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Physical pharmacy
lec3

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Learning objectives

✓ Understand the properties of the different states of matter.

✓ Perform calculations involving the boiling points ,the Clausius-Clapeyron equation, heats of fusion and melting points.

✓ Describe the pharmaceutical application of the different states of matter to drug delivery systems

✓ Describe the solid state and crystallinity.

States of matter part3

The Liquid State

➢ **General properties**

➢ **Liquefaction of gases**

➢ **Vapor pressure of liquids**

➢ **Boiling point**

General properties

✓ Liquids are denser than gases and occupy a definite volume and density due to the presence of <u>vanderWaals forces</u>.

✓ Unlike gases, liquids do not disperse to fill all the space Of a container .

✓ Liquids have translational motion i:e liquids move as a whole (the molecules can slide over each other but they cannot break away from the intermolecular forces while in the liquid state)
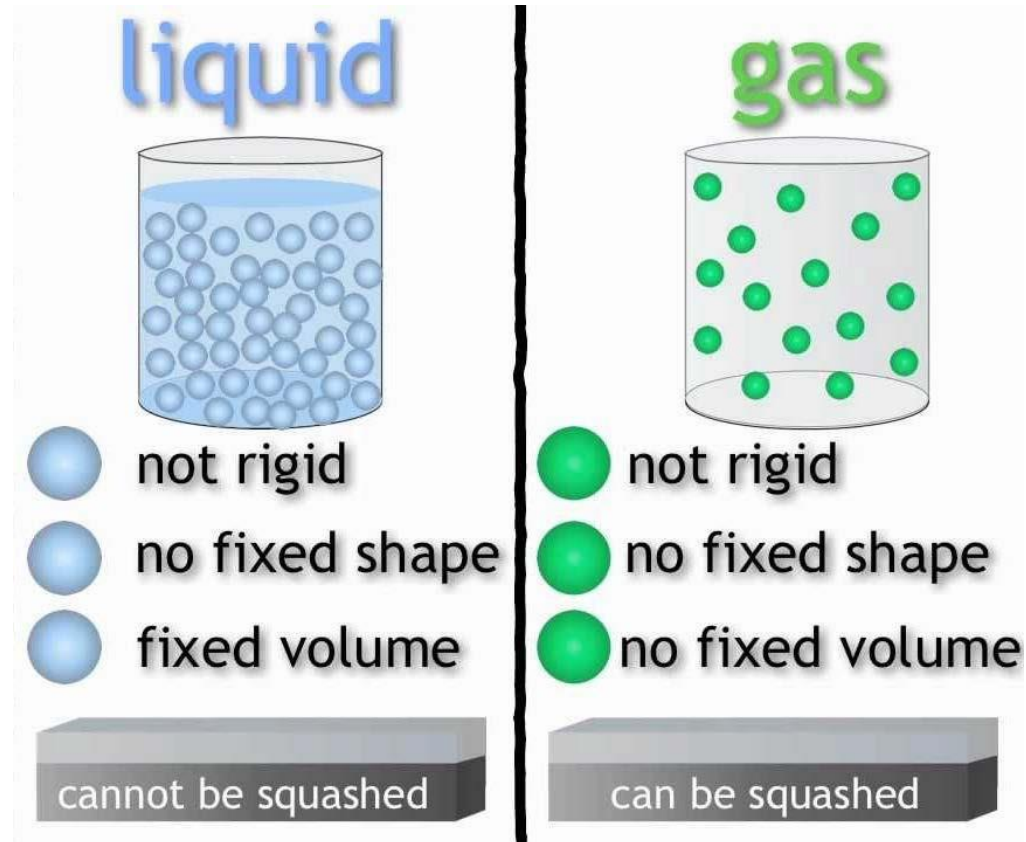
Liquefaction of gases

Effect of temperature and pressure

The transitions from a gas to a liquid and from a liquid to a solid depend on both temperature and pressure.

When a gas is <u>cooled</u> ,it loses some of its <u>kinetic energy</u> in and the <u>velocity</u> of the molecules <u>decreases</u>.

If pressure is applied to the gas ,the molecules are brought with in the range of the vanderWaals forces and pass in to the liquid state
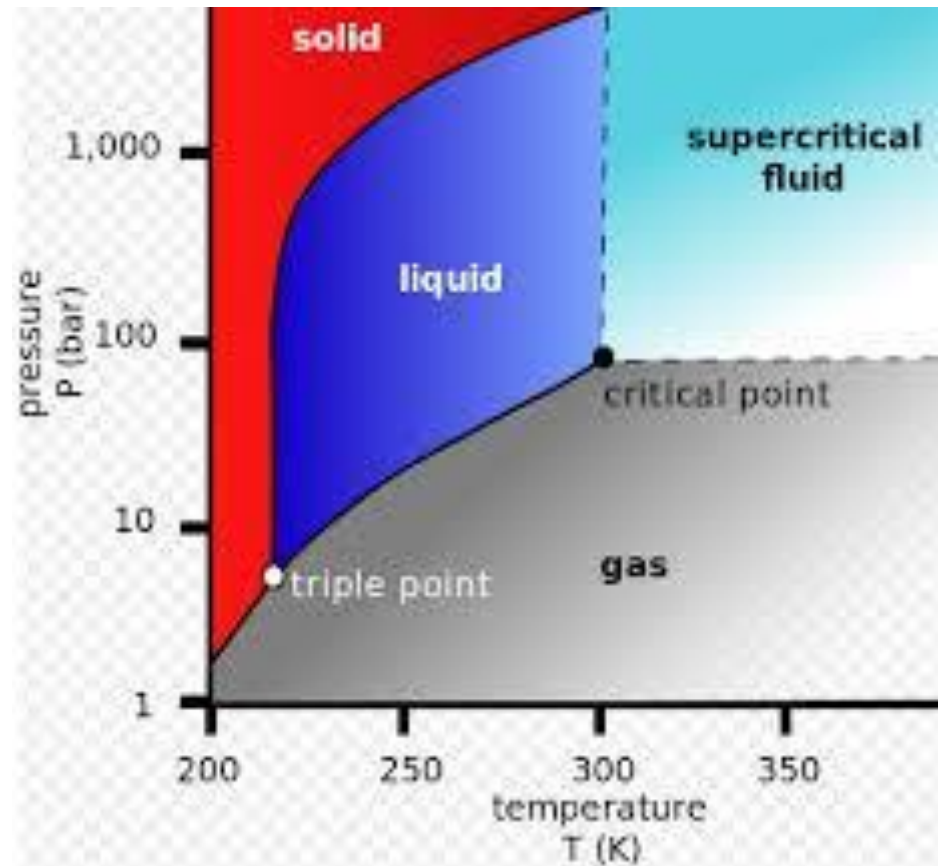

LIQUEFACTION OF GASES | XI FDC CHEMISTRY
CHAPTER 4
SIDRA JAVED

Critical temperature and pressure

If the temperature is elevated sufficiently, a value is reached above which it impossible liquefy a gas irrespective of the pressure applied. This temperature above which a liquid can no longer exist, is known as the **critical temperature**.

