UNIT 2

1. Pharmaceutical Calculations: Weights and Measures – Imperial & Metric System

8.1 Introduction

Pharmaceutical calculations are essential for ensuring the **accurate preparation, dispensing, and administration** of medications. Two common systems of weights and measures used in pharmacy are:

1. **Imperial (Apothecary) System**
2. **Metric System (International System of Units – SI)**

Understanding both is important for interpreting prescriptions, preparing formulations, and converting units as per modern practice.

8.2 The Imperial (Apothecary) System

The **Imperial System**, also known as the **Apothecary system**, was historically used in the UK and India, particularly in prescriptions and compounding.

8.2.1 Units of Weight in Imperial System

Unit	Abbreviation	Equivalent (Metric)
1 grain	gr	≈ 64.8 mg
1 scruple	℈	20 grains = 1.296 g
1 dram	ʒ	3 scruples = 60 grains = 3.888 g
1 ounce (oz)	℥	8 drams = 480 grains = 28.35 g
1 pound (lb)	lb	12 ounces = 5760 grains = 373.24 g

8.2.2 Units of Volume in Imperial System

Unit	Abbreviation	Equivalent (Metric)
1 minim	min	≈ 0.0616 mL
1 fluid dram	flʒ	60 minims = ≈ 3.6967 mL
1 fluid ounce	fl℥	8 flʒ = ≈ 29.57 mL
1 pint	pt	20 fl℥ = ≈ 473 mL
1 gallon	gal	8 pints = ≈ 3.785 L

8.3 The Metric System (SI Units)

The **Metric System** is the standard system used globally in pharmacy and science due to its **decimal-based structure**, which makes calculations easier and more accurate.

8.3.1 Units of Weight in Metric System

Unit	Symbol	Equivalent
1 microgram	µg	0.000001 g
1 milligram	mg	0.001 g
1 gram	g	1000 mg
1 kilogram	kg	1000 g

8.3.2 Units of Volume in Metric System

Unit	Symbol	Equivalent
1 millilitre	mL	0.001 L
1 centilitre	cL	10 mL
1 decilitre	dL	100 mL
1 litre	L	1000 mL

8.3.3 Units of Length in Metric System

Unit	Symbol	Equivalent
1 millimetre	mm	0.001 m
1 centimetre	cm	10 mm
1 metre	m	100 cm

8.4 Conversion Between Imperial and Metric Units

Imperial Unit	Metric Equivalent
1 grain	≈ 64.8 mg
1 dram (ʒ)	≈ 3.888 g
1 ounce (oz)	≈ 28.35 g
1 minim	≈ 0.0616 mL

1 fluid dram (fl℥)	≈ 3.6967 mL
1 fluid ounce (fl℥)	≈ 29.57 mL
1 pint	≈ 473 mL
1 gallon	≈ 3.785 L

8.5 Common Abbreviations Used in Prescriptions

Abbreviation	Meaning
gr	grain
mg	milligram
mL	milliliter
fl℥	fluid dram
fl℥	fluid ounce
L	liter

2. Pharmaceutical Calculations Involving Percentage Solutions, Alligation, Proof Spirit, and Isotonic Solutions

Percentage Solutions

Percentage solutions express the **concentration of solute** in a solution. They are expressed in three common ways:

9.1.1 Types of Percentage Solutions

Type	Formula	Meaning
% w/v (Weight/Volume)	g of solute/100 mL solution	Used for solids in liquids (e.g., syrups)
% v/v (Volume/Volume)	mL of solute/100 mL solution	Used for liquids in liquids (e.g., alcohol)
% w/w (Weight/Weight)	g of solute/100 g solution	Used for ointments, creams, etc.

Example:

Prepare 100 mL of a 5% w/v NaCl solution.
→ It means **5 g NaCl** is dissolved in **enough water to make the final volume 100 mL**.

9.2 Alligation Method

Used to **calculate the quantity of two or more components of different concentrations** required to prepare a mixture of a desired concentration.

