# Unit-2

# Industrial Pharmacy-1

## B.Pharma 5th Sem Notes

### Unit: 2

**Tablets:**

- **Introduction**, ideal characteristics of tablets, classification of tablets. Excipients, Formulation of tablets, granulation methods, compression and processing problems. Equipment's and tablet tooling.
- **Tablet coating:** Types of coating, coating materials, formulation of coating composition, methods of coating, equipment employed and defects in coating.
- **Quality control tests:** In process and finished product tests.

**Liquid orals:**

- Formulation and manufacturing consideration of syrups and elixirs suspensions and emulsions; Filling and packaging; evaluation of liquid orals official in Pharmacopoeia.

# Tablets:

- **Introduction**, ideal characteristics of tablets, classification of tablets. Excipients, Formulation of tablets, granulation methods, compression and processing problems. Equipment's and tablet tooling.

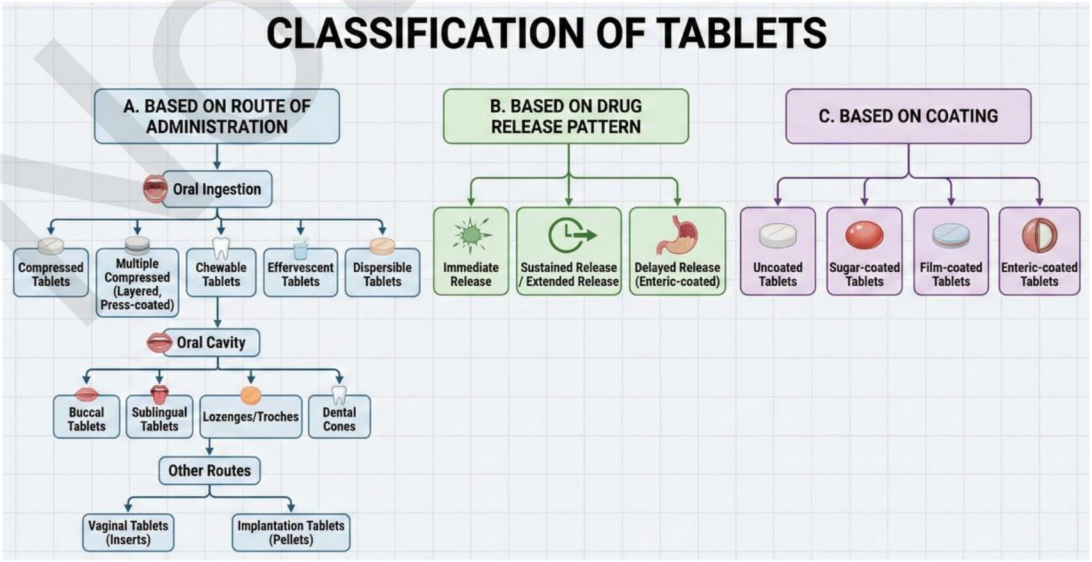
## Introduction:

- Tablets are solid unit dosage forms containing one or more active pharmaceutical ingredients (API) with suitable excipients.
- They are prepared by compression or molding and are the most widely used oral dosage forms due to their convenience, stability, and accuracy of dose.

### Ideal Characteristics of Tablets:

- Accurate and uniform dose of drug
- Sufficient mechanical strength (hardness and low friability)
- Rapid disintegration and dissolution (for conventional tablets)
- Chemical, physical, and microbial stability
- Elegant appearance and smooth surface
- Acceptable taste and odor
- Easy to swallow
- Should not cap, laminate, or crack during handling
- Uniform weight and thickness

### Classification of Tablets:



# Excipients

**Definition:**
Excipients are pharmacologically inactive substances added to the active pharmaceutical ingredient (API) to assist in the manufacturing process or to improve the stability, bioavailability, and patient acceptability of the final product.

Or

Excipients are pharmacologically inactive substances used along with the active drug to give bulk, stability, palatability, and proper manufacturing characteristics to tablets.

**Uses:**

- To give required size and shape to tablets
- To improve flow and compressibility
- To enhance stability of drug
- To improve taste, color, and appearance
- To control drug release and disintegration

**Ideal Characteristics of Excipients:**

- Chemically and physically stable
- Non-toxic and non-irritant
- Compatible with the drug
- Economical and easily available
- Should not interfere with drug action

**Advantages:**

- Improve manufacturability
- Improve patient acceptability
- Enhance tablet stability
- Ensure dose uniformity

**Disadvantages:**

- Possible drug–excipient incompatibility
- May cause allergic reactions in some patients
- Increase formulation cost

# Formulation of Tablets

**Definition:**
Formulation of tablets is the systematic process of selecting suitable drug substance, excipients, and manufacturing method to prepare tablets that are stable, effective, safe, and acceptable to patients.