The pressure required to liquefy a gas at its **critical temperature** is the **critical pressure** ,which is also the highest vapor pressure that the liquid can have the critical temperature of water is 374 C∘ or 647 K and its critical pressure is 218 atm.
The high critical values for water result from the strong dipolar forces between the molecules and particularly the hydrogen bonding that exists
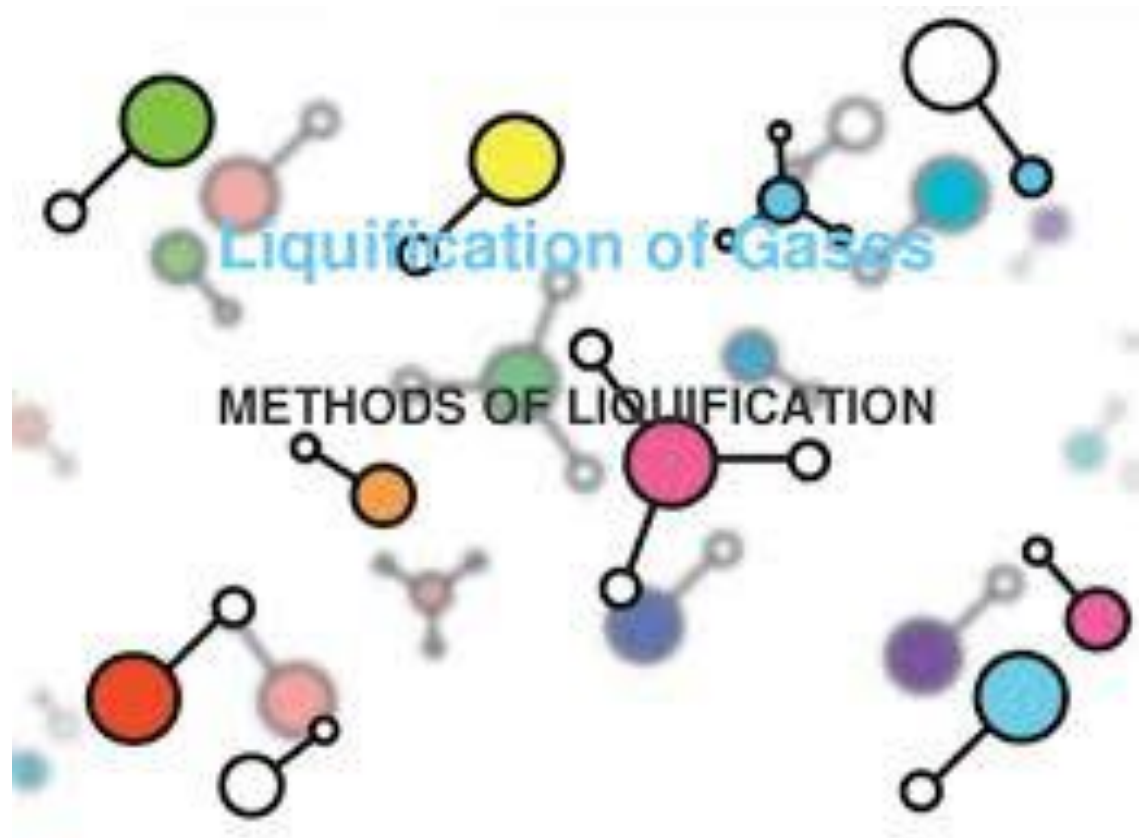
Aerosols

In pharmaceutical aerosols a drug is dissolved or suspended in a propellant a material that is liquid under the high pressure inside the container but forms a gas under normal atmospheric conditions) Part of the propellant exists as a gas and exerts the pressure necessary to expel the drug, whereas the remainder exists as liquid and provides a solution or suspension vehicle for the drug
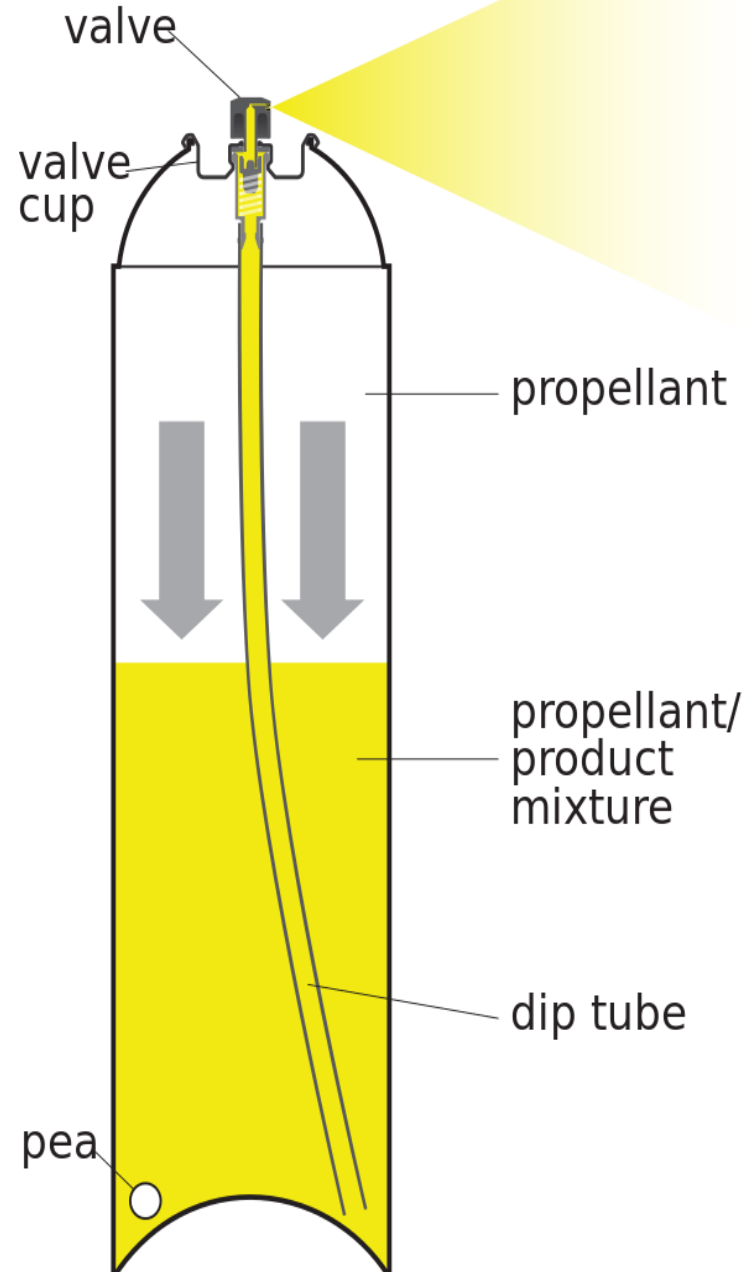
By depressing a valve on the container, some of the drug propellant mixture is expelled owing to the excess pressure inside the container Outside the container, the liquid propellant reverts to gas and vaporizes off, while the drug forms a fine spray
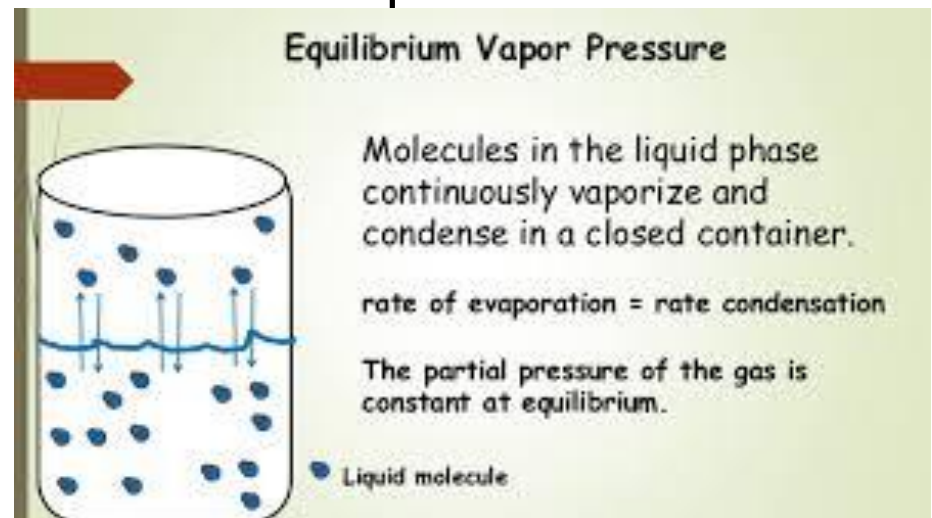
The filling process

