States of Matter

Lecture 4

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Physical pharmacy

Melting point and intermolecular forces

- Heat of fusion is the heat required to increase interatomic or intermolecular distance in crystals thus allowing melting (increase molecular motion).
- Because polymorphic forms represents different molecular arrangement leading to different crystalline form of the same compound due to different intermolecular forces.
- Paraffin's crystallise as thin leaflet composed of zigzag chain packed in parallel arrangement. The melting point of normal saturated hydrocarbon increases with molecular weight because vander wales forces between the molecules of crystal become greater with increasing number of carbon atom.

- The melting point of alkanes with an even number of carbon atom are higher than those hydrocarbon with odd number due to the fact that alkan with odd number of carbon atom pack in crystal less efficiently.

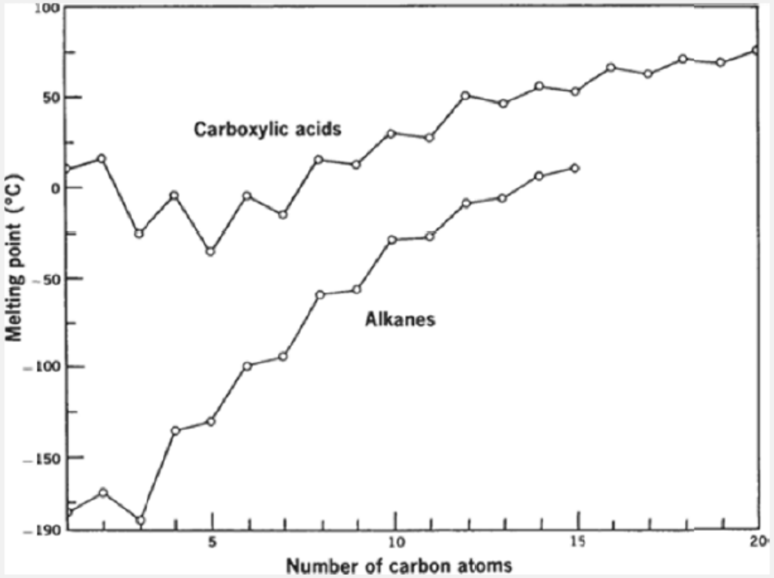


Fig. 2-13. The melting points of alkanes and carboxylic acids as a function of carbon chain length. (Modified from C. R. Noller, *Chemistry of Organic Compounds*, 2nd Ed., Saunders, Philadelphia, 1957, pp. 40, 149.)

- The melting point of carboxylic acid show this patterns.
- Fatty acid crystallise in molecular chains, one segment is shown in the following structure. The even number of carbon are arranged in the cystall as seen in the more asymmetric structure I wherase the odd number acid are arranged according to structure II. The carboxyl group are joined at 2 points in the even carbon compund hence the crystal lattice is more stable and the melting point is higher.

