Solubility

Solubility: Importance

- Solubility is the ability of a drug to dissolve in a solvent (usually water or biological fluids).
- It is one of the most important properties in pharmaceutical science.

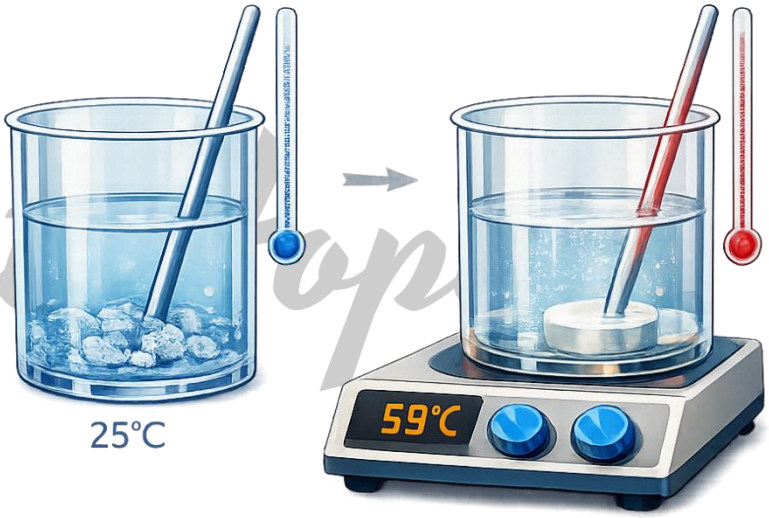


What solubility means in simple terms

- A drug must dissolve before it can be absorbed into the bloodstream
- If it does not dissolve, it cannot produce its therapeutic effect

Why solubility is important

1. **Drug absorption**
   - Drugs are absorbed in dissolved form
   - Poorly soluble drugs → poor absorption → low bioavailability
2. **Bioavailability**
   - Bioavailability means how much drug reaches systemic circulation
   - Higher solubility → better bioavailability
3. **Onset of action**
   - Faster dissolution → faster action
   - Poor solubility → delayed effect
4. **Dose design**
   - Poorly soluble drugs may require higher doses
   - This can increase risk of side effects
5. **Formulation development**
   - **Determines choice of dosage form:**
     - Solution (high solubility)



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- Suspension (low solubility)
- Tablets/capsules

6. Stability

- Some drugs degrade when dissolved
- Balance between solubility and stability is needed

7. Route of administration

- Injectable drugs must be highly soluble
- Oral drugs may tolerate lower solubility but still need adequate dissolution

Classification based on solubility (Biopharmaceutics Classification System – BCS)

- Class I: High solubility, high permeability
- Class II: Low solubility, high permeability
- Class III: High solubility, low permeability
- Class IV: Low solubility, low permeability

Experimental Determination of Solubility

- This refers to laboratory methods used to measure how much drug dissolves in a solvent.

Basic concept

- Add excess drug to solvent
- Allow it to reach equilibrium
- Measure the dissolved amount

Common Method: Shake-Flask Method

Principle

- A saturated solution is prepared by shaking excess drug with solvent until equilibrium is reached.

Steps Involved

1. **Preparation**
   - Take a known amount of solvent
   - Add excess drug (more than can dissolve)
2. **Shaking**
   - Mixture is shaken continuously

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- Ensures proper mixing
- Done using a shaker or water bath

3. **Equilibration**
   - Allow sufficient time (hours or days)
   - Drug dissolves until saturation is reached
4. **Filtration**
   - Remove undissolved drug particles
   - Use filter paper or membrane filter
5. **Analysis**
   - Measure concentration of dissolved drug

Analytical Methods Used

UV–Visible Spectrophotometry:

- Measures absorbance to determine concentration

HPLC (High-Performance Liquid Chromatography):

- Provides accurate and precise quantification

Other Methods for Solubility Determination

A. Turbidity Method

- Measures **cloudiness** of solution
- Indicates solubility limit (onset of precipitation)

B. Spectrophotometric Method

- Uses UV-visible spectroscopy
- Determines concentration based on absorbance

Important Experimental Conditions

- Temperature must be controlled
- pH should be maintained
- Sufficient time for equilibrium
- Proper agitation required

Factors affecting experimental results

- Temperature
- pH of solvent
- Agitation speed

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- Particle size of drug

Types of solubility measured

1. **Equilibrium solubility**
   - ➢ Maximum amount dissolved at equilibrium
2. **Intrinsic solubility**
   - ➢ Solubility of pure drug without influence of pH or additives

Phase Solubility Analysis

- Phase solubility analysis studies how drug solubility changes in the presence of another substance, usually a complexing agent.

Purpose

- To understand drug–carrier interactions
- Commonly used for **complexation studies** (e.g., cyclodextrins)

Basic principle

- Add increasing amounts of solubilizing agent to drug solution
- Measure solubility at each concentration
- Plot graph