| Filling | Insert the valve | Sealing | Filling propellant |
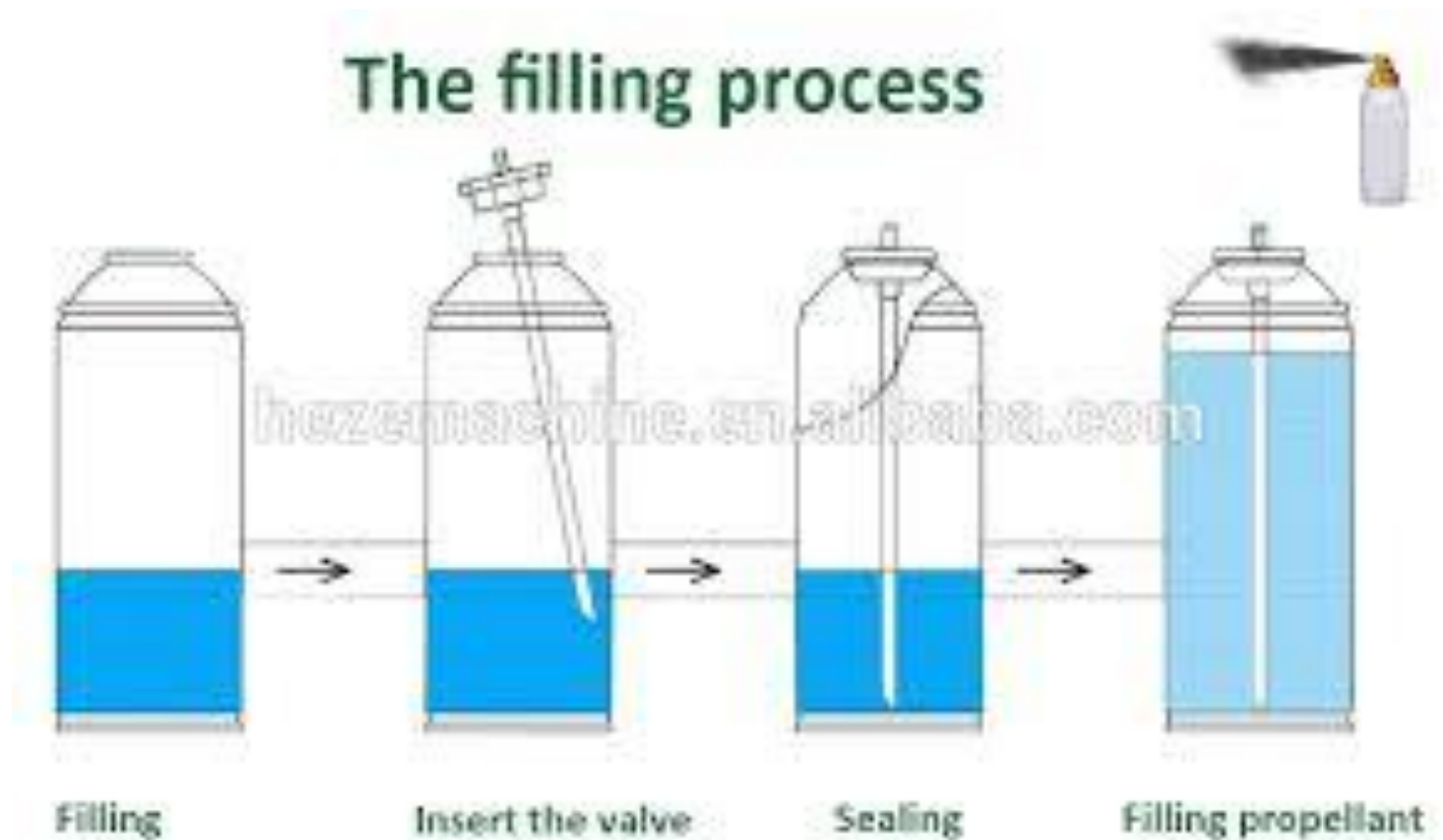
Vapor pressure of liquids

Equilibrium vapor pressure

When a liquid is placed in an evacuated container at a constant temperature ,the molecules with the highest energies break away from the surface of the liquid and pass in to the gaseous state (evaporate) ,and some of the molecules subsequently return to the liquid state (condense).

When the **rate of condensation** equals the **rate of vaporization** at a definite temperature ,the vapor becomes saturated and adynamic equilibrium is established.

The pressure of the saturated vapor above the liquid is then known as the **equilibrium vapor pressure**

Equilibrium Vapor Pressure

Molecules in the liquid phase continuously vaporize and condense in a closed container.

rate of evaporation = rate condensation

The partial pressure of the gas is constant at equilibrium.

Liquid molecule

Clausiusa Clapeyron equation معادلة كلاوزيوس-كلابيرون

the a condition in which the liquid and the vapor exist together in equilibrium If the temperature of any of the liquids is increased while the pressure is held constant, or if the pressure is decreased while the temperature is held constant, all the liquid will pass into the **vapor state**
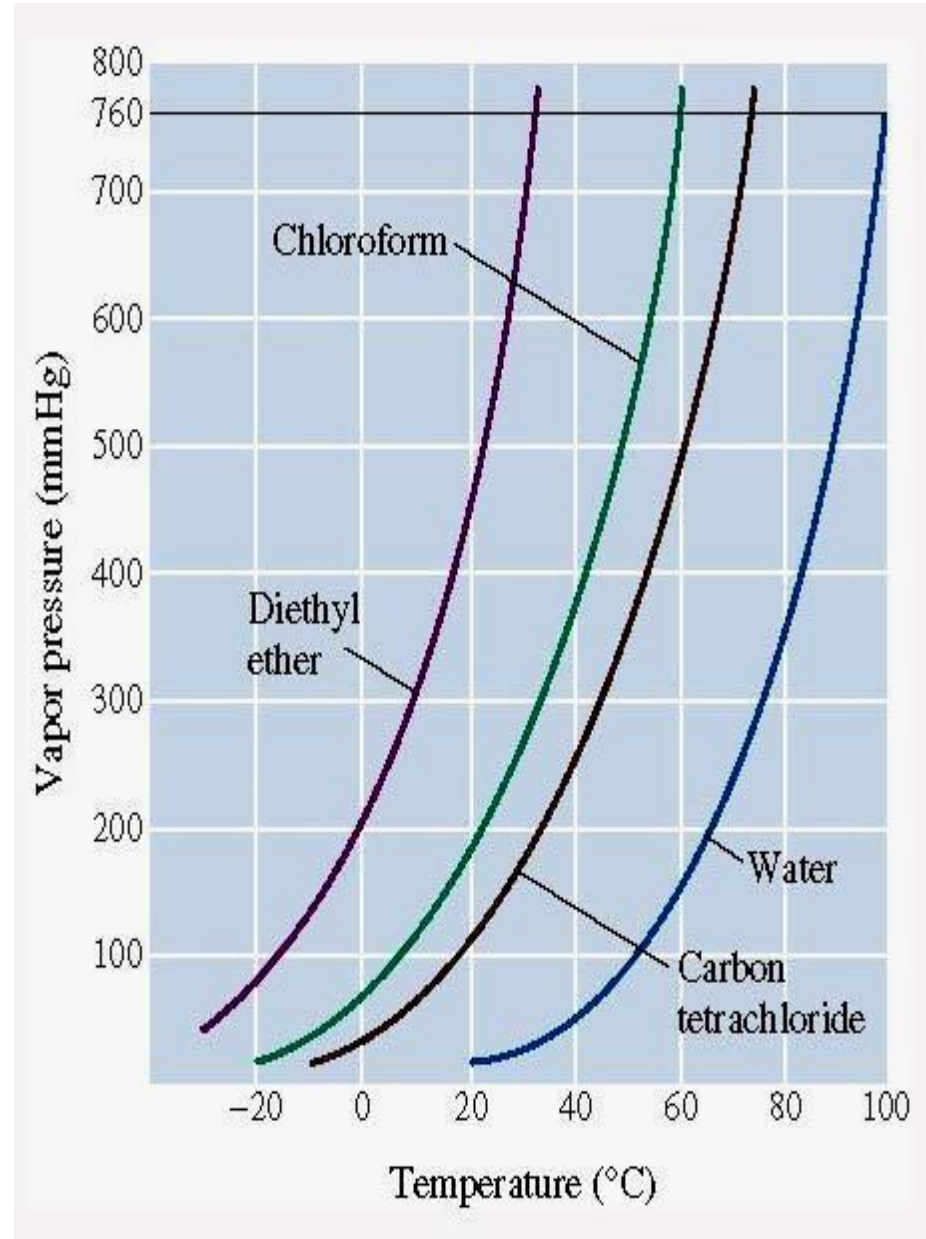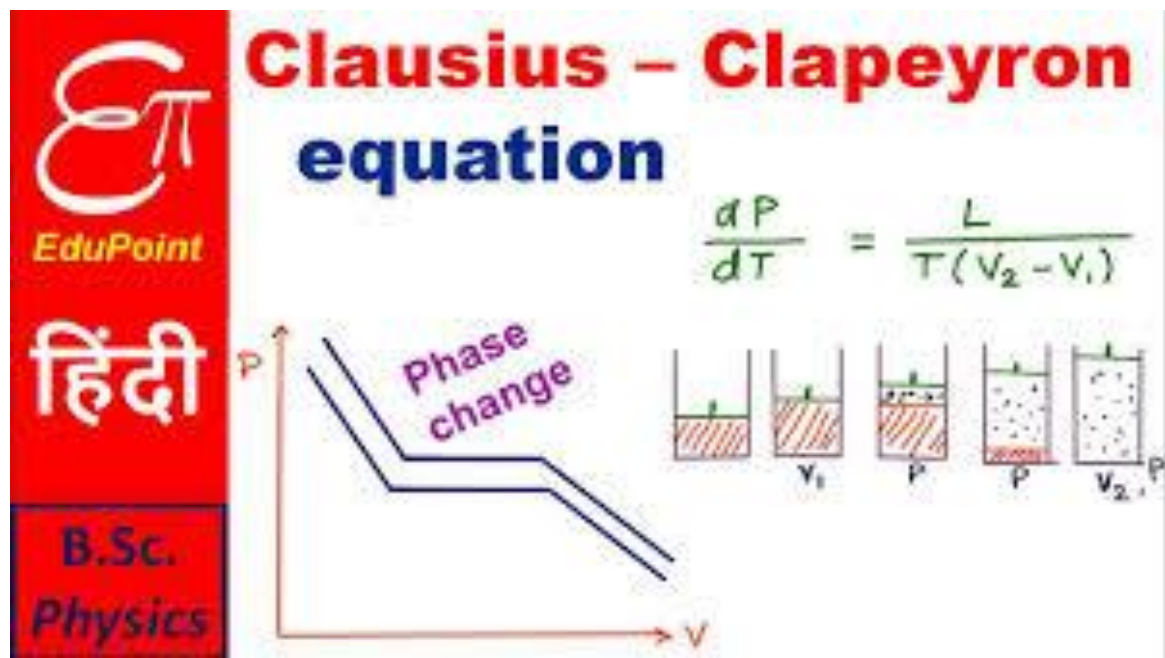
Clausius Clapeyron equation expresses the relationship between the vapor pressure and the absolute temperature of a liquid