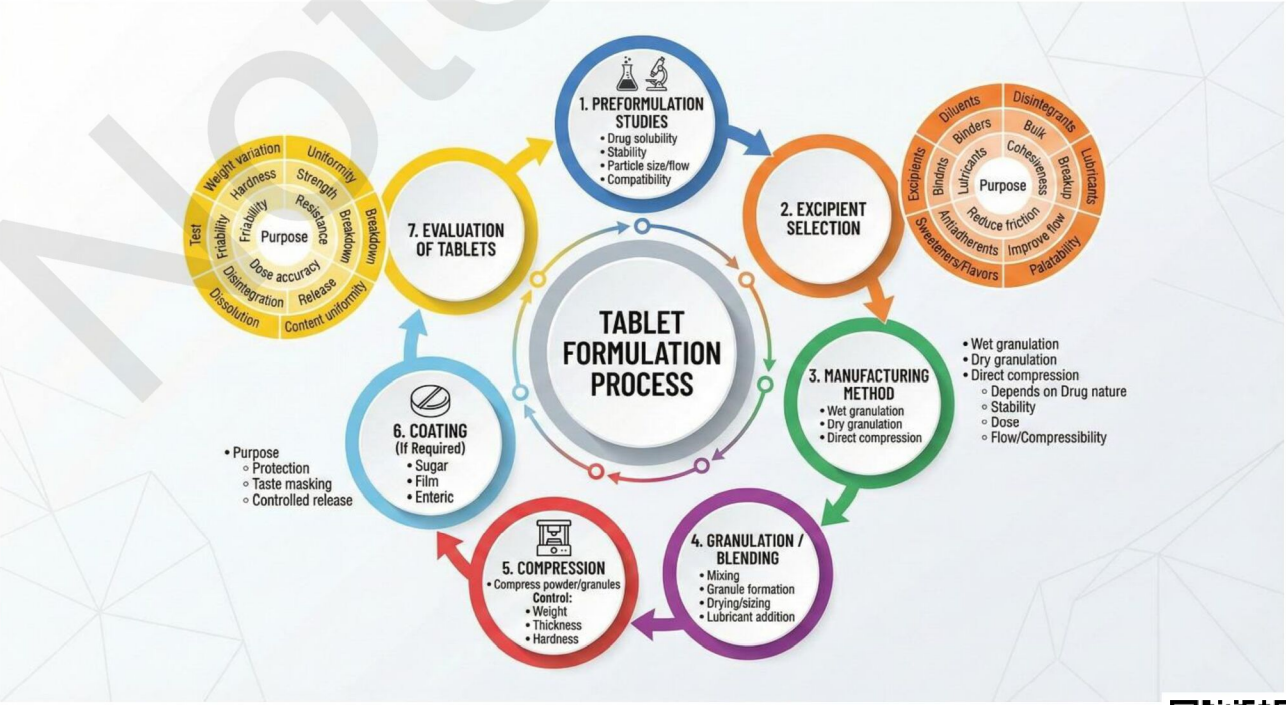
### Objectives of Tablet Formulation

- To deliver accurate and uniform dose
- To ensure chemical and physical stability of drug
- To provide desired drug release profile
- To achieve good hardness, friability, and disintegration
- To make tablets elegant and acceptable

## Ideal Characteristics of a Tablet Formulation

- Uniform weight and content
- Adequate mechanical strength
- Rapid and uniform disintegration (for conventional tablets)
- Good dissolution rate
- Stability during storage
- No interaction between drug and excipients

## Steps in Formulation of Tablets



1. **Preformulation Studies**
    - Drug solubility
    - Stability
    - Particle size and flow properties
    - Drug–excipient compatibility
2. **Selection of Excipients**

| Excipients | Purpose |
|---|---|
| **Diluents** | Increase bulk |
| **Binders** | Provide cohesiveness |
| **Disintegrants** | Break tablet into particles |
| **Lubricants** | Reduce friction |
| **Glidants** | Improve flow |
| **Antiadherents** | Prevent sticking |
| **Sweeteners/Flavors** | Improve palatability |

3. **Selection of Manufacturing Method**

- Wet granulation
- Dry granulation
- Direct compression

**Depends on:**

- Nature of drug
- Stability
- Dose size
- Flow and compressibility

4. **Granulation / Blending**

- Mixing of drug and excipients
- Granule formation (if required)
- Drying and size reduction
- Addition of lubricants

5. **Compression**

- Powder/granules are compressed into tablets
- Control of:
    - Weight
    - Thickness
    - Hardness

6. **Coating (if required)**

- Sugar coating
- Film coating
- Enteric coating

**Purpose:**

- Protection of drug
- Taste masking
- Controlled release

7. **Evaluation of Tablets**

| Test | Purpose |
|---|---|
| Weight variation | Uniformity |
| Hardness | Mechanical strength |
| Friability | Resistance to abrasion |
| Disintegration | Breakdown time |
| Dissolution | Drug release |
| Content uniformity | Dose accuracy |

**Advantages of Proper Tablet Formulation**

- Accurate dosing
- Better therapeutic effect
- Improved stability
- Patient convenience
- Large-scale manufacturing

**Disadvantages / Limitations**

- Time-consuming development
- High cost of equipment
- Risk of processing problems (capping, sticking, lamination)
- Requires skilled formulation development



# Granulation Methods

**Definition:**
Granulation is the process of converting fine powders into free-flowing granules suitable for compression.

**Types:**

**A. Wet Granulation**
Uses:

- For drugs with poor compressibility
  Advantages:
- Good content uniformity
- Strong tablets
  Disadvantages:
- Time consuming
- Not suitable for moisture/heat sensitive drugs

**B. Dry Granulation**
Uses:

- For moisture and heat sensitive drugs
  Advantages:
- No use of liquid
- Fewer steps
  Disadvantages:
- Less uniformity for low-dose drugs

**C. Direct Compression**
Uses:

- When powders have good flow and compressibility
  Advantages:
- Simple and economical
- Fewer processing steps
  Disadvantages:
- Limited choice of excipients
- Risk of segregation

## Processing Problems in Tablets

**Definition:**
Processing problems are defects that occur during manufacturing, compression, or handling of tablets, which affect their quality, appearance, and performance.

