

# AL-Mustaqbal university Pharmacy college



## Physical pharmacy I

### Lec 4

Dr.Ghada Ali

[ghada.ali@uomus.edu.iq](mailto:ghada.ali@uomus.edu.iq)

# Learning objectives

- ❑ Understand phase equilibria and phase transitions between the three main states of matter
- ❑ Understand the phase rule and its application to different systems containing multiple components

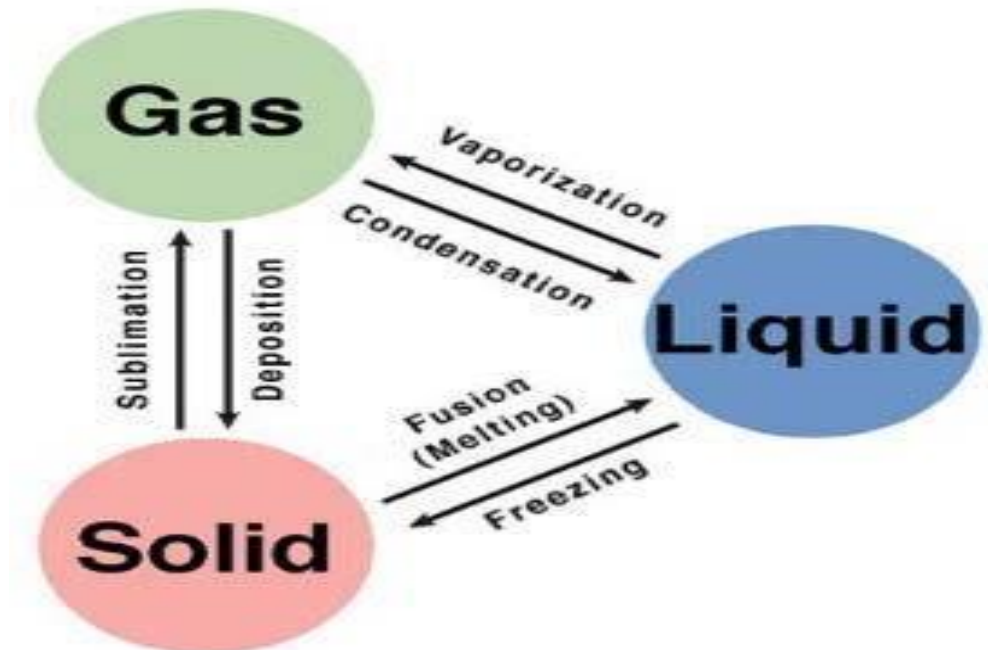
# Phase Equilibria and the Phase Rule

- The phase
- The phase diagram
- The Gibbs phase rule
- One component system
- Two component system (liquid phases)
- Two component system (solid/liquid phases)
- Three component systems (liquid phases)

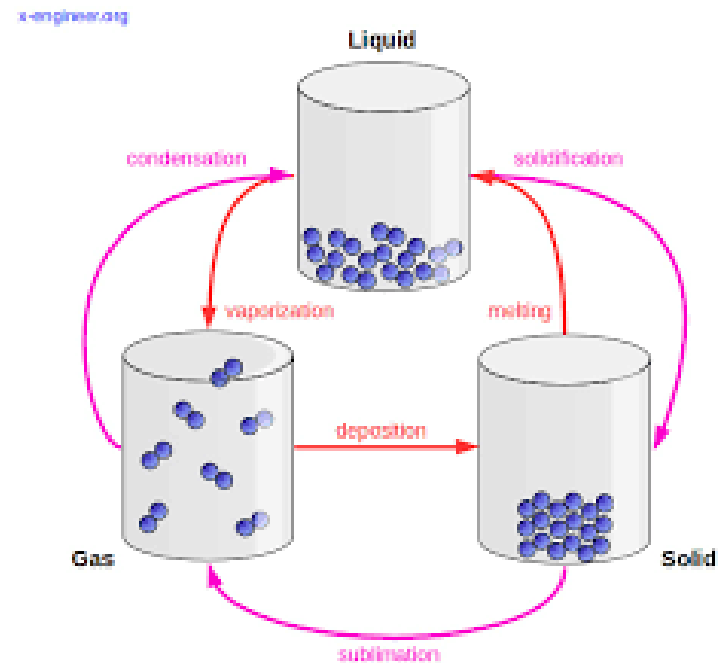
# The phase

## Definition

A phase is the part whose physical and chemical properties are completely **equal** and **homogenous**, it is separated from other parts of the system by interfaces. 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.



- **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.
- It is important to understand how phases coexist , and what are the rules that educator their existence and number of variables required to define the state of mater present under defined conditions



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## 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 .

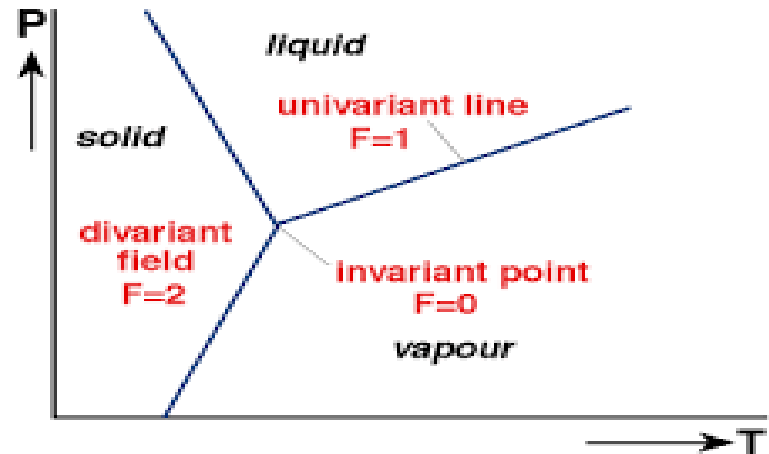
$\text{CaCO}_3 (s) \rightarrow \text{CaO} (s) + \text{CO}_2 (g)$  Number of phases 3

