

**AL-Mustaqbal university college  
Pharmacy department , under  
graduated Study, 2<sup>rd</sup> class Study  
year 2021-2022**



# **Physical pharmacy 1**

## **Lecture1**

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# 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 cooled, it loses some of its kinetic energy and the velocity of the molecules decreases.

If pressure is applied to the gas, the molecules are brought within the range of the vanderWaals forces and pass into the liquid state.



LIQUEFACTION OF GASES

XI FDC CHEMISTRY  
CHAPTER 4  
SIDRA JAVED

## **Critical point (thermodynamics)**

**Critical temperature ( $T_c$ ):** The maximum temperature at which a gas can be converted into a liquid by an increase in the pressure.

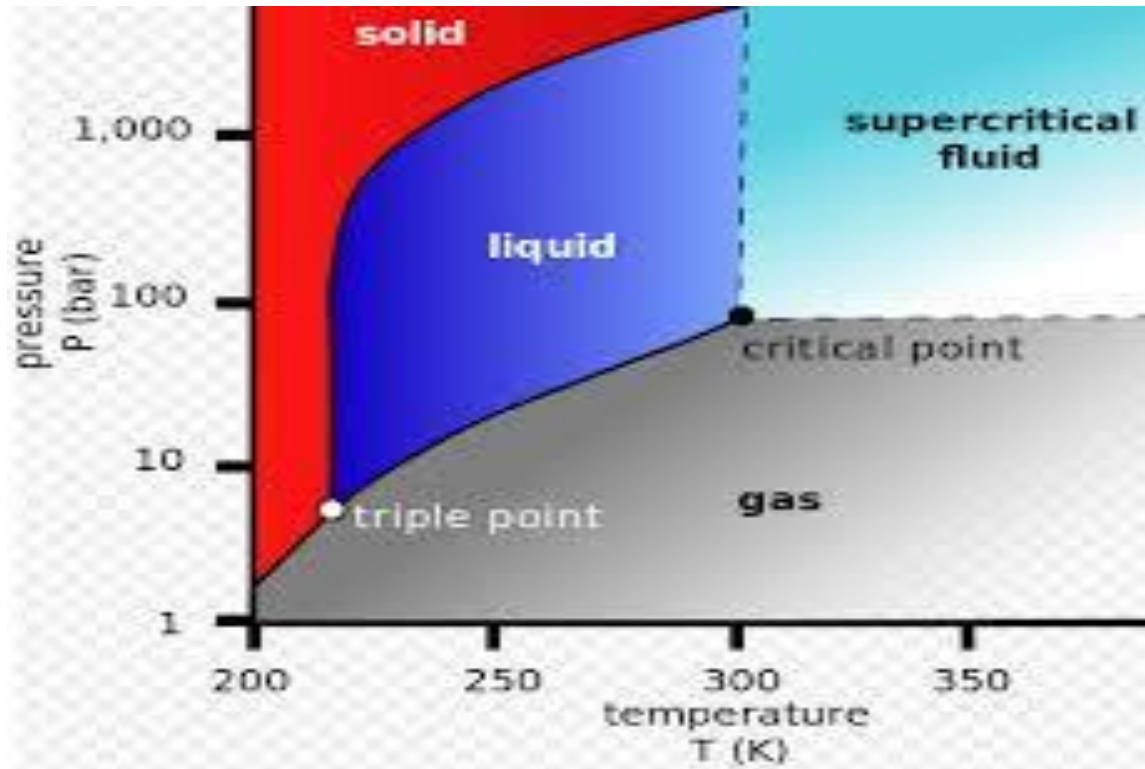
**Critical pressure ( $p_c$ ):** The minimum pressure which would suffice to liquefy a substance at its critical temperature. Above the critical pressure, increasing the temperature will not cause a fluid to vaporize to give a two-phase system.

**Critical point:** The characteristic temperature ( $T_c$ ) and pressure ( $p_c$ ) above which a gas cannot be liquefied.

**Supercritical fluid:** The defined state of a compound, mixture or element above its critical pressure ( $p_c$ ) and critical temperature ( $T_c$ ).

In physical chemistry, thermodynamics, chemistry and condensed matter physics, a critical point, also known as a critical state, occurs under conditions (such as specific values of temperature, pressure or composition) at which no phase boundaries exist. There are multiple types of critical points, including vapor–liquid critical points and liquid–liquid critical points.

# Critical temperature and pressure

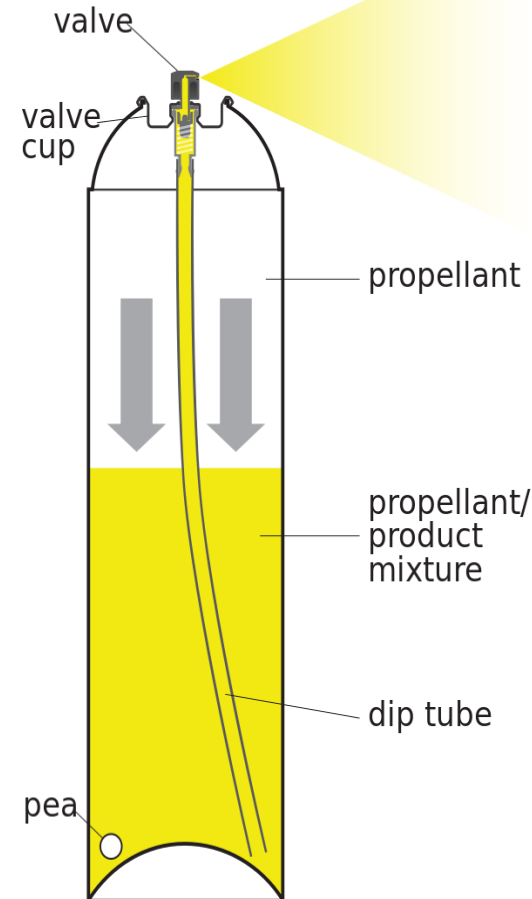


**the liquid can have the critical temperature of water is 374 C° or 647 K and its critical pressure is 218 atm.**

# 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.



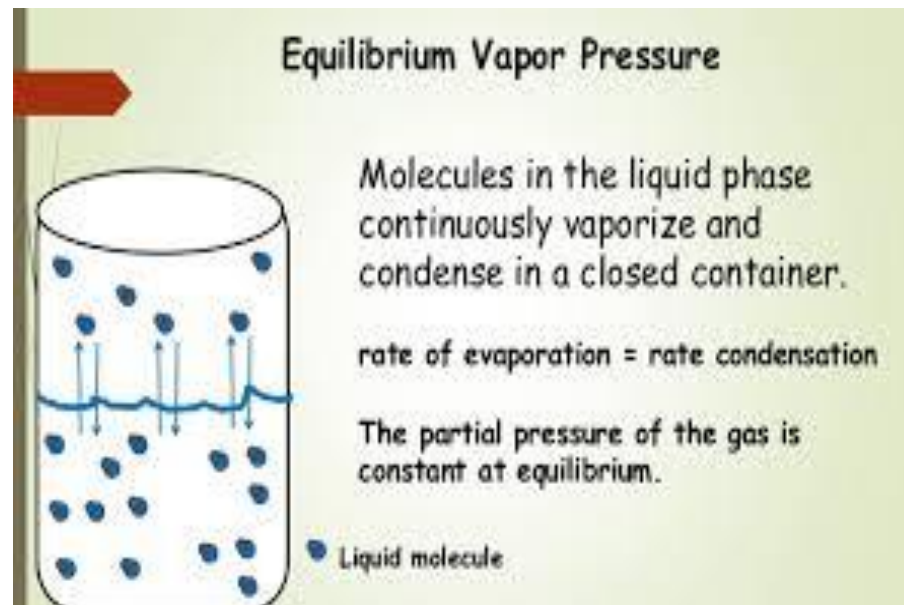
# Vapor pressure of liquids

## 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 dynamic equilibrium is established.**

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



## Clausius Clapeyron equation

## معادلة كلاوزيوس-كلايرون

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  $p_1$  and  $p_2$  are the vapor pressures at absolute temperatures  $T_1$  and  $T_2$ , and  $H_v$  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  $P_2$  at temperature  $T_2 = 373$  K (100°C) is **78** cm Hg, and  $R$  is expressed as 1.987 cal/deg mole.