First Hope

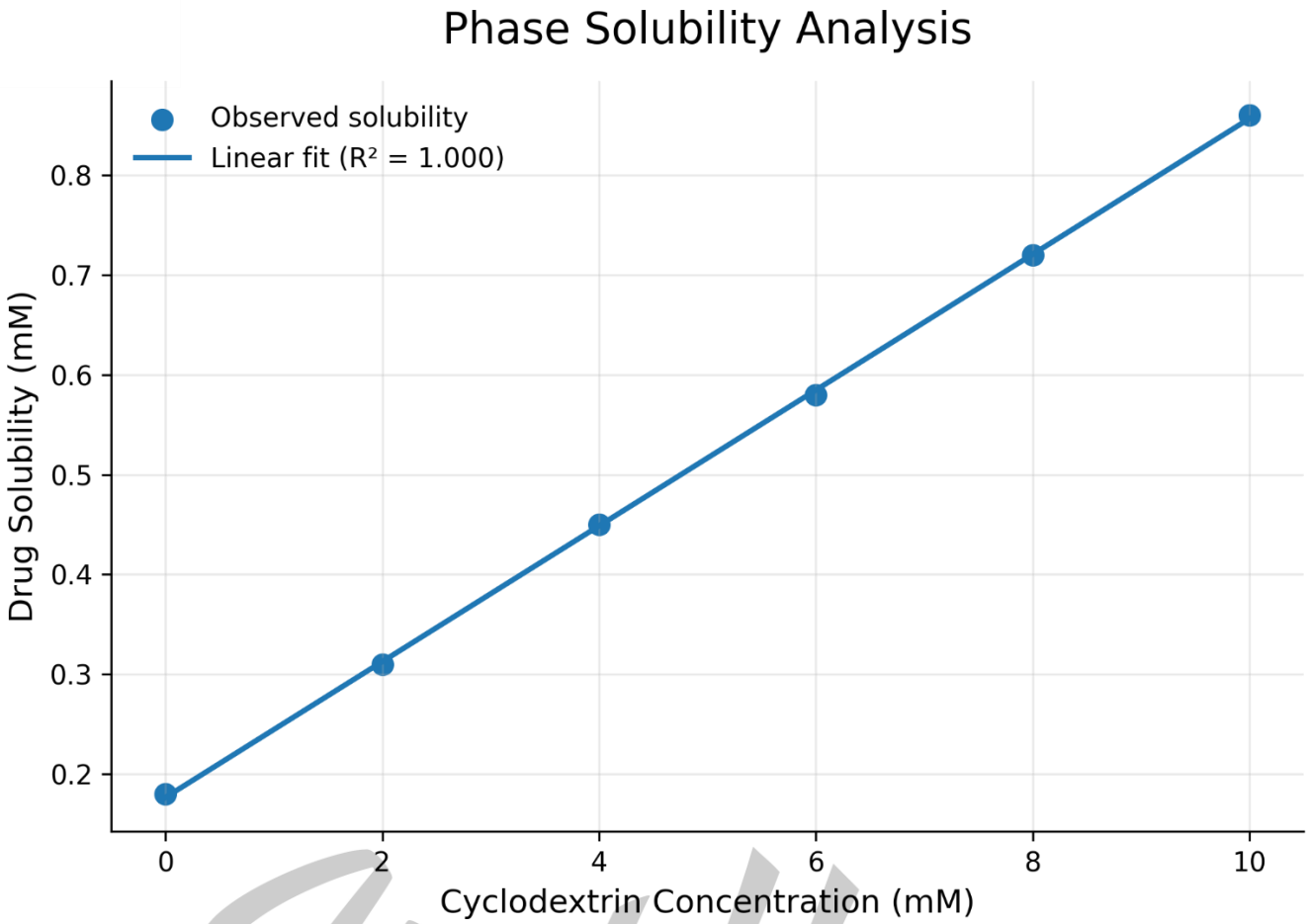
Method (Procedure)

1. Preparing solutions with increasing concentrations of complexing agent
2. Add excess drug to each solution
3. Shake until equilibrium is reached
4. Filter to remove undissolved drug
5. Analyze dissolved drug concentration

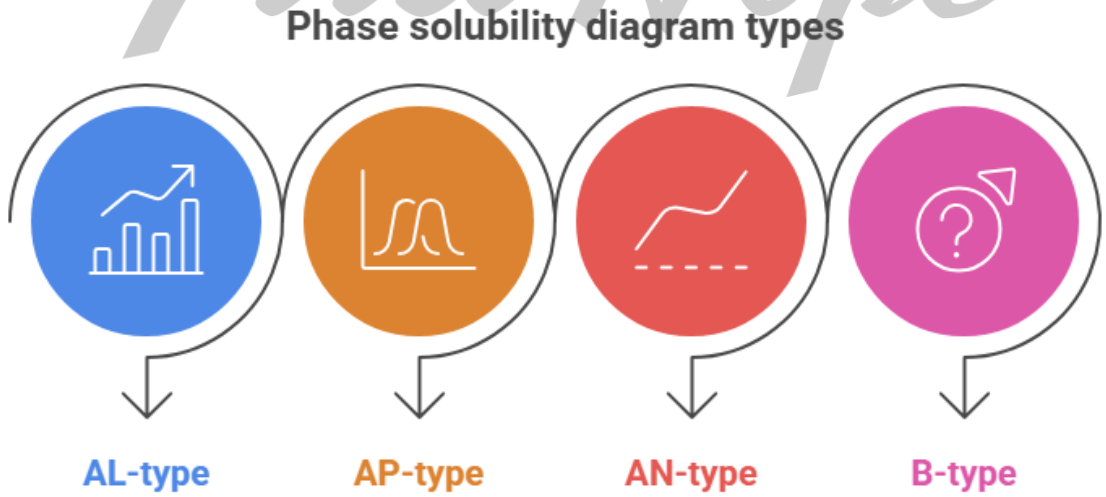
Graph

- X-axis: Concentration of solubilizing agent
- Y-axis: Drug solubility

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Types of phase solubility diagrams



1. **AL-type (Linear increase)**
   - Solubility increases linearly
   - Indicates formation of soluble complex
2. **AP-type (Positive deviation)**
   - Upward curve
   - Suggests higher-order complexes
3. **AN-type (Negative deviation)**

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