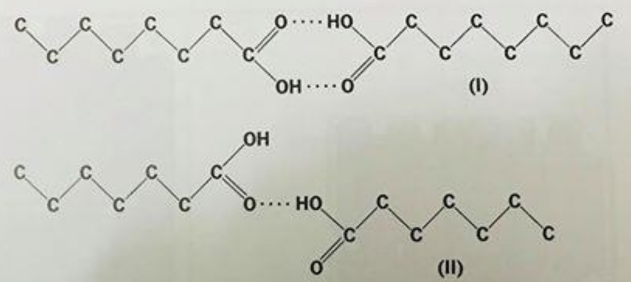
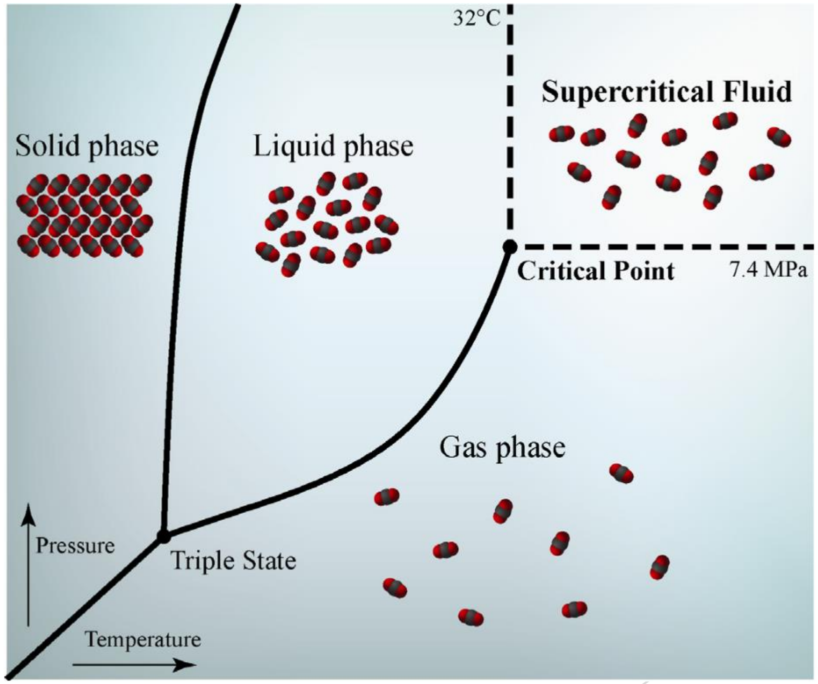


Fig. 2–14. Configuration of fatty acid molecules in the crystalline state. (Modified from A. E. Bailey, *Melting and Solidification of Fats*, Interscience, New York, 1950, p. 120.)

The supercritical fluid state

- It is intermediate between liquid and gas. The critical pressure is the minimum pressure required to liquefy a gas at a given temperature. Increasing the pressure results in increasing density without significant increase the viscosity. Application in extraction, crystallisation, preparation of polymer mixture and formation of nanoparticles.

