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INDUSTRIAL PHARMACY - I

UNIT 2

TOPIC :

- **Tablets :**

  a. Introduction, ideal characteristics of tablets, classification of tablets. Excipients, Formulation of tablets, granulation methods, compression and processing problems. Equipments and tablet tooling.

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

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

Tablets

- Tablets are solid unit dosage forms containing one or more medicaments, usually in combination with excipients.
- They are prepared by compression or molding methods.
- Each tablet is designed to deliver a precise amount of drug to the patient.
- Tablets are the most widely used dosage form due to their accuracy, convenience, stability, and cost-effectiveness.

Definition:

- A tablet is a solid pharmaceutical dosage form containing medicaments with or without excipients and prepared by compression or molding.

Advantages of Tablets

- Accurate dosage – each tablet contains a fixed quantity of drug.
- Convenient and portable.
- High stability compared to liquid forms.
- Easy to administer and handle.
- Mask unpleasant taste and odor by coating.
- Economical to manufacture and transport.
- Controlled release possible with modified formulations.

Disadvantages

- Difficult for children and unconscious patients to swallow.
- Drug absorption may be slower than liquids.
- Not suitable for drugs with poor compressibility or instability to heat/moisture.
- Inflexible dosing (cannot divide easily for all types).

Ideal Characteristics of Tablets

An ideal tablet should possess the following properties:

Characteristic	Description
Appearance	Elegant, smooth, uniform in color and shape.
Size and Weight	Consistent and easy to handle.
Hardness	Sufficient to resist mechanical shock during handling.
Friability	Should not break or crumble under stress.
Disintegration	Should disintegrate within a specified time (usually within 15 min for uncoated tablets).
Dissolution	Should release the drug completely in the specified time.
Stability	Maintains potency and integrity during storage.
Bioavailability	Provides reproducible and uniform drug release.

Classification of Tablets

Tablets can be classified based on route of administration, method of manufacture, and function.

A. Based on Route of Administration

1. Oral Tablets:
    - Compressed tablets: Swallowed whole (e.g., Paracetamol tablet).
    - Chewable tablets: Chewed before swallowing (e.g., Antacid tablets).
    - Sublingual tablets: Placed under the tongue for rapid absorption (e.g., Nitroglycerin tablet).
    - Buccal tablets: Placed in buccal pouch for slow absorption (e.g., Testosterone tablet).
    - Effervescent tablets: Release CO_2 in water before ingestion (e.g., Dispirin).
2. Tablets for Other Routes:

- Vaginal tablets (inserts): Dissolve in vaginal fluid (e.g., Clotrimazole).
- Implant tablets: Placed subcutaneously for long-term action (e.g., Leuprolide acetate).

B. Based on Method of Manufacture

1. Compressed tablets – prepared by direct compression or granulation.
2. Molded tablets – prepared by moistening and molding into shape.
3. Freeze-dried tablets (lyophilized) – for rapid dissolution in the mouth.

C. Based on Function

1. Immediate-release tablets – disintegrate quickly for fast action.
2. Modified-release tablets:
   - Enteric-coated tablets – resist gastric acid and dissolve in intestine.
   - Sustained-release / Controlled-release tablets – release drug over prolonged period.
3. Coated tablets:
   - Sugar-coated for taste masking.
   - Film-coated for protection and identification.

Excipients of Tablets

- Excipients are the inert or non-active ingredients added to a tablet formulation along with the active pharmaceutical ingredient (API).
- They perform various technological and biopharmaceutical functions to ensure the efficacy, stability, bioavailability, and manufacturability of the final product.
- A proper selection of excipients is essential for producing a stable, uniform, and acceptable dosage form.

