

Aim :- To determine the solubility of drug at room temperature.

Reference :

Y. Shaikh Tanvir, Dr. N. Shaikh Siraj, "A practical book of physical pharmaceutics - I", first edition, Nisali Publication, June 2018, Page No. - 3-6.

Requirements :

Apparatus :- Analytical balance, Beaker, Thermostat, Stirrer, UV-visible spectrophotometer, Pipette.

Chemicals :- Paracetamol, Distilled water.

Principle :

The solubility and dissolution properties of drugs perform a valuable role in the process of formulation development.

Definition of solubility :

Solubility is defined in quantitative terms as the concentration of solute in saturated solution at a certain temperature.

Qualitatively, it is defined as the spontaneous

interaction of two or more substances to form a homogeneous molecular dispersion.

Saturated Solution of Drug:

It means one in which drug (solute) is in equilibrium with solid phase.

An Unsaturated solution of Drug:

It means one containing dissolved drug (solute) in concentration below the saturated solution at specific temperature.

Supersaturated solution of drug:

It means one that containing more dissolved drug (solute) than necessary for preparation of the saturated solution at specific temperature.

Factors affecting solubility:

1. Particle Size.
2. Temperature
3. Pressure.
4. Nature of the solute and solvent.
5. Molecular size.
6. Polarity

Table 1.1 : Descriptive terms of solubility

Descriptive terms	Parts of solvent required for 1 part of solute.
Very soluble	Less than 1
Freely soluble	1 to 10
Soluble	10 to 30
Sparingly soluble	30 to 100
Slightly soluble	100 to 1000
Very slightly soluble	1000 to 10000
Practically insoluble or insoluble	More than 10000

7. Polymorphs.Importance of Solubility Determination:

Drug absorption requires that molecules be in solution at the absorption site. Dissolution of solid dosage forms in gastro intestinal fluids is a prerequisite to the delivery of a drug to the systemic circulation following oral administration. The improvement in oral bioavailability be able to attain by decrease the hepatic first pass metabolism by increasing solubility. Solubility determination is important in formulation of dosage forms also prediction of stability, dose of drug.

Techniques of Solubility Improvement:

As solubility and permeability are the deciding factors for the ~~in-vitro~~ in-vivo absorption of the drug, these can be altered or modified by enhancement techniques like:

A) Physical Modifications1) Particle size reductiona) Micronizationb) Nanosuspensionc) Sonocrystallisation.

Standard plot of paracetamol in distilled water

Sr. No.	Concentration (µg/ml)	Absorbance at 247 nm
1	0	0.4
2	2	0.5
3	4	0.6
4	6	0.7
5	8	0.8
6	10	0.9

Solubility of paracetamol in distilled water.

Sr. No.	Temperature (°C)	Volume of Sample taken	Absorbance	Concentration of drug (µg/ml)
1.				
2.				
3.				

Calculation: Put value of absorbance in $Y = MX + C$ equation generated from standard calibration curve and determine solubility.

- d) Supercritical fluid process
- e) Spray drying.

2.) Modification of the crystal habit.

3.) Drug dispersion in carriers.

4.) Complexation

- a) Stacking complexes
- b) Inclusion complexes

5.) Solubilization by surfactants

a) Microemulsions

b) Self microemulsifying drug delivery systems.

6.) Novel drug - drug solid dispersion.

B.) Chemical Modifications

1. pH adjustment

2. Salt formation.

c) Other Techniques.