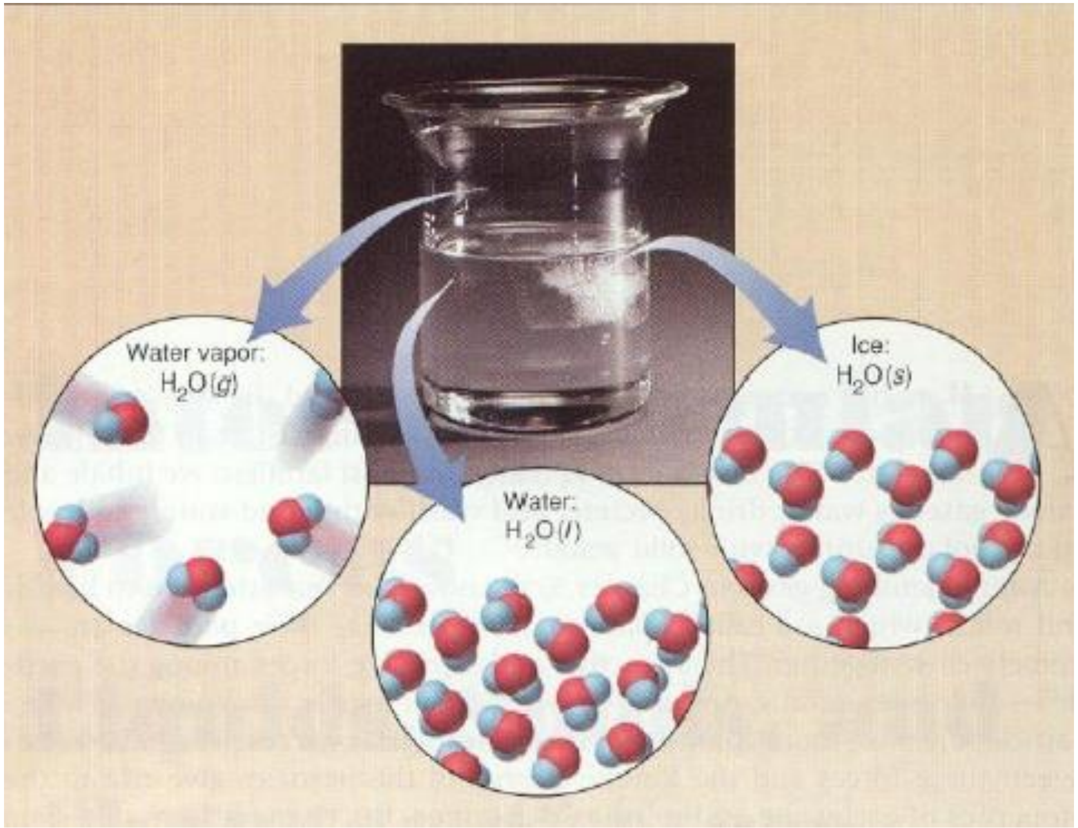


Advantages of supercritical fluids

- Extraction and purification of compound at low temperature.
- Solvent volatility under ambient conditions,
- selectivity of the extracted compound.
- Low energy and lower viscosity than solvents.
- Reduce toxicity of the gas.

Example is decaffeination of caffeine.

Phase Equilibria & The Phase Rule



Water and ice in hot summer is 3 phase system. Suspension consist of solid drug in liquid and evaporation may take place.

- **Phase Equilibrium**: A stable phase structure with lowest free-energy (internal energy) of a system, and also randomness or disorder of the atoms or molecules (entropy).
- Any change in Temperature, Composition, and Pressure causes an increase in free energy and away from equilibrium thus forcing a move to another 'state'.
- The phase rule: A relationship between number of intensive variables (temperature, concentration, density and pressure) that can be changed without changing the equilibrium state of the system,

- **A phase** is defined as any homogeneous and physically distinct part of a system which is separated from other parts of the system by interfaces.

- ✓ A phase may be gas, liquid or solid.
- ✓ A gas or a gaseous mixture is a single phase.
- ✓ Totally miscible liquids constitute a single phase.
- ✓ In an immiscible liquid system, each layer is counted as a separate phase.
- ✓ Every solid constitutes a single phase except when a solid solution is formed.
- ✓ A solid solution is considered as a single phase.
- ✓ Each polymorphic form constitutes a separate phase.

1. Liquid water, pieces of ice and water vapor are present together.

The number of phases is 3 as each form is a separate phase.

Ice in the system is a single phase even if it is present as a number of pieces.

2. Calcium carbonate undergoes thermal decomposition.

The chemical reaction is: $CaCO_3(s) \rightarrow CaO(s) + CO_2\ (g)$

Number of phases = 3 : This system consists of 2 solid phases, CaCO3 and CaO and one gaseous phase, that of CO_2.

3. A solution of NaCl in water Number of phases = 1

Components

- The number of components of a system at equilibrium is the smallest number of independently varying chemical constituents using which the composition of each and every phase in the system can be expressed.

Examples

- Counting the number of components

1. The sulphur system is a one component system. All the phases, monoclinic, rhombic, liquid and vapour – can be expressed in terms of the single constituent – sulphur.

2. A mixture of ethanol and water is an example of a two component system. We need both ethanol and water to express its composition.

Degrees of freedom (or variance)

- The degrees of freedom or variance of a system is defined as the minimum number of variables such as:

✓ temperature

✓ pressure

✓ concentration

which must be fixed in order to define the system completely.