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

4-Liquid water + water vapor Number of phases 2

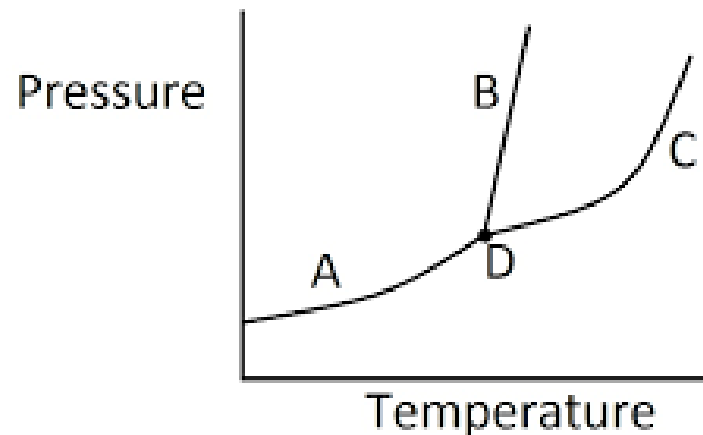
5-Liquid water + water vapor air Number of phases 2

### One component phase diagram $C=1$



# Phase Diagrams

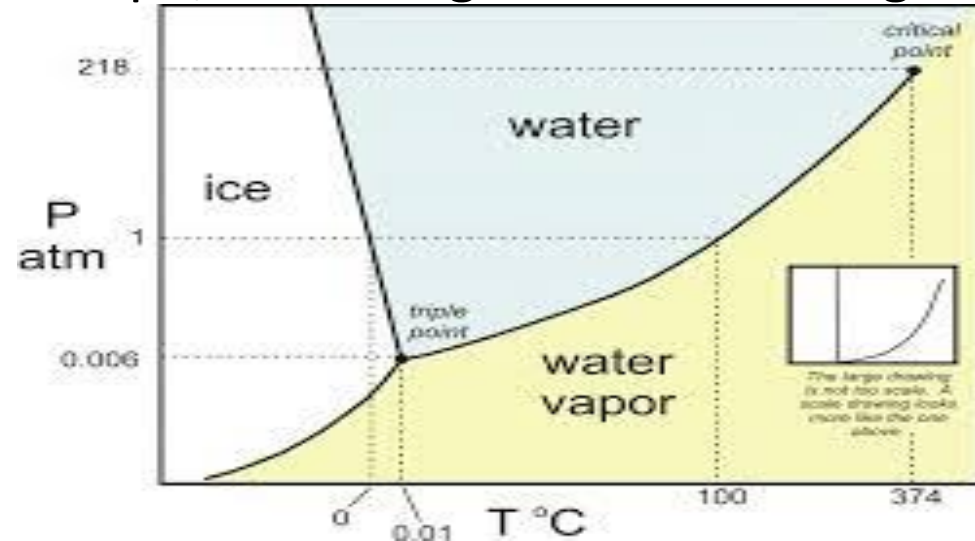
- ❖ A **phase diagram** is a chart used to illustrate the stable phases and phase changes of a substance as a function of temperature (on the  $x$ -axis) and pressure (on the  $y$ -axis).
- ❖ Each **region** of the phase diagram corresponds to a set of conditions where that particular phase is stable.
- ❖ 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.