Write

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

$$100^\circ\text{C} + 273 = 373\text{k}$$

$$95^\circ\text{C} + 273 = 368\text{k}$$

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

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

## Example

Compute the vapor pressure of water at **120°C**. The vapor pressure  $p_1$  of water at **100°C** is **1** atm, and  $\Delta H_v$  may be taken as **9720** cal/ mole for this temperature range. and  $R$  is expressed as 1.987 cal/deg mole. Thus,

$$393 \text{ k} = 120^\circ\text{C} + 273$$

$$100^\circ\text{C} + 273 = 373\text{k}$$

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

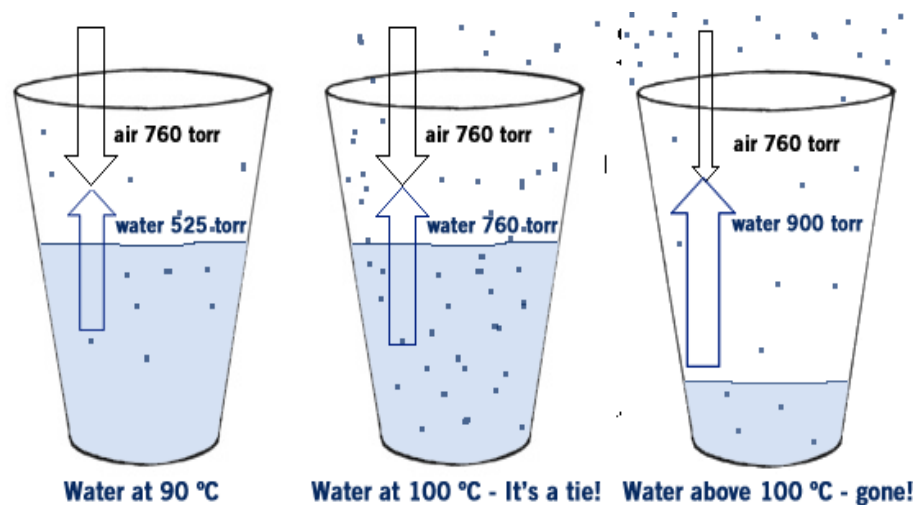
$$p_2 = 1.95 \text{ atm}$$



# 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..



**The temperature at which the vapor pressure of the liquid equals the external or atmospheric pressure is known as the boiling point .**

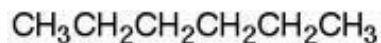
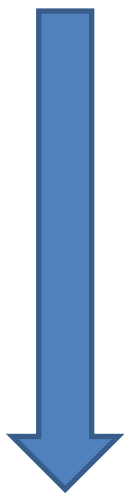
The heat that is absorbed when water vaporizes at the normal boiling point (i.e., the heat of vaporization at 100°C) is 539 cal/g or about 9720 cal/mole. For benzene, the heat of vaporization is 91.4 cal/g at the normal boiling point of 80.2°C. These quantities of heat, known as **latent heats** of vaporization,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

## 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.

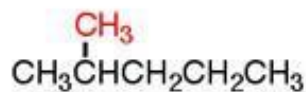
The boiling point of a compound, like the heat of vaporization and the vapor pressure, depends on the magnitude of the attractive forces.

- ❑ **Non polar substances have low boiling points and low heats of vaporization (Why)?**
- ❑ because the molecules are held together generally by the weak London forces.
- ❑ **Polar molecules (e.g water) exhibit high boiling points and high heats of vaporization (Why)?**
- ❑ 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

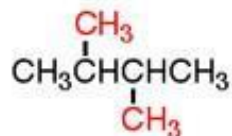


**boiling point**

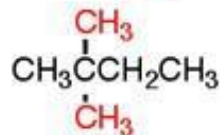
69 °C



60 °C



58 °C



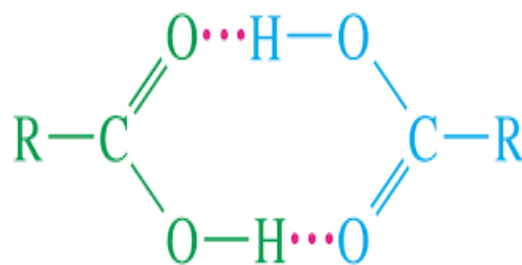
50 °C

□ **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

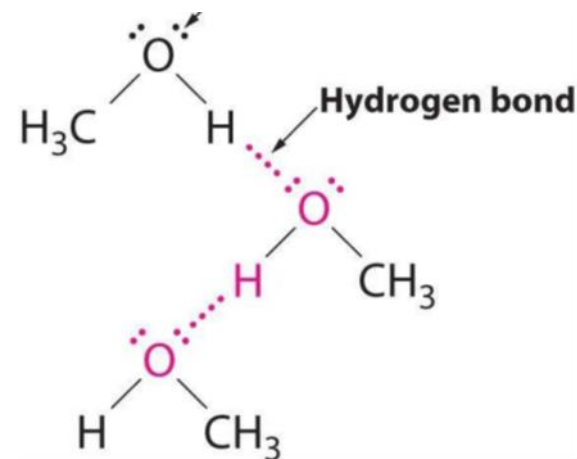
The boiling points of **carboxylic acids**

are higher than that of alcohols

because the acids form dimers through hydrogen bonding

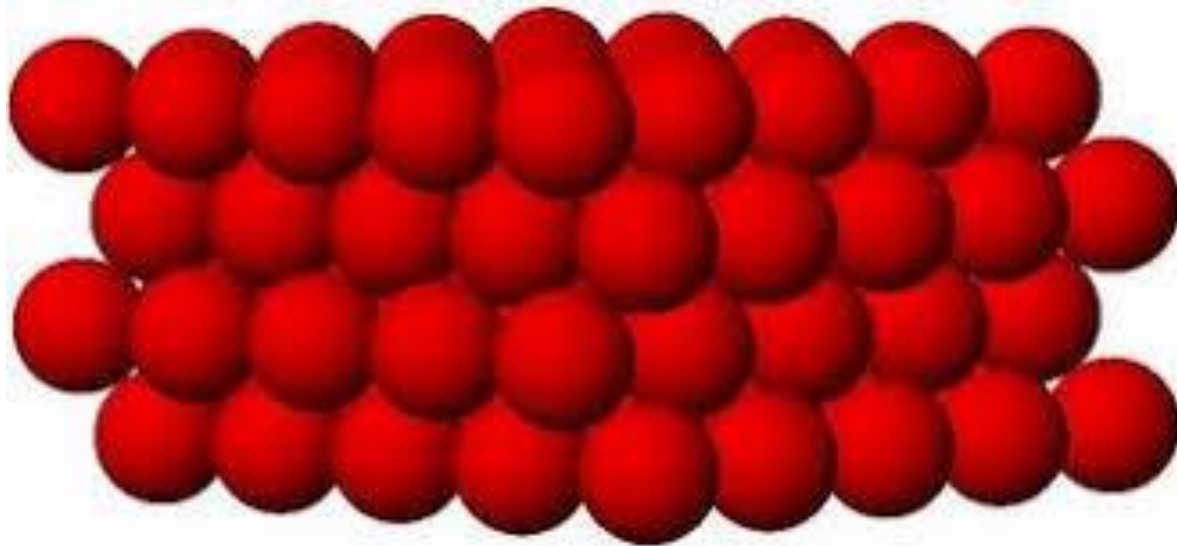


hydrogen-bonded acid dimer



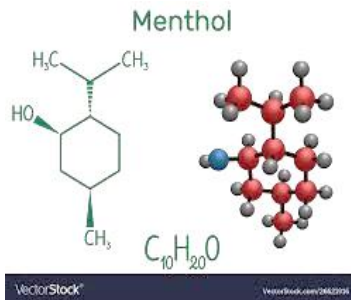
# The Solids State

- General properties
- Crystalline Solids
- Amorphous Solids
- Melting point



## Crystalline Solids

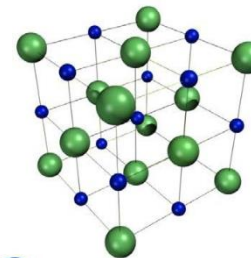
Crystalline solids, such as ice, sodium chloride, and menthol, are composed of structural units arranged in fixed geometric patterns or lattices.