$$F = C - P + 2$$

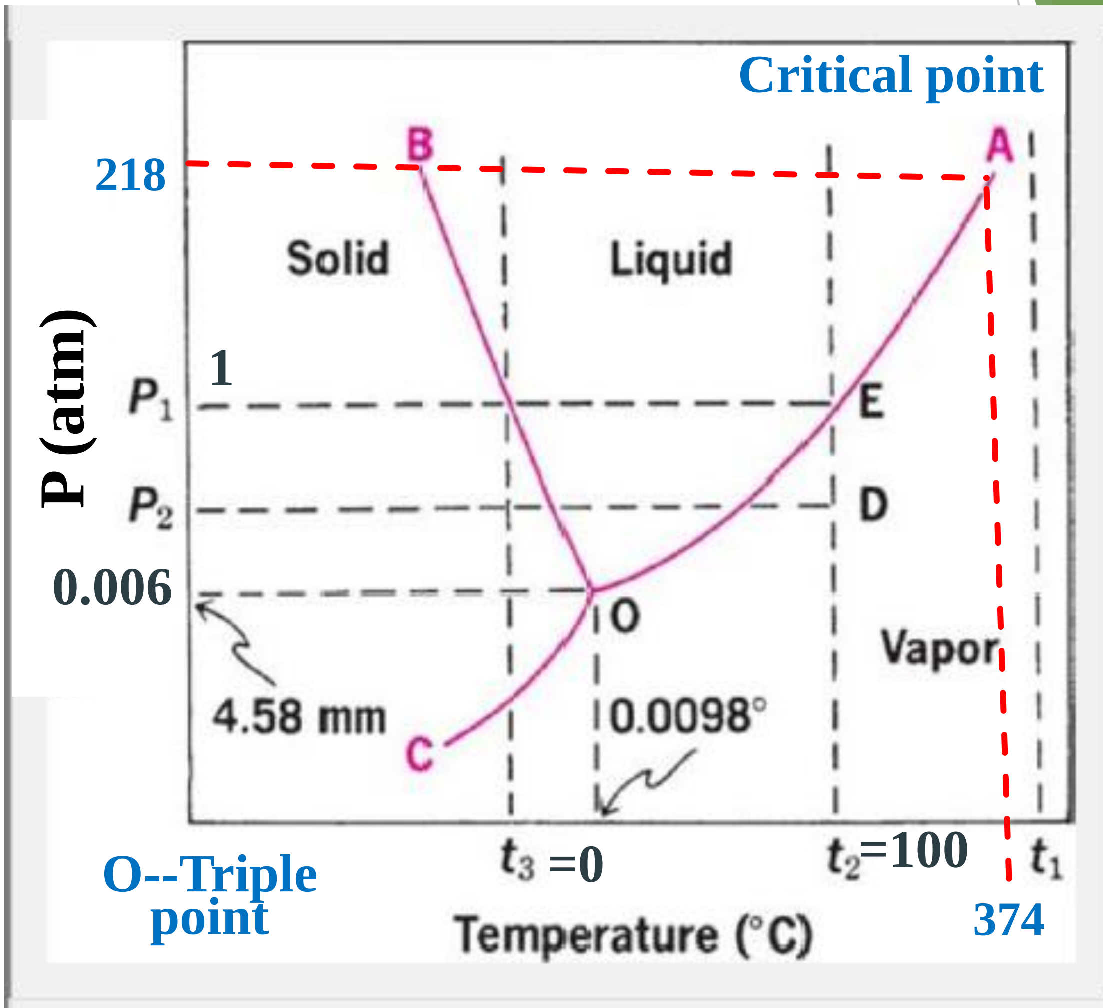
One-component systems

Phase diagram of water

Curve O-A
Vaporization
Condensation

Curve O -B
Melting
Freezing

Curve O -C
Sublimation
Deposition



$$F = C - P + 2$$

Table 2-7 Application of the Phase Rule to Single-Component Systems*

System	Number of Phases	Degrees of Freedom	Comments
Gas, liquid, or solid	1	$\mathbf{F} = C - P + 2 = 1 - 1 + 2 = 2$	System is *bivariant* ($\mathbf{F} = 2$) and lies anywhere within the area marked vapor, liquid, or solid in Figure 2-22. We must fix two variables, e.g., P_2 and t_2, to define system D.
Gas–liquid, liquid–solid, or gas–solid	2	$\mathbf{F} = C - P + 2 = 1 - 2 + 2 = 1$	System is *univariant* ($\mathbf{F} = 1$) and lies anywhere along a *line* between two-phase regions, i.e., AO, BO, or CO in Figure 2-22. We must fix one variable, e.g., either P_1 or t_2, to define system E.
Gas–liquid–solid	3	$\mathbf{F} = C - P + 2 = 1 - 3 + 2 = 0$	System is *invariant* ($\mathbf{F} = 0$) and can lie only at the *point* of intersection of the lines bounding the three-phase regions, i.e., point O in Figure 2-22.