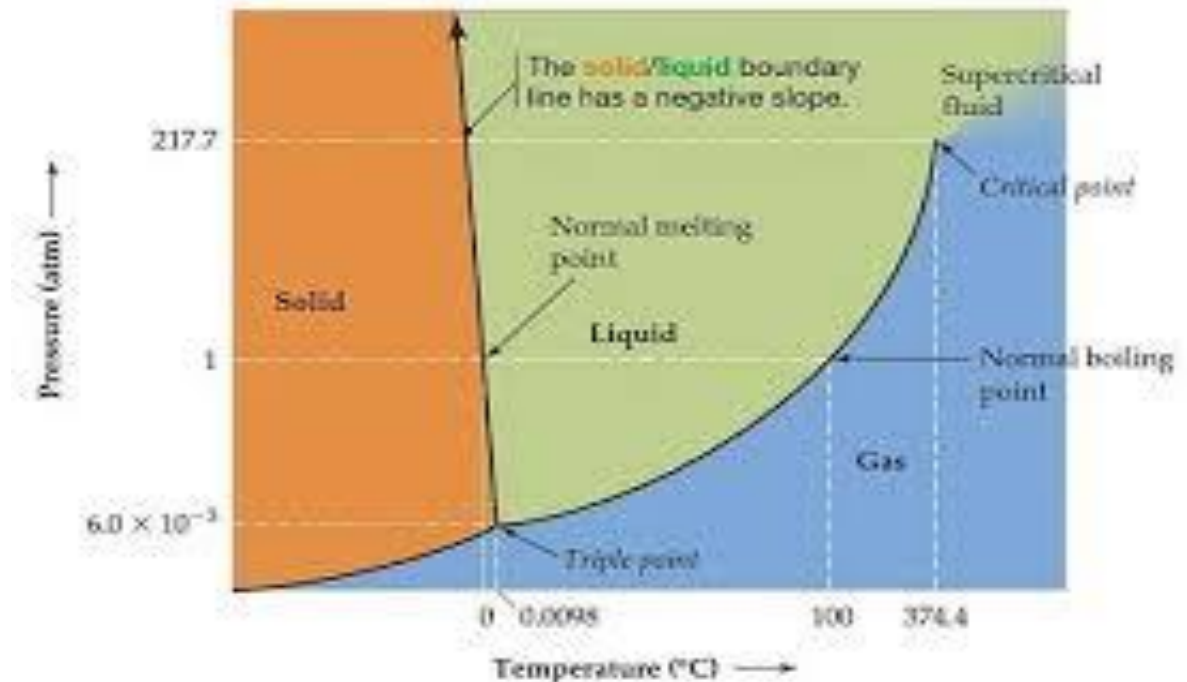


# Parts of a Phase Diagram

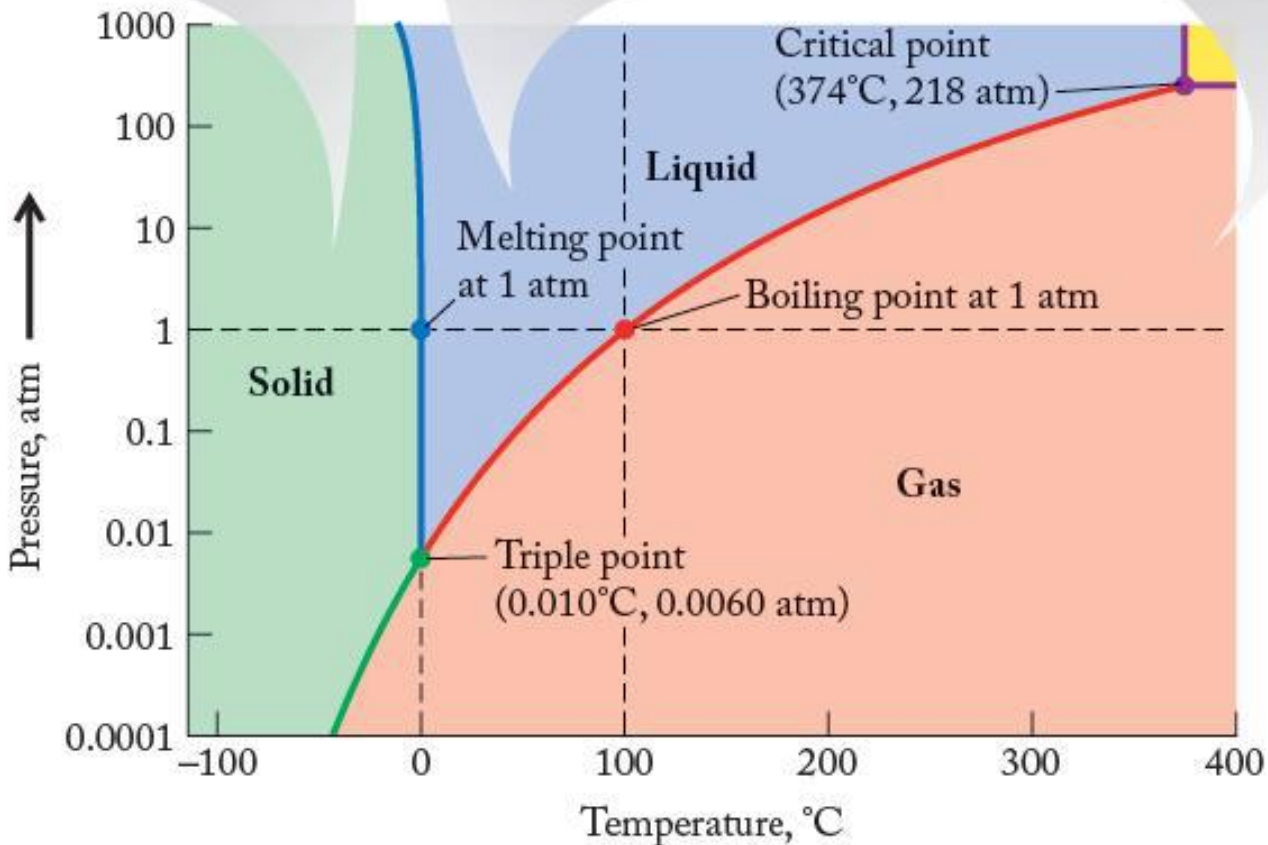
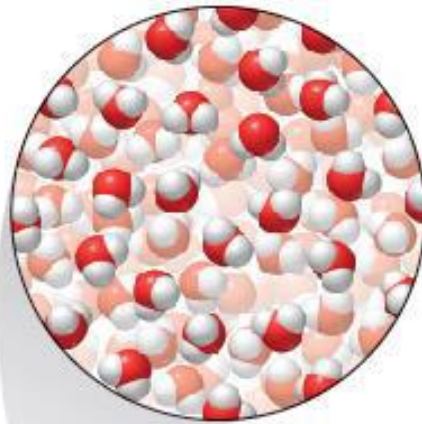
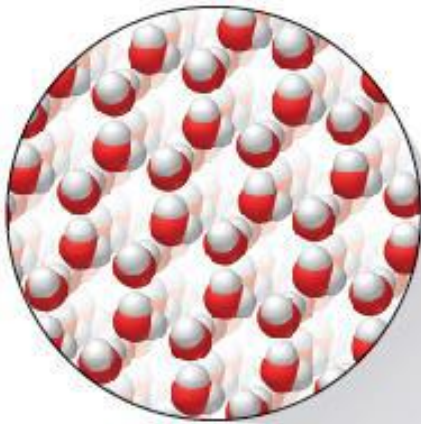
- ❖ The **triple point** is where all three phase boundaries meet; at this temperature and pressure all three phases are in equilibrium. (For  $\text{H}_2\text{O}$ , this occurs at  $0.0098^\circ\text{C}$  and  $0.0060\text{ atm}$ .)
- ❖ The solid-liquid boundary in water has a slight **negative** slope.
  - 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.



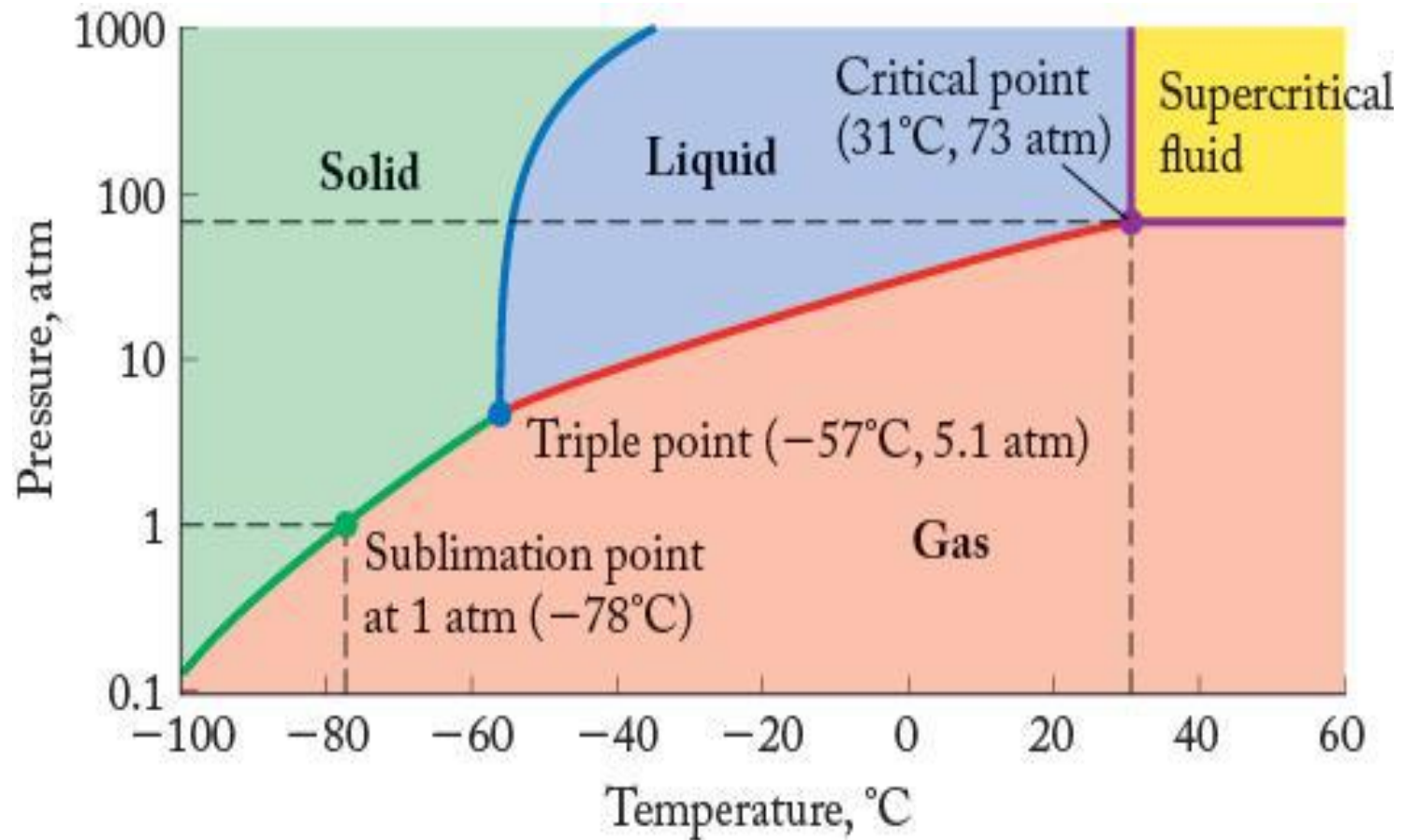
- ❖ At the **critical point** the liquid-gas line ends; the critical temperature(  $T_c$ ) is the temperature beyond which a gas cannot be liquefied, no matter how much pressure is applied. (For water, this occurs at  $374.4^\circ\text{C}$  and  $217.7$  atm.)
- ❖ At and above the critical point, the gas and liquid phases become indistinguishable; the substance is said to be a **supercritical fluid**.
- ❖ Supercritical fluids often make **good solvents**; coffee can be decaffeinated using supercritical carbon dioxide



