Program	B. Pharmacy
Semester	1st semester
Subject /Course	General Pharmacy (Theory)
Subject/Course ID	BP 102T
Module No.	03
Module Title	Solid Dosage Forms
Course coordinator	Dr. Gurjeet Singh

Learning Outcome of Module-

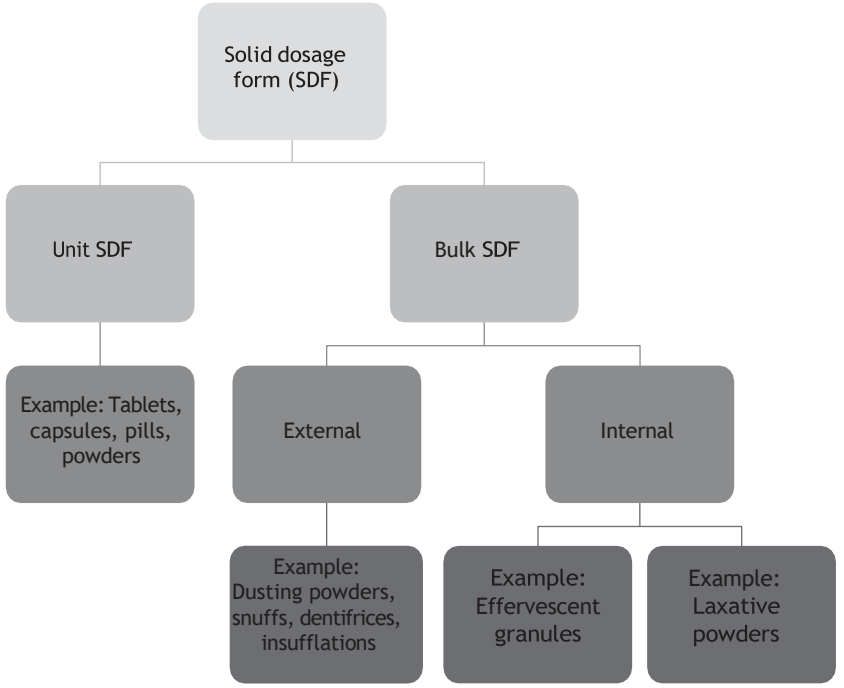
LO	Learning Outcome (LO)	Course Outcome Code
LO1	Classify different types of powders and explain the preparation methods for effervescent, hygroscopic, and eutectic mixtures.	BP102.3
LO2	Define and distinguish between various types of tablets, including molded tablets and pills.	BP102.3
LO3	Evaluate the advantages and disadvantages of capsules compared to other solid oral dosage forms.	BP102.3
LO4	Identify appropriate excipients required for the formulation of stable solid dosage forms.	BP102.3
LO5	Describe the manufacturing processes and standard sizes available for hard and soft gelatin capsules.	BP102.3

Module Content Table

No.	Topic
1.	Powders: Classification, advantages and disadvantages; dusting powders, effervescent powders, efflorescent powders, hygroscopic powders and eutectic mixtures; introduction to excipients and methods of preparation
2.	Tablets: Definition, types of tablets including moulded tablets and pills with examples; advantages and disadvantages; introduction to excipients and methods of preparation.
3.	Capsules: Definition, types of capsules, advantages and disadvantages, capsule sizes; introduction to excipients and methods of preparation.

INTRODUCTION

Solid dosage forms (SDFs) are the drug delivery devices formulated as both single



and bulk dose forms suitable for oral administration. It mainly comprises of tablets, capsules, cachets, pills, powders and granules (Fig.). The oral route offers several advantages such as accurate dosing, physicochemical integrity of the active medicament, elegant appearance, flexibility in formulating the cost- effective formulations with an assured patient compliance. The two most important rate determining steps governing the overall bioavailability of drugs are disintegration and dissolution.

TABLETS

Definition

Tablets are unit SDF each containing a single dose of one or more active medicaments with or without excipients prepared by molding or compression method.

Advantages

1. Enhanced physical and chemical stability when compared to liquid dosage forms.
2. They provide an accurately measured dose and low content variability of the unit dose.
3. Low manufacturing cost.
4. Easy for packaging and shipping.
5. Easy to identify.
6. Manufacturing processes and techniques can provide tablets with special properties. Examples are enteric coating, sustained release and fast dissolving tablets.

Disadvantages

1. Poor bioavailability of poorly soluble drugs or poorly absorbable drugs.
2. Some drugs may cause local Gastrointestinal tract (GIT) irritation effect.

3. Difficulty for swallowing in some patients such as pediatrics and geriatrics.
4. Onset of action is slow in conventional tablets when compared to other dosage forms as it has to undergo disintegration and dissolution before the drug is being released. Exceptions are soluble tablets, dispersible tablets, melt tablets and effervescent tablets.

Classification of Tablets

1. According to drug release rate from the tablet

a) **Immediate release tablet/Fast dissolving tablet:** It is the most common type and includes the following:

(i) Disintegrating tablets
(ii) Chewable tablets
(iii) Sublingual tablets
(iv) Soluble tablets
(v) Effervescent tablets

b) **Modified release tablet:** They have drug release features based on time, course, or location. They must be swallowed intact. They include the following:

(i) Extended release tablet
(ii) Delayed release tablet

1. According to method of manufacture

a) Compressed tablet
b) Molded tablet

2. According to route of administration

a. Oral tablets

(i) Uncoated tablets
(ii) Sugar coated tablets
(iii) Enteric coated tablets

(iv) Non-enteric coated tablets

(v) Sustained release tablets

(vi) Controlled release tablets

(vii) Time release tablets

b. Oral cavity tablets

(i) Buccal tablets

(ii) Sublingual tablets

(iii) Lozenges

(iv) Dental cones

Formulation of Tablets

Compressed tablets usually contain active medicament/s mixed with a number of inert substances known as excipients or additives. These additives are added to give good quality tablets. Although these additives are termed inert, they have great influence on stability, bioavailability and process by which dosage forms are prepared.

According to the activity of the additives in the preparation of tablet they may be classified as follows:

1. **Diluents:** When the dose of drug is very small, it is not practicable to compress such small amount in the form of a tablet, and then the inert substances are added to increase the bulk of the powders to be easily compressible into the tablets.

Example: Lactose, starch, mannitol, calcium carbonate and dicalcium phosphate.

2. **Binders:** The agents used to impart cohesiveness or glue to powdered substances are known as binders. They keep tablet intact after compression. The type of binder depends upon bind- ing force required to form granules and its compatibility with other compounds. The optimum concentration of the binder addition into the tablet formulation is very critical as it is one of the rate limiting

steps for the disintegration, onset of action and bioavailability (Table).

Table: List of Binders, Their Solvents and Their Optimum Concentration

Binder	Solvent	Concentration
Acacia	Water/water-alcohol mixture	2–5%
Tragacanth	Water	1–3%
Acacia	Water/water-alcohol mixture	2–5%
Gelatin	Water	1–4%
Sucrose	Water	2–20%
Starch	Water	1–4%
Sodium carboxymethyl cellulose	Water	1–4%
Ethyl cellulose	Water/water-alcohol mixture	0.5–2%
Polyvinylpyrrolidone	Water/water-alcohol mixture	2–6%

3. Disintegrating agents/Disintegrants: These are the substances added to facilitate the disin- tegration or breaking apart of the tablet into small particles in GIT after administration and facilitating dissolution. Usually disintegrants are added in two steps:

a. **Intragranular disintegrants:** Disintegrants are added during granulation process and it enhances the disintegration of the granules.

b. **Intergranular disintegrants:** Disintegrants are added during the blending or lubrication stage before the compression process to facilitate bursting of the tablet into granules, when it comes in contact with the liquid.