| Problem | Definition | Causes | Remedies |
|---|---|---|---|
| Capping | Partial or complete separation of the top or bottom of tablet | Air entrapment, low binder, high speed | Increase binder, reduce compression speed |
| Lamination | Tablet splits into layers | Excess compression, air entrapment | Reduce pressure, improve granulation |
| Sticking | Tablet material sticks to punches | Moist granules, insufficient lubricant | Dry granules, add lubricant |
| Picking | Material removed from tablet surface by punch | Rough punch surface, sticky granules | Polish punches, add antiadherent |
| Chipping | Breaking of tablet edges | Low hardness, worn tooling | Increase compression force |
| Mottling | Uneven color distribution | Improper mixing, dye migration | Improve mixing, use pigments |
| Cracking | Small cracks on tablet surface | Large granules, rapid drying | Reduce granule size, control drying |
| Double impression | Duplicate logo on tablet | Free rotation of punches | Use anti-turning devices |
| Weight variation | Unequal tablet weights | Poor flow of granules | Improve flow, proper granulation |
| Hardness variation | Uneven tablet strength | Uneven compression force | Machine calibration |

## Equipment Used in Tablet Manufacturing

Equipment are machines used for different stages of tablet production, from mixing to evaluation.

### Major Equipment and Their Uses

| Equipment | Use |
|---|---|
| **Rapid Mixer Granulator (RMG)** | Mixing and wet granulation |
| **Fluidized Bed Dryer (FBD)** | Drying of wet granules |
| **Multi-mill / Co-mill** | Size reduction |
| **Double Cone Blender** | Mixing of powders |
| **Tablet Compression Machine** | Compression of tablets |
| **Coating Pan / Auto Coater** | Tablet coating |
| **Hardness Tester** | Measures hardness |
| **Friabilator** | Measures friability |
| **Disintegration Test Apparatus** | Measures disintegration time |
| **Dissolution Apparatus** | Measures drug release |

### Advantages of Equipment:

- High production rate
- Consistent quality
- Automation possible

### Disadvantages:

- High initial cost
- Needs skilled operation
- Maintenance required

## Tablet Tooling

**Definition:**
Tablet tooling refers to the punches and dies used in tablet compression machines to shape tablets.

### Components of Tooling

- Upper punch
- Lower punch
- Die

### Types of Tooling

- **B tooling** – Common, medium-sized tablets
- **D tooling** – For large tablets

### Uses

- Determines tablet size, shape, and embossing
- Controls tablet thickness and weight

### Advantages

- Uniform tablet production
- High manufacturing efficiency

### Disadvantages

- Wear and tear of punches and dies
- Expensive replacement
- Requires regular maintenance

**Tablet coating:** Types of coating, coating materials, formulation of coating composition, methods of coating, equipment employed and defects in coating.

## Tablet Coating –

### Introduction:

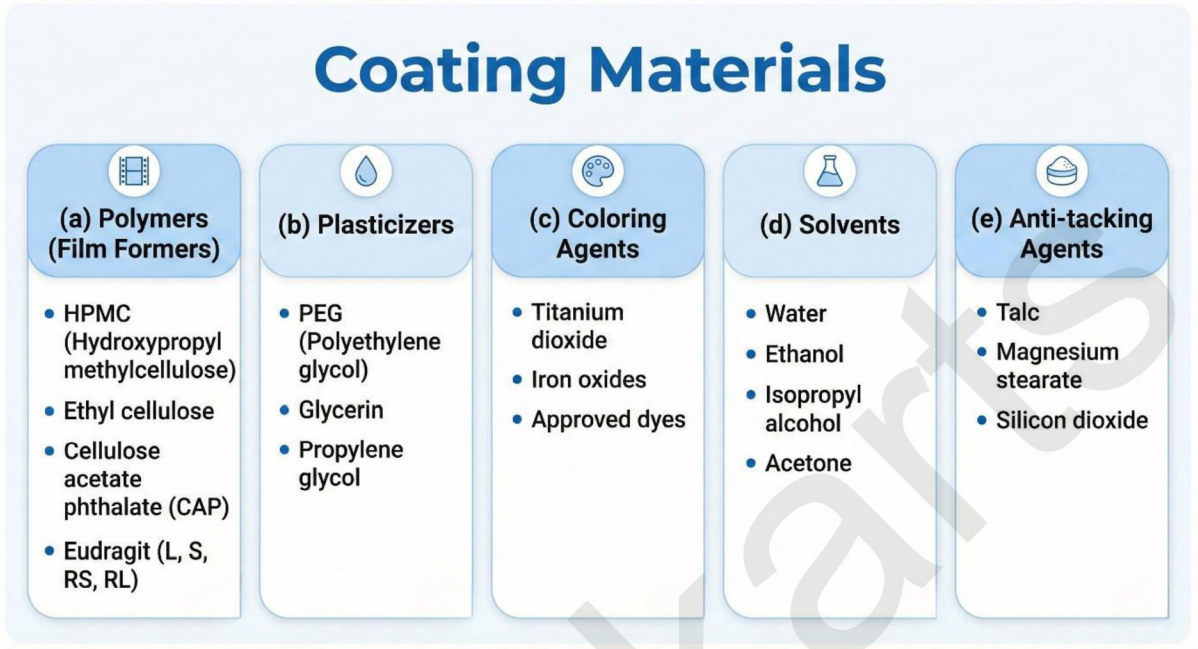
Tablet coating is the process of applying a **thin layer of coating material** on the surface of tablets to:

- Protect the drug from environment
- Mask unpleasant taste/odor
- Improve appearance & patient compliance
- Control drug release (enteric/controlled)

### Types of Tablet Coating

| Type of Coating | Description | Examples |
|---|---|---|
| **Sugar Coating** | Tablets coated with sugar syrup | Vitamins, lozenges |
| **Film Coating** | Thin polymer film on tablet | Paracetamol, antibiotics |
| **Enteric Coating** | Prevents drug release in stomach | Aspirin, Omeprazole |
| **Controlled / Sustained Release Coating** | Controls rate of drug release | SR tablets |
| **Compression Coating** | Dry coating using compression | Sensitive drugs |

## Coating Materials




### (a) Polymers (Film Formers)

- HPMC (Hydroxypropyl methylcellulose)
- Ethyl cellulose
- Cellulose acetate phthalate (CAP)
- Eudragit (L, S, RS, RL)

### (b) Plasticizers

- PEG (Polyethylene glycol)
- Glycerin
- Propylene glycol

### (c) Coloring Agents

- Titanium dioxide
- Iron oxides
- Approved dyes

### (d) Solvents

- Water
- Ethanol
- Isopropyl alcohol

- Acetone

**(e) Anti-tacking Agents**

- Talc
- Magnesium stearate
- Silicon dioxide

**Formulation of Coating Composition**

**Typical Film Coating Formula**

| S.No | Ingredient | Function |
|---|---|---|
| 1. | Polymer | Forms coating film |
| 2. | Plasticizer | Improves flexibility |
| 3. | Colorant | Provides color |
| 4. | Solvent | Dissolves polymer |
| 5. | Anti-tacking agent | Prevents sticking |

**1. Film-Forming Polymers**

The polymer is the most critical ingredient. It must be soluble in the solvent of choice and capable of forming a continuous, tough, and elegant film.

- **Non-Enteric (Gastric Soluble):** These dissolve quickly in the stomach.
  - **HPMC (Hydroxypropyl Methylcellulose):** The industry standard. It is cheap, flexible, and provides a high-quality finish.
  - **HPC (Hydroxypropyl Cellulose):** Very tacky; often used in combination with other polymers to improve adhesion.
  - **Vinyl Polymers (PVP/Povidone):** Highly water-soluble but can be slightly brittle.
- **Enteric (Gastro-Resistant):** These protect the drug from stomach acid or protect the stomach from irritating drugs. They only dissolve at pH > 5.5.
  - **CAP (Cellulose Acetate Phthalate):** Traditional but requires plasticizers.
  - **Eudragit (Methacrylic acid copolymers):** Highly versatile; different grades allow for release at specific points in the intestine.

**2. Plasticizers**

Without a plasticizer, the polymer film would be like dry glass—it would crack or peel off as the tablet expands or contracts. Plasticizers "soften" the polymer chains.

- **Mechanism:** They reduce the **Glass Transition Temperature ($T_g$)** of the polymer.
- **Common Types:**
  - **Polyols:** Glycerin, Propylene Glycol, Polyethylene Glycols (PEG).
  - **Organic Esters:** Citrate esters (Triethyl citrate), Phthalate esters (Diethyl phthalate).
  - **Oils/Glycerides:** Fractionated coconut oil, Castor oil.

### 3. Colorants and Opacifiers

These are used for brand recognition, aesthetics, and to protect light-sensitive active pharmaceutical ingredients (APIs).

- **Lakes:** These are aluminum salts of FD&C dyes. They are preferred for coating because they are water-insoluble and provide consistent, "non-bleeding" color.
- **Inorganic Pigments:** Iron oxides (Yellow, Red, Black) are very stable and provide excellent opacity.
- **Opacifiers (Titanium Dioxide):** This is a white pigment added to make the coating opaque. It helps hide the color of the tablet core and provides a "blank canvas" for other colors.

### 4. Solvents (The Vehicle)

The solvent carries the ingredients to the tablet surface. Once the spray hits the warm tablet, the solvent must evaporate quickly.

- **Water:** The most common choice. It is safe, non-flammable, and eco-friendly, but it requires more energy (heat) to evaporate.
- **Organic Solvents:** (e.g., Ethanol, Methanol, Isopropyl Alcohol, Methylene Chloride). These evaporate very fast but require specialized "explosion-proof" equipment and solvent recovery systems to prevent environmental damage.

### 5. Miscellaneous Additives

- **Anti-Tack Agents:** (e.g., **Talc** or Magnesium Stearate). These prevent the tablets from sticking to each other ("twinning") during the coating process.
- **Surfactants:** Added to help the coating liquid spread evenly over the tablet surface.
- **Flavoring/Sweeteners:** Used primarily for chewable tablets to mask the bitter taste of the drug.

## Formulation Breakdown Table

| Ingredient Class | Typical Concentration (% w/w) | Purpose |
|---|---|---|
| **Polymer** | 7% – 18% | Forms the actual film |
| **Plasticizer** | 0.5% – 2.0% | Provides flexibility |
| **Colorant/Opacifier** | 0.1% – 1.0% | Appearance and light protection |
| **Solvent/Vehicle** | 80% – 90% | Dissolves/suspends ingredients |

## Methods of Tablet Coating

### (a) Sugar Coating Method

Steps:

1. Sealing
2. Sub-coating
3. Syrup coating
4. Coloring
5. Polishing

### (b) Film Coating Method

- Polymer solution is **sprayed**
- Hot air dries tablets simultaneously

### (c) Enteric Coating Method

- Uses **pH-sensitive polymers**
- Drug released only in intestine

### (d) Compression Coating

- Dry process
- Tablet core surrounded by coating powder

### Equipment Employed in Tablet Coating

| Equipment | Description |
|---|---|
| **Conventional Coating Pan** | Used in sugar coating |
| **Perforated Coating Pan** | Efficient film coating |
| **Fluidized Bed Coater** | Uniform coating |
| **Spray System** | Atomizes coating solution |
| **Hot Air Blower** | Drying tablets |

## Equipment Employed in Tablet Coating

Tablet coating requires specialized equipment to ensure **uniform coating, efficient drying, and defect-free tablets**. The commonly used equipment are explained below in an **exam-oriented** manner.