Functions of Excipients

Excipients serve the following important roles:

- Bulk formation (increase tablet size for proper handling and compression)
- Aid in powder flow and compression
- Facilitate tablet disintegration and dissolution
- Improve stability and appearance
- Mask unpleasant taste or odor
- Enhance patient acceptability and compliance

Classification of Tablet Excipients

Class of Excipient	Purpose / Function	Examples
1. Diluents / Fillers	Increase bulk and provide uniform weight	Lactose, Starch, Microcrystalline cellulose, Dicalcium phosphate, Mannitol, Sorbitol
2. Binders / Adhesives	Provide cohesiveness and improve tablet hardness	Starch paste, PVP (polyvinylpyrrolidone), Gelatin, Acacia, HPMC, Sucrose solution
3. Disintegrants	Promote breakup of tablet after administration	Starch, Sodium starch glycolate, Crospovidone, Croscarmellose sodium, Alginates
4. Lubricants	Reduce friction between tablet and die wall during compression	Magnesium stearate, Calcium stearate, Stearic acid, Talc
5. Glidants	Improve flow properties of powder or granules	Colloidal silicon dioxide, Talc, Corn starch
6. Antiadherents	Prevent sticking of granules to punches and dies	Talc, Magnesium stearate
7. Wetting agents	Enhance penetration of dissolution medium	Sodium lauryl sulfate, Tween 80
8. Coloring agents	Give attractive appearance and product identification	FD&C dyes, Iron oxides, Titanium dioxide
9. Flavoring agents	Mask unpleasant taste and odor	Menthol, Peppermint, Vanilla, Fruit essences
10. Sweetening agents	Improve palatability	Sucrose, Mannitol, Aspartame, Saccharin sodium
11. Preservatives	Prevent microbial growth	Parabens (methyl, propyl), Benzoic acid, Sodium benzoate
12. Film formers / Coating agents	Provide aesthetic appeal, protect from moisture, mask taste	HPMC, Shellac, Ethyl cellulose, PEG, Eudragit polymers
13. Buffering	Maintain pH for	Citric acid, Sodium phosphate,

agents	stability	Sodium citrate

Formulation of Tablets

- Tablets are solid unit dosage forms that contain one or more active pharmaceutical ingredients (APIs) along with excipients.
- The process of tablet formulation involves designing a combination of drug and excipients that can be compressed into a stable, effective, and elegant dosage form.
- A successful tablet formulation must ensure:
  - Uniform dose in each tablet
  - Mechanical strength and chemical stability
  - Bioavailability and patient acceptability

Objectives of Tablet Formulation

1. To produce a uniform and reproducible dosage form.
2. To ensure drug stability during processing and storage.
3. To obtain desired disintegration and dissolution characteristics.
4. To produce tablets of acceptable appearance, taste, and size.
5. To optimize manufacturing efficiency and cost-effectiveness.

Basic Components of Tablet Formulation

A tablet formulation generally consists of the following key components:

Component	Function	Examples
Active Ingredient (API)	Therapeutic component responsible for pharmacological effect	Paracetamol, Ibuprofen, Metformin
Diluents / Fillers	Add bulk to make tablets of practical size	Lactose, Dicalcium phosphate, Starch, MCC
Binders / Adhesives	Provide cohesiveness to powders or granules	Starch paste, PVP, HPMC, Gelatin
Disintegrants	Promote tablet breakup after administration	Starch, Crospovidone, Sodium starch glycolate
Lubricants	Reduce friction between die wall and tablet	Magnesium stearate, Stearic acid
Glidants	Improve powder flow	Talc, Colloidal silicon dioxide
Coloring, Flavoring & Sweetening Agents	Enhance appearance and palatability	FD&C dyes, Sucrose, Aspartame

Coating Agents	Protect tablets, mask taste, improve appearance	HPMC, PEG, Shellac, Eudragit

Stages in Formulation of Tablets

→ Formulation development involves selection, optimization, and processing of ingredients.

Step 1: Preformulation Studies

- Conducted to understand physicochemical properties of drug substances.
- Includes:
  - Solubility and pH studies
  - Particle size and shape
  - Hygroscopicity
  - Compatibility with excipients
  - Polymorphism and stability

Purpose: To identify potential formulation and processing problems before full development.

Step 2: Selection of Excipients

- Choose appropriate excipients based on:
  - Dose of drug
  - Desired release profile
  - Compatibility with the drug
  - Manufacturing process (e.g., wet/dry granulation, direct compression)

Step 3: Determination of Manufacturing Method

Three main methods are used for tablet manufacture:

1. Wet Granulation
   - Most common method.
   - Steps: Mixing → Wet massing with binder → Screening → Drying → Lubrication → Compression.
   - Advantages: Good content uniformity, improved compressibility.