Disintegration mechanism is of the following two types:

(a) Substances that swell up when they come in contact with moisture or solvent.

(b) Substances that react with effervescence when they come in contact with

moisture. *Example:* Maize starch, potato starch, Veegum, methyl cellulose, agar, bentonite, CMC, and sodium starch glycolate, citric acid, tartaric acid with sodium bicarbonate.

4. Lubricants: These are the substances, which are added to granules during blending process to facilitate the easy ejection of tablet from the die cavity after compression.

Example: Magnesium stearate, Calcium stearate, Talc, etc.

5. Glidants: These are the substances, which are added during blending process before compres- sion of tablet for easy flow of granules from hopper into die cavity. They act by reducing the inter particle friction between granules such that flow property is increased.

Example: Silicates and colloidal silica.

6. Anti-adherents: These are the substances used to prevent sticking of tablet surface material to the punches and the tablet die wall. It avoids processing problems of sticking and picking, which occur due to the presence of excess of moisture.

Example: Talc and corn starch. Some more examples are provided in the table below.

Ingredient	**Usual Concentration**	**Glidant Property**	**Anti-adherent**	**Lubricant**
Metallic starch	1% or <	Poor	Good	Excellent
Purified talc	1–5%	Good	Excellent	Poor
Corn starch	5–10%	Excellent	Excellent	Poor
Stearic acid	1–5%	None	Poor	Good
Metallic starch	1% or <	Poor	Good	Excellent

7. Coloring agents: They are used to impart elegance to the tablets. They are also

used to identify the different types of tablets. Only FD&C approved color dyes are used. The colorants should be physically and chemically stable with other excipients, effective in low concentration, pharmacologically inert and should not interfere with the assay procedure of the medicament. *Example:* Frequently used colorants and their common names are mentioned in the table below.

Colorants	**Common Name**
FDC Blue #1	Brilliant blue
FDC Blue #2	Indigo tine
FDC Red #3	Erythromycin
FDC Yellow #5	Tartrazine
FDC Yellow #6	Sunset yellow

8. Flavoring agents: These are the substances usually used to increase the palatability of oral cavity tablets. The choice of the flavoring agent depends on the patient age and type of preparation also. *Example:* Peppermint oil, mango flavor, fruit flavor, chocolate flavor and vanilla flavor.

9. Sweetening agents: They are added to tablets, which are required to be dissolved in buccal cavity and to mask the unpleasant or bitter taste of the drug. The bases for the formulation are already sweet and they impart sweetness of varying degree.

Example: Lactose, sucrose, saccharin, and cyclamates.

Compressed tablets are manufactured by the following two methods:

1. Dry method

a) Direct compression

b) Slugging or double compression

2. Wet method

Dry Method

Direct compression: Most manufacturers agree that direct compression is superior with few steps since it does not require much equipment's and handling expenses as required for wet method of tablet manufacture. The medicaments with large doses having good bulk density, flowability and compressibility can be directly compressed.

There are few crystalline substances such as inorganic salts (e.g. NaCl, KCl, and KBr), which may be compressed directly with very few additives such as lubricants and glidants. However, sometimes these compressed tablets may not disintegrate in the given time limit, and hence, substances such as disintegrating agents are added. The different stages involved are as follows:

1. Milling or size reduction
2. Blending
3. Compression

Advantages

1. Less amount of additives are used in the formulation.
2. Number of steps involved is minimum.
3. Less equipments are used.
4. Less time consuming.

Disadvantage

1. All medicaments cannot be compressed directly.

Requirements for direct compression

1. Dose of medicament or drug should be more.
2. The medicaments should have very good mechanical strength and cohesiveness.
3. Medicament should have very good compressibility and other derived properties such as bulk density, angle of repose, etc.

Slugging or double compression: This method is used for those drugs, which are sensitive to heat, moisture, or both. This method is also called as granulation by compression or double compression method. The various process steps involved are as follows:

1. Size reduction: In this step, the size of the drug is reduced and passed through sifter to get the desired particle size of the drug.

2. **Mixing:** In this step, drug along with additives that are compressible like dicalcium phosphate granules, which are prepared previously are mixed along with glidant and lubricant and punched or compressed into compact masses called slugs by using flat punches using high compression force using multi-station tablet compression machine.

3. **Milling:** In this step, slugs are size reduced by using multi mill and passed through sifter to get the desired granules.

4. **Blending:** The obtained granules are then blended with additives such as disintegrating agents, lubricants and glidants for sufficient period of time using double cone blender.

5. **Compression:** The lubricated granules are finally compressed into tablets of desired weight, hardness, and thickness using multi station tablet compression machine.

Wet Method

The various process steps involved in wet method are as follows:

1. **Sifting/milling:** Weighed ingredients are passed through the desired sieve number such that the drug and the additives are of uniform size and shape.

2. **Dry mixing:** In this process, the drug along with additives such as diluents, disintegrating agents (half the weighed quantity as intragranular disintegrating

agent), and color lakes if present in the formulae are mixed in a suitable mixer for a predetermined time.

3. **Granulation:** In this stage, the powder mixture is converted into granules by adding binder in form of solution and mixed for suitable time period to get a coherent mass or dough mass. The concentration of binder and amount of solution added should be optimized; oth- erwise, the granules obtained may contain large amounts of fines and may be fragile with less concentration of binder or with excess binder the granules obtained may be very hard and sometimes sticky in nature, which may impose problems during compression and disintegration.

4. **Wet sifting:** The dough mass or coherent mass obtained is then passed through a specified sieve to get the desired size wet granules. The sieve number is usually selected based on the weight of the tablet to be compressed. For example, for weights above 500 mg of the tablet weight, the sieve no. selected can be 12, for weights between 200–400 mg, the sieve no. selected can be 16.

5. **Drying:** Wet granules obtained were dried in a suitable dryer for a predetermined period of time and temperature to get the dried granules with the required moisture content.

6. **Regranulation:** Dried granules are then passed through desired sieve number to get the gran- ules as per requirement.

7. **Blending:** In this stage, granules are transferred into a suitable blender such as double cone blender, V-cone blender, and other additives such as lubricants, glidants, anti-adherents and remaining quantity of disintegrating agents (intergranular disintegrating agent) were added and mixed for a suitable time period.

8. **Compression:** The blended granules should be carefully handled and the granules are com- pressed into tablets with predetermined weight, hardness and thickness using suitable punches and dies in a multi-station tablet compression

machine.

Manufacturing Defects in Tablets

During production of tablets, defects arise with finished tablets, which may be due to fault in the for- mulation or in the tableting equipment and sometimes due to both of these reasons. Table 5.2 details few common production problems that arise during manufacturing.