## 1. Conventional Coating Pan (Standard Pan)


### Description

- Circular, stainless-steel pan mounted on an inclined stand
- Pan rotates while coating solution is poured or sprayed

### Uses

- Mainly for **sugar coating**

### Advantages

- Simple design
- Low cost

### Disadvantages

- Non-uniform coating
- Longer processing time
- High labor requirement

## 2. Perforated Coating Pan

### Description

- Pan has **perforations** for better air flow
- Hot air passes through tablets during coating

### Uses

- Widely used for **film coating**

### Advantages

- Faster drying
- Uniform coating
- Better process control

### Examples

- Accela-Cota
- Hi-Coater

## 3. Fluidized Bed Coater (Air Suspension Coater)

**Description**

- Tablets are suspended in a stream of hot air
- Coating solution is sprayed onto fluidized tablets

**Uses**

- Film coating
- Enteric coating
- Controlled-release coating

**Advantages**

- Highly uniform coating
- Efficient heat transfer

**Disadvantages**

- High equipment cost
- Skilled operation required

## 4. Spray System

**Description**

- Consists of spray guns or nozzles
- Atomizes coating solution into fine droplets

**Function**

- Ensures **uniform distribution** of coating material

**Types**

- Air spray nozzle
- Airless spray nozzle

### 5. Hot Air Drying System

**Description**

- Supplies heated air during coating process

**Function**

- Removes solvent
- Speeds up drying
- Prevents tablet sticking

# Quality control tests: In process and finished product tests.

## Quality control tests:

Quality control (QC) tests are carried out to ensure that tablets are **safe, effective, uniform, and of acceptable quality**. These tests are divided into:

1. **In-Process Quality Control (IPQC) Tests**
2. **Finished Product Quality Control Tests**

### 1. In-Process Quality Control (IPQC) Tests

These tests are performed *during* the manufacturing process (granulation, blending, compression) to monitor the process and prevent defects. If a problem is found here, the machine can be adjusted immediately, saving the batch from being rejected later.

### A. Tests on Granules (Pre-Compression Parameters)

Before the powder/granules are compressed into tablets, their flow properties are checked.

- **Angle of Repose:**
  - **Definition:** The maximum angle possible between the surface of a pile of powder and the horizontal plane.
  - **Purpose:** Measures flowability. Lower angles (<30°) indicate excellent flow; higher angles (>40°) indicate poor flow.
  - **Formula:** $\tan(\theta) = h/r$ (where h is height and r is radius of the pile).
- **Bulk Density & Tapped Density:**
  - Used to determine how much the powder settles.
  - **Carr's Index (Compressibility Index):** Measures the tendency of powder to be compressed.
  - **Hausner's Ratio:** Another measure of flow capability.
- **Moisture Content (LOD - Loss on Drying):**
  - **Purpose:** To ensure granules have enough moisture to bind together but not enough to cause sticking or degradation.
  - **Method:** A sample is weighed, heated to remove moisture, and weighed again.

### B. Tests During Compression (Processing Parameters)

These are checked periodically (e.g., every 15-30 minutes) while the tablet press is running.

- **Thickness & Diameter:**
  - **Importance:** Ensures consistent tablet size for packaging (blister packs) and uniform appearance.
  - **Tool:** Vernier Caliper or Micrometer.
  - **Limit:** usually ± 5% variation is allowed.
- **Hardness (Crushing Strength):**
  - **Definition:** The force required to break a tablet across the diameter.
  - **Importance:** If too soft, it breaks during shipping; if too hard, it may not dissolve in the stomach.
  - **Standard:** Usually 4–8 kg/cm² (varies by tablet size).
  - **Equipment:** Monsanto, Pfizer, or Digital Hardness Testers.

## 2. Finished Product Quality Control (FPQC) Tests

These tests are performed on the final tablets after the batch is completed. They are categorized into **Official (Pharmacopoeial)** and **Non-Official (General)** tests.

### A. General / Non-Official Tests

These are critical for quality but are not always specified in the main monograph of pharmacopoeias (USP/BP/IP).

- **Organoleptic Properties:**
  - **Appearance:** Visual check for capping, lamination, or chipping.
  - **Color:** Must be uniform without mottling (uneven color distribution).
  - **Odor/Taste:** Checks for specific sensory characteristics (e.g., chewable tablets).

- **Friability Test:**
  - **Definition:** Measures the tablet's resistance to abrasion and shock (crumbling) during packaging and transport.
  - **Equipment:** Roche Friabilator.
  - **Procedure:**
    1. Weigh a sample of tablets ($W_{initial}$).
    2. Place them in the drum.
    3. Rotate at 25 RPM for 4 minutes (100 drops).
    4. Dedust and weigh again ($W_{final}$).
  - **Acceptance Limit:** Weight loss should not exceed **1.0%**.

**B. Official Tests (Pharmacopoeial)**

These are mandatory tests described in IP, BP, and USP.