9.2.1 Alligation Alternate Formula

Quantity of stronger part=Cd−Cw/Cs−Cw×Total qty

Where:

- Cs: Concentration of stronger solution
- Cw: Concentration of weaker solution
- Cd: Desired concentration

9.2.2 Alligation Method (Cross Method)

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```
        Strong sol.   40%
                ↘
                →      Desired: 20%
                ↗
        Weak sol.     10%
```

Difference: 10 parts (20–10)

20 parts (40–20)

Mix in the ratio: Strong : Weak = 10 : 20 = 1 : 2

So, to prepare 300 mL of a 20% solution from 10% and 40%:

- Use 100 mL of 40% and 200 mL of 10%

9.3 Proof Spirit Calculations

Used in alcohol preparations. The strength of alcohol is expressed as **"proof spirit"**.

9.3.1 Definitions

Term	Definition
Proof Spirit	Alcohol containing **49.5% v/v** of ethanol at 15.56°C
Overproof (O.P.)	Contains **more than 49.5% v/v** ethanol
Underproof (U.P.)	Contains **less than 49.5% v/v** ethanol

9.3.2 Conversion Formula

To convert **alcohol % v/v** to **proof strength**:

Proof strength = % alcohol/{49.5}

Example:
Convert 70% v/v alcohol to proof spirit:
= 70×10049.5=141.41∘ proof → **Overproof (O.P.)**

9.4 Isotonic Solutions (Freezing Point & Molecular Weight Method)

Isotonic solutions have the same **osmotic pressure** as body fluids (like blood plasma or tears), which prevents **cell damage** due to osmotic imbalance.

9.4.1 Freezing Point Depression Method

- **Normal freezing point of blood plasma**: **–0.52°C**
- To make a solution isotonic, it must **depress freezing point to –0.52°C**

Steps:

1. Find **freezing point depression of the drug** in 1% solution (given or from table).
2. Use formula:

% drug required for isotonicity = 0.52/Freezing point depression of 1% solution

Example:

If 1% solution of a drug lowers freezing point by 0.08°C:
Then, % required to make it isotonic:
= 0.52/0.08=6.5%

9.4.2 Sodium Chloride Equivalent Method (E-value method)

NaCl required=(0.9−E×drug amount)

0.9: isotonic NaCl concentration (%)

- **E**: amount of NaCl equivalent to 1 g of drug
- **drug amount**: in grams

Example:

Prepare isotonic solution with 0.5 g of drug having E = 0.18.
NaCl needed = $0.9-(0.18\times0.5)=0.9-0.09=0.81g$

9.4.3 Molecular Weight Method (van't Hoff Law)

Used when **molecular weight and dissociation** of solute is known.

$\pi=iMRT$
Where:

- π: osmotic pressure
- i: dissociation factor
- M: molar concentration
- R: gas constant
- T: temperature in Kelvin

For isotonicity: equate π of solution to plasma

Rarely used in routine pharmacy, but important for **precision dosing and formulation design**.

3. Powders

3.1 Definition

"Powders are **intimate mixtures** of dry, finely divided drugs or chemicals that may be **intended for internal or external use**."

These are among the **simplest pharmaceutical dosage forms**, widely used in both **compounding** and **industrial formulations**.

3.2 Classification of Powders

Powders are classified based on **route of administration**, **composition**, and **method of preparation**.

3.2.1 Based on Route of Administration

Type	**Example**
Oral powders	Antacids, Oral rehydration salts
Topical powders	Dusting powders, Medicated talc
Inhalation powders	Dry powder inhalers (DPI)
Dental powders	Tooth powders

3.2.2 Based on Number of Doses

Type	Description
Bulk powders	Intended to be measured before use (e.g. ORS)
Divided powders	Pre-divided into individual doses (e.g. sachets)

3.2.3 Based on Composition or Ingredients

Type	Example
Simple powders	Contain one drug (e.g., Paracetamol powder)
Compound powders	Contain two or more ingredients
Effervescent powders	Release CO_2 when mixed with water (e.g., ENO)
Hygroscopic powders	Absorb moisture from air (e.g., Ammonium chloride)
Deliquescent powders	Absorb moisture and liquefy (e.g., Calcium chloride)
Eutectic mixtures	Form a liquid when mixed (e.g., camphor + menthol)

3.3 Advantages of Powders

1. **Flexibility in Compounding**
    - Easy to formulate for specific dose needs.
2. **Stability**
    - More stable than liquid forms (especially for antibiotics, probiotics).
3. **Rapid Onset of Action**
    - No disintegration step—acts faster when taken with water.
4. **Better Palatability**