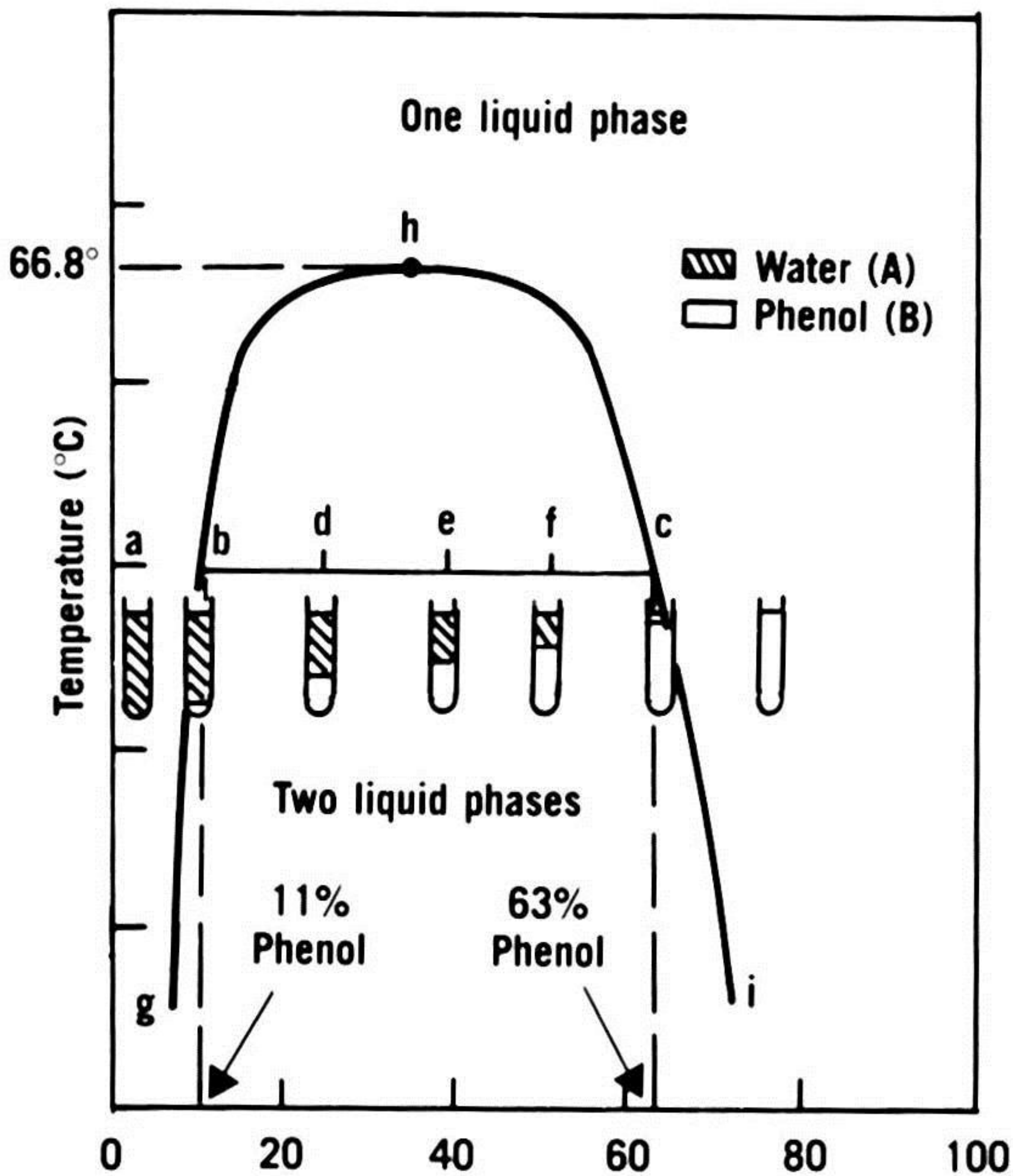
*Key: C = number of components; P = number of phases.

$$F = C - P + 2$$

Two component system

- For two component system F can be 3, (3D model is needed), e.g. T, p and concentration , usually we fix p = 1atm , *the vapor phase is neglected, and F is reduced to 2*

- For three component system the pressure and temperature are fixed

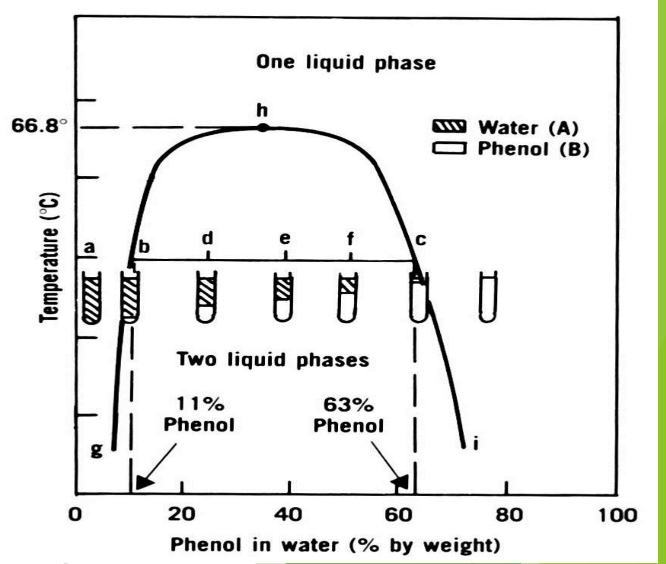

One liquid phase
h
66.8°
Water (A)
Phenol (B)
Temperature (°C)
a
b
d
e
f
c
Two liquid phases
11%
Phenol
63%
Phenol
g
i
0
20
40
60
80
100

The Critical Solution Temperature: CST

- Is the maximum temperature at which the 2-phase region exists (or upper consolute temperature).

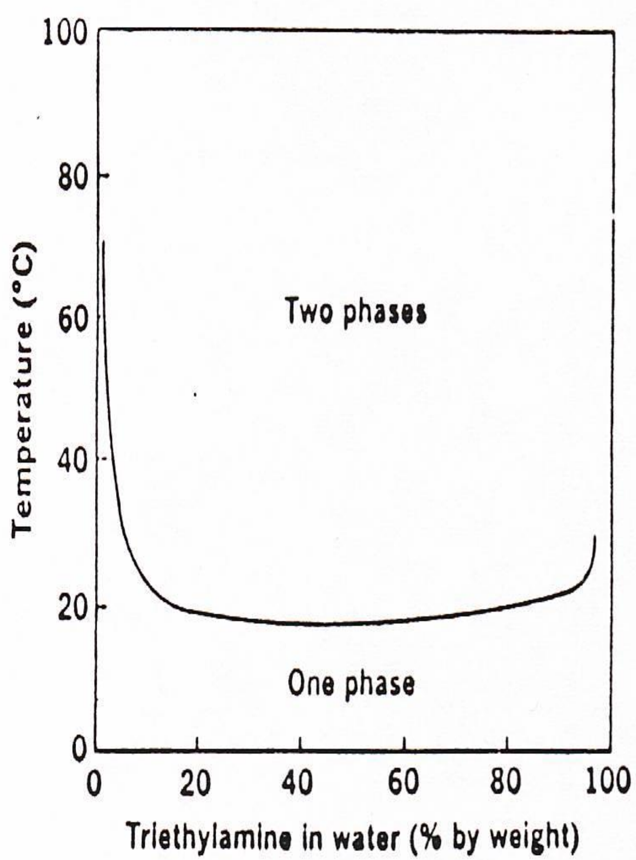
- In the case of the phenol-water system, this is 66.8°C (point h)

- All combinations of phenol and water > CST are completely miscible and yield 1-phase liquid systems.



Systems Showing a Decrease in Miscibility with Rise in Temperature

- A few mixtures, exhibit a lower critical solution temperature (low CST), e.g. triethylamine plus water. The increased miscibility with reduced in temperature.



Systems Showing Upper and Lower CSTs

nicotine-water system has both lower and upper consolute temperature