**1. Weight Variation Test**

- **Purpose:** Ensures that each tablet contains the correct amount of drug (assuming the mixture is uniform).
- **Procedure:**
  1. Weigh 20 tablets individually.
  2. Calculate the average weight.
  3. Compare individual weights to the average.
- **IP/BP Limits (Percentage Deviation Allowed):** | Average Weight of Tablet | Maximum % Deviation Allowed | | :--- | :--- | | 80 mg or less | ± 10% | | More than 80 mg to less than 250 mg | ± 7.5% | | 250 mg or more | ± 5% | *(Note: No more than 2 tablets can cross the limit, and none can cross twice the limit.)*

**2. Content Uniformity**

- **Purpose:** Used for potent drugs (low dose) to ensure every tablet has the exact amount of active drug (API), not just the correct weight.

- **Procedure:** 10 tablets are assayed individually. The amount of active ingredient usually must lie within 85%–115% of the label claim.

**3. Disintegration Test (DT)**

- **Definition:** The time required for a tablet to break down into small particles under experimental conditions.
- **Equipment:** Disintegration Apparatus (basket rack assembly moving up and down in a water bath at 37°C).
- **Limits (General):**
  - **Uncoated Tablets:** NMT (Not More Than) 15 minutes.
  - **Coated Tablets:** NMT 60 minutes.
  - **Enteric Coated:** Should *not* disintegrate in acid (2 hrs) but *must* disintegrate in buffer (1 hr).
  - **Dispersible/Soluble:** NMT 3 minutes.

**4. Dissolution Test**

- **Definition:** Measures the rate and extent at which the drug goes into solution (bioavailability indicator). This is more critical than disintegration because a drug must be dissolved to be absorbed.
- **Equipment:**
  - Type 1: Basket Apparatus.
  - Type 2: Paddle Apparatus.
- **Procedure:** A single tablet is placed in a vessel containing buffer at 37°C. Samples are withdrawn at intervals to analyze drug concentration.
- **Acceptance:** Typically, $Q+5\%$ (where Q is the amount specified in the monograph, usually 75-80% dissolved in 30-45 mins).



Noteskarts
MAKING NOTES SIMPLE

## Summary Table for Quick Revision

| Test | Type | Key Limit / Standard |
|---|---|---|
| Angle of Repose | IPQC (Granules) | < 30° is excellent flow |
| LOD (Moisture) | IPQC (Granules) | Depends on product (often 1-3%) |
| Hardness | IPQC/FPQC | 4–8 kg/cm² (typically) |
| Friability | FPQC | NMT 1.0% weight loss |
| Weight Variation | FPQC (Official) | ± 10%, 7.5%, or 5% |
| Disintegration | FPQC (Official) | Uncoated: < 15 mins |
| Dissolution | FPQC (Official) | Measure of bioavailability |

# Liquid orals:

- Formulation and manufacturing consideration of syrups and elixirs suspensions and emulsions; Filling and packaging; evaluation of liquid orals official in Pharmacopoeia.

**Liquid Oral Dosage Forms (Detailed Notes)**

**Liquid orals** are pharmaceutical preparations intended for **oral administration** in liquid form. They are especially useful for **pediatric, geriatric, and dysphagic patients** and for drugs requiring **rapid onset of action**.

**1. Classification of Liquid Orals**

**A. Monophasic Liquid Orals**

(Drug completely dissolved)

- **Syrups**
- **Elixirs**
- **Linctus**
- **Oral drops**
- **Solutions**

**B. Biphasic Liquid Orals**

(Drug dispersed, not dissolved)

- **Suspensions**
- **Emulsions**

**2. Syrups**

**Definition:**
Syrups are **concentrated aqueous solutions of sugar (usually sucrose)** with or without medicaments.

**Ideal Characteristics**

- Clear and transparent
- Pleasant taste
- Free from crystallization

- Microbiologically stable

**Composition**

- Sucrose (60–85%)
- Purified water
- Active drug
- Flavoring & coloring agents
- Preservatives (if needed)

**Advantages**

- Good palatability
- Self-preserving at high sugar concentration

**Disadvantages**

- Not suitable for diabetic patients
- Risk of crystallization

**3. Elixirs**

**Definition:**
Elixirs are **clear, sweetened, flavored hydro-alcoholic solutions** for oral use.

**Composition**

- Alcohol
- Water
- Sweeteners
- Flavoring agents
- Active drug

**Advantages**

- Suitable for alcohol-soluble drugs
- Better chemical stability

**Disadvantages**

- Alcohol content limits pediatric use

### 4. Linctus

**Definition:**
Linctus is a **viscous, sweetened oral liquid** used mainly for **relief of cough**.

**Characteristics**

- Taken in small doses
- Should be swallowed slowly
- Forms soothing film on throat

**Examples**

- Codeine linctus
- Simple linctus

### 5. Oral Drops

**Definition:**
Oral drops are **concentrated liquid preparations** intended to be administered in **small volumes** using a dropper.

**Uses**

- Pediatric medicines
- Vitamins
- Potent drugs

### 6. Suspensions

**Definition:**
Suspensions are **biphasic liquid dosage forms** in which **finely divided insoluble drug particles** are dispersed in a liquid medium.

**Ideal Characteristics**

- Uniform particle size
- Easily redispersible
- No caking

**Components**

- Drug
- Suspending agents (CMC, xanthan gum)

- Wetting agents
- Preservatives
- Vehicle (water)

**Advantages**

- Suitable for insoluble drugs
- Better stability than solutions

**Disadvantages**

- Physical instability
- Sedimentation issues

**7. Emulsions**

**Definition:**
Emulsions are **biphasic liquid preparations** consisting of **two immiscible liquids**, one dispersed in the other using an emulsifying agent.

**Types**

- **Oil-in-water (O/W)** – Oral use
- **Water-in-oil (W/O)** – Rare in oral use

**Components**

- Oil phase
- Aqueous phase
- Emulsifying agent
- Preservatives
- Flavoring agents

**Advantages**

- Masks unpleasant taste of oils
- Improved absorption of lipophilic drugs

**Disadvantages**

- Risk of phase separation
- Requires careful formulation

**Advantages of Liquid orals:**

- **Faster Absorption:** Unlike tablets, liquid orals don't need to disintegrate, so the drug is absorbed more quickly.
- **Flexible Dosing:** Dose can be easily adjusted (e.g., 5 mL vs. 10 mL) based on patient needs.
- **Ease of Administration:** Ideal for patients with **dysphagia** (difficulty swallowing).
- **Uniformity:** In monophasic liquids, the drug is uniformly distributed.

**Disadvantages of Liquid orals:**

- **Stability Issues:** Drugs are generally less stable in liquid form than in solid form (prone to hydrolysis or oxidation).
- **Microbial Growth:** High water content makes them a breeding ground for bacteria and fungi.
- **Taste Masking:** It is much harder to hide the bitter taste of a drug in a liquid than in a coated tablet.
- **Portability:** Bulky to carry and prone to breakage or leakage.

### 1. Syrups (Aqueous Solutions)

Syrups are concentrated, viscous, aqueous preparations of a sugar or sugar substitute.

#### Formulation Considerations

- **Sucrose Concentration:** Traditionally 66.7% w/w (IP) or 85% w/v (USP). This high concentration provides **osmotic preservation**, meaning it inhibits microbial growth by drawing water out of microorganisms.
- **Polyols:** Sorbitol or glycerin are often added to prevent "Cap Locking" (crystallization of sugar in the bottle neck).
- **Inversion:** If heated too high, sucrose breaks down into glucose and fructose (invert sugar). While sweeter, this can make the syrup more prone to fermentation and darkening.

#### Manufacturing Steps

1. **Hot Process:** Sucrose is added to purified water and heated until dissolved. Best for heat-stable components.
2. **Agitation without Heat:** Used for heat-sensitive drugs. It takes longer but prevents sugar inversion.
3. **Percolation:** Water is passed slowly through a bed of crystalline sucrose.
4. **Finishing:** The syrup is strained or filtered, and the volume is adjusted.

### 2. Elixirs (Hydro-alcoholic Solutions)

Elixirs are clear, sweetened, hydro-alcoholic liquids intended for oral use.

#### Formulation Considerations

- **Alcohol Content:** Usually ranges from 5% to 40%. Alcohol acts as a co-solvent to dissolve drugs that aren't water-soluble.
- **Self-Preserving:** Elixirs containing more than 10-12% alcohol usually do not require additional preservatives.
- **Sweeteners:** They use less sugar than syrups (making them less viscous) and often utilize saccharin for extra sweetness.

### Manufacturing Steps

1. **Two-Pot Method:** Dissolve water-soluble ingredients in water and alcohol-soluble ingredients in alcohol.
2. **Mixing:** The **aqueous phase is added to the alcoholic phase** (never the reverse) to maintain the highest possible alcohol concentration during mixing, preventing drug precipitation.
3. **Clarification:** Often filtered using Talc or Siliceous earth to absorb excess oils and ensure a brilliant, clear appearance.

## 3. Suspensions (Biphasic: Solid in Liquid)

Suspensions are used when the drug is insoluble or to mask a bitter taste (since the drug isn't dissolved, it doesn't hit the taste buds as quickly).

### Formulation Considerations

- **Wetting Agents:** Surfactants (like Polysorbates) reduce the interfacial tension so the liquid can "wet" the individual drug particles.
- **Flocculating Agents:** Electrolytes that create "flocs" (loose clusters). While these settle faster, they are easily redistributed with a shake.
- **Suspending Agents:** (e.g., Xanthan gum, CMC) Increase viscosity to slow down the settling rate of particles.

### Manufacturing Steps

1. **Particle Size Reduction:** The drug must be finely micronized (usually via a colloid mill).
2. **Wetting:** The drug powder is mixed with a wetting agent to form a smooth paste.
3. **Dispersion:** The paste is diluted with the vehicle containing the dissolved preservatives and flavors.
4. **Homogenization:** The final mixture is passed through a homogenizer to ensure uniform particle distribution.