    - Bitter drugs can be masked with sweeteners or flavors.
5. **Suitable for Large Doses**
    - Large doses (e.g., ORS) are more easily taken as powder.
6. **Useful for Children or Elderly**
    - Can be mixed with food or water.
7. **Cost-effective**
    - Simple to prepare, pack, and store—reduces production costs.

3.4 Disadvantages of Powders

1. **Less Accurate Dosing in Bulk Form**
    - Patient must measure the dose; risk of under/overdosing.
2. **Unpleasant Taste**
    - Some drugs (e.g., metronidazole) have poor palatability.
3. **Not Suitable for Moisture-sensitive Drugs**
    - May require special packaging (e.g., desiccants).
4. **Risk of Incompatibility**
    - Powders containing multiple actives may react (e.g., eutectics).
5. **Irritation Potential**
    - Dust may irritate respiratory tract (especially fine powders).
6. **Not Ideal for Unstable or Volatile Substances**
    - Volatile oils or oxidation-sensitive drugs degrade easily.
7. **Difficult to Store Hygroscopic Substances**
    - Absorb moisture and deteriorate.

4. Simple and Compound Powders – Official Preparations

4.1 Simple Powders

Definition:

A **simple powder** is a pharmaceutical powder that contains only **one medicinal substance**, sometimes with an inert diluent.

Characteristics:

- Usually dispensed in **bulk** or **divided doses**.
- Easy to prepare and dispense.
- Suitable when a **single drug** is prescribed.

Examples of Official Simple Powders (IP/BP/USP):

Official Name	Use	Details
Paracetamol Powder IP	Analgesic and antipyretic	May be dispensed in divided doses
Magnesium Sulphate Powder IP	Laxative, also used externally	Hygroscopic; must be stored in airtight container
Light Kaolin Powder BP	Antidiarrheal	Used as adsorbent in diarrhea
Sulphanilamide Powder USP	Antibacterial (topical)	Used for infected wounds

4.2 Compound Powders

Definition:

Compound powders are pharmaceutical powders that contain **two or more ingredients**, which may be active or inert.

Characteristics:

- Used to achieve **synergistic action**, mask taste, or combine therapeutic effects.
- Require careful weighing and **mixing to ensure uniformity**.
- Often used in **bulk or divided** forms.

4.3 Official Compound Powder Preparations

Official Name	Ingredients	Uses
Compound Sodium Bicarbonate Powder IP	Sodium bicarbonate, Citric acid, Sodium carbonate	As antacid; effervescent preparation
Oral Rehydration Salts IP (ORS)	Glucose, NaCl, KCl, $NaHCO_3$ or citrate	Treats dehydration due to diarrhea
Compound Rhubarb Powder BP	Rhubarb, Light Magnesium Carbonate, Ginger, etc.	Mild laxative
Compound Sulphur Powder IP	Sublimed sulphur, Precipitated sulphur	Skin conditions (scabies, acne)

4.4 Key Points in Preparation :

- **Weighing**: Each ingredient must be accurately weighed.
- **Comminution**: If any material is coarse, it must be finely powdered.

- **Mixing**: Done using geometric dilution to ensure uniform distribution.
- **Packaging**: Divided powders are wrapped in cachets or sachets; bulk powders in wide-mouthed containers.
- **Labeling**: Should mention dose, route, storage, and auxiliary instructions.

5. Dusting Powders and Effervescent Powders

5.1 Dusting Powders

5.1.1 Definition

Dusting powders are **finely divided, non-irritating powders** meant for **external application** on the skin to provide a **soothing, protective, antiseptic, or absorbent effect**.

They are **not intended for application on open wounds** unless they are **sterile**.

5.1.2 Classification

Type	**Use**
Medical (Therapeutic)	Antiseptic, antifungal, or protective functions
Surgical	Used during surgery, must be **sterile**
Cosmetic	Talcum powder, deodorants for personal care

5.1.3 Desirable Properties

- **Free-flowing** and fine
- **Non-irritating**
- Chemically and physically **stable**
- **Sterile** (especially surgical types)
- Free from gritty materials

5.1.4 Common Ingredients

Substance	**Function**
Talc	Lubricant, absorbent
Zinc oxide	Protective, mild antiseptic
Starch	Absorbent
Kaolin	Adsorbent, soothing
Salicylic acid	Antifungal
Boric acid	Mild antiseptic

5.1.5 Official Examples

Preparation	Use
Dusting Powder IP	Antiseptic or antifungal external use
Zinc Oxide Dusting Powder	Protective for diaper rash, eczema
Surgical Dusting Powder	Applied to surgical gloves or instruments

5.2 Effervescent Powders

Effervescent powders are **granular or powdered mixtures** containing **acid and carbonate or bicarbonate salts** which **release carbon dioxide** when dissolved in water. This results in **effervescence**.

5.2.2 Composition

Ingredient	Function
Citric acid	Acid component
Tartaric acid	Acid component
Sodium bicarbonate	Alkali (effervescent base)
Active drug	Therapeutic agent
Sweetener/flavor	Palatability

5.2.3 Ideal Properties

- Quick and complete **effervescence**
- Pleasant **taste** (due to carbon dioxide release)
- Stable in **dry form**
- Easily **soluble** in water
- Releases **CO_2** which can aid **gastric emptying** and reduce bloating

5.2.4 Method of Preparation

Dry/fusion method:

- Citric acid is used in crystalline form.
- The ingredients are **blended and heated gently** (not exceeding 60°C).
- Water in citric acid aids granule formation.

Wet method:

- A small amount of alcohol or water is added to prepare a **dough-like mass**, which is passed through a sieve and dried.

5.2.5 Advantages

- Improves **taste and palatability**
- Increases **drug solubility**
- Enhances **absorption** due to fast dissolution
- Easy to carry and administer

5.2.6 Disadvantages

- **Moisture sensitive** – requires tight packaging
- May cause **gastric distension** in some individuals
- Not suitable for **patients on sodium-restricted diets**

5.2.7 Official Examples

Preparation	**Use**
Effervescent Granules of Aspirin	Analgesic, antipyretic
Citric Acid + $NaHCO_3$ + Drug	Antacids (e.g., Eno)
ORS IP (Effervescent Type)	Oral rehydration, faster fluid replacement

5.3 Packaging and Storage

Type	**Requirement**
Dusting powders	Stored in **sifter-top containers**
Effervescent powders	Packed in **airtight, moisture-proof containers** (e.g., glass jars or aluminium tubes with desiccants)

6.1 Efflorescent Powders

6.1.1 Definition:

Efflorescent powders are **crystalline substances** that contain **water of crystallization** and may **lose this water when exposed to air**, becoming **damp or liquefied**.

These powders **liberate water** upon standing in **dry or warm environments**, which can cause:

- Clumping
- Caking
- Inaccurate dosing

6.1.2 Examples of Efflorescent Substances

Substance	Water of crystallization	Comment
Citric acid monohydrate	1 molecule	Used in effervescent preparations
Caffeine (some forms)	Variable	May lose water during storage
Atropine sulphate	Crystalline form	Can liquefy in dry atmosphere
Codeine phosphate	Crystalline form	Tends to lose water on storage

6.1.3 Problems with Efflorescent Powders

- Loss of water leads to **inaccurate dosing**.
- Resultant moisture may **cause clumping** or affect **other ingredients** in a powder mixture.

6.1.4 Pharmaceutical Handling

- Mix with **a suitable absorbent** (e.g., light kaolin, starch).
- Use **anhydrous form** of the drug if possible.
- Store in **tightly closed, moisture-resistant containers**.
- Avoid unnecessary heating during drying.

6.2 Hygroscopic Powders

6.2.1 Definition:

Hygroscopic powders are substances that **absorb moisture from the air** but **do not liquefy** (unlike deliquescent substances).

The absorbed moisture can cause:

- Caking
- Clumping
- Degradation of the active ingredient

6.2.2 Examples of Hygroscopic Substances

Substance	Comment
Magnesium oxide	Common antacid and laxative
Zinc chloride	Strongly hygroscopic
Calcium chloride	Highly hygroscopic and deliquescent
Ferric chloride	Very moisture-sensitive

Note: **Some substances** may be both **hygroscopic and deliquescent**, depending on storage conditions.

6.2.3 Problems with Hygroscopic Powders

- **Loss of flowability**
- Affects **uniformity of dose**
- May lead to **chemical instability**

6.2.4 Pharmaceutical Handling

- Store in **airtight containers with desiccants**.
- Use **anhydrous or less hygroscopic substitutes** if available.
- Avoid exposure to **humid environment**.
- **Rapid dispensing and minimal handling** recommended.

6.3 Comparison Table: Efflorescent vs. Hygroscopic Powders

Parameter	Efflorescent Powders	Hygroscopic Powders
Moisture Behavior	**Lose water** of crystallization	**Absorb moisture** from air
Effect	Becomes **damp**, may cause other powders to clump	Becomes **clumpy**, sticky
Action	**Release** water	**Gain** water
Examples	Citric acid, Atropine sulphate	Magnesium oxide, Zinc chloride
Handling	Mix with absorbents; use anhydrous forms	Use desiccants; store in airtight containers

7.1 Eutectic Mixtures

A **eutectic mixture** is a combination of two or more solid substances that, when mixed together, form a **liquid or soft mass** due to **reduction in their melting points** below room temperature.

This happens even though each component is **solid at room temperature** on its own.

7.1.2 Mechanism

- Substances **interact physically** when mixed in powdered form.
- They **lower each other's melting point**.
- Result: A **semi-solid, oily, or liquefied mass** is formed.

7.1.3 Common Eutectic Substances

Substance	**Melts when mixed with**
Camphor	Menthol, thymol, phenol, salol
Menthol	Camphor, thymol, chloral hydrate
Thymol	Menthol, camphor
Phenol	Camphor
Chloral hydrate	Menthol

7.1.4 Pharmaceutical Problems

- Uncontrolled eutectic reaction leads to **liquefaction**, making the powder **unsuitable for packaging or dosing**.
- Creates **non-uniform mixtures**, affecting drug delivery.

7.1.5 Handling Techniques (as per RM Mehta)

- Mix eutectic substances **separately** with inert absorbent powders like:
    - Light kaolin
    - Talc
    - Starch
    - Magnesium carbonate
- Then **combine all mixtures** using **geometric dilution**.
- **Double-wrapping** may be required when dispensing in paper sachets.

7.1.6 Example Formulation Approach

To mix **camphor and menthol** (both eutectic):

1. Mix camphor with starch.
2. Mix menthol with light kaolin.
3. Combine both mixtures carefully.

7.2 Geometric Dilution

Definition

Geometric dilution is a **pharmaceutical mixing method** used to ensure **uniform distribution** of a **small quantity of potent drug** with a large amount of diluent or excipient.

7.2.2 Principle

- Equal quantity of **drug and diluent** are mixed first.
- Then, **equal quantity of this mixture** is further mixed with diluent.
- Repeated until all the diluent is mixed.

7.2.3 Importance

- Ensures **homogeneous blending** of low-dose drugs (e.g., potent corticosteroids, antibiotics).
- Prevents **hot spots** or **uneven dosing**.
- Particularly used in **compounding of powders and granules**.

7.2.4 Step-by-Step Process

Example: Mix 1 g of potent drug with 15 g of lactose.

Step	Mixture
1	Mix 1 g drug + 1 g lactose → 2 g mixture
2	Add 2 g mixture + 2 g lactose → 4 g mixture
3	Add 4 g mixture + 4 g lactose → 8 g mixture
4	Add final 7 g lactose (if needed) and mix

This method uses **doubling technique** to maintain proportional blending.

7.2.5 Applications

- Compounding of **bulk powders** and **divided powders**.
- Preparation of **tablets** and **capsules** containing small doses.
- Used when mixing **eutectic powders** with absorbents.

8. Liquid Dosage Forms: Advantages and Disadvantages

Liquid dosage forms are **preparations containing one or more active ingredients** dissolved or suspended in a suitable liquid vehicle. They may be intended for **oral, parenteral, external, or mucosal administration**.

8.2 Types of Liquid Dosage Forms (Brief Overview)

Type	Example
Solutions	Syrups, elixirs, oral drops
Suspensions	Antacid suspensions
Emulsions	Cod liver oil, lotions
Injectables	IV fluids, vaccines
Ear/Nasal Drops	Nasal decongestants
Gargles/Mouthwashes	Chlorhexidine gargle
Lotions/Liniments	Calamine lotion

8.3 Advantages of Liquid Dosage Forms

8.3.1 Accurate Dosing (Flexible Doses)

- Especially useful in **pediatrics** and **geriatrics**.
- Dose can be **easily adjusted** using a measuring cup, spoon, or dropper.

8.3.2 Rapid Onset of Action

- No **disintegration** needed as in tablets.
- Drugs are **already dissolved or dispersed**, promoting faster absorption.

8.3.3 Suitable for Certain Routes

- Ideal for **oral, topical, parenteral, rectal, and mucosal** administration.
- Useful for **local effects** (e.g., throat pain, skin infection).

8.3.4 Ease of Swallowing

- Preferred in **patients who have difficulty swallowing** tablets or capsules, such as:
    - Infants
    - Elderly
    - Post-operative patients

8.3.5 Taste Masking

- Sweeteners and flavors can be added to **mask bitterness**.

8.3.6 Uniform Distribution

- For **multi-dose therapy**, suspensions/emulsions can be easily **shaken to redisperse**.

8.3.7 Better Bioavailability

- Especially in case of **solutions**, as drug is already in dissolved form.

8.4 Disadvantages of Liquid Dosage Forms

8.4.1 Poor Stability

- More prone to **chemical degradation**, hydrolysis, oxidation.
- Suspensions and emulsions may suffer **physical instability** (settling, creaming).

8.4.2 Shorter Shelf Life

- Due to microbial growth risk, they often require **preservatives**.
- Have **lower shelf stability** compared to solids.

8.4.3 Inconvenient Packaging and Transport

- Require **bulkier, leak-proof containers** (glass/plastic bottles).
- **Breakable**, heavier, and more expensive to ship.

8.4.4 Dosage Inaccuracy

- Patient-administered doses can vary due to **improper measuring** (especially without calibrated devices).

8.4.5 Unpleasant Taste

- If not properly flavored or sweetened, some drugs (e.g., metronidazole) may still taste bitter.

8.4.6 Storage Conditions

- Sensitive to **light, air, temperature**, and **microbial contamination**.
- Require **airtight, often amber-colored containers**.

8.4.7 Preservative Issues

- Preservatives like **parabens** or **benzalkonium chloride** may cause **allergic reactions** or instability in sensitive formulations.

9. Excipients Used in Formulation of Liquid Dosage Forms

Introduction

Excipients are **pharmaceutically inactive substances** added to a formulation alongside the active pharmaceutical ingredient (API) to improve **stability, palatability, solubility, viscosity, appearance, and patient compliance**. In liquid dosage forms, excipients perform **functional roles** such as solubilizing the drug, enhancing taste, preventing microbial growth, or improving viscosity and pourability.

Types of Excipients and Their Functions

Vehicles (Solvents)
Vehicles are the **major component** in liquid dosage forms. They act as carriers for active ingredients.

- **Aqueous Vehicles**: Purified water, aromatic water, syrup, water for injection
- **Non-aqueous Vehicles**: Alcohol, glycerin, propylene glycol, oils (e.g., castor oil, sesame oil)
  These solvents dissolve or suspend the drug and provide volume to the preparation.

Preservatives
Preservatives are added to prevent **microbial contamination** in multi-dose liquid products. They are essential for maintaining product safety and shelf life.
Examples include:

- Parabens (methylparaben, propylparaben)
- Benzalkonium chloride
- Sodium benzoate
- Sorbic acid
  Selection depends on the pH and nature of the formulation.

Sweetening Agents
These are added to improve **taste and palatability**, especially important in pediatric and oral preparations.
Examples include:

- Sucrose (most common)
- Sorbitol
- Saccharin sodium
- Aspartame
- Stevia (natural alternative)

Flavoring Agents
Used to **mask unpleasant taste or odor** of drugs. Choice of flavor depends on the drug's characteristics and patient preference.

- For bitter drugs: Chocolate, mint, raspberry
- For sour drugs: Orange, lemon
- For salty drugs: Butterscotch, vanilla

Coloring Agents
Color improves **aesthetic appeal** and helps in product identification.
Examples:

- Tartrazine, sunset yellow, amaranth (synthetic)
- Natural colors like caramel or beetroot extract
  Colors used must be **non-toxic and approved by regulatory bodies**.

Buffers
Buffers maintain the **pH of the preparation** to ensure stability and solubility of the drug.
Examples:

- Citrate buffer
- Phosphate buffer
- Acetate buffer
  Proper pH also enhances preservative efficacy.

Antioxidants
Antioxidants prevent **oxidative degradation** of the drug, especially in vitamins and oils.
Examples:

- Sodium metabisulfite
- Ascorbic acid
- Butylated hydroxyanisole (BHA)
- Butylated hydroxytoluene (BHT)

Chelating Agents (Sequestering Agents)
These bind **metal ions** that catalyze oxidation, enhancing antioxidant effectiveness.
Examples:

- EDTA (ethylenediaminetetraacetic acid)
- Citric acid

Viscosity Enhancers / Thickening Agents
Used to **improve mouthfeel**, suspend particles in suspensions, and enhance stability.
Examples:

- Methylcellulose
- Hydroxypropyl methylcellulose (HPMC)
- Acacia
- Xanthan gum
- Sodium carboxymethylcellulose (NaCMC)

Emulsifying Agents
Used in **emulsions** to stabilize the mixture of immiscible liquids like oil and water.
Examples:

- Tween 80 (polysorbate 80)
- Span 20
- Lecithin
- Gum acacia

Suspending Agents
Used in **suspensions** to keep solid particles uniformly distributed throughout the liquid.
Examples:

- Bentonite
- Tragacanth
- Sodium alginate
- Carbopol

Solubilizing Agents / Co-solvents
Used when the drug is **poorly soluble in water**. They help to increase solubility.
Examples:

- Alcohol
- Glycerin
- Propylene glycol
- Polyethylene glycol (PEG)

Surface-Active Agents (Surfactants)
Reduce surface tension and aid in **wetting, solubilization, and emulsification**.
Examples:

- Sodium lauryl sulfate
- Polysorbates
- Sorbitan esters

10. Solubility Enhancement Techniques

Introduction

Many drugs have **poor aqueous solubility**, which limits their **bioavailability**, especially in oral dosage forms. Therefore, **enhancing solubility** is a major challenge in formulation development. Solubility enhancement techniques are strategies used to **increase the solubility and dissolution rate** of poorly soluble drugs, thereby improving their **therapeutic effectiveness**.

Classification of Solubility Enhancement Techniques

Solubility can be enhanced by using **physical, chemical, and miscellaneous methods**. Each method is selected based on **drug characteristics** and **intended dosage form**.

A. Physical Methods

Particle Size Reduction
Reducing particle size increases **surface area**, enhancing the rate of dissolution.
Techniques:

- Micronization
- Nanosuspension
- Milling or grinding

Modification of the Crystal Habit
Converting the drug from **crystalline to amorphous form** (which has higher energy) improves solubility.

- Amorphous solids are more soluble than crystalline solids.

Use of Surfactants
Surfactants reduce **interfacial tension** and increase **wetting of drug particles**, leading to improved solubility.
Examples:

- Sodium lauryl sulfate
- Polysorbate 80 (Tween 80)
- Cremophor RH

Use of Co-solvents
Addition of a **water-miscible organic solvent** increases drug solubility in aqueous systems.
Common co-solvents:

- Ethanol

- Glycerin
- Propylene glycol
- PEG 400

Solid Dispersion Technique
The drug is dispersed in an inert, hydrophilic carrier in the **solid state**, enhancing solubility and dissolution.
Carriers used:

- Polyvinylpyrrolidone (PVP)
- PEG
- Urea
  Methods:
- Melting method
- Solvent evaporation method

Complexation
The drug is complexed with another substance that improves its solubility.
Most common:

- Cyclodextrin complexes (β-cyclodextrin)
  These form inclusion complexes where the drug molecule is trapped in the hydrophobic cavity.

Hydrotropy
A large amount of a **hydrotropic agent** is added to increase the solubility of a poorly soluble drug.
Examples:

- Sodium benzoate
- Sodium salicylate
- Urea

B. Chemical Methods

Salt Formation
Converting the drug into its **salt form** enhances aqueous solubility.
Example:

- Aspirin (acid) → Sodium salicylate (salt)
  This is suitable for drugs with **ionizable functional groups**.

pH Adjustment
Altering the **pH of the solvent system** can improve solubility of **weak acids and bases**.

- Weak acids dissolve better in alkaline pH.
- Weak bases dissolve better in acidic pH.

Prodrug Approach
The drug is chemically modified into a **more soluble derivative** (prodrug), which is converted into the active drug in the body.

C. Miscellaneous Techniques

Use of Superdisintegrants
Used in solid dosage forms like tablets to **promote rapid disintegration** and improve dissolution.
Examples:

- Cross-linked PVP
- Sodium starch glycolate

Micellar Solubilization
Use of surfactants above their **critical micelle concentration (CMC)** to form **micelles**, which solubilize the drug inside their hydrophobic core.

Self-Emulsifying Drug Delivery Systems (SEDDS)
A mixture of oil, surfactant, and drug that **spontaneously emulsifies** in the GIT to improve drug solubility and absorption.

Nanotechnology-Based Methods
Nanoparticles and nanosuspensions provide **high surface area**, increasing dissolution and solubility.