$$\log \frac{p_2}{p_1} = \frac{\Delta H_v(T_2 - T_1)}{2.303\,R T_1 T_2}$$

where p1 and p2 are the vapor pressures at absolute temperatures T1 and T2, and Hv is the molar heat of vaporization, that is, the heat absorbed by 1 mole of liquid when it passes into the vapor state.

Application of the Clausius–Clapeyron Equation

The average heat of vaporization of water can be taken as about **9800** cal/mole within the range of 20∘C to 100∘C. What is the vapor pressure at **95**∘C? The vapor pressure P2 at temperature T2 = **373** K (100∘C) is **78** cm Hg, and R is expressed as 1.987 cal/deg mole. Write

$$\log \frac{p_2}{p_1} = \frac{\Delta H_v (T_2 - T_1)}{2.303\, R\, T_1\, T_2}$$

100∘C+273=373k

95∘C+273=368k

$$\log \frac{78.0}{P_1} = \frac{9800}{2.303 \times 1.987} \left(\frac{373 - 368}{368 \times 373} \right)$$

$$P_1 = 65 \text{ cm Hg}$$

Example

Compute the vapor pressure of water at **120**◦C. The vapor pressure p1 of water at **100**◦C is **1** atm, and ΔHv may be taken as **9720** cal/ mole for this temperature range. and R is expressed as 1.987 cal/deg mole. Thus,

120◦C+273=393 k
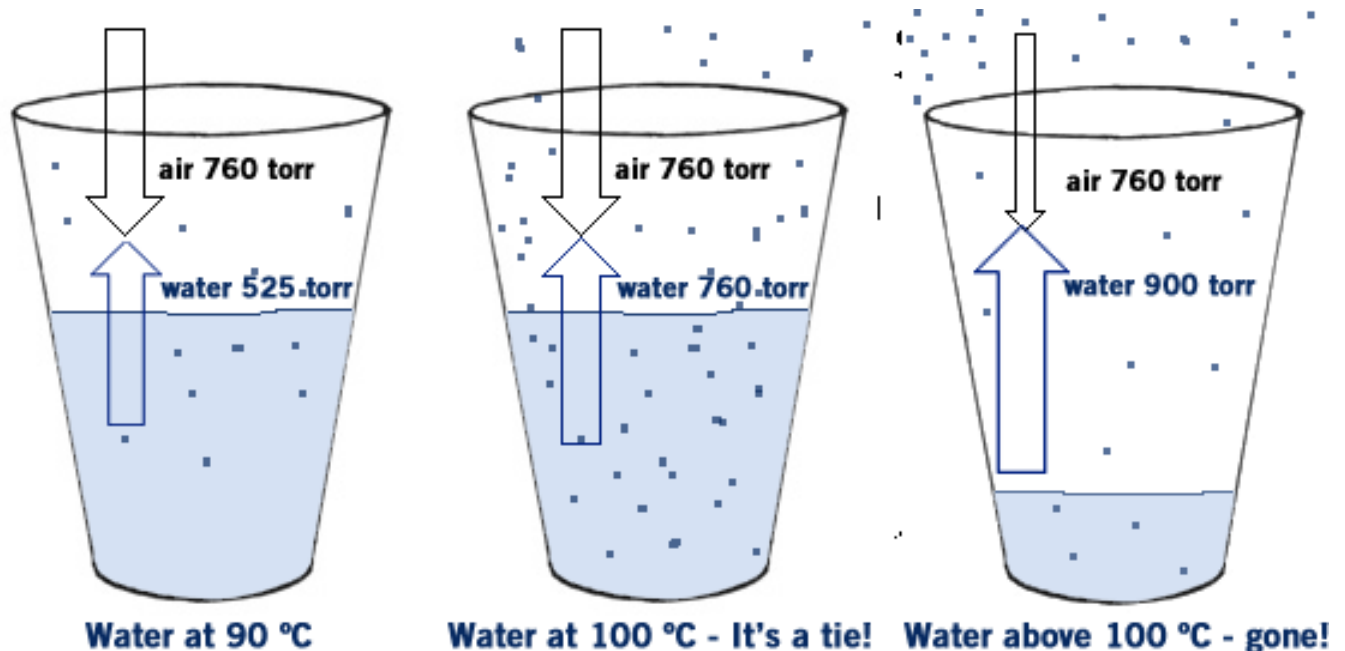
100◦C+273=373k

$$\log \frac{p_2}{1.0} = \frac{9720 \times (393 - 373)}{2.303 \times 1.987 \times 393 \times 373}$$
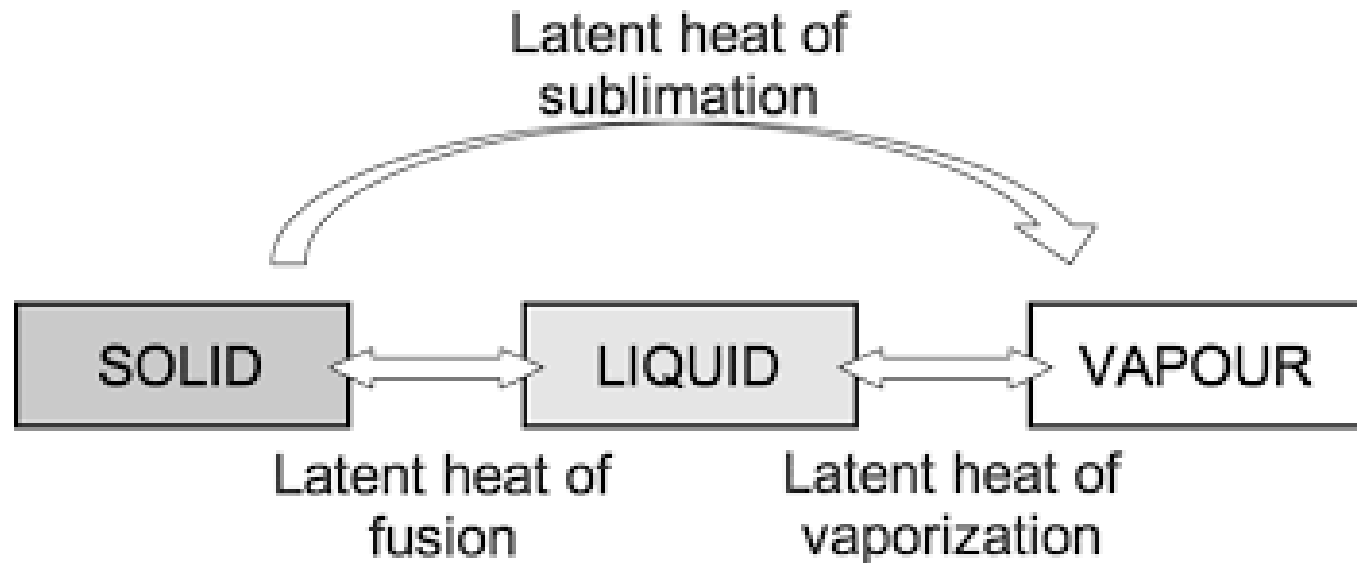
$$p_2 = 1.95 \text{ atm}$$

Boiling point

Definition

If a liquid is placed in an open container and heated until the vapor pressure equals the atmospheric pressure, the vapor will form bubbles that rise rapidly through the liquid and escape into the gaseous state..

air 760 torr
water 525 torr
Water at 90 °C

air 760 torr
water 760 torr
Water at 100 °C - It's a tie!

air 760 torr
water 900 torr
Water above 100 °C - gone!