Table: Production Problems with Tablet Quality

Tablet Problems	Possible Causes	Corrective Action
1. Non-uniform tablet weight	1. Feeders starved or choked 2. Granulation lost or gained after proper filling of die 3. Dies not filling 4. Lower punch pulled down before die is filled 5. Wide variation in thickness of lower punch	• Excessive recirculation of granulation • Excessive vacuum pressure, or nozzle improperly located • Check speed or shape of feeder paddle • Inadequate recirculation of granulation • Check that head thickness of lower punches is within ± 0.10 inch of TSM specification
2. Non-uniform tablet thickness	1. Non-uniform tablet weight 2. Non-uniform punch lengths	• Same as above • Check that working length is within ± 0.001 inch of TSM specification
3. Non-uniform tablet density (friability)	1. Non-uniform tablet weight and thickness 2. Low moisture content	• Same as above • Add moisture to aid bonding

Tablet Problems	Possible Causes	Corrective Action
4. Dirt in product (black specks)	1. Dust, dirt, or press lubrication in the granulation	• Clean press more frequently; Use proper punch dust cups
5. Capping and lamination	1. Air entrapment 2. Rapid expansion of tablet upon ejection 3. Weak granulation 4. Excessive dry granulation 5. Punch cavity too deep	• Reduce press speed; Reduce quantity of fine particles; Ensure punch to die clearance is correct • Taper dies • Increase quantity of binder; use strong binder • Increase level of lubricant • Use punches with less concave depth
6. Picking and sticking	1. Excessive moisture 2. Poor embossing design	• Check moisture content of granulation • Check room humidity; Redesign embossing as per TSM guidelines
7. Mottled or marked tablets	1. Contamination by grease, oil, chutes, or feed hoppers 2. High moisture content 3. High drying rate	• Clean and reset components correctly • Re-dry granulation • Optimize drying rate

Tablet Problems	Possible Causes	Corrective Action
8. Chipping or splitting	1. Poor surface finish on punch tips; worn punches/dies 2. Poor tooling design (sharp embossing or bisect line)	• Polish punch tips, replace punches and dies
9. Splitting of layered tablets	1. Excessive pressure 2. Excessive lubrication of granules	• Decrease pressure • Reduce the amount of lubricant
10. Indistinct break line or embossing	1. Incorrect embossing design 2. Worn punch tips 3. Excessively coarse granulation 4. Inadequate binder 5. Picking	• Redesign embossing as per TSM guidelines • Replace punch • Reduce particle size • Increase binder strength • Compress granulation at lower pressure
11. Double impression of embossing	1. Rotation or jerk of punches during compression	• Adjust anti-turning device; Use keyed punches

Some more problems that give rise to defective tablet quality are discussed below:

Binding in the die: During binding in the die, the ejection of tablet is difficult and is accompanied by a characteristic noise. The edges of the tablet become rough. This defect occurs due to poor lubrication of granules, under dried granules and worn out dies.

Capping and lamination of tablets: In capping or splitting, the upper or lower

surface of the tablet is partially or completely separated out from the main body of the tablet. In lamination, the tablet separates out into two or more layers.

Causes: Capping occurs due to the following reasons:

1. Entrapment of air in the granules during compression
2. Presence of excess of fine powder in granules
3. Use of too soft granules leads to capping
4. Wear and tear of punches and dies
5. Incorrect setting of dies and punches

Picking: The surface of tablet material is removed by punches and adheres to the surface of the punches.

Causes: Picking occurs due to the following reasons:

1. Presence of scratches on punches
2. Use of wet granules

Sticking: Granules adhere to the die and lower punches cannot move freely.

Causes: Sticking occurs due to the following reasons:

1. Use of damp granules
2. Worn out dies or punches

Mottling: It occurs in colored tablets. Due to the unequal distribution of color in the tablet, different shades appear on the tablet.

Causes: Mottling occurs due to the following reasons:

1. Difference in color used, drug and the excipient
2. Migration of dyes during drying

Weight variation: This problem arises during filling of granules into die cavity.

Causes: Weight variation occurs due to the following reasons:

1. Poor flow of granules into die cavity
2. Presence of fines in granules
3. Non-uniform separation of granules
4. Improper mixing of lubricants

Hardness variation: Hardness of the tablets varies due to variation in weight of material, pressure applied on upper punches, improper space between upper and lower punches and excessive use of fatty lubricants like magnesium stearate.

Double impression: This occurs in tablets when a monogram is printed during compression.

Cause: The defect may be due to loosening of the punches in the socket grooves.

Quality Control Tests for Tablets

Tablets when formulated may undergo physical and chemical changes thereby altering the bioavailability of the dosage form. The manufactured tablet batches are to be evaluated before dispensing to ascertain stability and bioavailability throughout its shelf life.

Evaluation of tablets can be carried out by the following tests.

Unofficial Tests

Tablet appearance: The tablet appearance is considered as one of the most important factor in evaluation based on the consumer acceptance. It also ensures whether the lot of batch of tablets produced has maintained uniformity in its elegance, which includes color, taste, presence of flavor, identifying marks, surface texture, etc.

Organoleptic parameters: The organoleptic parameters, which are considered in tablets, mainly include its color, taste and odor.

1. **Color of the tablet:** The color distribution within the tablets should be uniform,

and it should not vary from one lot to another. Non-uniform distribution of color within a tablet is known as mottling. Mottling should be avoided as it not only provides a poor appearance to the tablet but also does not give a satisfactory look to the consumer. Hence, color distribution in a tablet is quantitatively evaluated by the following instruments:

(a) Tristimulus calorimetric measurements

(b) Reflectance spectrophotometry

(c) Micro reflectance photometer

2. **Odor of the tablet:** This helps to know whether the tablet has deteriorated thereby stability of the tablet is affected. For example, Aspirin tablet—instability indicated by a characteristic acetic acid odor.

Identification markings on tablet: These include name or symbol of the company and code of the product. These symbols are engraved and printed on the tablet surface, which helps in quick referral of the tablet when searched for identification.

Size and shape of the tablet: Tablets are designed to allow rapid production, to enable good consumer acceptance and also for identification.

Thickness of the tablet: The thickness of the tablet is influenced by the amount of fill material in the die cavity, die diameter and the compaction force applied. Thickness specification is characteristic to each tablet product, but in general the tablet thickness is required to be within □5% of the prescribed values.

Factors affecting tablet thickness

1. The true and bulk density and also the crystalline nature of the raw material influence the tablet thickness.
2. The particle size and size distribution of the granules affect the tablet thickness.
3. The length of both upper and lower punches should be uniform, if not it affects the tablet thickness.

Thickness of the tablet is evaluated by micrometer digital readout sliding caliper scale

method.

Hardness of the tablet: It is also termed as its crushing strength. It may be defined as the compres- sional force required to break or fracture the tablet when such force is applied diametrically. It is influenced by three variables—bonding strength, internal strain and brittleness. It is determined using the instrument Monsanto Hardness Tester or Pfizer Hardness Tester, and expressed with the units kg/cm^2.

Official Tests

Friability test Friability in addition to hardness gives the measure of tablet strength. It is defined as its resistance to shock and abrasion encountered during the process of manufacture, packing, transport and ultimately its usage.

Factors contributing to tablet friability are deep concave punches used during the compression leading to formation of whiskered tablets, high moisture content of the granules, over drying of the granules, etc. It is determined using the instrument Roche friabilator, and the value is calculated using the following equation:

$$Fraibility\% = \frac{Initial\ Weight \times Final\ Weight}{Initial\ Weight} \times 100$$

The batch tablets pass the test for friability, if the value is less than 1%.

Weight variation test: The average weight is determined by randomly selecting 20 tablets and weigh- ing them individually. Not more than two of the individual weights deviate from the average weight by more than the percentage given in the pharmacopeia and none deviates by more than twice that per- centage. IP limits for tablet weight variation are given as follows:

IP/BP	**Limit**
80 mg or less	10%
More than 80 mg and less than 250 mg	7.5%
250 mg or more	5%

Drug content: Thirty tablets are selected randomly. Ten of these tablets are assayed individually. The tablet passes the test if 9 of the 10 tablets contain not less than 85% and not more than 115% of the labeled drug content (±15%) and the 10th tablet may not contain less than 75% and more than 125% of the labeled content (±25%). If these conditions are not met, then the remaining 20 tablets are assayed individually. The batch sample complies with the test if the drug content of not more than 3 individual tablets out of the total 30 sampled tablets is outside the limits by ±15% and none may fall outside of the limits of ±25%.