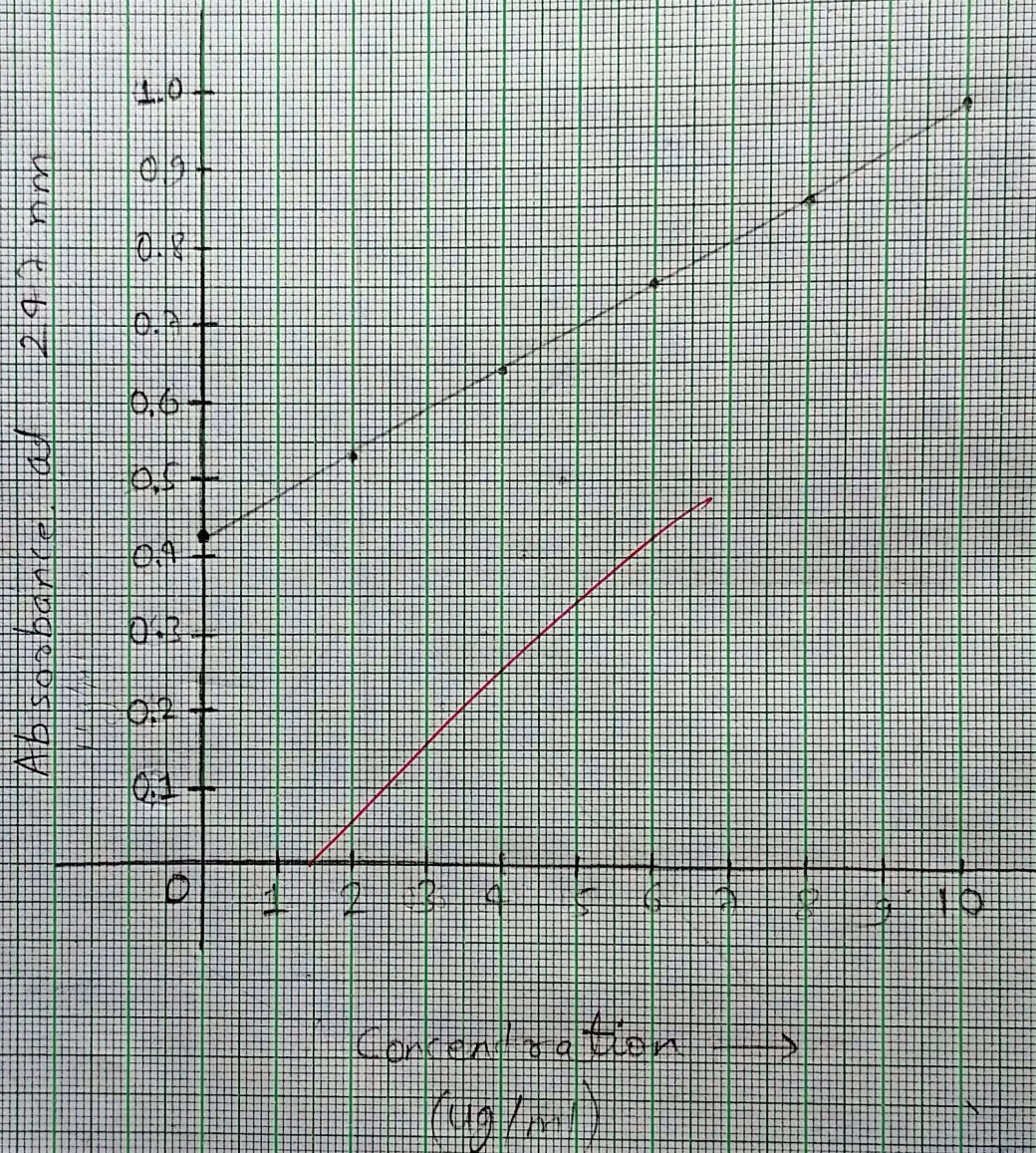
1.) Co-crystallisation.

2.) Co-solvency.

3.) Hydrotropy.

4.) Nanotechnology approaches.

5.) Nanocrystal.



Procedure :

1. Thoroughly clean all the necessary glasswares with acid and wash 2 times with fresh distilled water.
2. Take about 60 ml of distilled water in a flask.
3. Add excess amount of paracetamol in flask containing distilled water and simultaneously stir it.
4. After saturation. keep the flask in a rotating chamber at 37°C at 60 rpm for overnight.
5. In distilled water prepare standard solution of paracetamol.

Dissolve an accurately weighed quantity of paracetamol (100 mg) in small amount of distilled water and make up to 100 ml with distilled water to generate a primary stock solution having a concentration of 100 $\mu\text{g/ml}$.

Further dilute 1 ml of primary stock solution to 100 ml with distilled water to produce a secondary stock solution having a concentration of 10 $\mu\text{g/ml}$. Pipette out 2, 4, 6, 8 and 10 ml from secondary stock solution to further dilute to 10 ml to produce standard

solutions having concentrations of 2, 4, 6, 8 and 10 $\mu\text{g/ml}$. Measure the absorbance of the solutions at 297 nm using double beam UV-visible spectrophotometer against stability chamber as blank. Plot absorbance vs. concentration ($\mu\text{g/ml}$) curve and subject the data to linear regression analysis in Microsoft excel.

6. Measure absorption by using UV-visible spectrophotometer.
7. Determine solubility of paracetamol by using standard calibration curve.

Result:

The solubility of paracetamol in distilled water was found to be ($\mu\text{g/ml}$).