- Disadvantages: Time-consuming, not suitable for moisture-sensitive drugs.

2. Dry Granulation (Slugging / Roller compaction)
    - Used when the drug is moisture or heat-sensitive.
    - Steps: Mixing → Slugging or roller compaction → Screening → Lubrication → Compression.
    - Advantages: No heat or moisture.
    - Disadvantages: Produces dusty material and harder tablets.
3. Direct Compression
    - Directly compressible powders are mixed and compressed without granulation.
    - Advantages: Simple, fast, cost-effective.
    - Disadvantages: Requires good flow and compressibility of ingredients.

Step 4: Optimization of Tablet Formulation

- Adjust excipient levels for:
    - Desired hardness and friability
    - Proper disintegration and dissolution
    - Uniform weight and content
- Evaluate compatibility between ingredients.

Step 5: Compression of Tablets

- Using a tablet compression machine with dies and punches.
- Critical parameters during compression:
    - Weight variation
    - Hardness
    - Thickness
    - Disintegration time
    - Friability

Step 6: Coating (if required)

- Purpose: Protection from light/moisture, masking taste, modifying release.
- Types of coatings:
  - Sugar coating
  - Film coating
  - Enteric coating
  - Controlled-release coating

Step 7: Packaging and Storage

- Tablets are packed in blister packs or bottles.
- Packaging protects against:
  - Moisture
  - Light
  - Mechanical shock
- Storage under controlled conditions (e.g., 25°C, 60% RH).

Evaluation of Tablets (Post-Formulation Tests)

Test	Purpose	Limit/Standard
Appearance	Color, odor, shape, size	Should be uniform
Weight Variation	Ensure dose uniformity	±5% for <250 mg tablets
Hardness Test	Measure mechanical strength	4–8 kg/cm²
Friability Test	Measure tablet resistance to abrasion	≤1% weight loss
Disintegration Test	Measure time for tablet breakup	≤15 minutes for uncoated tablets
Dissolution Test	Measure rate of drug release	As per pharmacopeial standards
Content Uniformity	Ensure uniform drug distribution	85–115% of label claim

Factors Affecting Tablet Formulation

- Physicochemical properties of drug (e.g., solubility, stability)

- Type and amount of excipients
- Compression force
- Granule size and moisture content
- Lubricant concentration
- Manufacturing process parameters

Importance of Tablet Formulation

- Ensures therapeutic efficacy and patient compliance
- Improves stability and bioavailability of the drug
- Ensures economical and large-scale production
- Helps in developing modified release formulations (e.g., sustained or controlled release)

Granulation Methods

- Granulation is the process of enlarging powder particles to form granules, which improves flow properties, compressibility, and uniformity for tablet manufacturing.
- The goal of granulation is to produce a uniform mixture that can be compressed into tablets with desired physical and chemical properties.

Objectives of Granulation

- To improve flow properties of powder mix.
- To increase compressibility for tablet formation.
- To prevent segregation of different-sized particles.
- To enhance uniformity of drug distribution.
- To reduce dust generation during processing.
- To improve uniformity of tablet weight and content.

Methods of Granulation

Granulation methods are mainly divided into three types:

A. Wet Granulation Method

➢ A process in which the powder mixture is moistened with a binder solution, screened, dried, and then compressed into tablets.

Steps Involved :

1. Weighing and mixing of drug and excipients.
2. Preparation of binder solution (e.g., starch paste, PVP solution).
3. Wet massing – binder solution is added to powder to form a damp mass.
4. Screening – wet mass is passed through a sieve to form granules.
5. Drying – granules are dried in a tray dryer or fluid bed dryer.
6. Sizing – dried granules are resized by sieving.
7. Lubrication and blending – lubricants, glidants, and disintegrants are added.
8. Compression – final blend is compressed into tablets.

Advantages:

- Produces strong granules and good compressibility.
- Ensures uniform distribution of low-dose drugs.

- Reduces segregation and improves flow.

Disadvantages:

- Time-consuming process.
- Requires more equipment and labor.