Disintegration test: This method is used to evaluate the rate of disintegration of SDF of tablets. Disintegration is defined as the breakdown of SDF into small particles after it is ingested. The time of disintegration is a measure of the quality. If the disintegration time is too high, it suggests that the tablet is highly compressed. Also, if the disintegration time is not uniform in a set of samples being analyzed, it indicates batch inconsistency and lack of batch uniformity. The test is performed by ran- domly selecting six tablets using the instrument Disintegration Test Apparatus. Some of the types of dosage forms and their disintegration tests are as follows:

1. **Uncoated tablets:** Tested using distilled water as medium at 37 □ 2 □C at 29–32 cycles per minute. The test is completed if all the tablets disintegrate within 15 minutes. It is acceptable when there is no palpable core at the end of the cycle and if the mass does not stick to the immersion disc.

2. **Coated tablets:** The test procedure given for uncoated tablets is adopted. For film coated tab- lets, the disintegration time limit is 30 minutes and for sugar coated tablets it is 60 minutes.

3. **Enteric coated/Gastric resistant tablets:** The test is carried out first in 0.1 M -HCl (up to 2 hours during which all the tablets should be completely intact followed by replacement with phosphate buffer pH 6.8 for 1 hour during which the tablets

should disintegrate.

Dissolution test: Dissolution is pharmaceutically defined as the rate of mass transfer from a solid surface into the dissolution medium or solvent under standardized conditions of liquid or solid interface, temperature and solvent composition. It is a dynamic property that changes with time and explains the process by which a homogenous mixture of a solid or a liquid can be obtained in a solvent.

Dissolution test can be performed in two ways—*in vitro, in vivo*.

In vivo test is performed in selected animal and human subjects (expensive and time consuming).

In vitro test is performed using dissolution test apparatus (inexpensive and less time consuming).

Factors to be considered for designing *in vitro* dissolution test are as follows:

- Factors related to the dissolution apparatus
- Factors related to dissolution fluid or medium
- Factors related to the test medium

Dissolution test apparatus-1 (basket type): The sample which floats in the test media is placed in a small wire mesh basket attached to the bottom of the shaft connected to a variable speed motor. The basket is immersed in a dissolution medium (as specified in monograph) contained in a 1000 ml flask. The flask is cylindrical with a hemispherical bottom. The flask is maintained at 37□0.5 □C by a constant temperature bath. The motor is adjusted to turn at the specified speed and samples of the fluid are withdrawn at predetermined time intervals to determine the amount of drug in solutions.

Dissolution test apparatus-2 (paddle type): It is same as apparatus-1, except the basket is replaced by a paddle. The dosage form is allowed to sink to the bottom of

the flask before stirring. For dissolution test USP specifies the dissolution test medium and volume, type of apparatus to be used, rpm of the shaft, time limit of the test, and assay procedure for the same. The test tolerance is expressed as a percentage of the labeled amount of drug dissolved in the time limit.

CAPSULES

Definition

Capsules are solid unit dosage form of medicament in which the drug is enclosed in a hard or soft container or shell made of suitable form of gelatin.

Advantages

1. They are attractive in appearance.
2. Drugs with unpleasant odor and taste can be enclosed in the shell.
3. The dose and combination of drug can be altered.
4. They are economical.
5. Ease of administration and portability.
6. Less formulation additives and processing steps when compared to tablets.
7. Disintegration time is lesser when compared to ordinary tablets.

Disadvantages

1. Drugs that are hygroscopic, deliquescent, effervescent or efflorescent are not suitable for filling into capsules.
2. Irritant GIT drugs cannot be formulated in capsule form.
3. They are not tamper proof resistant.

Classification of Capsules

Hard Gelatin Capsule

Manufacture of hard gelatin capsules includes the following steps:

Manufacture of capsule shells

Extraction of gelatin: Gelatin is a heterogeneous product derived by irreversible hydrolytic extraction of treated collagen obtained from animal bones and skin (Fig. 5.2). The properties of gelatin that are to be evaluated are as follows:

1. **Bloom Strength:** It is defined as assessment of cohesive strength of cross-linking taking place in between the molecules of gelatin. It is also known as gel strength of gelatin and depends on the molecular weight of gelatin. The harder the gelatin higher the bloom strength. The weight required to move a standard plunger in to standard 6⅔ %w/v gelatin solution determines the bloom strength of gelatin. Bloom strength must be between 150 and 250 bloom grams.

2. **Viscosity:** Viscosity of gelatin is required to control the thickness of the film, which is meas- ured by standard 6⅔ %w/v gelatin solution maintained at 60 □C. The range of viscosity should be between 30 and 60 millipoise.

3. **Iron content:** Iron is present in both raw gelatin and water used for manufacturing gelatin capsule shells. Excess amount of iron can affect Food drug and cosmetics (FDC) certified dyes and may react with other organic compounds. Iron is used in a concentration not more than 15 ppm.

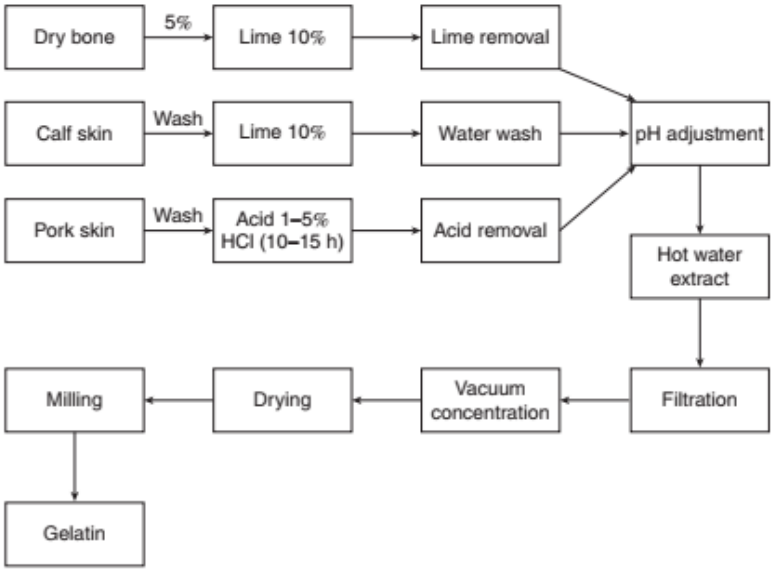


Figure: Schematic Representation for Extraction of Gelatin

Two types of gelatin used are as follows:

1. *Type A gelatin* is derived from acid treated precursor and exhibits an isoelectric point in the region of pH 9.
2. *Type B gelatin* is derived from alkali treated precursor and has an isoelectric point of pH 4.7.

Capsules can be made from either type of gelatin but usually a mixture of both is used. Bone gelatin produces a tough film but it becomes hazy and brittle. However, the pork skin gelatin contributes the plasticity, clarity and elasticity producing a transparent film. Blends of bone and pork skin gelatin of relatively high gel strength are normally used for hard capsule shell production.