# Phase Diagram for H<sub>2</sub>O



## Phase Diagram for CO<sub>2</sub>



## Phase rule:

- Phase is a homogeneous, physically distinct portion of a system that is separated from other portions of the system by bounding surfaces (interfaces)
- Phases coexistence can only occur over a limited range. For example, ice does not last as long in boiling water as it does in cold water.

## Examples of phases coexistence:

- 1)The mixture of ice and water have two phase which is solid and liquid
- 2)The mixture of oxygen gas and nitrogen gas have one phase which is gas phase (the system is homogeneous)
- 3)The mixture of oil and water have 2 same phase (liquid). Oil and water are not homogeneous and have the boundaries to separate both phase

## The Gibbs phase rule

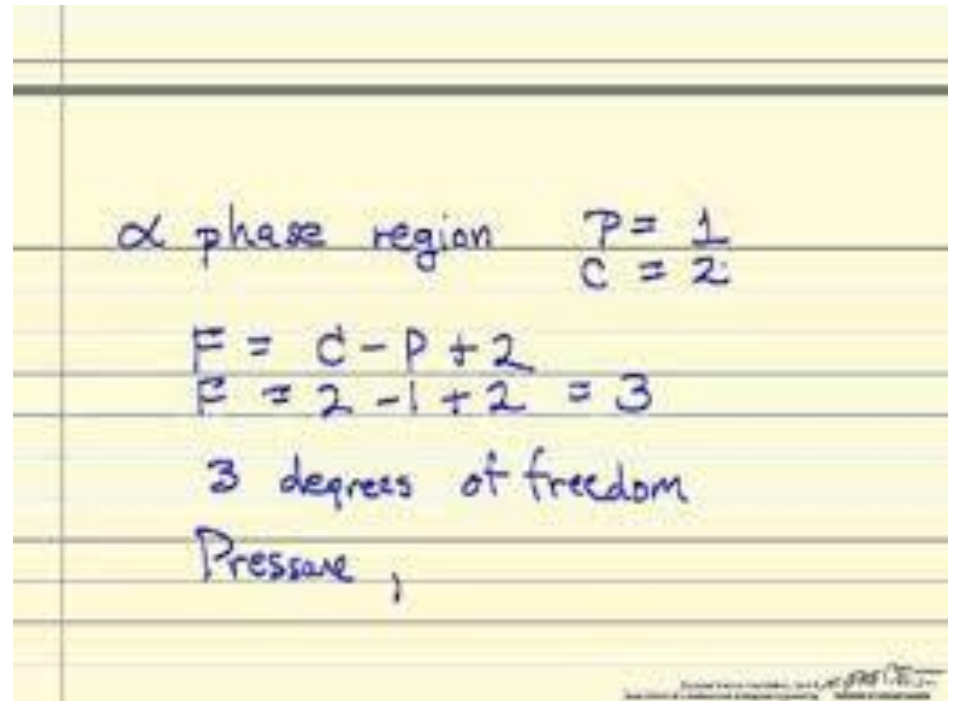
The Gibbs phase rule is expressed as follows:

$$F = C - P + 2$$

F : the number of degrees of freedom of the system (number of independent variables (e.g. temperature, pressure, and concentration) that may affect the phase equilibrium)