### Types of crystalline solids

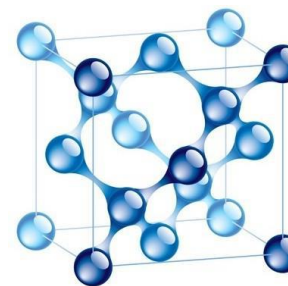
#### ➤ Ionic Solid

Lattice units consist of ions held together by ionic bonds e.g NaCl



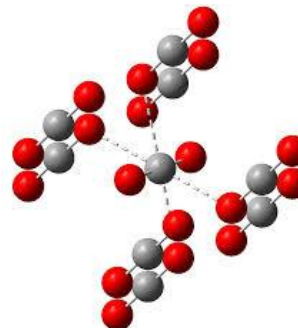
#### ➤ Atomic Solid

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



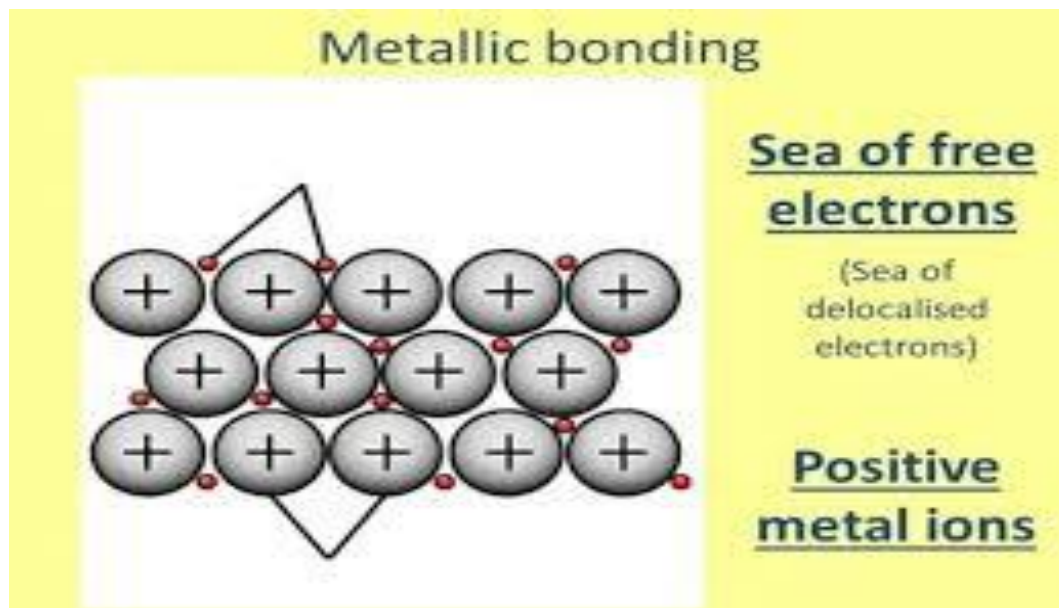
#### ➤ Molecular Solid

Lattice units consists of molecules held together by vanderWaals forces e.g Solid CO<sub>2</sub>



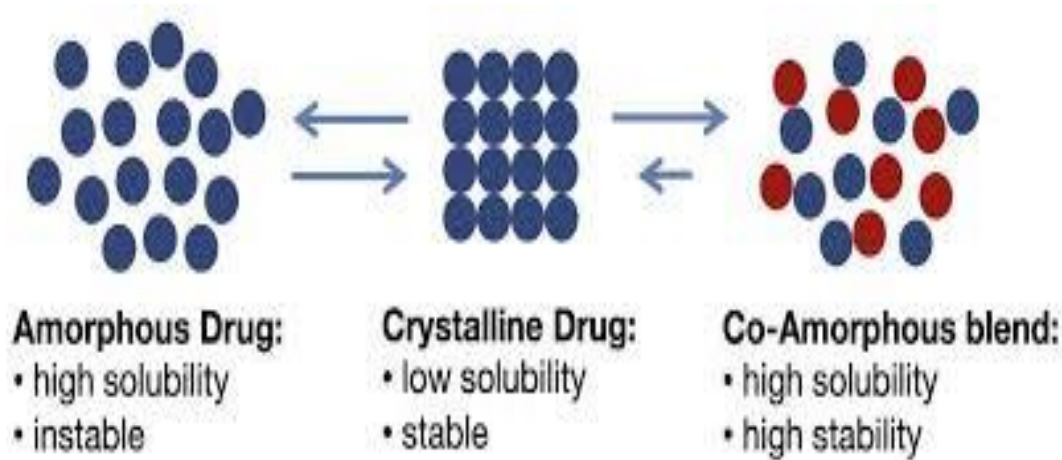
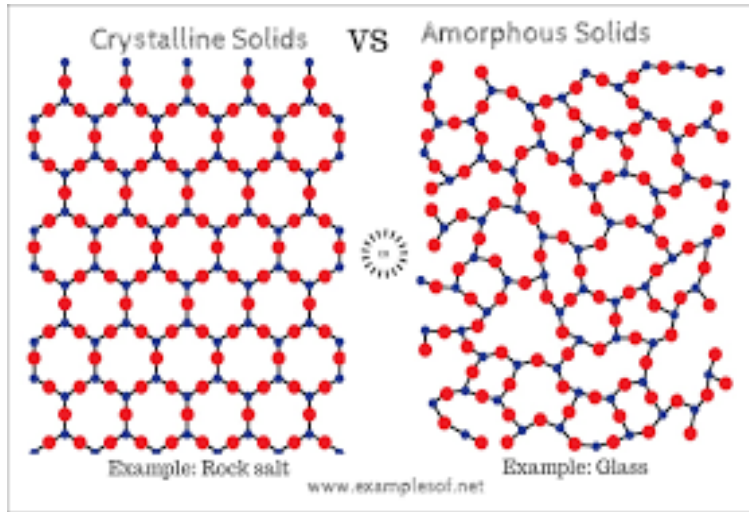
- Ionic and atomic crystals in general are **hard and brittle** and have **high melting points**, while molecular crystals are **soft** and have relatively **low melting points**.
- Metallic crystals are composed of positively charged ions in a field of freely moving electrons. The atoms are held together 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



# Amorphous Solid

Amorphous solids may be considered as super cooled liquids in which the molecules are arranged in a somewhat random manner as in the liquid state



They differ from crystalline solids in that they tend to flow when subjected to sufficient pressure over a period of time, 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)**

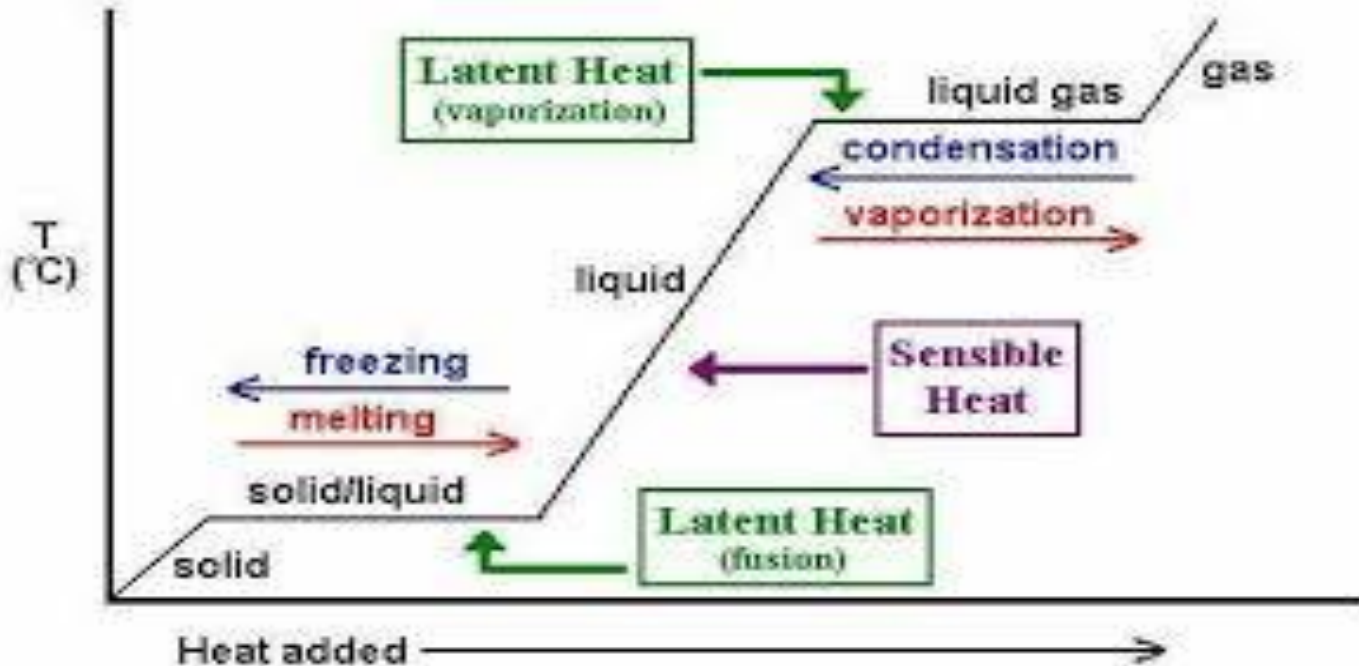


# Melting Point and Heat of Fusion

**Melting point** : is that melting is the process of changing the state of a substance from solid to liquid by heating it

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.

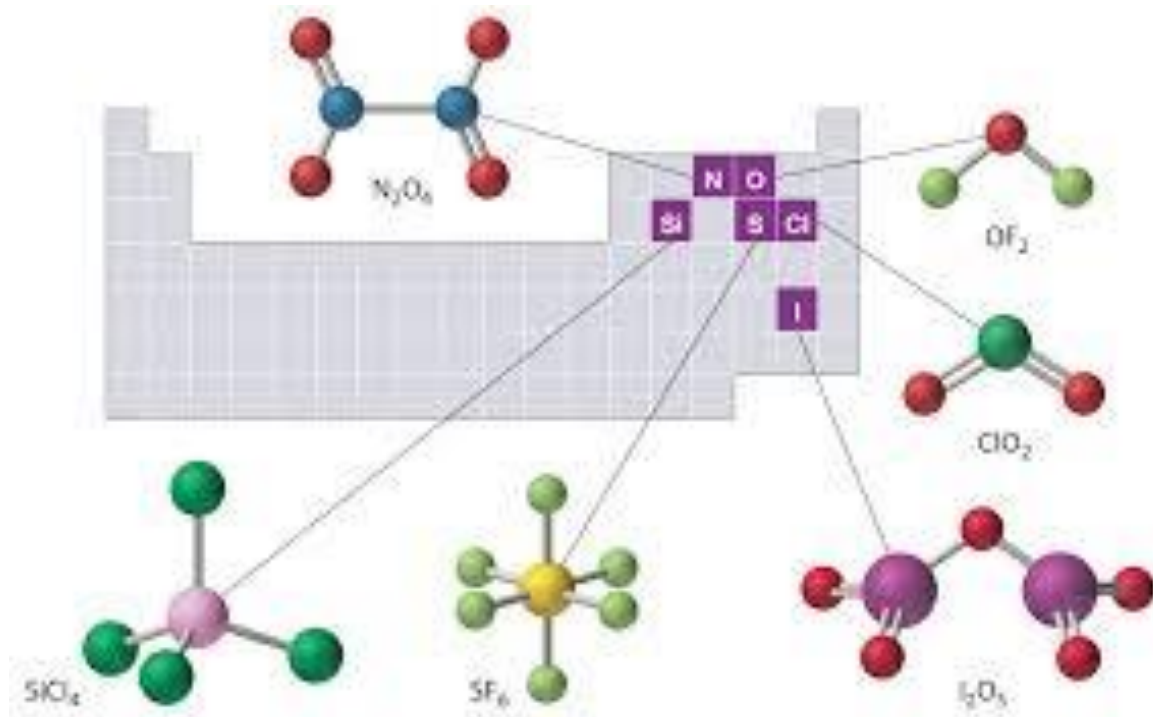
**The heat of fusion is the amount of heat required to melt the frozen solvent.** ... The magnitude of heat of fusion and heat of vaporization is related to the nature and strength of forces which hold the molecules of the solvent together in the solid or the liquid state





# 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)



# PHASE

**A phase** : any homogeneous part of a system having all physical and chemical properties the same throughout.

A system may consist of one phase or more than one phases.

(1) only liquid water is **one-phase** ( $P = 1$ )

(2) liquid water and water vapour is a **two-phase** ( $P = 2$ ).

(3) liquid water, water vapour and solid ice is a **three-phase** ( $P = 3$ )

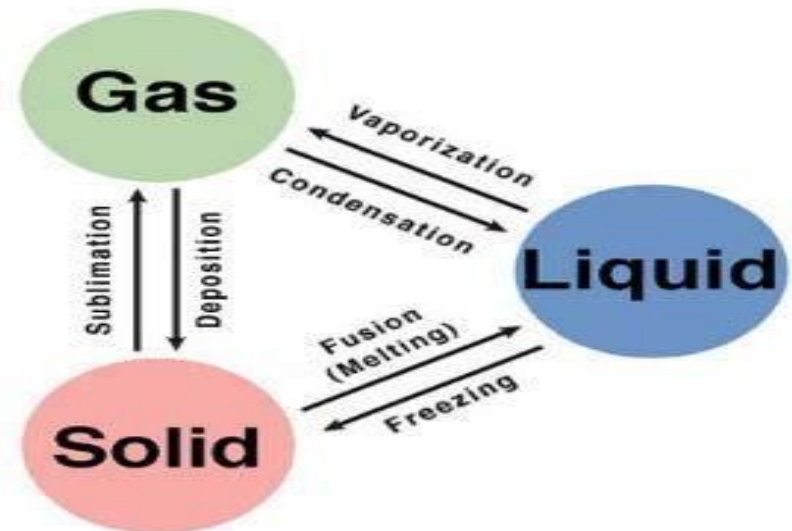
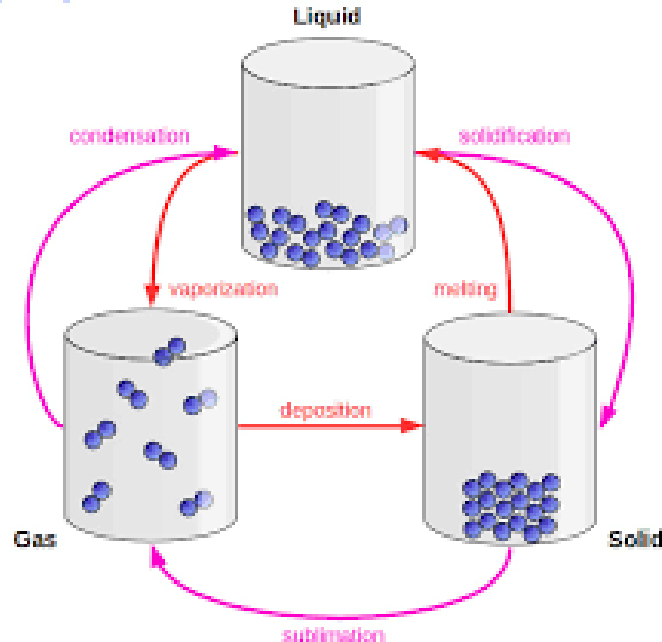
A system consisting of one phase only is called a **homogeneous system**.

A system consisting of two or more phases is called a **heterogeneous system**.

A system containing water and its vapor is a two phase system .An equilibrium mixture of ice, liquid water, and water vapor is a three phase system

- A phase may be gas, liquid or solid. A gas or a gaseous mixture is a single phase. Completely **miscible liquids** constitute a single phase. In **an immiscible liquid** system, each layer is counted as a separate phase.
- The three primary phases (solid, liquid, and gaseous) of matter are often defined individually under different conditions, but in most systems we usually encounter phases in coexistence.

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- **For example**, a glass of ice water on a hot summer day comprises **three coexisting phases**: ice (solid), water (liquid), and vapor (gaseous).
- The amount of ice in the drink depends heavily on several variables including the amount of ice placed in the glass, the temperature of the water in which it was placed, and the temperature of the surrounding air.



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# PHASE

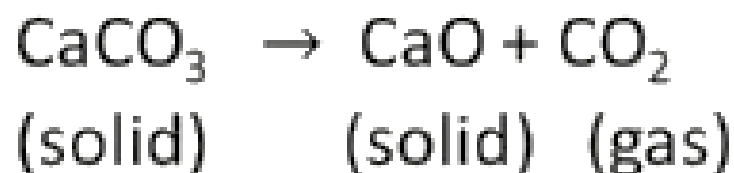
- (1) **Pure substances** (made of one chemical species only): one phase ( $O_2$ ), ( $C_6H_6$ ), and ice ( $H_2O$ ) are all 1-phase systems.
- (2) **Mixtures of gases**. All gases mix freely to form homogeneous mixtures.
- (3) **Miscible liquids**. Two completely miscible liquids yield a uniform solution. Thus a solution of ethanol and water is a 1-phase system.
- (4) **Non-miscible liquids**. A mixture of two non-miscible liquids on standing forms two separate layers. Hence a mixture of chloroform ( $CHCl_3$ ) and water constitutes a 2-phase system.
- (5) **Aqueous solutions**. An aqueous solution of a solid substance such as sodium chloride (or sugar) is uniform throughout. Therefore it is a 1-phase system. However, a saturated solution of sodium chloride in contact with excess solid sodium chloride is a 2-phase system.
- (6) **Mixtures of solids**. (i) By definition, a phase must have throughout the same physical and chemical properties. Ordinary sulphur as it occurs in nature is a mixture of monoclinic and rhombic sulphur. These allotropes of sulphur consist of the same chemical species but differ in physical properties. Thus mixture of two allotropes is a 2-phase system.

# PHASE

*(ii)* **A mixture of two or more chemical substances contains as many phases.**

Let us consider the equilibrium system :

the **Decomposition of Calcium carbonate**. When calcium carbonate is heated in a closed vessel, we have



There are two solid phases and one gas phase.

Hence it is a 3-phase system.

## Examples

How many phases in each of the following systems?

1-Liquid water, pieces of ice and water vapor are present together. Number of phases 3

2-Calcium Carbonate under goes thermal decomposition .

$\text{CaCO}_3(\text{s}) \rightarrow \text{CaO}(\text{s}) + \text{CO}_2(\text{g})$  Number of phases 3

3-A solution of NaCl in water Number of phases 1

4-Liquid water + water vapor Number of phases 2

5-Liquid water + water vapor air Number of phases 2

## COMPONENTS

The least number of independent chemical constituents in terms of which the composition of every phase can be expressed by means of a chemical equation.

# COMPONENTS

(1) **Water and sulphur systems are 1-component systems.** Water system has three phases : *ice, water, and water vapour.*

The composition of all the three phases is expressed in terms of one chemical individual H<sub>2</sub>O.

Sulphur system has four phases : rhombic sulphur, monoclinic sulphur, liquid sulphur and sulphur vapour.

The composition of all these phases can be expressed by one chemical individual sulphur (S). Hence it is a 1-component system.

(2) **Mixture of gases.** A mixture of gases, say O<sub>2</sub> and N<sub>2</sub>, constitutes one phase only. Its composition can be expressed by two chemical substances O<sub>2</sub> and N<sub>2</sub>.

(3) **Sodium chloride solution.** A solution of sodium chloride in water is a 1-phase system. Its composition ( $x\text{NaCl}.y\text{H}_2\text{O}$ ) can be expressed in terms of two chemical individuals, sodium chloride and water.



# Gibbs Phase Rule

The number of intensive variables that must be defined to determine the state of a system.

## Variables

- Extensive variables – dependent on quantity (V, m, n, ...)
- Intensive variables – not dependent on quantity (T, P,  $\rho$ , ...)

## State

Knowing all variables of a system (V, m, n, T, P,  $\rho$ , ...)

# Gibbs Phase Rule

$$F = C - P + 2$$

F = number of degrees of freedom (intensive variables to define T, P).

P = number of phases.

C = number of independent components

2 = constant

# Phase Rule

## Gibbs phase rule

**“In a heterogeneous system in equilibrium is not affected by gravity or by electrical and magnetic forces, the number of degrees of freedom(F) of the system is related to the number of component(C) and the number of phases(P) existing at equilibrium”.**

It is expressed by mathematically,

$$\mathbf{F = C - P + 2}$$

where,

F - number of degrees of freedom

C - number of components

P - number of phases

2 - additional variables of temperature and pressure

# DEGREES OF FREEDOM

Degree of Freedom ( $F$ ):the least number of variable factors (concentration, pressure and temperature) which must be specified so that the remaining variables are fixed automatically and the system is completely defined

A system with  $F = 0$  is known as **nonvariant** or having no degree of freedom.

A system with  $F = 1$  is known as **univariant** or having one degree of freedom.

A system with  $F = 2$  is known as **bivariant** or having two degrees of freedom.

# ONE-COMPONENT SYSTEM

For a one-component system we can write the phase rule equation as :

$$F = C - P + 2 = 1 - P + 2 = 3 - P$$

Three cases may arise :

**Case 1.** When only **one phase** is present,

$$\therefore F = 3 - 1 = 2$$

Thus the system is **bivariant**. It can be completely defined by specifying the two variables, temperature and pressure. Or that, both the temperature and pressure can be varied independently.

Therefore a **single phase** is represented by an area on P, T-graph.

# ONE-COMPONENT SYSTEM

**Case 2.** When **two phases** are in equilibrium,

$$F = 3 - 2 = 1$$

The system then has one degree of freedom and is termed **monovariant**. This means that the pressure cannot be changed independently if we change the temperature. The pressure is fixed automatically for a given temperature. **A two-phase system is depicted by a line on a P, T-graph.**

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# ONE-COMPONENT SYSTEM

**Case 3.** When **three phases** are in equilibrium,

$$F = 3 - P = 3 - 3 = 0$$

$$\therefore F = 0$$

The system has zero degree of freedom and is termed **nonvariant or invariant**. This special condition can be attained at a definite temperature and pressure. The system is, therefore, defined completely and no further statement of external conditions is necessary.

**A three-phase system is depicted by a point on the P, T-graph.** At this point the three phases (solid, liquid, vapour) are in equilibrium and, therefore, it is referred to as the **Triple point**.

# Phase Rule

## Examples

### (i) Sulphur system

(a) monoclinic sulphur, (b) rhombic sulphur (c) liquid sulphur  
(d) sulphur vapour. **(C = 1; P = 4)**

### (ii) Water system

solid, liquid and vapour  
**(C = 1 ; P = 3)**

### (iii) Salt + water system

- Certain salts are capable of existing as hydrates with different number of water molecules of crystallization.  
The system is a two component. **(C = 2 , P = 1)**
- The composition of each phase of the hydrates is completely described in terms of the anhydrous salt and water alone. e.g.,  
**Na<sub>2</sub>SO<sub>4</sub> + water**

# Phase Rule

## Degrees of Freedom

“It is defined as the minimum number of independent variables such as temperature, pressure and concentration which should be specified in order to define the system completely”.

Examples

(i) State of a pure gas can be specified by two variables **P and T** or **P and V**, third variable can be calculated.

Hence pure gas has degree of freedom two ( $F = 2$ )

(ii)  $\text{H}_2\text{O}_{(l)} \rightleftharpoons \text{H}_2\text{O}_{(g)}$  ( $F = 1$ ) **Monovariant**

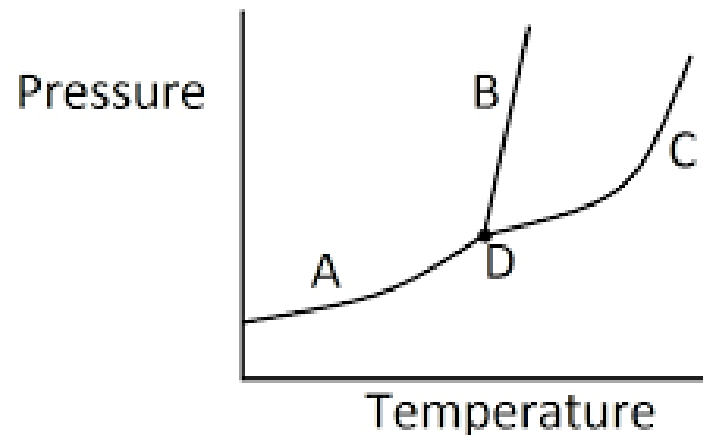
(ii) A gaseous mixture say  $\text{N}_2$  and  $\text{O}_2$  gases is completely defined when three variables (T, P and C).

( $F=3$ ) **Trivariant.**



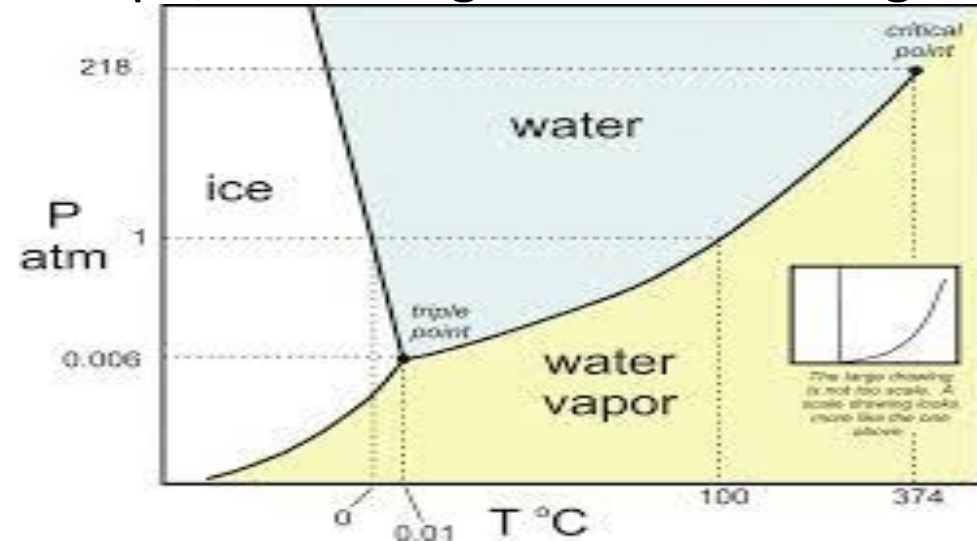
# Phase Diagrams

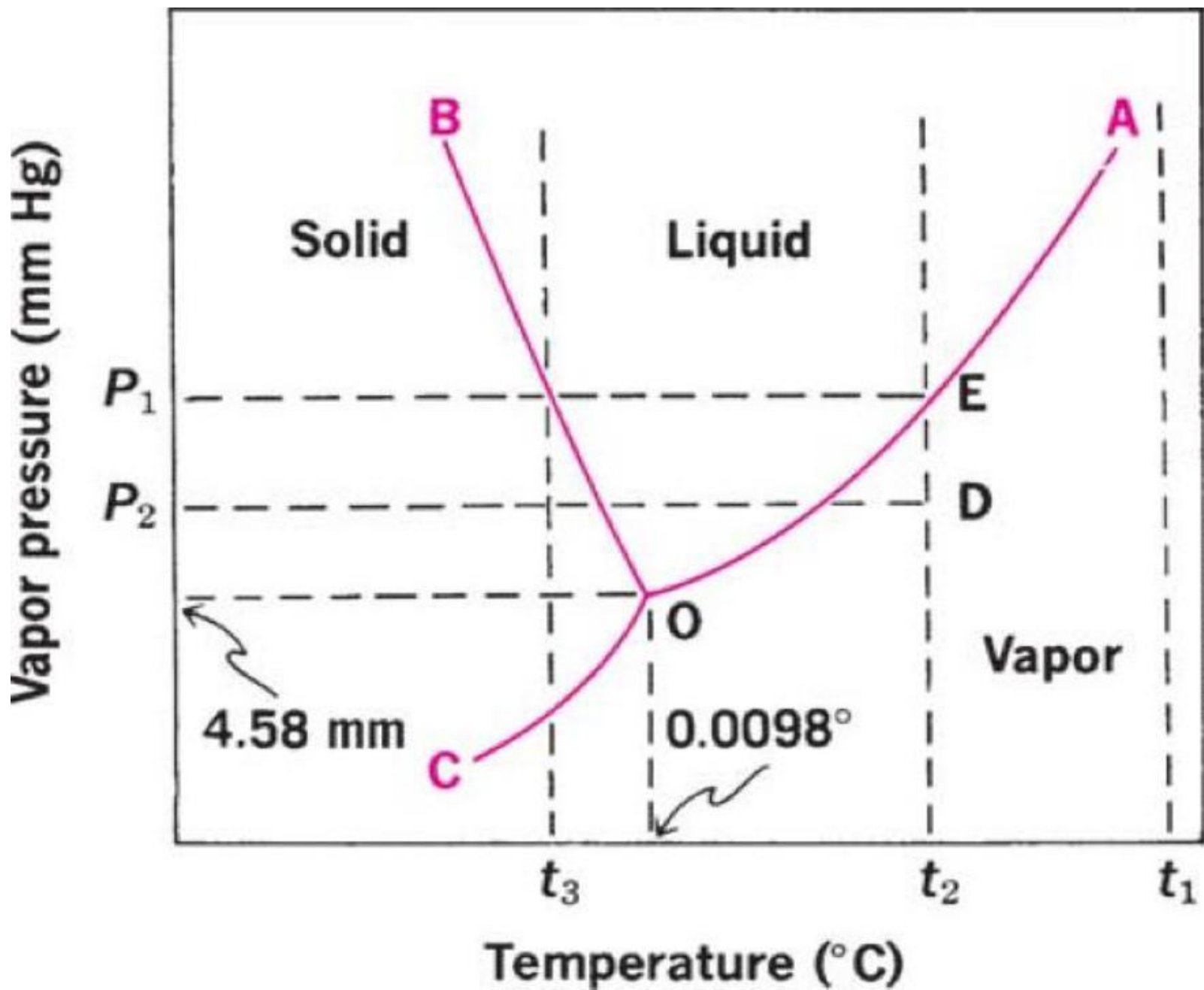
- ❖ A **phase diagram** is a chart used to illustrate the stable phases and phase changes of a substance as a function of temperature (on the x-axis) and pressure (on the y-axis).
- ❖ Each **region** of the phase diagram corresponds to a set of conditions where that particular phase is stable.
- ❖ The **lines** separating the regions represent the transitions between the different phases, where those two phases are at equilibrium at a particular temperature and pressure.

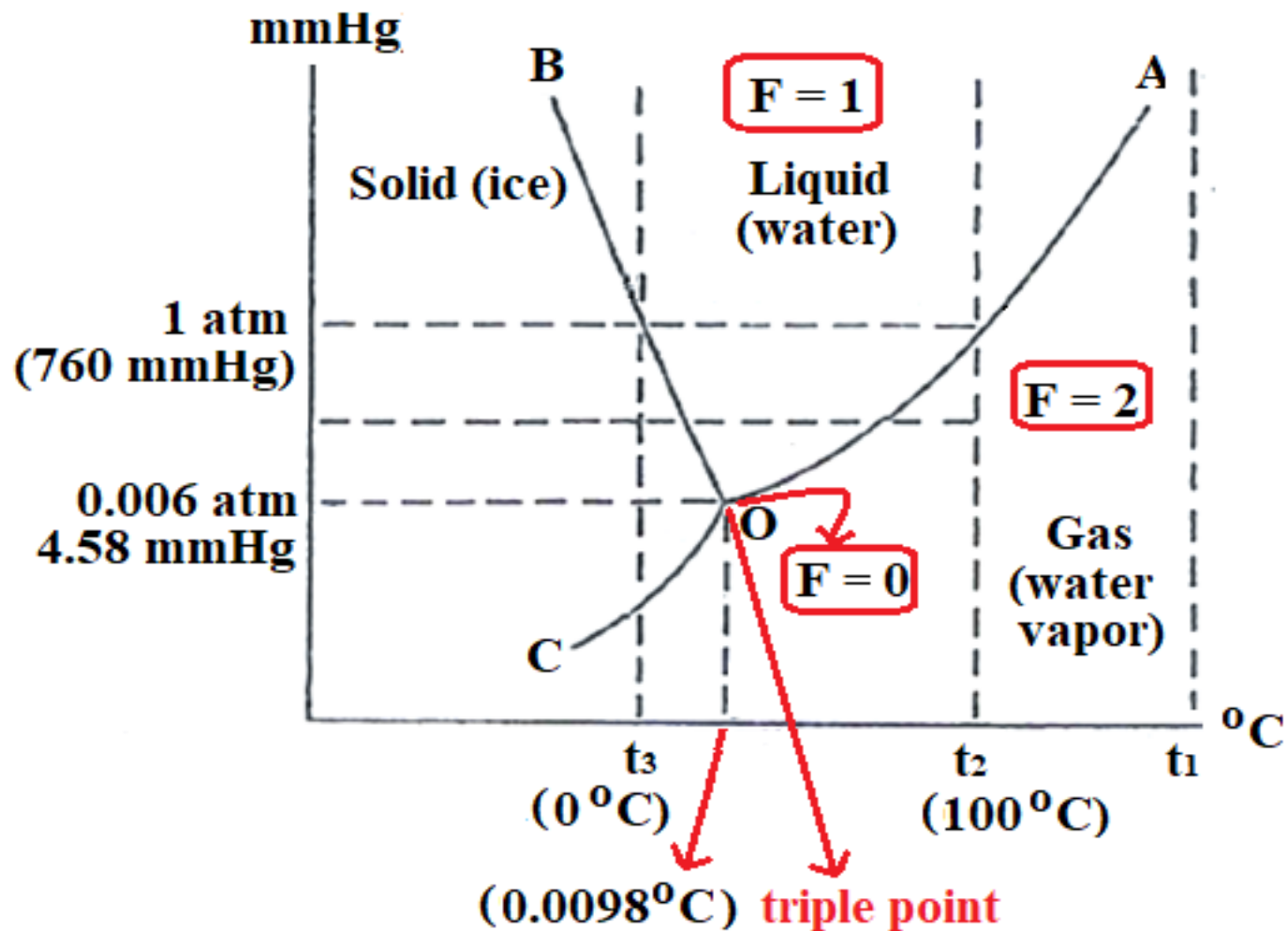


# Parts of a Phase Diagram

- ❖ The **triple point** is where all three phase boundaries meet; at this temperature and pressure all three phases are in equilibrium. (For  $\text{H}_2\text{O}$ , this occurs at  $0.0098^\circ\text{C}$  and  $0.0060\text{ atm}$ .)
- ❖ The solid-liquid boundary in water has a slight **negative** slope.
  - because the melting point of ice decreases as the pressure increases.
  - Because ice is less dense than liquid water; increasing the pressure favors the liquid phase.
- ❖ Most substances become less dense when melted, and the solid-liquid boundary line has a positive slope, indicating that the melting point increases with pressure.







**Phase diagram for water at moderate pressures**

## **Two Component Systems Containing Solid and Liquid Phases : Eutectic Mixtures**

An eutectic mixture is the composition of two or more compounds that exhibits a melting temperature lower than that of any other mixture of the compounds .Here ,the components are completely **miscible** in liquid state but completely **immiscible** as solids.

- Examples of such systems are salol-thymol , salol-camphor ,and acetaminophen-propyphenazone .
- In **salol and camphor system** containing **56% by weight of salol in camphor eutectic point is 6°C.**

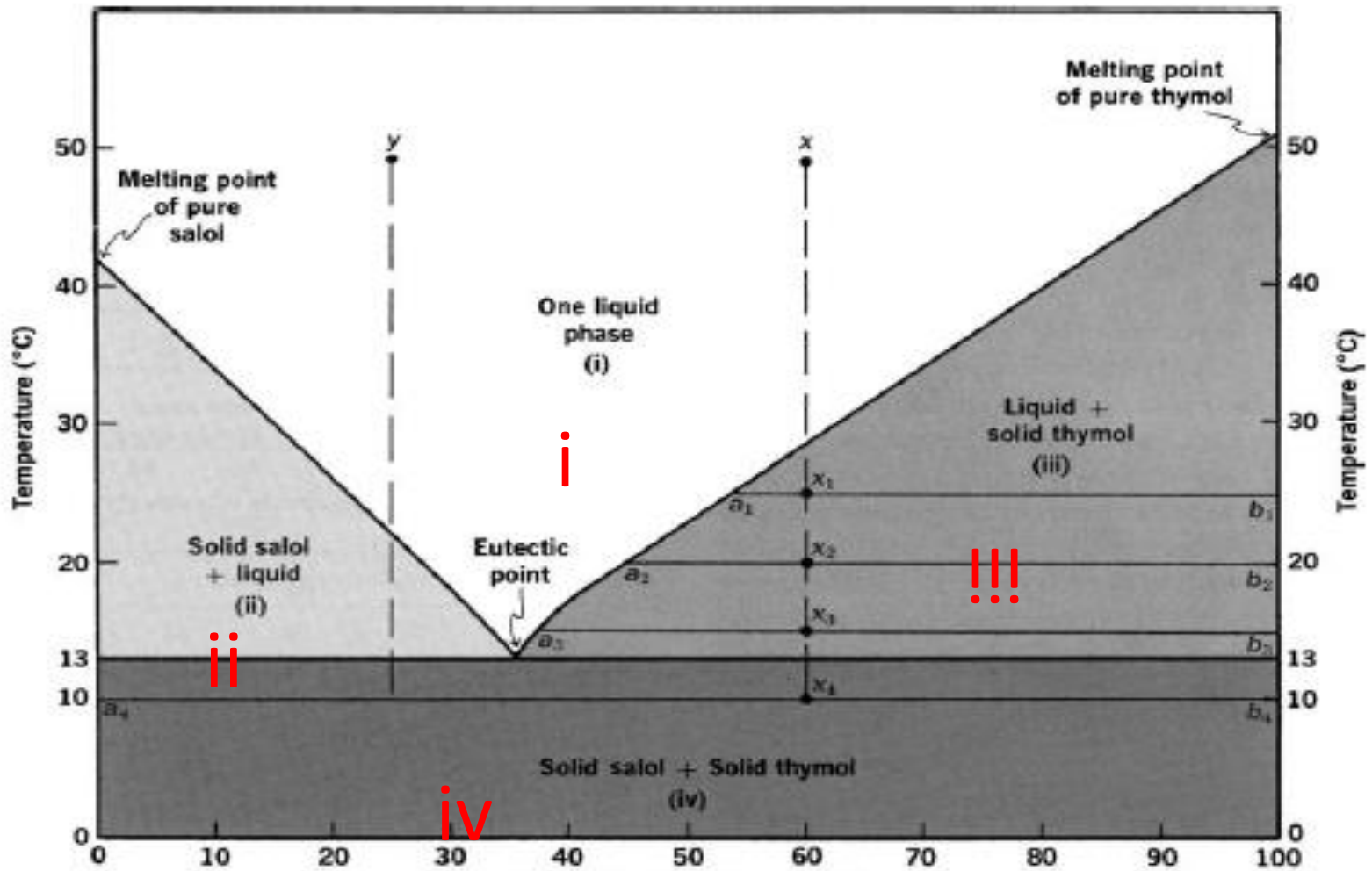
**Eutectic systems are examples of solid dispersions.**

- Solid dispersions may offer a means of facilitating the dissolution and frequently ,therefore ,the **bioavailability** of poorly soluble drugs when combined with freely soluble“ carriers” such as urea or polyethylene glycol.

## Example:

- Salol -thymol mixture shows eutectic point
- When the mixture has 34% thymol in salol over a temperature of 13 °C system will be in a single liquid form
- This point (13°C) on the phase diagram is known as the Eutectic Point for the given concentration of salol thymol mixture
- At the eutectic point, three phases ( solid salol, and solid thymol coexist ).The eutectic point therefore denotes an invariant system because, in a condensed system,

System containing 60% of thymol in salol at 50 °C is represented by x  
 This system remains as single liquid until 29°C. At (x1) solid thymol separates out to form two phase system. Below 13 °C the liquid phase disappears completely. And the system contains two solid phases of pure salol and pure thymol



# Phase Equilibria in Three Component Systems

In a non-condensed system containing three components but only one phase,

$$F=3-1+2=4$$

(temperature ,pressure ,and the concentrations of two of the three components)

- Only two concentration terms are required because the **sum** of these **subtracted** from the total will give the concentration of the third component.
- Because we are dealing with a three-component system, it is more convenient to use triangular coordinate graphs, although it is possible to use rectangular coordinates..



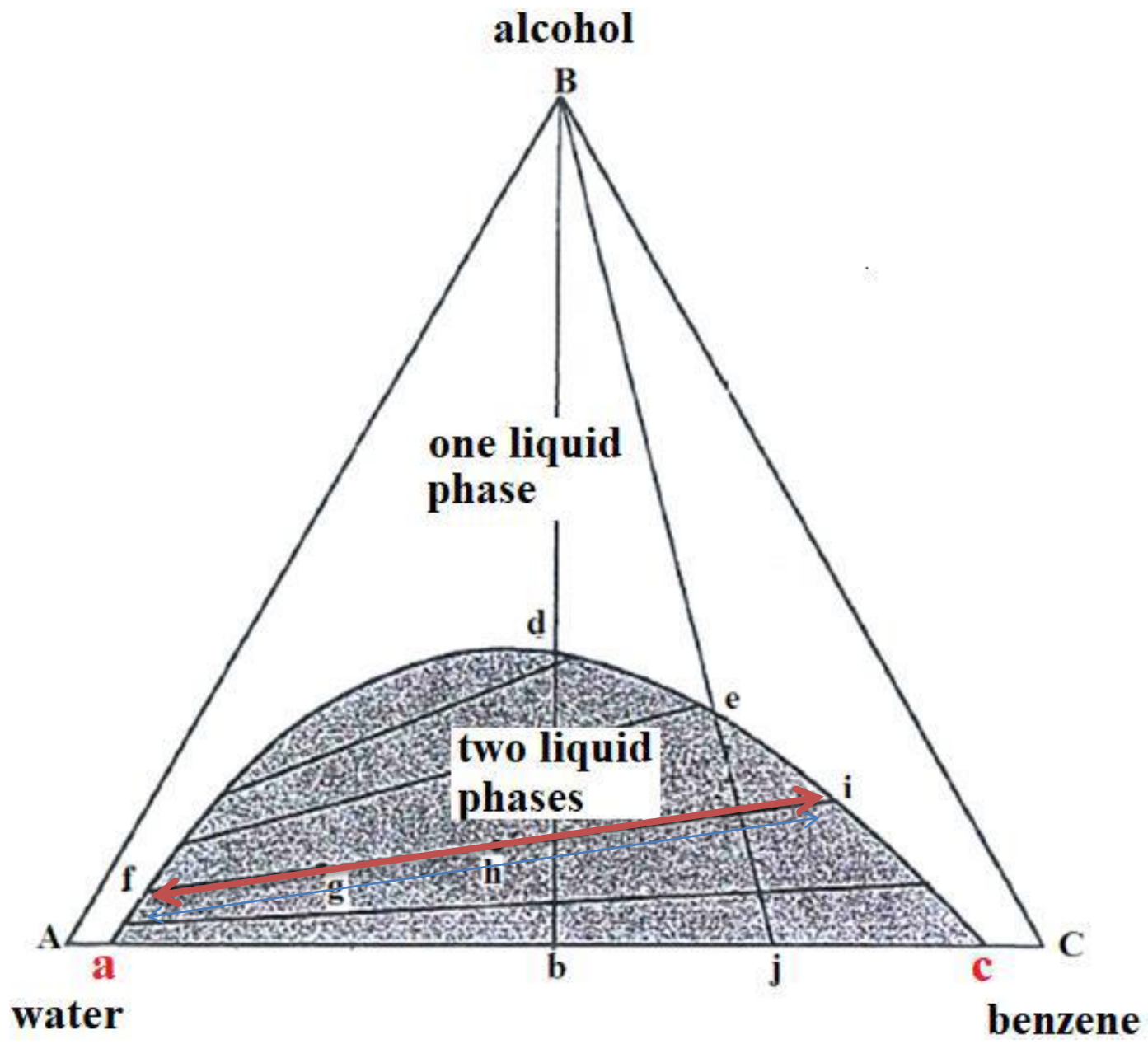
## **Ternary Systems with One Pair of Partially Miscible Liquids :**

### **Example: The addition of alcohol to the benzene–water system**

- Water and benzene are miscible only to a slight extent, and so a mixture of the two usually produces a two-phase system
- The heavier of the two phases consists of water saturated with benzene ;while the lighter phase is benzene saturated with water.
- Alcohol is completely miscible with both benzene and water and serves as a co-solvent.
- Addition of sufficient alcohol to a two-phase system produces a single liquid phase in which all three components are miscible

## Line AC binary mixtures of A and C

- ✓ Point a: solubility of C in A
- ✓ Point c: solubility of A in C
- ✓ Binodal curve afdeic: two-phase region
  
- ✓ Point g, in equilibrium, will separate into two phases, f and i:
- ✓ The ratio of phase f to phase i, on a weight basis, is  $g_i:g_f$ .
  
- ✓ System h contains equal weights of the two phases.
  
- ✓ Addition of component B to a 50:50 mixture of A+C will produce a phase change from a two-liquid system to a one-liquid system at point d.



## Application of Phase Diagrams to Pharmaceutical Systems

Phase diagrams were used as;

- Solubilization of two-and three-component pharmaceutical systems.
- Formulation of microcapsule, Nano capsule and emulsion type systems,
- stability studies and examination of biological activity.

A close-up photograph of a white card with the words "Thank you" written in a cursive, purple ink. The card is placed on a light-colored surface. To the left of the card is a bouquet of small purple flowers with green foliage. To the right of the card, a black pen with a white textured grip lies horizontally. Further to the right, a piece of red and white striped string is coiled and draped over the surface. The overall scene is a still life composition related to gift-giving or gratitude.

Thank  
you