and polarizability is given by **Clausius-Mossotti equation** as;

$$\left[ \frac{(\epsilon - 1)}{(\epsilon + 2)} \right] = \left[ \frac{4}{3} \right] [\pi n \alpha]$$

**$n$  = no. of molecules per unit volume**

- The total polarization is the sum of induced molar polarization and temporary polarization.

$$P = P_i + P_o$$

- Since  $\pi = 0$ ,  $P_o$  is zero. To obtain an induced molar polarization ( $P_i$ ) equation can be multiplied by **the  $M/\rho$  on both sides**.



Therefore,

$$\begin{aligned}\left[\frac{(\epsilon-1)}{(\epsilon-2)}\right] &= \left[\frac{4}{3}\right] [\pi n M \alpha p] \\ &= \left[\frac{4}{3}\right] [\pi n \alpha p] \\ &= P_i\end{aligned}$$

- A condition in which electric field **strength of condenser (V/m)** is unity,  $\pi$  represents the **induced molar polarization**.

### ❖ Application

1. The **ease of solution of salt soluble** like water & glycerin 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 :**

- **In a polar molecule**, the separation of positively and negatively charged regions can be permanent, and the molecule will possess a **permanent dipole moment**.
- **It is denoted by  $\mu$**
- The **unit of  $\mu$  is the debye**, named after the scientist P. debye.

$$\mu = q \times r$$

**Where,**

$\mu$  = dipole moment

$q$  = charge on atom

$r$  = distance of separation of charge



## ❖ Determination of Dipole Moment

### ➤ Vapour Temperature Method

- In this dielectric constant of a substance and its density of vapour are determined at **series of temperatures**. If the substance decomposes on heating then observations can be made **under reduced pressures**.

✓ **But according to Debye**

$$P = a + \frac{b}{T}$$

**Where,**

$$a = \frac{4}{3} \pi N \alpha, \quad b = \frac{4}{3} \pi N \left( \frac{\mu^2}{3k} \right)$$

**$K = 1.38 \times 10^{-16}$  ergs per degree,  $N = \text{Avogadro's number}$ .**

- By plotting the **values of  $P$  on Y-axis and  $\frac{1}{T}$  on X-axis** we obtain a straight line with slope equal to  $b$ . The dipole moment is **calculated by equation,**

$$\mu = 0.0128 \sqrt{b} \times 10^{-18}$$

- The other methods involved in the determination of dipole moment include **Refraction Method and Dilute Solution Method** which are not frequently used.

## ❖ Application of Dipole Moment

**1. For drug-receptor binding.**

**2. In knowing the crystalline arrangement of substances composed of molecules with permanent dipole moments.**

**3. It also helps in determining the biological activity of certain compounds.**

**E.g.: DDT (Insecticidal activity)**



## ❑ 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 example,**  $\text{HCN} + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{O}^+ + \text{CN}^-$

**This is often regarded as a straight forward dissociation into ions.**



➤ **For an acid**

$$K_a = \frac{[\text{H}^+] \times [\text{CN}^-]}{[\text{HCN}]}$$

The concentration of water  $[\text{H}_2\text{O}]$  can be taken as constant. Similarly, for a base, the equilibrium in following reaction is also dissociation;



➤ **For a base**

$$K_b = \frac{[\text{NH}_4^+] \times [\text{OH}^-]}{[\text{NH}_3]}$$

**Where,  $K_a$  or  $K_b$  is the measures of the strength of the acid (base).**

### ❖ Determination of dissociation constant

- There are various methods like conductivity method, visible or UV **absorption spectrometer**, potentiometer etc. Potentiometric pH is most widely used
- Dissociation constant of acid  $K_a = [\text{H}_3\text{O}^+] [\text{A}^-] / [\text{HA}]$
- When equimolar concentration of salt  $\text{A}^-$  and an acid  $[\text{HA}]$  are present, the  **$K_a$  dissociation constant** is numerically equal to the **hydronium ion concentration**.  
 $K_a = [\text{H}_3\text{O}^+] \text{ when } [\text{A}^-] = [\text{HA}]$



➤ **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.**