C: number of components

P: Number of phases



$\alpha$  phase region  $P = 1$   
 $C = 2$

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

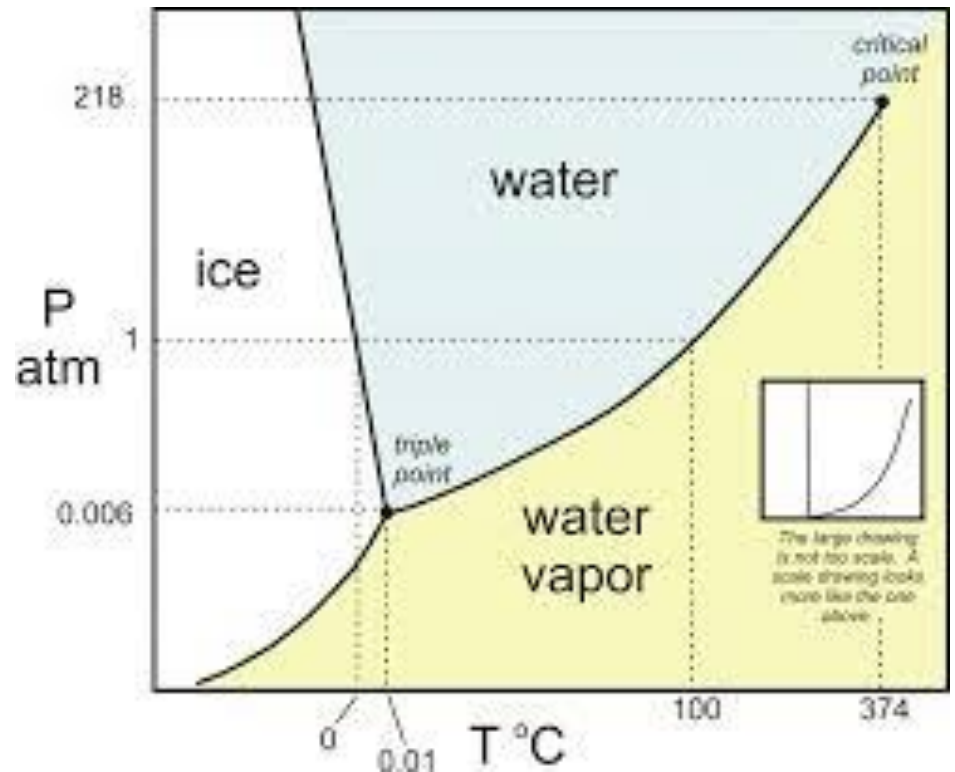
3 degrees of freedom  
Pressure,

## Number of components

The number of components of a system is the number of constituents expressed in the form of a chemical formula.

**For example** in the 3-phase system ice, water, water vapor, the number of components is 1, since each phase is expressed as **H<sub>2</sub>O**.

A mixture of salt and water is a 2 component system since both chemical species are independent but one phase .



## Example 1

1 Consider a given volume of water vapor

$$F = C - P + 2$$

$$1 - 1 + 2 = 2$$

Number of degrees of freedom (F)

It is the least number of intensive variables that must be fixed/known to describe the system completely. According to the phase rule, two independent variables are required to define the system. Variable like temperature or pressure must be known to define the system completely

## Example 2

2 Consider a system water with its vapor

$$F = C - P + 2$$

$$1 - 2 + 2 = 1$$

By stating the temperature, we define the system completely because the pressure under which liquid and vapor can coexist is also defined





## **Systems Containing One Component**

The phase diagram for the ice-water-water vapor system (phase diagram graphical representation which indicates the phase equilibrium

Each area correspond to a single phase.

The number of degrees of freedom in each area is :