Preparation of gelatin solution

1. **Gelatin**—Gelatin extracted of Type A and Type B are used.
2. **Plasticizer**— normally used are glycerin or sorbitol or in combinations. The ratio of gelatin and plasticizer is (0.4:1).
3. **Preservatives**—usually mixture of 0.2% w/v of methyl paraben and propyl paraben are used. Others like sodium sulfite or sodium metabisulpfite can also be used.
4. **Coloring agents**—Various FDC approved dyes and pigments are used.
5. **Opacifying agents**—Titanium dioxide (0.3%) is generally used to make the shell opaque, which is specially used to provide protection against light.
6. **Sugar—**included in the formulation up to 5%, which acts as a sweetening agent and also increases the viscosity of the gelatin solution.
7. **Demineralized water—**used as a vehicle for the gelatin solution preparation.

Processing of capsule shells

1. **Dipping:** The required pairs of stainless steel mould pegs or pins (long length with lesser diam- eter for body and short length with larger diameter for cap) are dipped in gelatin solution for a period of 12 s, which helps in achieving proper

length and thickness of shells.

2. **Spinning:** After dipping, the pins are rotated for uniform distribution of gelatin solution and withdrawn with a blast of cold air.
3. **Drying:** The gelatin coated pins are introduced into the drying chamber and dried at specified temperature and humidity.
4. **Stripping:** After drying, the cap and body portions are stripped off from the pins by using jaws made of bronze.
5. **Trimming:** The body and cap portions are trimmed to required sizes. The trimmed cap and body are joined and capsule shells are sent to sorting section for inspection.

Formulation of the blend

1. **Drug:** Medicament may be single or multicomponent.
2. **Bulking agent/Diluents:** If the dose of the drug is very less and to increase the bulk volume for filling of the capsules as per the size of the capsule shell selected, bulking agent is used. For example, lactose, starch, sucrose, and mannitol.
3. **Disintegrating agent:** To enhance the rate of disintegration of capsules, especially for water insoluble drugs are used. For example, starch, sodium CMC, PVP and sodium starch glycolate.
4. **Glidant and lubricant:** For the easy flow of the powder blend from the hopper in to the body of capsule shell and also for easy ejection of the filled capsule from the capsule filling machine the above ingredients are added. For example, purified talc and magnesium stearate.

Filling, sealing and packing of capsules

Capsules are manufactured as depicted in Figure.

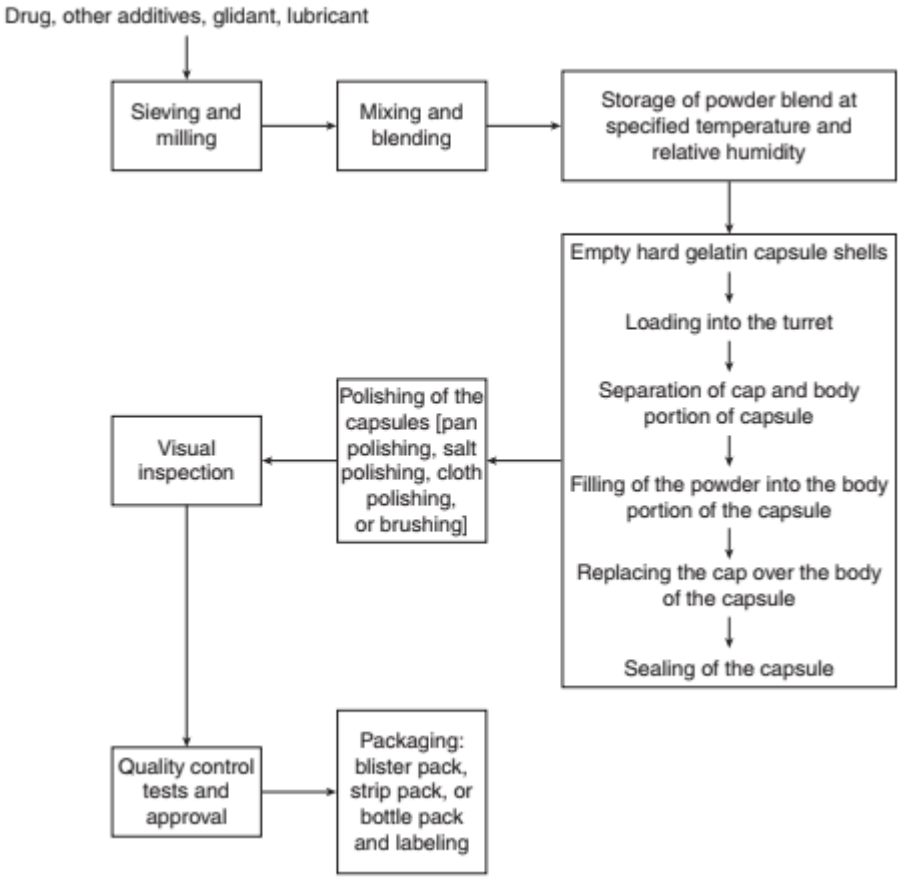


Figure: Process Layout of Capsule Manufacture

Soft Gelatin Capsules

It can be defined as the unit SDF in which the drug is enclosed in a soft shell made up of gelatin. The drug enclosed is usually in the form of solid, liquid or semi-solid.

It is a unit SDF available in various sizes and shapes such as spherical, tubular, oblongated, and ovoid.

Advantages

- It is suitable for solids, liquids, suspension, emulsions, volatile oils, semi-solids, etc.
- Disintegration is faster compared to hard gelatin capsules and tablets.
- Available in various sizes and shapes.
- It can be easily swallowed when compared to hard gelatin capsules.

Disadvantages

- It cannot be used for drugs that are hygroscopic, effervescent and deliquescent in nature.
- It is not suitable for acidic drugs, ketones and aqueous products.
- The drugs that irritate the stomach extremely cannot be given in this dosage form.

Formulation of the capsule shell: The capsule shell is composed of gelatin material, water with higher concentration of plasticizer. It also contains additional ingredients such as preservatives, color- ing agents, opacifying agents, flavoring agents, etc.

Some of the specifications during the manufacturing process are as follows:

1. **Gel strength or bloom strength:** It is measured by using bloom gelometer, which determines the weight in grams required to depress a standard plunger from a fixed dispenser into the surface of a 6-2/3 %w/v of gelatin solution under standard conditions. It measures the cohesive strength of the cross link between gelatin molecules, and it is directly proportional to the molecular weight of the gelatin. The standard range for bloom strength is between 150 and 250 bloom grams.

2. **Viscosity:** 25–45 mps (millipoise).

3. **Iron content:** The iron content of the gelatin used for the manufacture of the soft gelatin capsules should not be more than 15 ppm because of its effects on the color used in the preparation and also possible chemical reaction in the product.

4. **Plasticizer:** Its concentration to that of the gelatin should be in the range of 0.8:1, which renders the shells of elasticity and increases its plasticity. For example, glycerin, sorbitol, or combination.

Formulation of the blend: During the formulation of the blend when a product is determined to be dispensed in the liquid form, then the following two parameters are to be monitored:

1. **Base absorption factor:** Formulation of suspension for gelatin encapsulation, the factor base absorption factor is considered. It can be defined as the number of grams of the liquid base required to produce an encapsulated mixture when mixed with 1 g of the solid drug.

This can be determined by the following formula:

Base absorption factor Weight of the base/Weight of the solid

2. **Minim per gram factor:** It can be defined as the volume in minims occupied by 1 g of the solid drug along with the weight of the liquid base required to form an

encapsulated mixture.

$$M/g = (BA + S)V/W$$

M/*g* = Minim per gram factor

BA= Weight of the base

S= 1 g of the solid

V= Volume occupied by encapsulated mixture

W= Weight of the encapsulated mixture

1 minim= 0.06 ml

Thus, lower the base absorption of the solids, higher will be the density of the mixture and hence smaller will be the size of the capsule shell.