The temperature at which the vapor pressure of the liquid equals the external or atmospheric pressure is known as the **boiling point** . The heat that is absorbed when water vaporizes at the normal boiling point (i.e., the heat of vaporization at 100∘C) is 539 cal/g or about 9720 cal/mole. For benzene, the heat of vaporization is 91.4 cal/g at the normal boiling point of 80.2∘C. These quantities of heat, known as **latent heats** of vaporization, are taken up when the liquids vaporize and are liberated when the vapors condense to liquids

Latent heat of
sublimation

SOLID $\longleftrightarrow$ LIQUID $\longleftrightarrow$ VAPOUR

Latent heat of
fusion

Latent heat of
vaporization

Intermolecular forces

The boiling point can be considered the temperature at which thermal agitation can overcome the attractive forces between the molecules of a liquid.

The boiling point of a compound ,like the heat of vaporization and the vapor pressure ,depends on the magnitude of the attractive forces.

- ❑ **Non polar** substances have low boiling points and low heats of vaporization because the molecules are held together predominantly by the weak London forces.

- ❑ **Polar** molecules (e.g water) exhibit high boiling points and high heats of vaporization because they are associated through hydrogen bonds

- ❑ The boiling points of normal hydrocarbons ,simple alcohols ,and carboxylic acids increase with molecular weight because vanderWaals forces become greater with increasing numbers of atoms.

☐ **Branching** of the chain produces a less compact molecule with reduced intermolecular attraction, and a decrease in the boiling point
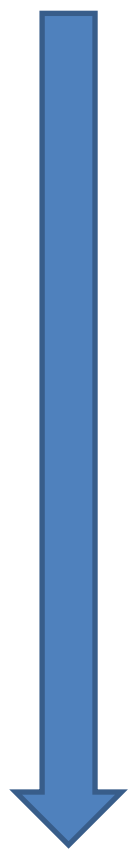
boiling point

$CH_3CH_2CH_2CH_2CH_2CH_3$ 69 °C

$CH_3\overset{\displaystyle CH_3}{\underset{|}{C}}HCH_2CH_2CH_3$ 60 °C

$CH_3\overset{\displaystyle CH_3}{\underset{|}{C}}H\underset{|}{C}HCH_3$ 58 °C
CH_3

$CH_3\overset{\displaystyle CH_3}{\underset{|}{C}}CH_2CH_3$ 50 °C
CH_3

- ❑ **Alcohols** boil at a much higher temperature than saturated hydrocarbons of the same molecular weight because of association of the alcohol molecules through hydrogen Bonding .

- ❑ The boiling points of **carboxylic acids** are higher than that of alcohols because the acids form dimers through hydrogen bonding
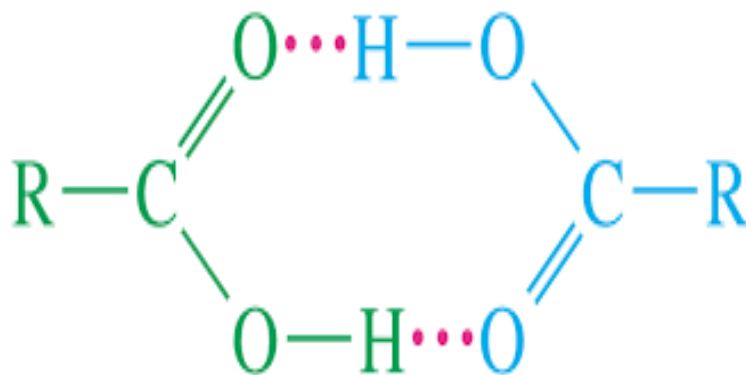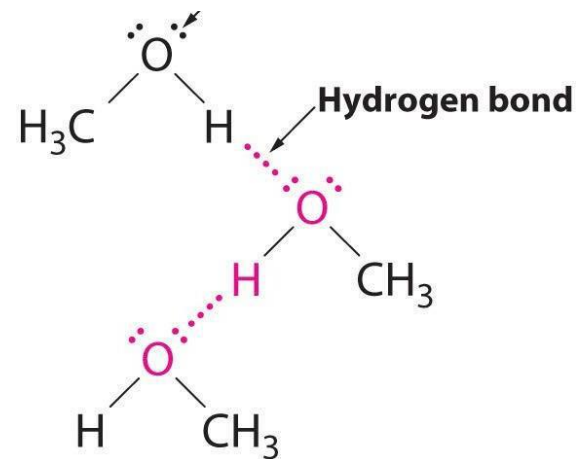
hydrogen-bonded acid dimer

The Solids State

➢ General properties
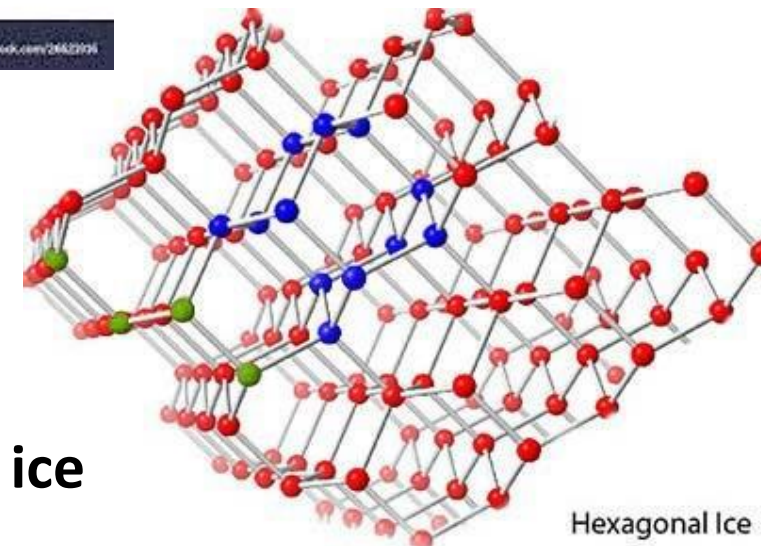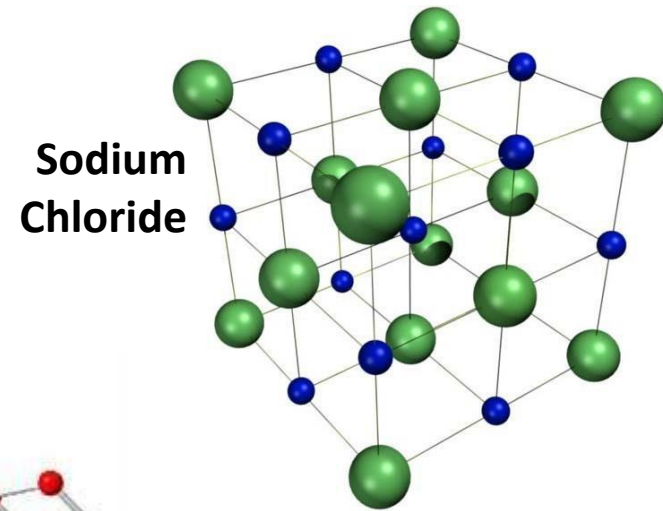➢ Crystalline Solids
➢ Amorphous Solids
➢ Melting point
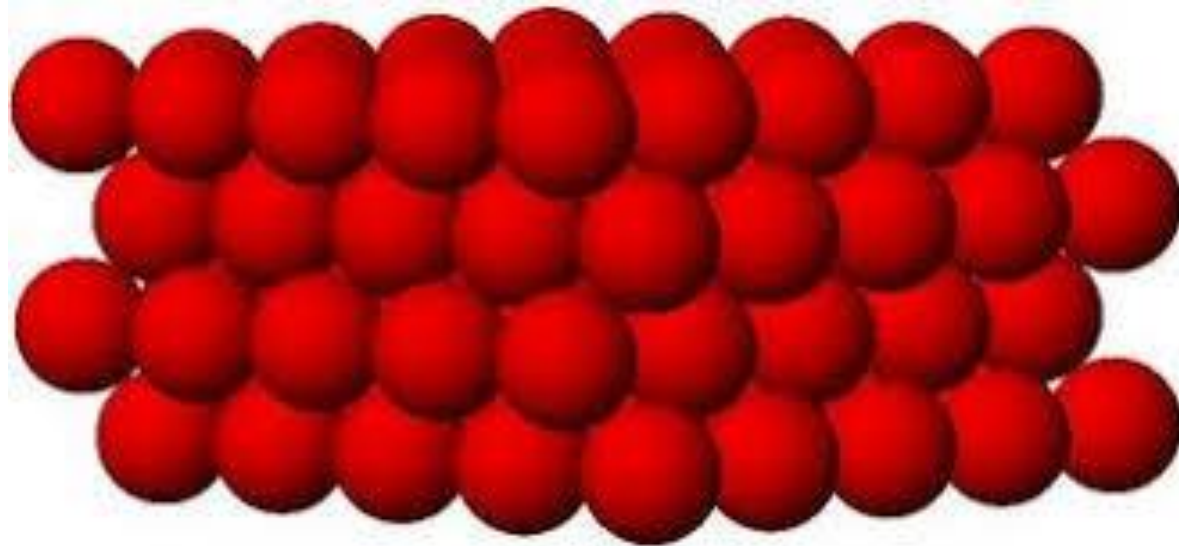
General properties