B. Dry Granulation Method

➢ The process of compressing powders into large slugs or ribbons, which are then milled and screened into granules — no water or heat is used.

Steps :

1. Mixing of drug and excipients.
2. Slugging (large tablets) or roller compaction to form ribbons.
3. Milling and screening of slugs/ribbons to obtain granules.
4. Addition of lubricant and glidant.
5. Compression into tablets.

Advantages:

- Suitable for heat- and moisture-sensitive drugs.
- Fewer processing steps.

Disadvantages:

- Produces more dust.
- Granules may have poor uniformity.

C. Direct Compression Method

➢ A process in which tablets are produced directly from the powder blend without granulation.

Steps:

1. Mixing of drug with directly compressible excipients.
2. Addition of lubricant and disintegrant.
3. Direct compression into tablets.

Examples of directly compressible excipients:

- Microcrystalline cellulose (MCC)
- Spray-dried lactose

Advantages:

- Simple, fast, and economical.
- Fewer processing steps and less equipment.

Disadvantages:

- Requires excellent flow and compressibility.

- Risk of segregation of ingredients.

Tablet Compression

Principle

➢ Compression involves the reduction in volume of powder by applying pressure through punches in a die cavity to form a tablet.

Compression Stages

1. Filling: Granules enter the die cavity.
2. Metering: Amount of powder is adjusted for uniform tablet weight.
3. Compression: Upper and lower punches press granules together.
4. Ejection: Tablet is pushed out of the die.

Processing Problems in Tablet Manufacture

A. During Granulation

Problem	Cause	Remedy
Over-wetting	Excess binder or moisture	Control binder quantity and drying time
Under-wetting	Insufficient binder	Increase binder or mixing time
Non-uniform granules	Poor mixing or screening	Proper mixing and sieving

B. During Compression

Problem	Description	Cause	Remedy
Capping	Partial or complete separation of top/bottom of tablet	Entrapped air, poor granule binding	Reduce compression speed, optimize binder
Lamination	Tablet splits into layers	Air entrapment, too much lubrication	Reduce compression speed, adjust lubricant
Picking	Material sticks to punch face	Moisture, low melting ingredients	Use anti-adherent like talc, maintain humidity
Sticking	Powder adheres to die wall	Over-wet granules	Proper drying and lubrication
Mottling	Uneven color distribution	Improper mixing, dye migration	Use lake colors, ensure uniform drying
Chipping	Breaking at tablet edges	Low binder, high	Adjust binder and

		friability	compression force
Weight variation	Non-uniform die filling	Poor flow of granules	Improve flow with glidants

Equipment Used in Tablet Manufacturing

A. Mixing Equipment

- Used for blending drug and excipients.
- Double cone blender →

- V-blender
- Ribbon blender

B. Granulation Equipment

Wet granulation:

- Sigma blade mixer →

- High shear mixer-granulator

Dry granulation:

C. Drying Equipment

- Tray dryer →

- Fluid bed dryer (FBD)
- Vacuum dryer

D. Sieving / Milling Equipment

- Multimill →

- Oscillating granulator
- Vibro sifter

E. Compression Equipment

Tablet Compression Machines:

1. Single-punch machine (eccentric press): →

   - Used for lab-scale production.
   - Produces one tablet per cycle.
2. Rotary tablet press:
   - Multiple punches and dies.
   - High-speed production (thousands of tablets per minute).

F. Coating Equipment

- Conventional coating pan
- Perforated pan coater
- Fluid bed coater

Tablet Tooling

Components

1. Dies: Hollow cavity that defines tablet size, shape, and weight.
2. Punches: Upper and lower metallic rods that compress powder.
3. Cam tracks: Control punch movement.
4. Tablet press turret: Holds dies and punches in rotary machines.

Tablet Shape and Identification

- Determined by the die cavity shape and punch face design.
- Punches may contain engraved markings (letters, logos) for identification.

Common Tablet Shapes:

- Round (most common)
- Oval
- Capsule-shaped (oblong)
- Triangular, square (for brand identity)

Tablet Coating

- Tablet coating is the process of applying a thin layer of coating material on the surface of a compressed tablet.
- Objectives of coating:
    1. Mask unpleasant taste or odor.
    2. Protect the tablet from moisture, light, and air.
    3. Improve appearance and patient acceptability.
    4. Facilitate swallowing.
    5. Control drug release (enteric or sustained release).