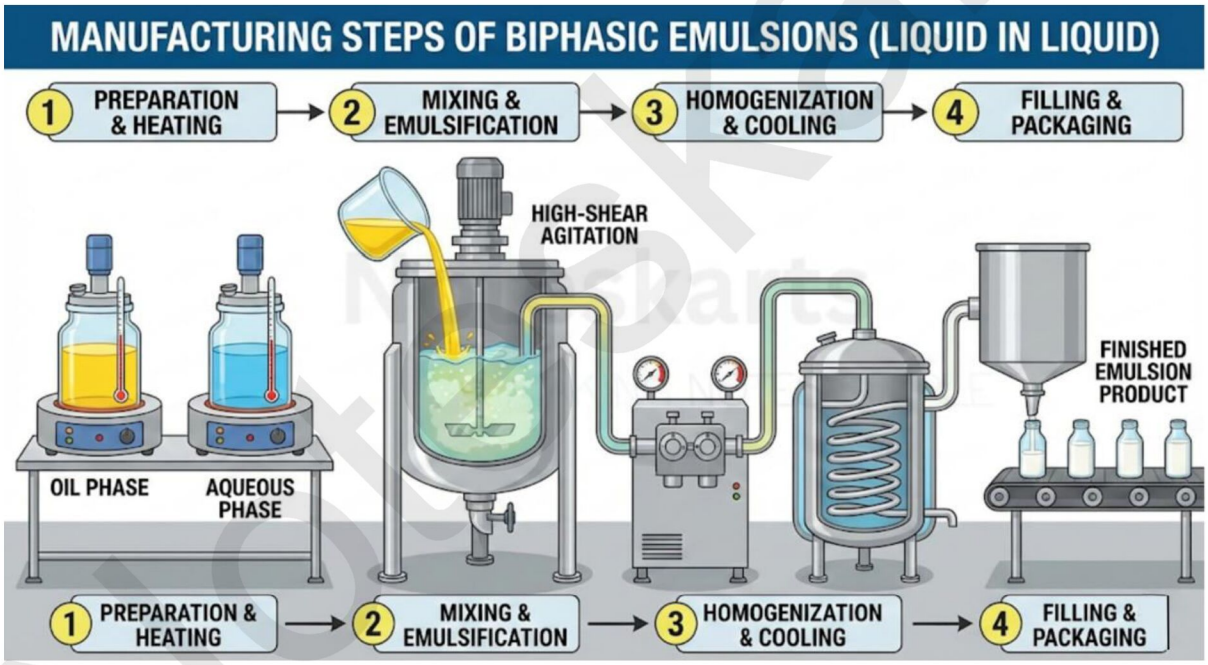
### 4. Emulsions (Biphasic: Liquid in Liquid)

Emulsions consist of two immiscible liquids (Oil and Water) stabilized by an emulsifying agent.

#### Formulation Considerations

- **Emulsifying Agents (Emulgents):** Critical for stability. Examples include Acacia, Tragacanth, or synthetic surfactants (HLB value is key here).
- **Phase Volume Ratio:** Usually, the internal phase makes up 40-60%of the total volume.
- **Antioxidants:** Essential if the oil phase is prone to rancidity.

#### Manufacturing Steps




### 1. Filling and Packaging of Liquid Orals

The filling process must be precise to ensure dose uniformity and prevent contamination.

#### Filling Operations

- **Volumetric Filling:** The most common method. A piston pumps a specific volume of liquid into the container. Highly accurate for thin liquids like elixirs.

- **Level Filling:** Fills the bottle up to a certain height. It looks better on a shelf (uniform levels) but is less accurate if bottle thickness varies.
- **Vacuum Filling:** Used for high-speed lines to prevent foaming and dripping.

**Packaging Components**

- **Containers:** * **Glass:** Type III (soda-lime) or Type I (borosilicate). Amber glass is used for light-sensitive drugs.
    - **Plastic:** PET or HDPE are popular for being lightweight and shatterproof.
- **Closures (Caps):** Must provide a moisture-proof seal. Child-resistant closures (CRC) are often required for potent liquid medications.
- **Induction Sealing:** A foil seal applied to the bottle rim to ensure the product is tamper-evident.

**II. Evaluation of Liquid Orals (Official in Pharmacopoeia)**

Quality control tests are performed to ensure the liquid oral preparation meets the safety and efficacy standards set by Pharmacopoeias like the **United States Pharmacopeia (USP)**, **British Pharmacopoeia (BP)**, or **Indian Pharmacopoeia (IP)**.

**1. Physical Parameters (General)**

- **Appearance:** Checked for clarity (solutions), homogeneity (emulsions/suspensions), color, and odor.
- **pH:** The pH is measured using a pH meter to ensuring it remains within the stability range of the drug.
- **Viscosity:** Measured using a viscometer (e.g., Brookfield). Crucial for "pourability" and the physical stability of emulsions/suspensions.
- **Specific Gravity/Density:** Measured using a pycnometer or hydrometer to ensure the correct concentration of solids/solvents.

**2. Official Pharmacopoeial Tests**

These are the mandatory tests specified in the monographs.

| Test Parameter | Description & Standard |
|---|---|
| **Deliverable Volume (USP <698>)** | Ensures the user can actually pour out the labeled amount from the bottle. |

| Test Parameter | Description & Standard |
|---|---|
| *or*<br><br>**Uniformity of Volume (BP/IP)** | **Method:** A random sample of containers (usually 10-30) is emptied, and the volume is measured.<br>**Acceptance:** The average volume must not be less than the labeled volume (e.g., 100% of label claim). |
| **Microbial Limit Test (MLT)** | Checks for the total count of bacteria and fungi and the absence of specific pathogens (e.g., *E. coli*, *Salmonella*).<br>Mandatory for aqueous preparations prone to microbial growth. |
| **Assay (Content Estimation)** | Determines the exact amount of active pharmaceutical ingredient (API) present.<br>**Method:** HPLC, UV-Spectroscopy, or Titration.<br>**Limit:** Typically **90% – 110%** of the labeled amount. |
| **Alcohol Content** | If the formulation contains ethanol (e.g., elixirs, tinctures), the percentage of alcohol is determined, usually by gas chromatography or distillation. |
| **Antimicrobial Preservative Effectiveness** | If a preservative is added, the formulation is challenged with specific microorganisms to ensure the preservative can prevent growth over time (Challenge Test). |

### 3. Specific Tests for Biphasic Liquids

If the liquid oral is an **Emulsion** or **Suspension**, additional tests are required:

- **Sedimentation Volume (F):** For suspensions, measures how quickly particles settle and how easily they redisperse.

- **Globule Size Analysis:** For emulsions, ensures oil droplets remain small enough to prevent coalescence (separation).
- **Zeta Potential:** Measures the electrical charge on particles/globules to predict long-term stability (higher charge = better stability).