✓ Solids are much denser than both gases and liquids due to the presence of very strong intermolecular forces.

✓ Solids are essentially incompressible (small empty spaces) Solids have definite volume and shape (rigid, not fluid)

✓ Solids have no translational motion (only vibration)
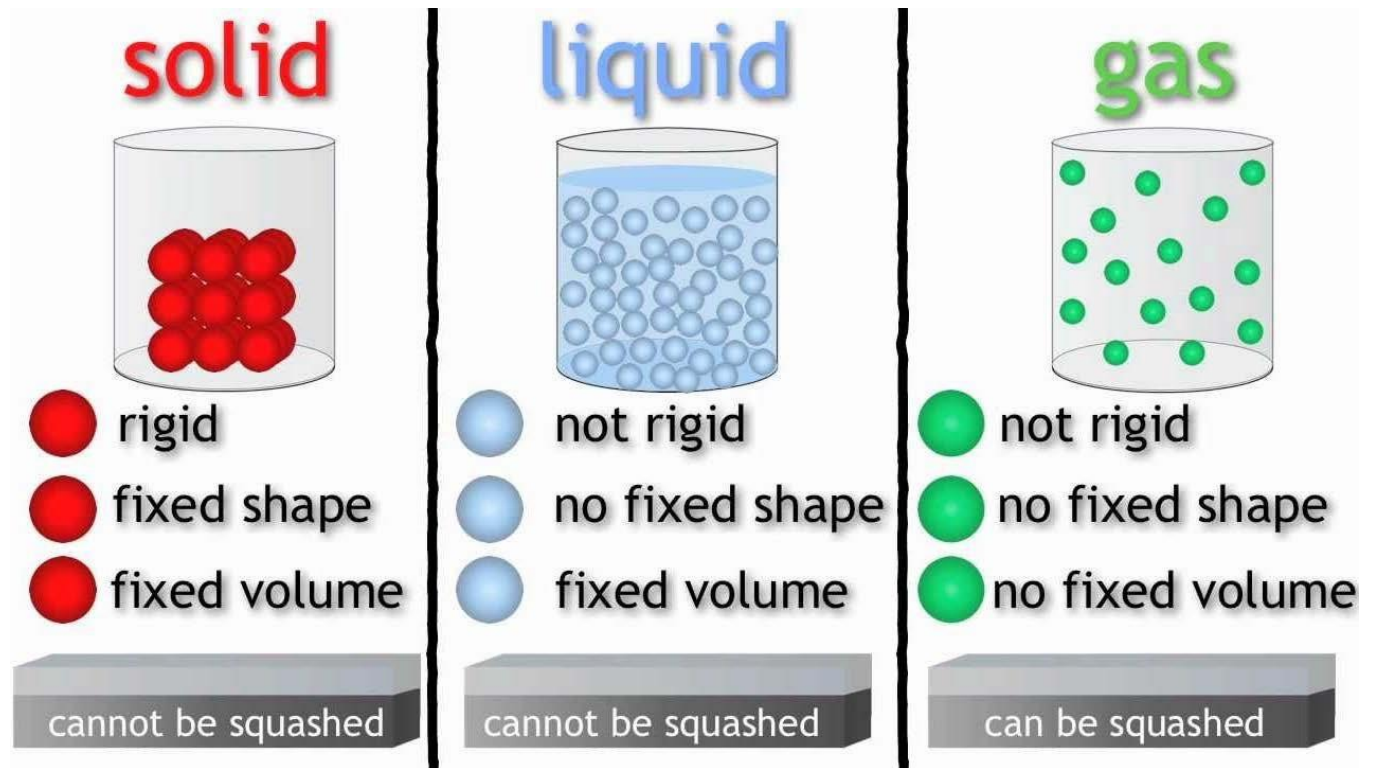
Crystalline Solids

Crystalline solids ,such as ice ,sodium chloride ,and menthol ,are composed of structural units arranged in fixed geometric patterns or lattices.

Menthol

$C_{10}H_{20}O$

Sodium Chloride

ice

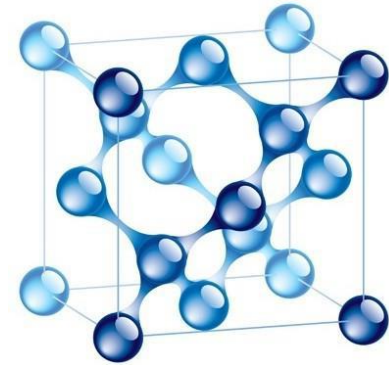Hexagonal Ice
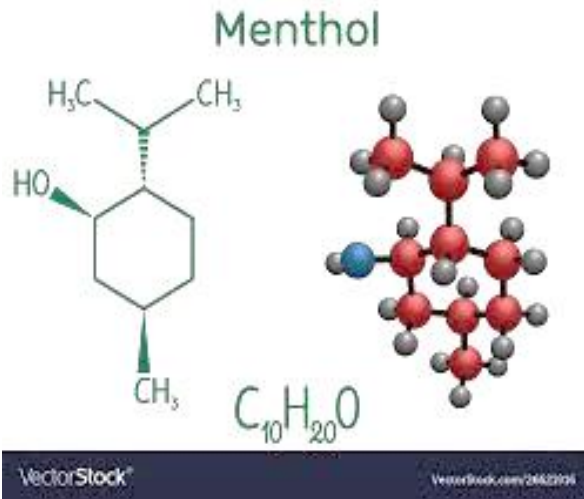
Types of crystalline solids

➤ Ionic Solid

Lattice units consist of ions held together by ionic bonds e g NaCl
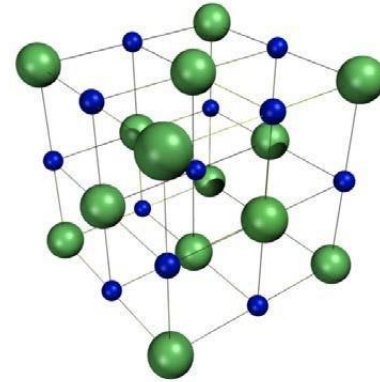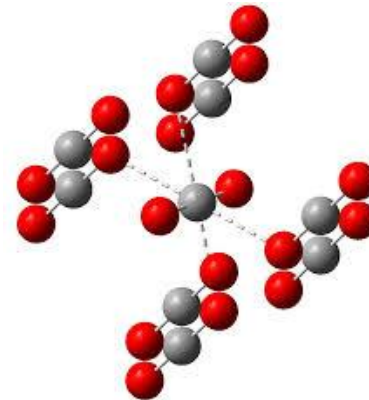
➤ Atomic Solid

Lattice units consist of atoms held together by covalent bonds e.g .diamond

➤ Molecular Solid

Lattice units consists of molecules held together by vanderWaals forces e.g Solid CO_2

➢ Ionic and atomic crystals in general are **hard and brittle** and have **high melting points**, while molecular crystals are **soft** and have relatively **low melting points.**

➢ Metallic crystals are composed of positively charged ions in a field of freely moving electrons .The atoms are held together by metallic bonding.

➢ Metals are good conductors of electricity because of the free movement of the electrons in the lattice Metals may be soft or hard and have low or high melting points

Metallic bonding

Sea of free electrons
(Sea of delocalised electrons)

Positive metal ions
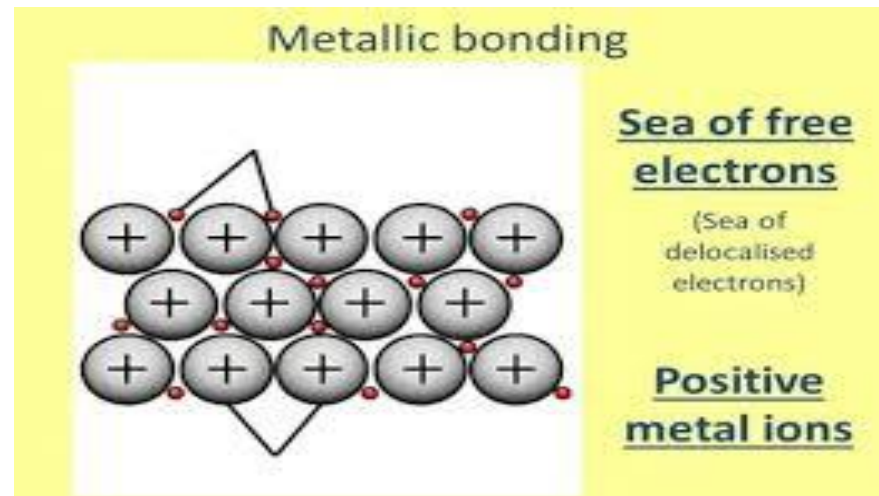
Amorphous Solid

Amorphous solids may be considered as super cooled liquids in which the molecules are arranged in a some what random manner as in the liquid state
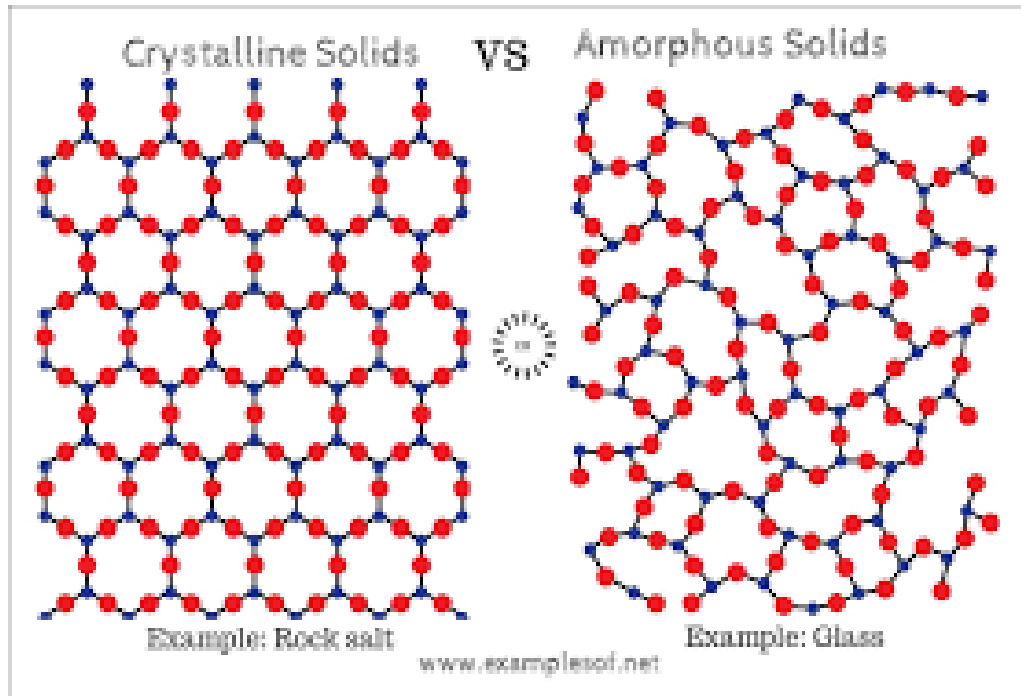
They differ from crystalline solids in that they <u>tend to flow when subjected to sufficient pressure over a period of time</u>, and they do not have definite melting points

The amorphous state is unstable compared to the crystalline solid (it has higher energy than crystalline solid) The pharmaceutical advantages of amorphous solid is its higher solubility and bioavailability .Its pharmaceutical disadvantages is its low stability over time, amorphous solid may transform to the more stable crystalline state)

Amorphous Drug:
• high solubility
• instable

Crystalline Drug:
• low solubility
• stable

Co-Amorphous blend:
• high solubility
• high stability

Crystalline   Polycrystalline   Amorphous
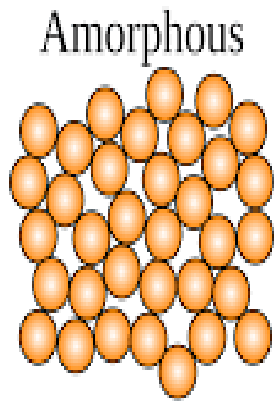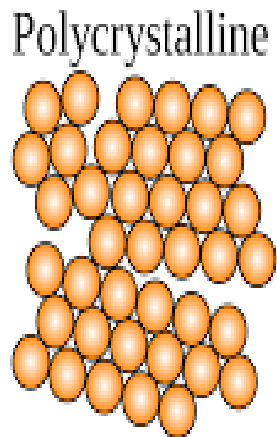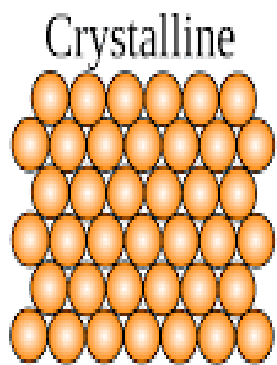
Classification of solids

Crystalline solids

Amorphous solids
Ex: Glass, rubber etc

- → Ionic crystals Ex: NaCl ,KCl

- → Covalent crystals Ex: Diamond, SiO_2

- → Molecular crystals Ex: naphthalene, anthracene, glucose

- → Metallic crystals Ex: All metallic elements
  (Na, Mg,Cu,Au,Ag etc..)

- → Atomic solids - ex: frozen elements of Group 18

Melting Point and Heat of Fusion

The temperature at which a liquid passes into the solid state is known as the *freezing point*. It is also the *melting point* of a pure crystalline compound. The freezing point or melting point of a pure crystalline solid is strictly defined as the temperature at which the pure liquid and solid exist in equilibrium..
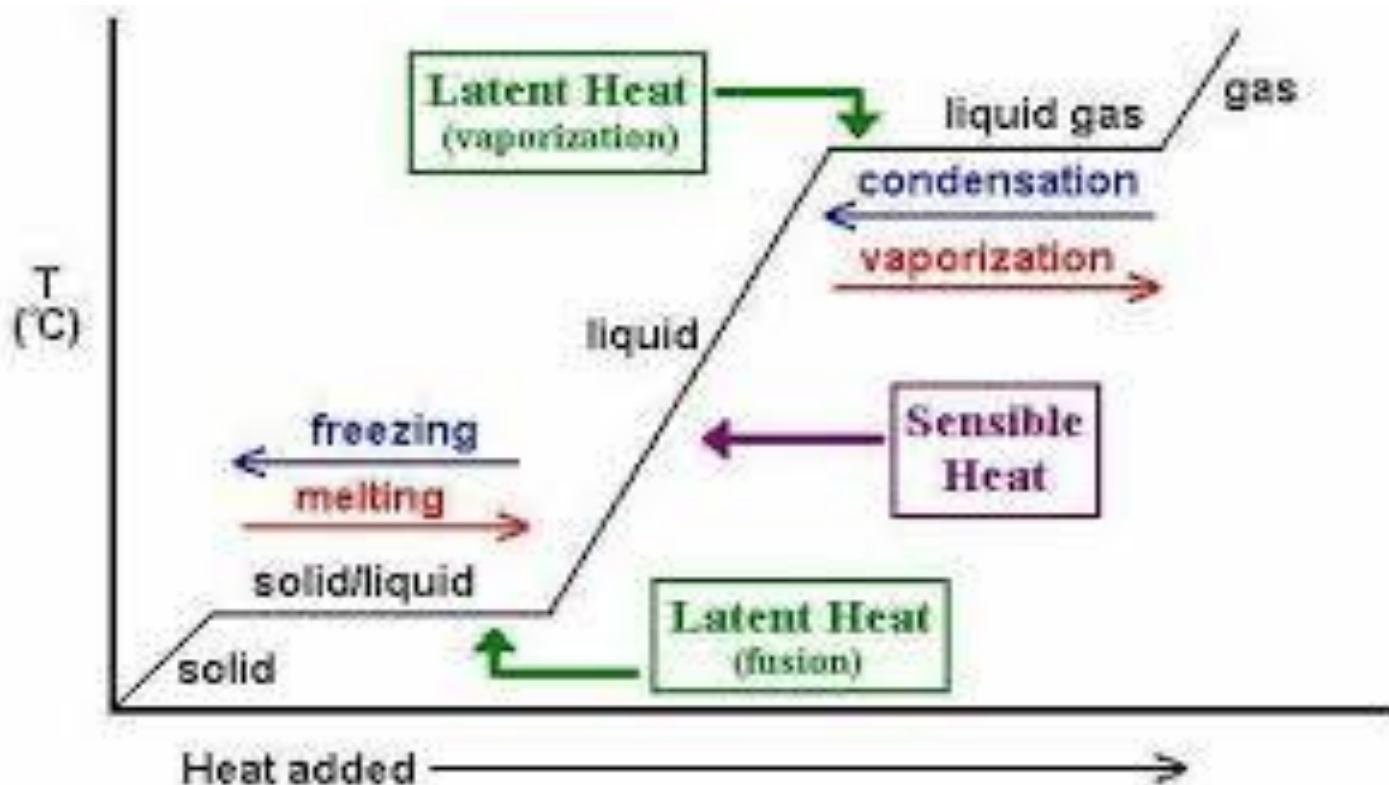
The heat (energy) absorbed when 1g of a solid melts or the heat liberate When it freezes is known as **latent heat of fusion**. Changes of freezing or melting point with the pressure can be obtained by using a form of the Claperon equation written as :-

$$\frac{\Delta T}{\Delta P} = T \frac{V_1 - V_s}{\Delta H_f}$$

V_l and V_s the molar volumes (cm^3/mole) of the liquid and solid, respectively .**Molar volume** is computed by dividing the gram molecular weight by the density of the compound

ΔH_f the **molar heat of fusion** the amount of heat absorbed when 1 mole of the solid changes into liquid

ΔT the change of melting point brought about by a pressure change of ΔP

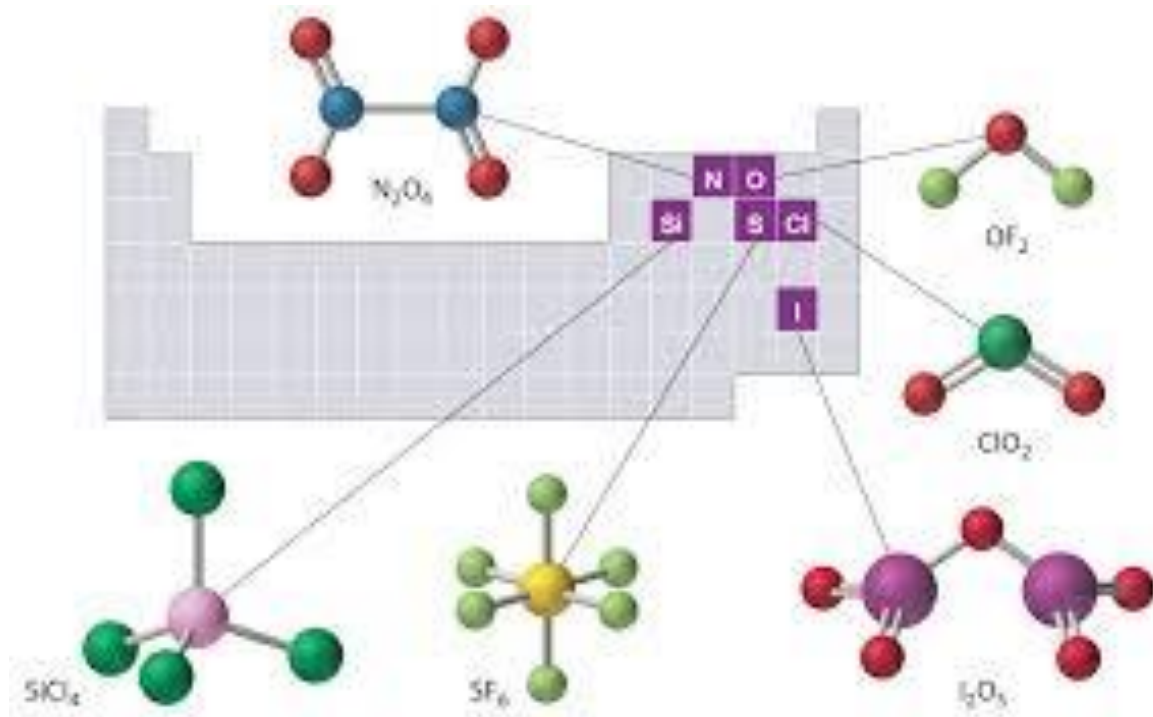# Intermolecular Forces

The heat of fusion may be considered as the heat required to <u>increase</u> the inter atomic or intermolecular distances in crystals ,thus all owing melting (increased molecular motion)to occur.
A crystal that is bound together by weak forces generally has a <u>low</u> heat of fusion and a <u>low</u> melting point ,where as one bound together by strong forces has a high heat of fusion and a high melting point.
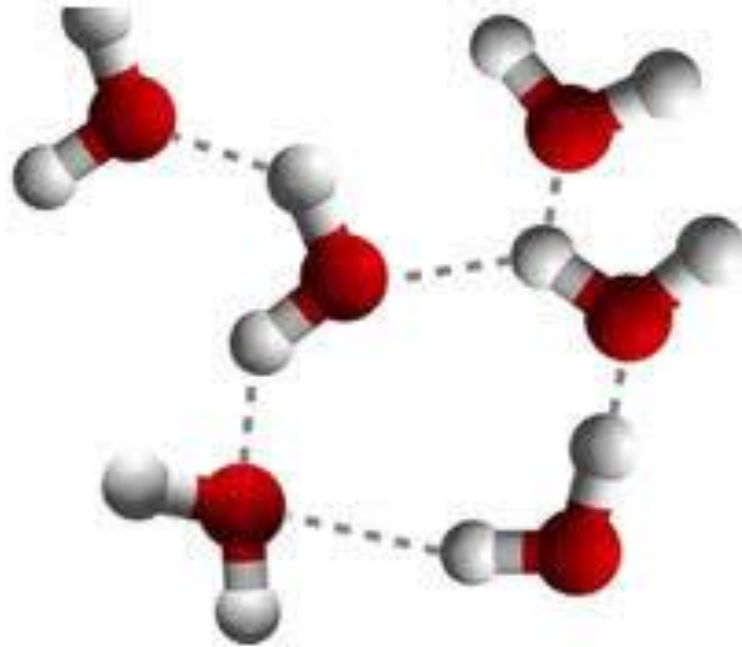
Applications Melting points for organic and inorganic compounds are often used to:

•Characterize organic and inorganic compounds.

•the melting point of a pure substance is always higher and has a smaller range than the melting point of an impure substance)