Preservatives: These substances are included to prevent the microbial contamination of the shells as gelatin are obtained from animal source. Usually a combination of methyl paraben and propyl paraben are used.

Coloring agents: FD&C approved color dyes, pigments and lakes are used.

Opacifying agents: Titanium dioxide, aluminum hydroxide, etc.

Drugs: The drug, which is used for the soft gelatin capsules, may be in the form of the solid, liquid, or semi-solid. The volume of the capsule fill may range from 0.3 to 30 ml.

Manufacture of soft gelatin capsules: The manufacture of soft gelatin capsules is done by using rotary die process by form fill and seal (FFS) technique. In this method, the gelatin mass is fed by gravity on to an air cooled rotating drums. Gelatin films of controlled thickness are produced, which may vary from 0.022 to 0.045 inches and the gelatin film passes through the guider and comes in contact with two identical die-rollers, which rotate in opposite direction maintained at controlled temperature so that the gelatin film cavity is formed. The medicament to be capsulated flows by grav- ity into a positive displacement pump, which accurately dispenses the medicament into the gelatin wedge. After filling, by the movement of the rollers, the dies come in contact with each other such that the sealing of the capsules occur. The sealing of the capsules is achieved by mechanical pres- sure applied on the die rollers with the controlled temperature and relative humidity maintained. The sealed capsules are cut uniformly by the cutter and then immediately conveyed through naphtha belt to remove the excess of mineral oil lubricant. Finally, filled capsules are subjected to IR drying to remove the

excess of moisture. Later the capsules are stored at specified temperature and humidity until packaged.

The soft gelatin capsules are usually blister or aluminum seal packed and the bulk package is car- ried out by using airtight plastic or glass container.

Differences between hard gelatin capsule and soft gelatin capsule are shown in Table.

Table: Differences between Hard Gelatin Capsule and Soft Gelatin Capsule

S. No.	Hard Gelatin Capsule	Soft Gelatin Capsule
1.	They are made up of cap and body portions.	They are made as a single entity.
2.	Only solid medicaments can be filled.	Solid, liquid, and semi-solid medicaments can be filled.
3.	Disintegration time is low.	They undergo fast disintegration.
4.	Capsule filled can be opened and sealed	Once opened they cannot be sealed.
5.	Capsule fill weight ranges between 100 and 950mg	Capsule fill volume ranges between 0.3 and 30ml.
6.	Available in only one shape.	Available in various shapes and sizes.
7.	Concentration of plasticizer to gelatin ratio is low (0.4:1)	Concentration of plasticizer to gelatin ratio is more (0.8:1)

Quality Control Tests for Capsules

Uniformity of Weight

This test is only applicable to those capsules that need to comply with the test for uniformity of content of the main active ingredient. Weigh the capsule and open the capsule carefully without any spillage to remove the encapsulated contents completely. For soft gelatin capsules, the shell has to be washed with *ether* or any other suitable solvent and allowing the shell to stand until the odor of the solvent gets completely removed. Weigh the empty shell

again and the difference between the weights is the actual weight of contents. Repeat the procedure for another 19 capsules. Record the average weight. Not more than two of the individual weights (capsules) should deviate from the average weight by more than the specified percentage deviation shown in Table and none of the capsules to deviate by more than twice that percentage.

Table : Official Limits for Uniformity of Weight

Average Weight of Capsule Contents	Percentage Deviation (%)
Less than 300 mg	10
300 mg or more	7.5

Uniformity of Content

The content of active ingredient in each of 10 capsules taken at random is determined according to the method given in the monograph or by following any other relevant analytical method of high accuracy and precision. The capsules pass the test if not more than one of the individual values is outside the specified limits 85–115% percent of the average value and none should be falling outside the limits of 75–125%. If two or three individual capsule values are lying outside the limits of 85–115% of the average values, the determination has to be repeated using another 20 capsules. The capsules comply with the test if from the total sample of 30 capsules, not more than 3 individual values are outside the 85–115% and none is outside the 75–125% limits of the average value.

Diameter Check

This test is carried out using a capsule diameter sorter. The capsules are fed from the hopper into sorter and are allowed to pass into next unit maintained at 0.02 inch above the theoretical diameter of capsule. The equipment is provided with a vibrator so that capsules fit into operator.

Disintegration Test

Hard gelatin capsules: IP uses disintegration test apparatus with 250 ml or 1 L of specified disintegration medium maintained at 37± 2^{O}C and for specified time as per monograph. If 1–2 capsules fail, repeat for another 12 different units. 16 out of 18 capsules indicate that the test is affirmative.

BP uses disintegration test apparatus with water or specified liquid medium. Add a

metal disc to prevent capsule from floating and operate for 30 min or as per monograph. If 1–2 fail, repeat for another 12 different units. Sixteen out of 18 indicate test is affirmative.

Soft gelatin capsules: IP uses disintegration apparatus with 250 ml or 1 L of specified medium at 37

$\pm 2^{O}$ C and for specified time as per monograph. To test for disintegration time, one capsule is placed in each tube and the basket rack is positioned in a 1-L beaker of water, simulated gastric fluid or simulated intestinal fluid at 37± 2^{O}C such that the sample remains 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement. Move the basket containing the capsules up and down through a distance of 5–6 cm at a frequency of 28–32 cycles per minute. If 1–2 fail, repeat for 12 different units. Sixteen out of 18 capsules indicate that the test is affirmative.

United States Pharmacopoeia (USP) procedure is similar to that of uncoated tablets. Place one dosage unit in each of the tubes of the basket with water or any other specified medium (depends on individual monograph) maintained at 37± 2^{O}C. Attach a removable wire cloth with a plain square weave of 1.8–2.2 mm of mesh aperture and a wire diameter of 0.60–0.655 mm to the surface of upper rack of the basket assembly. Observe the capsules for a time limit (specified in individual monograph), at the end of prescribed time, all of the capsules must have been disintegrated excluding the fragments from the capsule shell. No palpable material to remain on the mesh. If 1 or 2 capsules fail, the test should be repeated on additional of 12 capsules. Then, not lesser than 16 of the total 18 capsules tested should disintegrate completely.

Dissolution Test

Place each of the capsules in the apparatus-1 of dissolution tester, excluding air bubbles from the surface of the capsule. Operate immediately at specified rate within specified dissolution medium at 37± 0.5^{O}C. Aliquots should be withdrawn at specified time points or as mentioned in individual monograph and the volume of withdrawn sample should be replaced with the fresh media to maintain the sink conditions. The withdrawn aliquots are suitably diluted and analyzed for the percentage drug release by following reported analytical procedure and instrument.

PILLS

A pill is a small, round and unit solid pharmaceutical oral dosage form that was in use before the advent of tablets and capsules. They are prepared by blending or mixing the active ingredients with selected excipient glucose syrup in a mortar and pestle resulting in a paste, then rolling the resultant mass into a long cylindrical shape (pipe) and dividing it into equal portions. These portions are then rolled into balls and coated with sugar to make them more palatable. In a broad sense even tablet, capsules and caplets are still collectively referred to as "pills."

PASTILLES

Pastilles (also known as troche) are a type of candy or medicinal pill made of a thick liquid that has been solidified and is meant to be consumed by light chewing and allowing it to dissolve in the mouth. They are made by transferring a liquid, which is viscous into a mold with added sugar or wax and then the liquid is allowed to set and dry. The dried liquid substances when chewed slowly release the drugs and dissolve in the mouth. The released liquid is then absorbed by the mucous membrane of the oral cavity. The base of pastilles is usually a mixture of gums such as starch and gum arabic. The gums emulsify the ingredients and fix them in a hydrocolloidal matrix. The presence of gums helps in reducing in the rate at which the pastilles dissolve and controls the concentration of active ingredient delivery at different time intervals. It also helps in making the pastilles physically stable especially during storage and transport.

POWDERS

A powder is a homogenous mixture of more or less finely divided particulate material in dry form. Although the use of powders as a SDF has declined yet they are the starting material in the manufac- ture of many dosage forms. Powders are one of the oldest dosage forms and are used both internally and externally. They impart flexibility (with regard to a wide selection of drugs, combination and dos- age ranges), stability (drugs like aspirin and penicillin are more stable in powdered form than in solu- tion), rapid therapeutic effect (rapid attainment of therapeutic blood levels and rapid absorption from finely divided powders due to large specific surface area), and ease of administration to all categories of patients. However, the preparation of powders is not a suitable dosage form for unpleasant tasting, hygroscopic and deliquescent drugs.

Advantages

1. Powders are more physically and chemically stable when compared to liquid dosage form.
2. The drug product in the powder dosage forms is less prone to microbial contamination.
3. It is an ease mode of drug administration when the dose is very large.
4. It is well accepted by pediatric and geriatric patients.
5. The rate of dissolution and absorption is faster in powder dosage form when compared to any other SDF.

Disadvantages

1. Powders are bulky dosage form and causes difficulty in handling and transport.
2. They are not easily transferrable from a container and may spill.
3. The method of preparation and packaging are time consuming.
4. Drug substances that are having an unpleasant taste are not suitable to administer in powder form.
5. The substances that are hygroscopic, deliquescent, volatile and oxygen sensitive are not suitable to be administered in powder form.

Classification of Powders

The classification of powders is as follows:

1. **Aerosol powders:** Medicated powders that are taken or administered by inhalation with the help of a dry powder inhaler are aerosol powders. The products delivered by this route are intended for the treatment of asthma or bronchial disorders. The particle diameters, which are delivered by this route, are in the range of 1–6 μm. These products also contain inert propellants and pharmaceutical diluents to protect the powder from humidity, to aid in flow property and for the metering uniformity.
2. **Bulk powders:** Medication in bulk powder forms is limited to non-potent substances. Examples of powders taken in the bulk forms are medicated topical anti-infectives such as polymyxin B sulfate, tolnaftate, etc., douche powders for vaginal use such as Massengill powder, reconsti- tuted antacid preparation such as sodium bicarbonate, laxative such as psyllium, etc.
3. **Divided powders:** These are properly blended by using geometric dilution method and then based on the amount to be taken at a single time are divided as single dosing units. The divided powders are packed in small piece of paper folded to enclose the

medication. Examples: Powdered laxatives, douche powder and analgesic powders.

4. **Effervescent powders:** These powders when mixed with water shows effervescence with the liberation of carbon-di-oxide. The effervescence also helps in masking the bitter taste of active ingredients. The usual content of these powders are sodium bicarbonate, organic or inorganic acids such as citric acid, tartaric acid, etc.

5. **Explosive powders:** Substances such as an oxidizing agent and reducing agent when triturated in a mortar and pestle there are chances of explosion, which may occur due to the heat generation and may lead to serious consequences. To handle such type of powders each ingredient should be separately triturated and lightly mixed without applying any pressure. Alternatively the powders can be individually triturated and can be separately packed and dispensed with suit- able directions to the patient regarding its use.

   Some of the oxidizing and reducing agents are listed in Table

Table: List of Oxidizing and Reducing Agents

Oxidizing Agents	Reducing Agents
Potassium chlorate	Charcoal
Potassium dichromate	Sulfur
Potassium nitrate	Sulfides
Potassium permanganate	Tannic acid
Silver nitrate	Tannic acid

6. **Medicated powders for internal use:** These powders are available to be used both internally and externally. Internally used powders are added in water or directly taken internally. Internal medicated powders can also be inhaled for both local such as analgesics and systemic use such as laxatives. Medicated powders taken systemically will have faster rate of dissolution and absorption when compared to any other SDFs. These powders are also available in reconstituted form.

7. **Insufflations:** These powders are usually applied with an applicator known as insufflators. Insufflations are finely divided powder form introduced into different body cavities such as nose, ear, vagina, tooth sockets, etc. When the insufflator is compressed, a current of air distributes the powder particles in a stream of gas through the nozzle into the delivery site. Uniform dose delivery may not be obtained

by insufflations.

8. **Dusting powders:** Dusting powders are used externally for local application, not intended for systemic action. The desirable characteristics of dusting powders are non-irritability, homogeneity, free flow, good spreadability and covering capability, fine state of subdivision, and capacity to protect the skin from chafing and irritation caused by friction, moisture, and chemical irritants. The formulation usually contains substances such as kaolin, talc, zinc oxide, starch, and boric acid. These powders are micronized by passing through sieves #85 or 120. It should be preferably dispensed in sifter-top containers. Such containers provide the protection from air, moisture, and contamination as well as convenience of application. It should contain a label as "FOR EXTERNAL USE ONLY." The categories of drugs dispensed are lubricants, protectives, adsorbents, antiseptics, antipruritics, astringents and antiperspirants. Dusting powders can be classified into the following two types:
   (a) **Medicated dusting powders:** These are the bulk SDFs, which are intended to be applied on the intact skin for local action.
   (b) **Surgical dusting powders:** These are the bulk SDF, which are intended to be applied into the deep layers of the skin. These preparations need to be sterile as it comes in contact with open wounds and deep layers of the skin.
9. **Dentifrices:** Dentifrices are bulk powders for external use to clean teeth. They mainly contain an abrasive agent such as precipitated calcium carbonate or hydrous dibasic calcium phosphate. It also contains a surfactant, mild soap or detergent and sweetening agents.
10. **Douche powders:** These powders are most commonly used for vaginal use and intended for the action of cleansing agents or used as an antiseptic. They may also be used for nasal or ophthalmic route. The main criteria for these preparations are to ensure complete mixing and to maintain the micronized particle size by passing through sieve #85.

Preparation of Powders

1. **Trituration:** In this method, particle size reduction of coarse granular substances or lumps is carried out using a mortar and pestle or mill. Sometimes even dry powder substances are mixed using this method.

2. **Pulverization:** Soft and gummy substances are difficult to powder in mortar and pestle. Such substances are powdered by adding an inert material that helps in powdering and are removed afterwards. A typical example is camphor, which is powdered by moistening in presence of alcohol and after the preparation, alcohol is allowed to evaporate.
3. **Levigation:** In this method, a solvent is added to the dry powder to form a paste. The solvent is known as the levigating agent. The powder-solvent paste is then triturated using mortar and pestle. In the preparation of semi-solid dermatological preparations, ophthalmic ointments and suspensions, this method is used, which prevent the gritty feeling in these formulations. Typical example of levigating agent is liquid Paraffin.
4. **Spatulation:** In this method, the powders are blended in small amount by movement of a spatula on an ointment tile or on a small sheet of paper. The process is only suitable for small quantities of powder. Powders having potent substances or with a large quantity are not blended by this method, because the process does not ascertain a homogenous blending. Solid substances that form eutectic mixtures are suitable for blending with spatulation because compacting of the powders results from these. Examples of substances that can be blended by this method are— camphor, menthol, phenol, thymol, aspirin, etc.
5. **Tumbling:** Special motorized powder blenders are used in this process, whereby the powder is mixed by tumbling in a rotating chamber. The process is time consuming.
6. **Sifter mixing:** Powders are mixed by passing through sifters, which results in light and fluffy products. The process is not suitable for the incorporation of potent drugs into a powder mix.

Incorporation of Ingredients into Powders

In the preparation of powders, some special modifications are followed for incorporation of some of the substances. The modified procedures are as follows:

1. **Hygroscopic and deliquescent powders:** Substances such as sodium bromide, zinc chloride, etc., have strong affinity to absorb moisture from the atmosphere. When the moisture absorption crosses the limits, these substances even liquefy. Such substances are usually used in the granular form rather than powder form to expose

the lower surface area to the atmosphere. These types of powders should be double wrapped.

2. **Volatile substances:** Agents containing volatile oils undergoes volatilization in the atmosphere upon incorporation in the powder. The examples of such agents are camphor, menthol, etc. These agents should be packed by double wrapping with an inner waxed paper and outer bond paper cover by using heat sealed plastic bags.
3. **Eutectic powders:** Substances having low melting point when triturated and mixed together will form a powder blend with low melting point as compared to individual melting points and whose temperature would be less than the room temperature and hence liquify. Examples of eutectic substances are thymol, menthol, camphor, phenol, aspirin, etc. The components of these powders should be dispensed separately with directions like powder of each kind should be taken as a dose. Another alternative method is by addition of double the proportion of an inert high melting point diluent such as magnesium carbonate, light magnesium oxide, kaolin or talc, etc., and mixing together with the eutectic substances without applying pressure.
4. **Efflorescent powders:** Crystalline substances, which liberate water of crystallization when pre- sent, cause a powder to liquefy. Examples of these substances are citric acid, ferrous sulfate, caffeine, etc. Employment of anhydrous salt of these substances is a remedy.
5. **Liquids:** Incorporation of liquids into a powder substance is done by trituration of the liquid (small concentration) with an equal volume of powder and then addition of the remaining pow- der in several portions with trituration.

Granules

Granules are agglomerates of powders. Depending upon the application, various granules of different size can be prepared. The usual size ranges of granules are in the range of 4–12 sieve.

Advantages of Granules

1. They flow better than powders. The easy flow characteristics are important in supplying drug materials from the hopper or feeding container into the die cavities of the tablet compression machine. For this reason, powder mixtures are usually

granulated if they are intended to be compressed into tablets. Granules also eliminate or control dust.

2. They increase compressibility.
3. They have smaller surface area than a comparable volume of powders. This makes granules more stable physically and chemically than the corresponding powders.
4. They are more easily wetted by a solvent than certain powders, so that granules are also preferred in making solutions.

   Example: Ampicillin is unstable in aqueous solution, so it is usually prepared as granules and reconstituted with boiled and cooled water just prior to administration. The granules also contain colorants, flavorants and other pharmaceutical ingredients. So the resulting solution or sus- pension has all the desired medicinal and pharmaceutical features of a liquid pharmaceutical.
5. They produce particle-size uniformity and thus content uniformity.

Particle Size Analysis

Pharmaceutical powder particles range from about 10 mm in diameter to 1 micron or less. Particle size analysis is helpful in the determination of size, shape, distribution of drug and other components used in pharmaceutical formulations. Powder particle size influences a various physical and physiological factors. They are as follows:

1. Content uniformity or dose uniformity of drug substances in sold dosage forms.
2. Size reduction increases specific surface area of the active medicament and hence enhances the rate of dissolution and bioavailability.
3. In suspensions formulation, the particles suspendibility and uniform dispersion of solids in the liquid phase is increased.
4. In aerosol formulation, the drug particle in micronized form penetrate deep into the affected area of the body. Examples are bronchodilators, anti-inflammatory and steroidal drugs.
5. In semi-solid dosage forms such as ointments, creams and ophthalmic preparation, lack of grittiness of solid particles can be monitored.

Methods of particle size analysis

1. **Optical microscopy:** Determination of particle size by this method involves the use of micro- scope fitted with scaled eyepiece micrometer. Particle size ranging from 0.2 to 100 μm can be determined by this method.

2. **Sieving method:** A series of sieves are arranged in descending order of sieve number in a sieve shaker and the accurately weighed powder particles are passed through it. Then the proportion of powder passing through or being withheld on each sieve is determined. Particle size range of about 40–9500 μm can be determined accurately based on the sieve method.

3. **Sedimentation method:** In this method, Andreasen apparatus is used and the terminal settling velocity of particles through a liquid medium in a gravitational or centrifugal environment is determined. Stoke's law is used to calculate the rate of sedimentation. Particle size range of 0.8–300 μm can be determined by this method.

4. **Light scattering or light energy diffraction:** The process of light scattering involves the use of He–Ne laser, ultrasonic probe and silicon photo diode detectors for particle size determination. Range of particle size determined by this method is 0.02–2000 μm.

   Light energy diffraction involves the determination of particle size by the reduction in light reaching the sensor as particles dispersed in a liquid or gas pass through the sensing zone. Range of particle size determined is 0.2–500 μm by this method.

5. **Laser holography:** The method involves individually imaging and sizing of particles by three dimension photography with a holographic camera (in which a pulsed laser is fired through an aerosolized particle spray). The size range of particles determined by this method is 1.4–100 μm.

6. **Cascade impaction:** The principle of this method depends upon that when a particle moves through an airstream, it will hit a surface that comes across its path and the particles are rebounded and separated into different size ranges by increasing the velocity of the airstream in which the particles moves.

   For an exact determination of the size and shape parameter of the powder particles, a com- bination of above methods discussed is preferred. Commercially used particle size analyzers are automated and linked with computers for data processing, distribution analysis and printout.

Packaging of Powders and Granules

1. Depending upon the drug substances present in powders or/and granules the packaging is chosen. Single dose paper packets are used for powders and granules

containing stable drugs.

2. A double wrapped paper packet lined with waxed paper is used for moisture sensitive drugs.
3. A wide mouth airtight glass or plastic containers are used for effervescent or granular sub- stances. It is easy to withdraw the content from a wide mouthed container. Sometimes, a single dose or multiple dose aluminum foil is also used for packaging purposes.
4. Sifter-top packages or pressure aerosol containers are used for dusting powders.

Labeling of Powders and Granules

The following information should be there in the labels of powders and granules:

1. Name of the preparation.
2. Strength of the therapeutic agent present.
3. Directions for use like—dose frequencies for powders and granules to be taken internally, how to apply on the affected part for externally applied powders, etc.
4. It should be mentioned as "For external use only" and "Not to be applied to open wounds or to raw or weeping surfaces," in case of medicated dusting powders.
5. A warning indicating "Keep out of the reach of children."
6. Some legal requirements on the label are—batch number, license number, manufacturing date, expiry date and name of the company.

Storage Conditions

1. A cool and dry place should be chosen for the storage of powders and granules.
2. A light resistant container should be chosen for light sensitive preparation.

Points to be Remember

Powders: Differentiate between types like **dusting, effervescent, and hygroscopic powders**. Pay special attention to **eutectic mixtures**.

Tablets & Pills: Understand the definition and types of tablets (including molded tablets) and their specific advantages/disadvantages.

Capsules: Focus on the different **capsule sizes** and the pros/cons of using capsules versus other solid forms.

Preparation: For all three forms, you must know the general methods of preparation and the role of excipients.

Level 1: Remember (Knowledge)

1. **Which of the following is a type of powder that absorbs moisture from the atmosphere to form a solution?**

    A) Efflorescent powder
    B) Hygroscopic powder
    C) Deliquescent powder
    D) Eutectic mixture **Ans: C**

2. **The term used for powders that release water of crystallization when rubbed together is:**

    A) Efflorescent
    B) Hygroscopic
    C) