



**Physical pharmacy II  
Lab -1-**

**Solubility**

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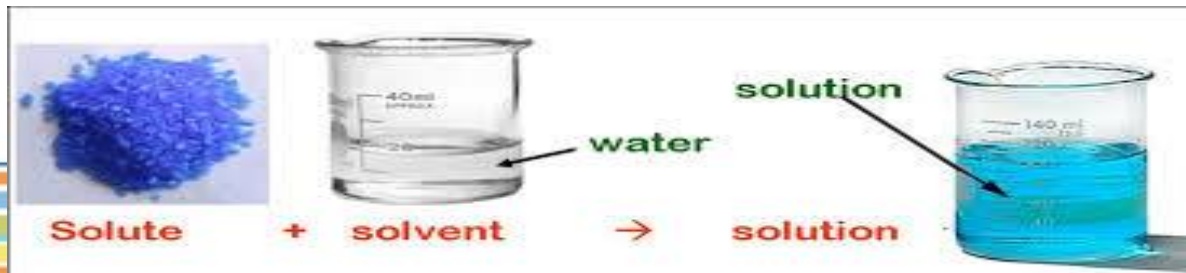


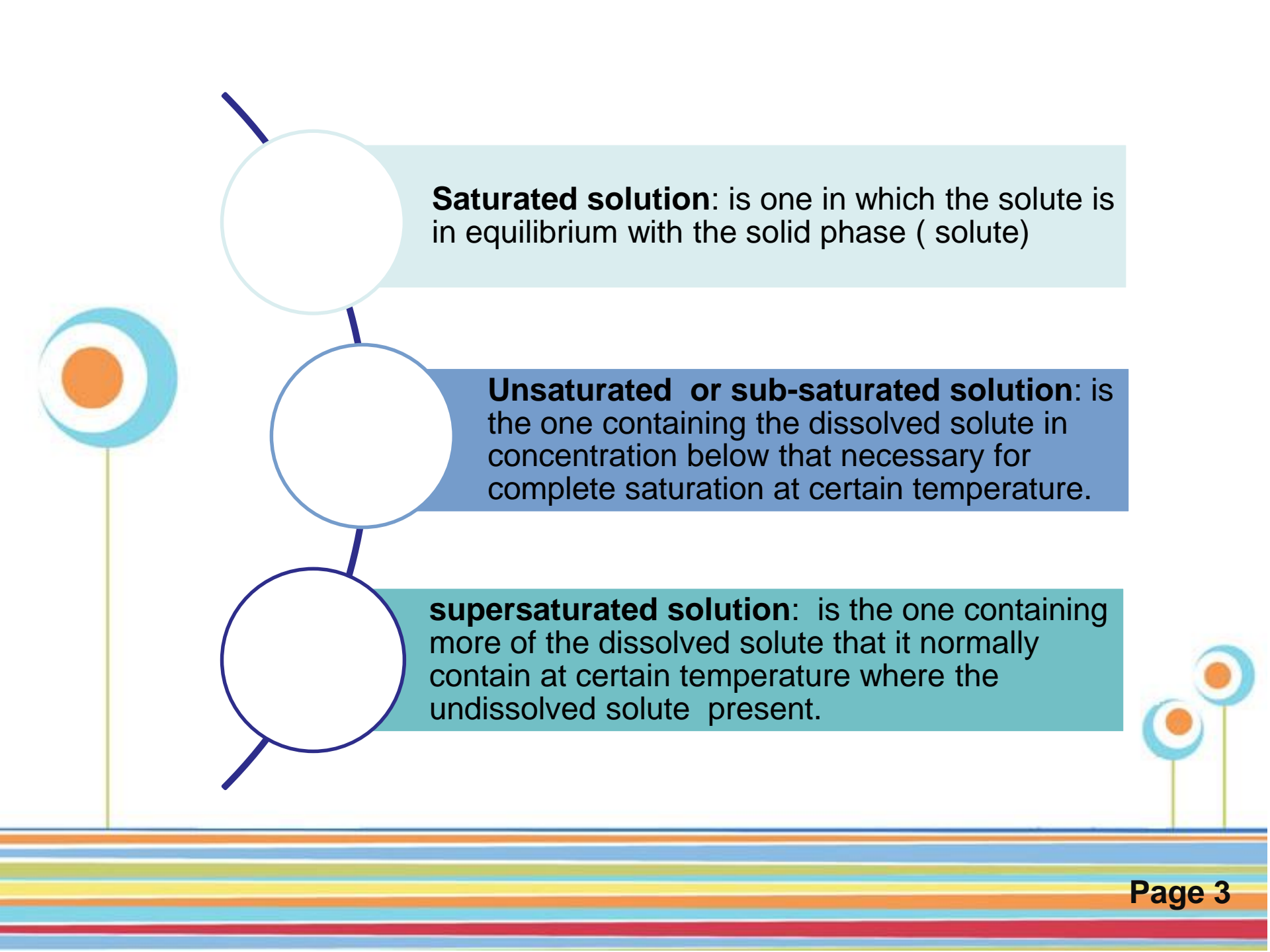
**2024**

The concentration Of solute in saturated solution at certain temperature. **(quantitatively)**

Spontaneous interaction of two or more substances to form homogeneous dispersion **(qualitatively).**

# *Solubility*





**Saturated solution:** is one in which the solute is in equilibrium with the solid phase ( solute)

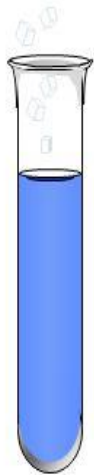
**Unsaturated or sub-saturated solution:** is the one containing the dissolved solute in concentration below that necessary for complete saturation at certain temperature.

**supersaturated solution:** is the one containing more of the dissolved solute that it normally contain at certain temperature where the undissolved solute present.

# Solubility

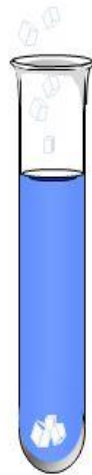
## UNSATURATED SOLUTION

more solute dissolves



## SATURATED SOLUTION

no more solute dissolves



## SUPERSATURATED SOLUTION

becomes unstable, crystals form



Increasing concentration

# FACTORS AFFECTING **SOLUBILITY**



The solubility of a compound depends upon the physical (e.g., particle size) and chemical properties of the solute and solvent.

Other factors:

- **Temperature:** in general as the temperature of medium increase the solubility of compound increase.
- **Pressure:** in case of solubility of gas in liquid solubility increases as pressure increases (e.g., as in aerosol)

## The interaction between solute and solvent (solubilization)

Interaction occur in three steps:

- ❖ the breaking of intermolecular or inter-ionic bond of solute
- ❖ the separation of molecules of solvent to provide a space for solute
- ❖ interaction between solvent & solute molecule or ion

“like dissolves like”





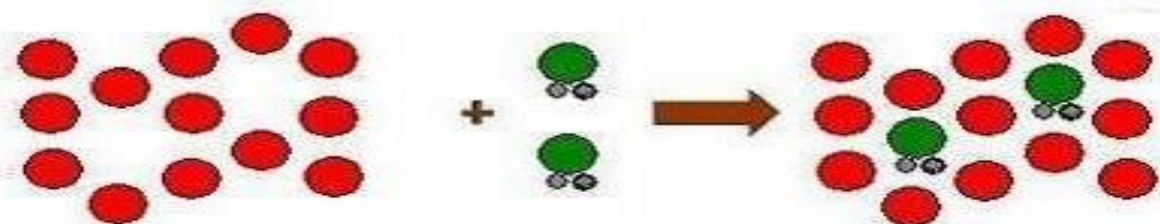
**Step 1: Holes opens in the solvent**



**Step 2: Molecules of the solid breaks away from the bulk**

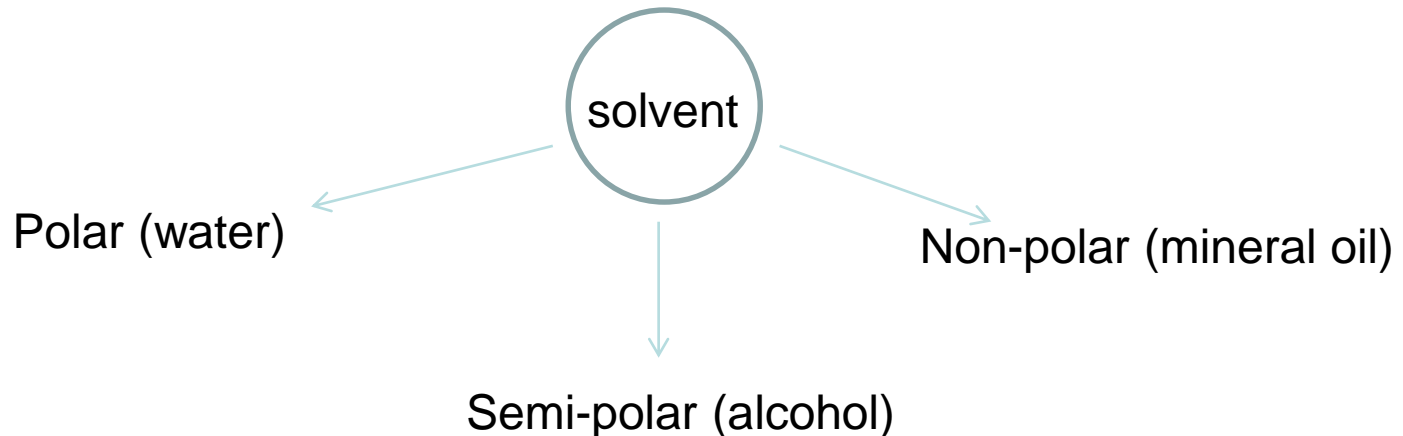


**Step 3: The free solid molecule is integrated into the hole in the solvent**



# Like dissolves like

- Water is good solvent for salt, sugar and similar compounds.
- Mineral oil is good solvent for substance that are normally slightly soluble in water.





# Solubility expression in USP

<b>Solubility definition</b>	<b>Part of solvent required for 1 part of solute</b>
Very soluble	Less than 1 part
Freely soluble	1-10 parts
Soluble	10-30 parts
Sparingly soluble	30-100 parts
Slightly soluble	100-1000 parts
Very slightly soluble	1000-10000 parts
Insoluble	More than 10000 parts



# Polar solvent

- Water is polar solvent, its solvation action is related to:
  1. Polarity or its dipole moment
  2. Solvation by H-bond
  3. By acid base reaction



# Polarity

- The difference in electronic density on H and O atoms of water molecule.
- So the water molecules acts as dipole (having +ve and -ve pole) which is expressed quantitatively as dipole-moment.
- Increasing in dipole moment increases polarity of the solvent.
- The -ve pole attract +ve ion of solute while +ve pole attract -ve ion of solute so water considered as good solvent for ionic compound (e.g., NaCl)



# H-bonding and solvation

- The ability of solute to form H-bond is more significant factor than polarity.
- Water dissolves phenol, aldehyde, ketone and amine and other nitrogen and oxygen containing compounds due to H bonding.



# acid-base

- water consider as good solvent for strong & weak electrolyte because it can break the covalent bond of the acid or base by acid-base reaction since water acts as amphiprotic ( proton donor & acceptor)



# Non-polar solvent

- Hydrocarbon and mineral oils can dissolve non-polar solutes (such as  $\text{CCl}_4$ , benzene, fatty acids and alkaloid bases).
- Non-polar solvent cannot dissolve ionic or polar solute because it is unable to decrease attraction between ions of its low dielectric constant compared to that of water.
- They cannot form H-bond.





# Semi-polar solvents

- Ketone and alcohol can induce certain degree of polarity in non-polar solvents.
- They act as intermediate solvent to bring about miscibility of polar and non-polar liquids.
- For example acetone increases the solubility of ether in water, and alcohol increases the solubility of chloroform in water.

# Methods to increase solubility

## 1. Physical method

- a. **Particle size reduction:** by decreasing particle size surface area will be increased and thus increasing solubility.
- b. **Solid dispersion**

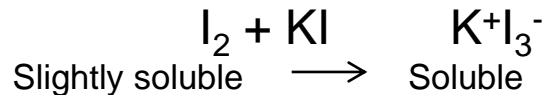
## 2. Chemical methods

- a. **pH change (salt formation):** for weak acid such as salicylic acid; increase in the pH increase the ionization of salicylic acid (i.e., increase concentration of ionized form and thus the solubility).

Since most of drugs are either weak acid or weak bases, their solubility can be enhanced by adjusting the pH of solution, so keep drug in ionized form (salt form). Salt of weak acid and weak base have higher solubility than weak acid and weak base.

- b. **Complexation:** it has been found that insoluble drug can form soluble complex with some compound.

Inorganic and organic material which do not ionize may be rendered soluble in polar solvent (e.g., water) by complexation with electrolyte.



- c. **Prodrugs**


### 3. Miscellaneous methods:

- a. **Co-solvent (solvent combination):** the solubility of solute is quantitatively related to the dielectric constant of solvent system. For example a given solute will have qualitatively similar solubility profile with respect to the same dielectric constant for various co-solvent combination.
- b. Using **surfactant (surface active agent)** in certain concentration.



# *Experimental work*

## 1. Solvent combination



**The objective of this experiment** is to increase the solubility of salicylic acid (a weak organic acid) slightly water soluble by solvent combination; By addition of alcohol (e.g., ethanol) to water the dielectric constant will change (decrease).

### **Materials and equipments:**

Salicylic acid, distilled water, ethanol 99%, conical flask, pipette, burette.



## Procedure

1. Weigh 0.1 g salicylic acid and place it in conical flask.
2. Add 10 ml distilled water and shake the flask to see the solubility of salicylic acid in water.
3. Add from burette drop by drop absolute alcohol i.e., ethanol (99.9%) with continuous shaking until salicylic acid crystals dissolve.
4. Measure the amount of ethanol in the final mixture.
5. Calculate % of alcohol in the final mixture (v/v%).
6. Express the solubility of salicylic acid as 1 part of salicylic acid soluble in X parts of Y% hydro-alcoholic solution.



# Steps of the experiment

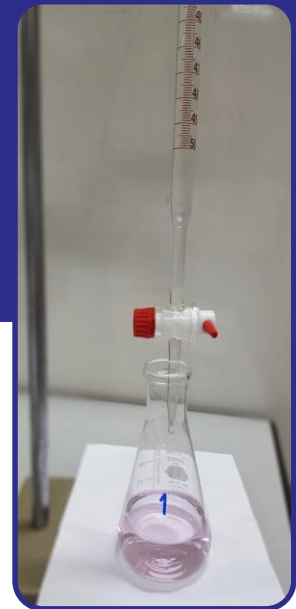
**Weigh 0.1 g  
salicylic acid**




**Add 10 ml  
distilled water  
and shake**



**Add from  
burette drop by  
drop absolute  
alcohol**








To find the conc. of alcohol in final mixture  
End point=5 mL

Final volume of the mixture= 10 +5=15 mL

$C_1 \cdot V_1 = C_2 \cdot V_2$   
100% \* end point = C2 \*final volume



## To express the solubility of Salicylic acid as no. of parts

0.1gm salicylic acid

15 mL (Final volume of mixture)

1 part

X

X= 150 parts of the solvent need  
(Which mean Slightly soluble)

## 2. Salt formation

**The objective of the experiment** is to increase the solubility of salicylic acid by salt formation using sodium carbonate ( $\text{Na}_2\text{CO}_3$ )

### **Material and equipment**

Salicylic acid, sodium carbonate, distilled water

Conical flask, pipette.

### **Procedure**

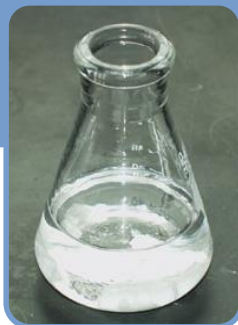
1. Weigh 0.1 g salicylic acid and place it in conical flask
2. Add 10 ml distilled water and shake the flask to check solubility of salicylic acid.
3. Add 0.1 g sodium carbonate and shake the flask and observe the result.
4. Add 5 ml diluted HCl (10%) slowly and see the result
5. Develop equation to account for observation in step 3 and 4.

# Steps of the experiment

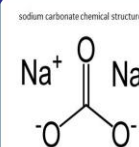
Weigh 0.1 g salicylic acid



Add 10 ml distilled water and shake



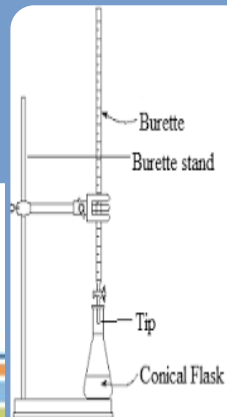
Add 0.1 g sodium carbonate



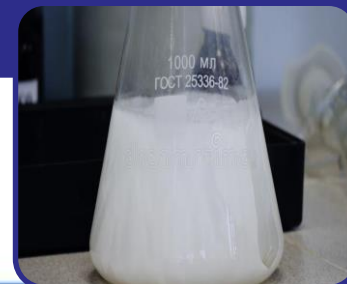
You obtain clear solution

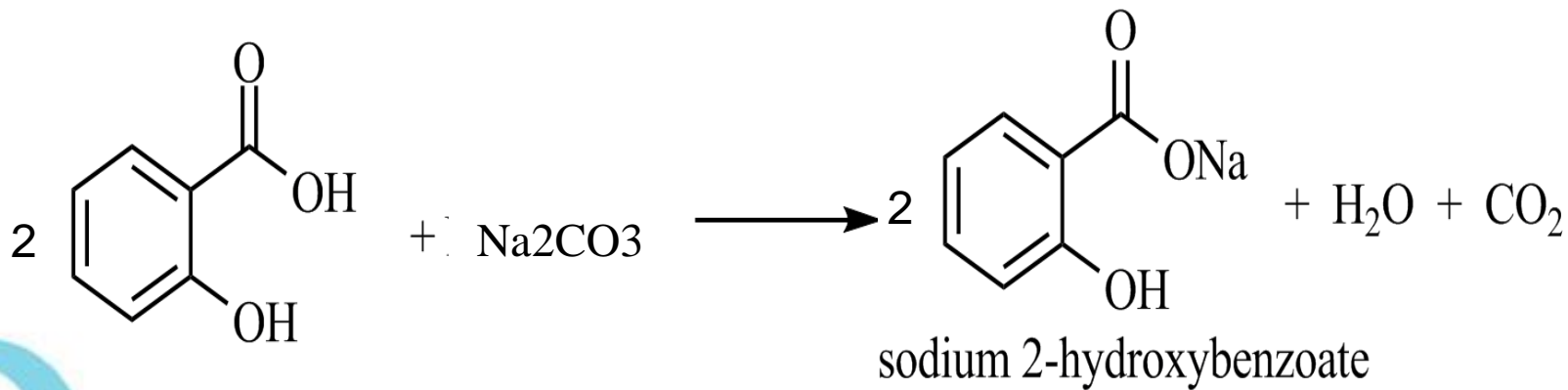


Add 5 ml diluted HCl (10%) slowly



Salicylic acid precipitate in the solution





## 3- complexation:

**The objective of the experiment:** is to increase solubility of Iodine in water by forming soluble Complex upon the addition of potassium iodide.

### **Material and equipment**

Iodine, potassium iodide, distilled water  
Conical flask, pipette.

### **Procedure**

- 1-put (0.1 gm) iodine in conical flask
- 2- add (10 ml) water , shake and observe
- 3- add (0.2 gm) of potassium iodide
- 4-observe the result with equation

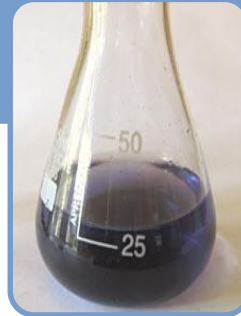


# Steps of the experiment

**Weigh 0.1 g iodine**



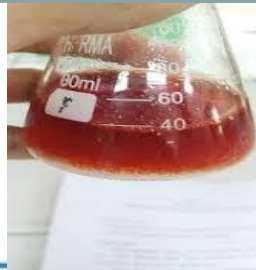
**Add 10 ml distilled water and shake**



**add (0.2 gm) of potassium iodide**



**Soluble complex**



# Thank You For Listening

**It's time for question???**