$$F = C - P + 2$$

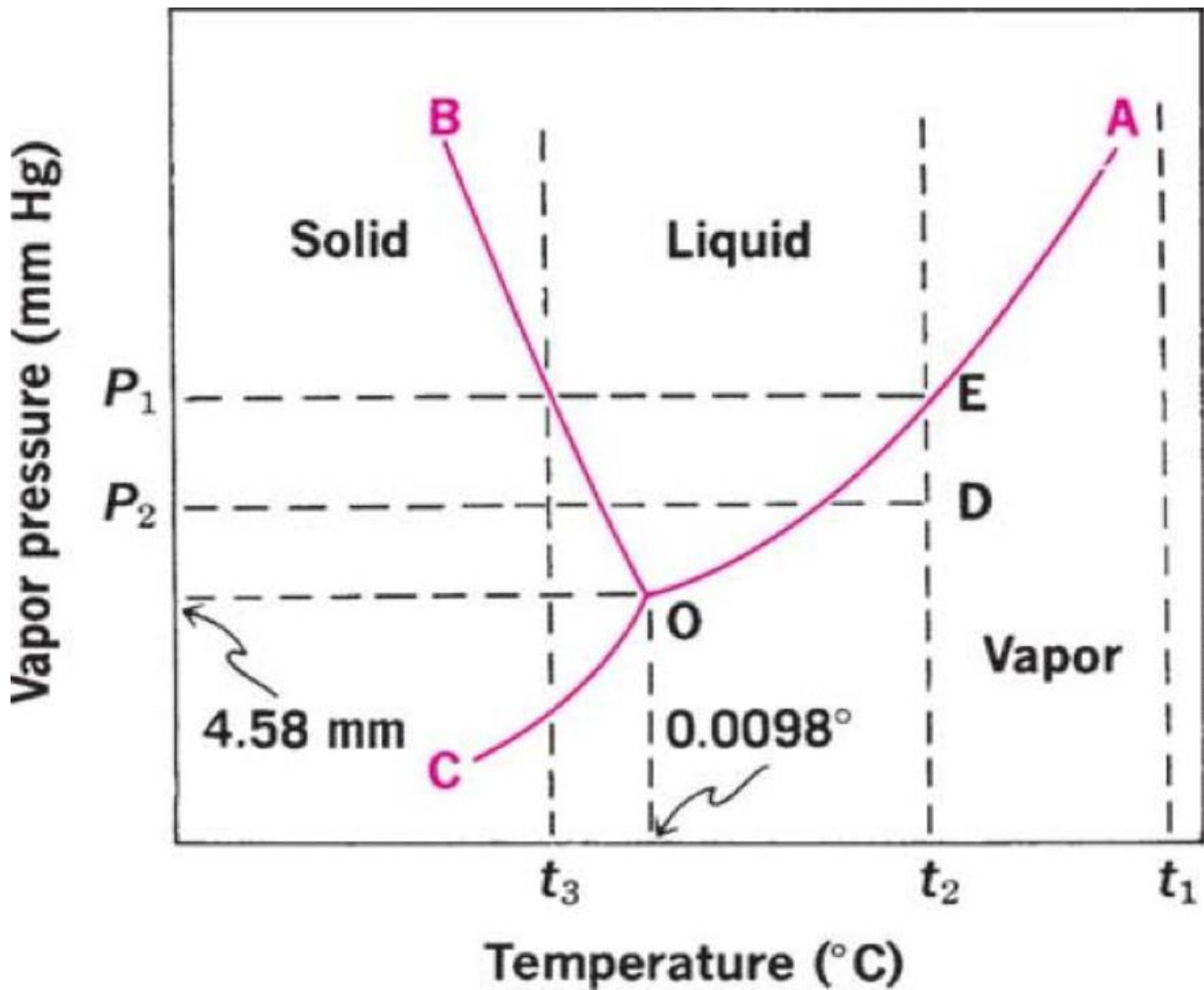
$$F = 1 - 1 + 2 = 2$$

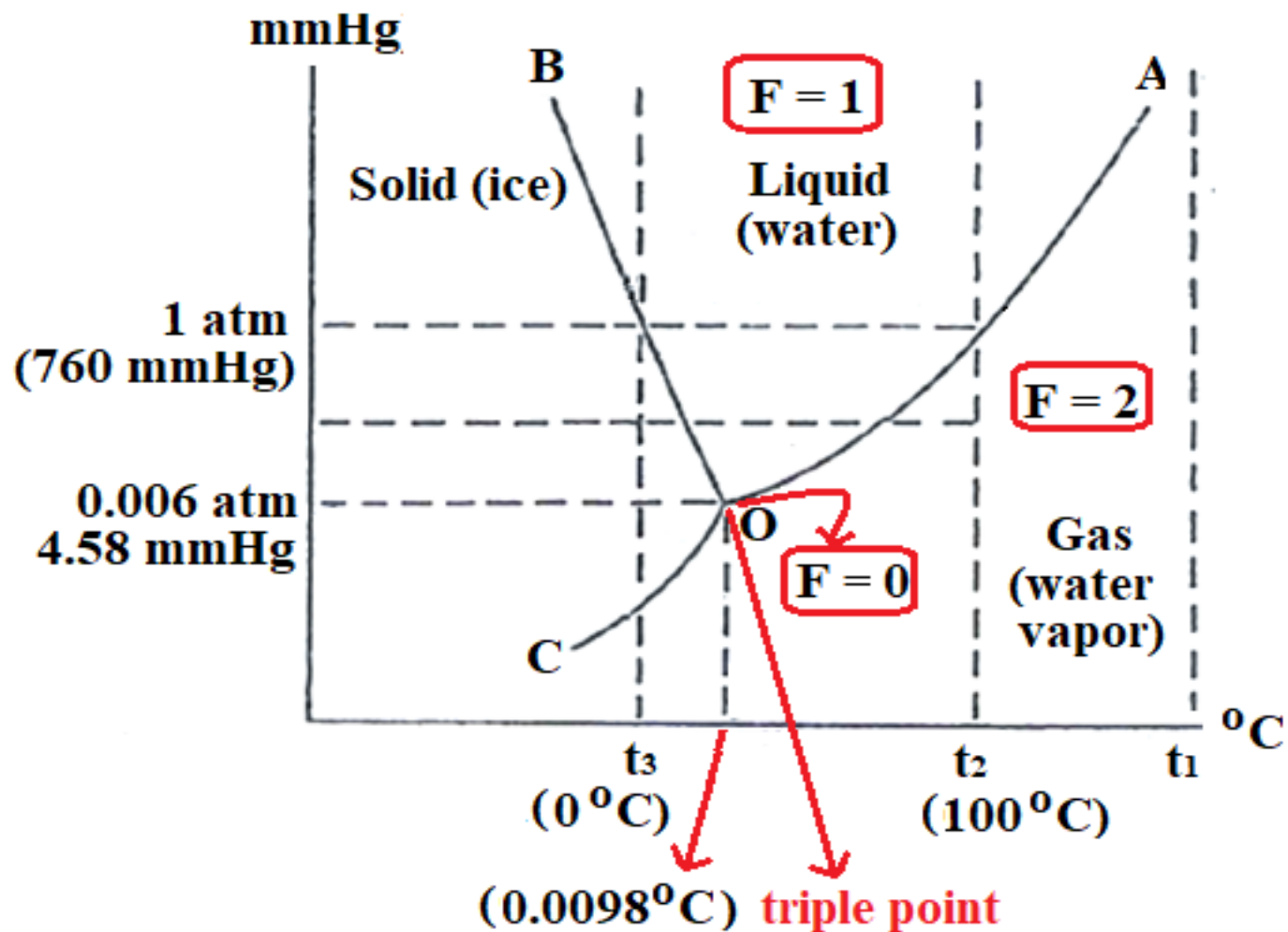
This means that temperature and pressure, volume and temperature, volume and pressure can be varied independently within these areas without change in number of phases

# Systems Containing One Component

## Water

- The curve **OA** in the  $P$ – $T$  (pressure–temperature) diagram is known as the **vapor pressure curve**. Its upper limit is at the critical temperature, 374°C for water, and its lower end terminates at 0.0098°C, called the triple point. Along the vapor pressure curve, vapor and liquid coexist in equilibrium..
- Curve **OB** is the **melting point curve**, at which liquid and solid are in equilibrium. The negative slope of OB shows that the freezing point of water decreases with increasing external pressure,
- .Curve **OC** is the **sublimation curve**, and here vapor and solid exist together in equilibrium..





**Phase diagram for water at moderate pressures**

## Condensed systems

- ✓ With two-component system having one liquid phase;

$$F=C-P+2$$

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

(pressure , concentration ,temperature)

- ✓ In a two-component system ,in which the vapor phase is ignored ,only solid and / or liquid phases are considered .They are termed **Condensed Systems** .
- ✓ There are only two variables (temperature and concentration ) remain in condensed systems ,and we are able to describe the interaction of these variables by the use of planar figures on rectangular-coordinate graph paper.
- ✓ solids can also have liquid phase(s) associated with them, and the converse is true. Therefore, even in an apparently dry tablet form, small amounts of “solution” can be present.

# Two Component Systems Containing Liquid Phases

## Phenol and Water

- ❖ The curve (*gbhci*) shows two liquid phases exist in equilibrium . The region outside this curve contains one liquid phase systems
- ❖ Point «*a*» has 100 % water at 50°C. When phenol is added between 11-63 % at 50°C( *points b to c*) two phases appear. When the total concentration of phenol exceeds 63% at 50°C, a single phenol-rich liquid phase is formed.
- ❖ The max °C (66.8 °C–point *h*) at which the two-phase region exists is termed as critical solution(upper consolute , critical °C).
- ❖ All combinations of phenol and water above this temperature are **completely miscible and yield one-phase liquid systems.**

- ❖ At point **d** there is 24% w/w phenol in the system . The weight of water (A) is greater than phenol B ) at point **d**
- ❖ Phenol has a higher density than water. At point **d** there will be more of water rich phase in the tube

$$\frac{\text{Weight of phase A}}{\text{Weight of phase B}} = \frac{\text{Length } dc}{\text{Length } bd}$$

Also, the percentage weight of phenol can be found . For example,

**b** =11%, **c** =63%, **d** =24%,

$dc/ bd = (63 -24)/(24 -11)$

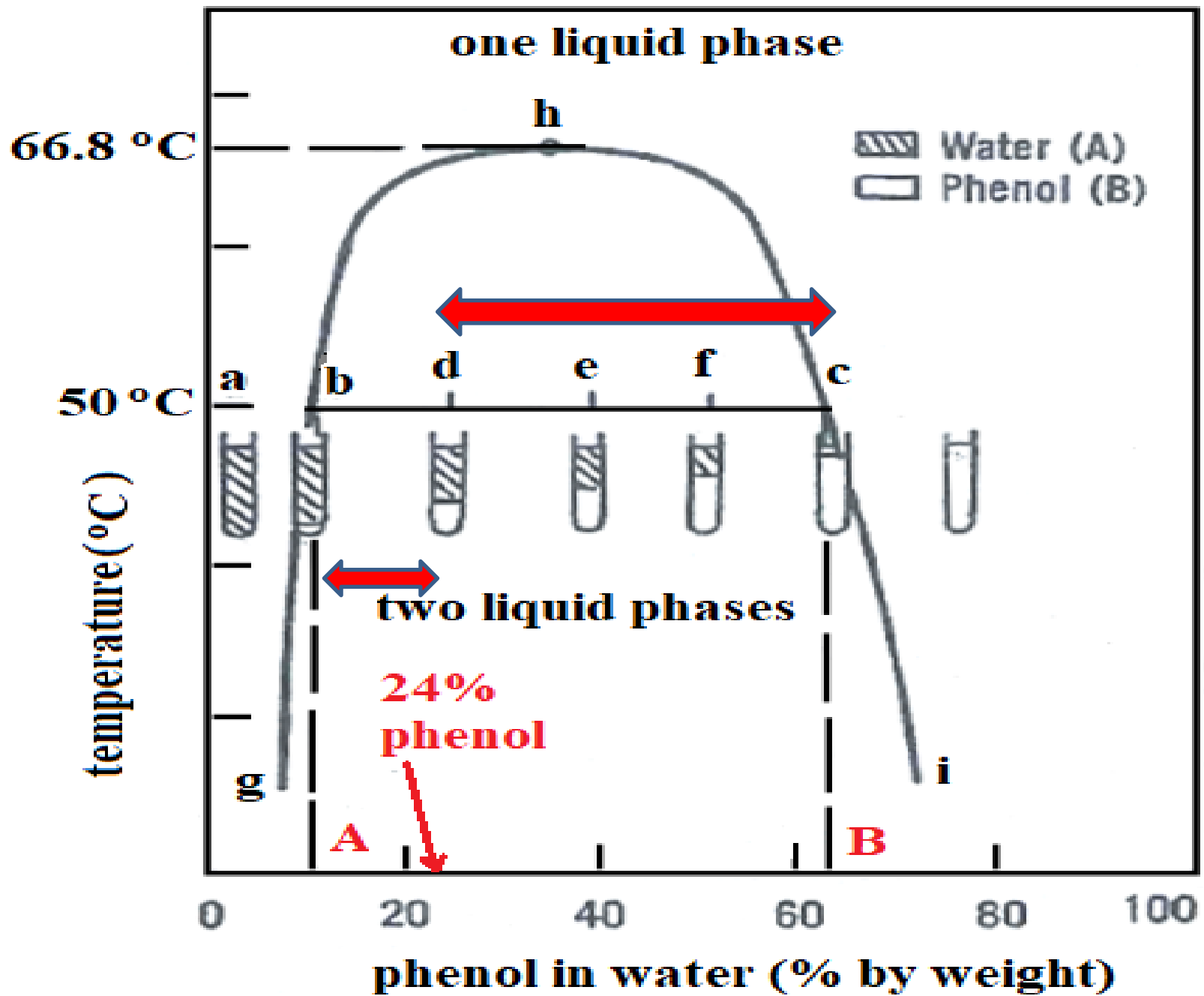
$= 39/13 =3/1$

For every 10 g of a liquid system in equilibrium represented by point **d**

, one finds 7.5 g of phase A (75%)

2.5 g of phase B (25%)





## Example

Let us suppose that we mixed 24 g of phenol with 76 g of water, warmed the mixture to 50°C and allowed it to reach equilibrium at this temperature.

On separation of the two phases, we would find 75 g of phase A (containing 11% by weight of phenol) and 25 g of phase B (containing 63% by weight of phenol). Phase A therefore contains a total of  $(11 \times 75) / 100 = \mathbf{8.25 \text{ g of phenol}}$ , Whereas phase B contains a total of  $(63 \times 25) / 100 = \mathbf{15.75 \text{ g of phenol}}$ . This gives a sum total of **24 g** of phenol in the whole system.

This equals the amount of phenol originally added and therefore confirms our assumptions and calculations.

## 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.**

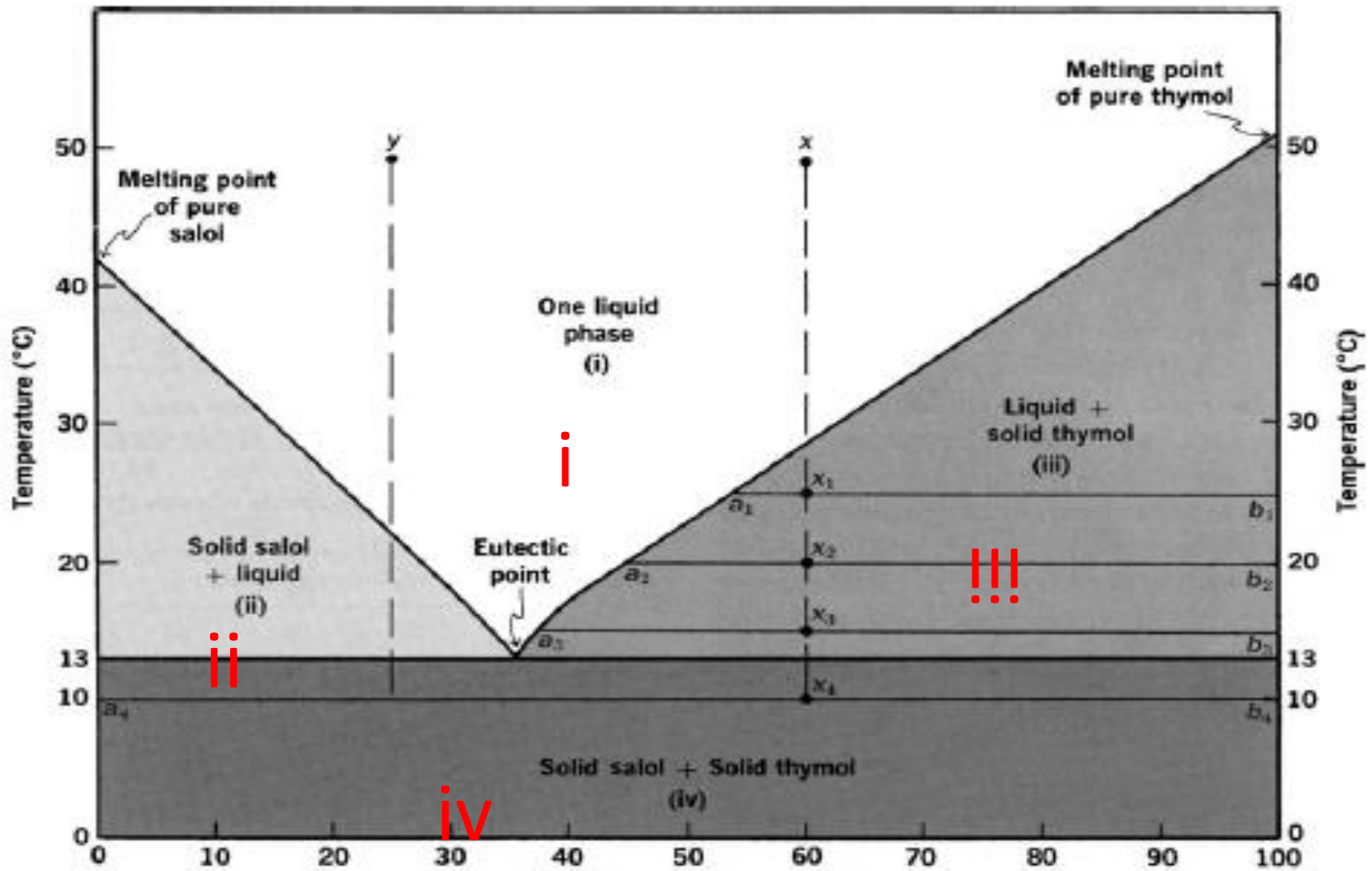
**Eutectic systems are examples of solid dispersions.**

- 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..

## Rules Relating to Triangular Diagrams

The concentration in ternary systems are accordingly expressed on a weight basis.

✓ The lines  $AB$ ,  $BC$ , and  $AC$  are used for **two-component mixtures** and can be divided into 100 equal units.

### Examples:

- ✓ Point  $y$ , on the line  $AB$ , represents a system containing 50%  $B$  and 50%  $A$
- ✓ Point  $z$ , along  $BC$ , signifies a system containing 75%  $C$ .
- ✓ Point  $x$ , 15% of  $B$  85% of  $A + C$





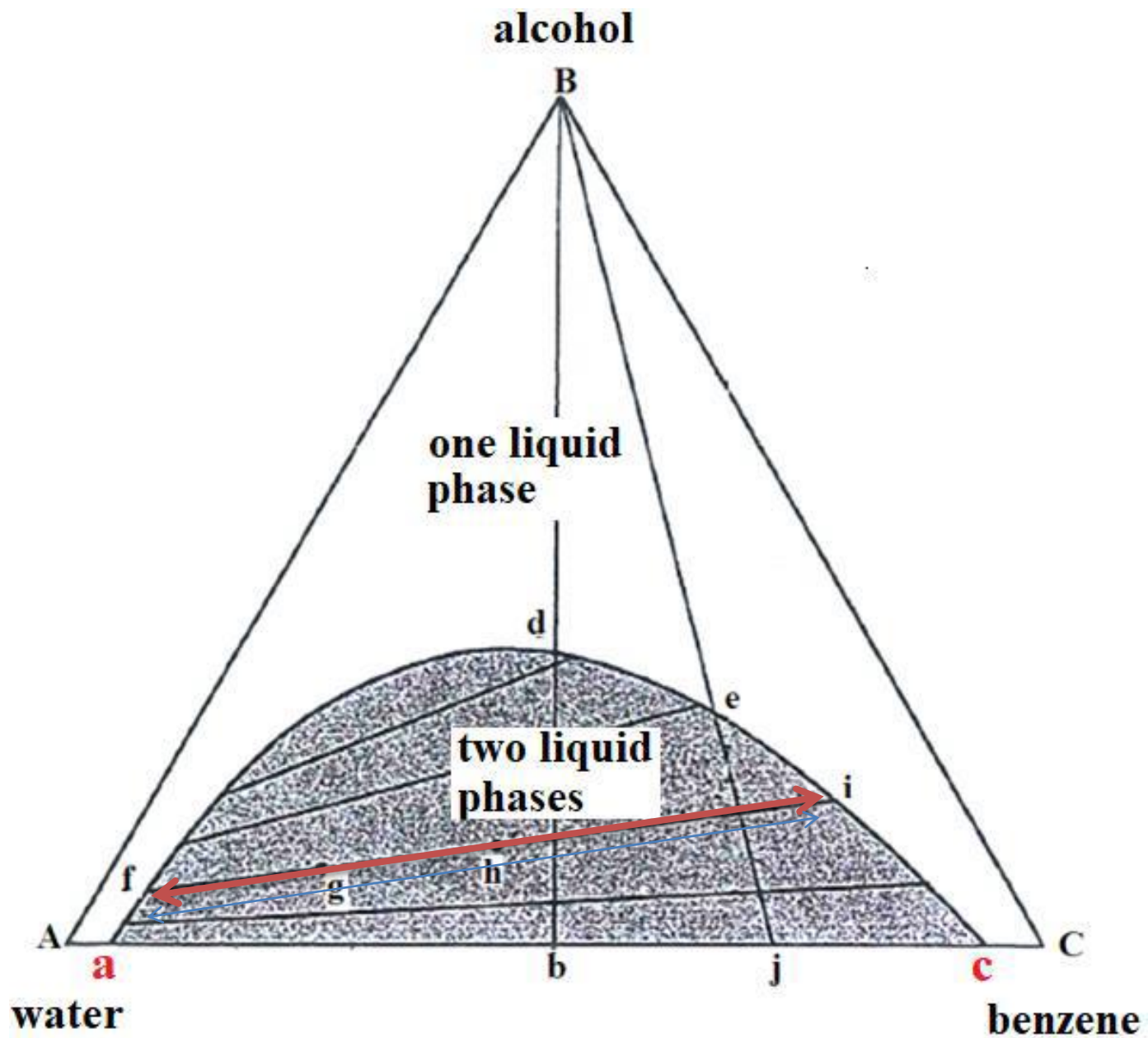
## **Ternary Systems with One Pair of Partially Miscible Liquids :**

### **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.

Thank  
you! 