Types of Tablet Coating

Type	Purpose / Characteristics
Sugar Coating	Traditional coating to mask taste and improve appearance; water-soluble.
Film Coating	Thin polymer layer; protects drug, masks taste, improves stability.
Enteric Coating	Resistant to gastric acid; dissolves in intestine for targeted release.
Compression Coating	Hard tablet layer compressed around core tablet; used for modified release or taste masking.
Functional Coating	Modified release coating (sustained, delayed, or controlled release).

Coating Materials

A. Sugar Coating

- Components:
    1. Syrup: Sucrose solution (60–70%)
    2. Coloring agents: FD&C dyes, natura
    3. Polishing agents: Talc, waxes
    4. Sealing agents: Shellac or cellulose acetate
- Function: Masks taste, provides glossy appearance.

B. Film Coating

- Polymers (film formers):
  - HPMC (Hydroxypropyl methylcellulose)
  - Ethyl cellulose
  - Polyvinyl alcohol (PVA)
- Plasticizers: Improve flexibility of the film
  - Glycerol, PEG, Propylene glycol
- Colorants: FD&C dyes, titanium dioxide
- Solvents: Water (aqueous coating) or organic solvents

C. Enteric Coating

- Polymers resistant to stomach acid:
  - Cellulose acetate phthalate (CAP)
  - Hydroxypropyl methylcellulose phthalate (HPMCP)
  - Methacrylic acid copolymers (Eudragit L/S)

D. Compression Coating

- Powdered excipients with binders are compressed around core tablets.
- Commonly used for taste masking or sequential drug release.

Formulation of Coating Composition

A. Sugar Coating:

1. Sealing solution: Protect core tablet (shellac or cellulose acetate)
2. Sub-coating: Bulk buildup (sugar + binder solution)
3. Smoothing: Surface smoothing with syrup
4. Coloring: Colored syrup or dye solution
5. Polishing: Talc or wax to produce glossy finish

B. Film Coating:

- Polymer (3–8%) + Plasticizer (0.5–2%) + Colorant (if needed) + Solvent

C. Enteric Coating:

- Enteric polymer dissolved in suitable solvent
- May include plasticizers and pigments

Methods of Coating

A. Sugar Coating Method

1. Sealing of core tablets (prevents moisture penetration)
2. Sub-coating (multiple layers of sugar-binder mixture)
3. Smoothing (rounds tablets, eliminates irregularities)
4. Coloring (spray colored syrup)
5. Polishing (talc or wax for gloss)

B. Film Coating Method

1. Prepare coating solution (polymer + plasticizer + solvent)
2. Spray over rotating tablets in coating pan or fluidized bed
3. Dry with warm air simultaneously
4. Achieve uniform film thickness (typically 2–4% weight gain)

C. Enteric Coating Method

- Similar to film coating but requires acid-resistant polymers
- Used for gastric-resistant drug delivery

D. Compression Coating Method

1. Place portion of coating powder in die
2. Place core tablet in center
3. Add remaining coating powder
4. Compress to form coated tablet

Equipment Employed

Equipment	Purpose
Coating pan (standard/tilting)	Rotate tablets for coating; traditional method
Perforated coating pan	Improved drying and coating efficiency
Fluidized bed coater	Spray coating in fluidized tablet bed; uniform and faster drying
Spray nozzles	Apply coating solution evenly
Hot air system	Dry coating solution rapidly

Compression tablet press	For compression coating method

Defects in Tablet Coating and Remedies

Defect	Description	Cause	Remedy
Picking / Peeling	Coating sticks to punches or flakes off	Over-wetting, high humidity	Adjust binder, reduce moisture, improve drying
Blistering / Blistering	Bubble formation under coating	Air or moisture trapped	Reduce pan speed, proper drying
Cracking / Capping	Film cracks or core splits	Excessive tablet expansion	Use plasticizers, optimize coating thickness
Orange peel effect	Rough surface of coated tablet	High spray rate, low pan speed	Optimize spray rate, pan speed, solvent
Sticking / Twinning	Tablets adhere together	Insufficient drying, sticky core	Increase drying, use anti-adherent (talc)
Color variation / Mottling	Uneven coloring	Non-uniform mixing, dye migration	Pre-mix color, adjust pigment concentration
Chipping	Small pieces break off	Poor tablet hardness or compression	Improve core hardness, reduce mechanical stress

Quality Control Tests of Tablets

- Quality Control (QC) ensures that tablets meet pharmacopoeial specifications for safety, efficacy, and stability.
- QC testing is performed at two stages:
  1. In-process (during manufacturing)
  2. Finished product (after tablet compression and coating)
- QC tests are essential for dose uniformity, mechanical strength, drug release, and appearance.

In-Process Quality Control Tests

These tests are conducted during tablet manufacturing to ensure that compression and granulation processes are under control.

Test	Purpose	Method / Specification
Weight Variation (during compression)	Ensure each tablet contains uniform drug amount	Randomly select 20 tablets, weigh individually, calculate % deviation (USP/ IP limits: ±5% for <250 mg, ±7.5% for 250–324 mg, ±10% for >324 mg)
Granule Flow Property	Ensures uniform die filling and compression	Measure angle of repose, Carr's index, Hausner ratio
Granule Moisture Content	Prevent capping, sticking, or lamination	Use Loss on drying (LOD) method; optimize drying
Particle Size Distribution of Granules	Uniformity for flow and compression	Sieve analysis; uniform granule size prevents segregation
Blend Uniformity	Ensure homogenous mixing of drug and excipients	Collect samples from different parts of blender; assay for API content
Lubrication Uniformity	Prevent ejection problems and	Blend thoroughly and check sample tablets for hardness/friability

	variable hardness	

Finished Product Quality Control Tests

→ After compression (and coating if applied), tablets are subjected to pharmacopoeial tests:

A. Physical Tests

Test	Purpose	Limit / Specification
Appearance	Visual inspection for color, shape, size, uniformity	Tablets should be smooth, uniform, free from cracks, chips, or blemishes
Weight Variation	Check uniformity of drug content indirectly	±5% for <250 mg, ±7.5% for 250–324 mg, ±10% for >324 mg
Thickness	Ensures uniformity and coating uniformity	Measure using a Vernier caliper; ±5% variation
Hardness / Crushing Strength	Evaluate mechanical strength and resistance to handling	Typically 4–8 kg/cm² for uncoated tablets
Friability	Measure tablet resistance to abrasion during handling/packaging	Using Roche friabilator; % weight loss ≤1%
Disintegration Time	Time required for tablet to break into granules	Uncoated: ≤15 min; Coated: ≤60 min; Enteric-coated: no disintegration in 0.1 N HCl for 2 hrs
Content Uniformity / Assay	Ensure each tablet contains correct API amount	85–115% of label claim (USP/IP)
Moisture Content / Loss on Drying	Evaluate hygroscopic drugs and coated tablets	As per pharmacopeial specification

B. Chemical and Biopharmaceutical Tests

Test	Purpose	Specification / Method
Dissolution Test	Evaluate rate and extent of drug release	Using USP dissolution apparatus (I/II); % drug release at specified time
Assay / Content Determination	Determine API potency	UV-Vis, HPLC, or titration method
Uniformity of Dosage Units	Ensures each tablet meets content requirements	10–30 tablets assayed; must comply with pharmacopeial limits
pH of Soluble Tablets	For effervescent or dispersible tablets	Must comply with pharmacopeial pH range
Stability Testing	Evaluate shelf life and storage conditions	Accelerated and long-term stability per ICH guidelines

C. Specialized Tests (for specific types)

Tablet Type	Special QC Test
Enteric-coated tablets	Acid resistance test; disintegration in 0.1 N HCl for 2 hrs, then dissolution in phosphate buffer
Modified-release tablets	In vitro release profile (sustained/controlled release)
Effervescent tablets	CO_2 evolution rate and complete dissolution in water
Chewable tablets	Texture and hardness suitable for chewing; disintegration in saliva simulant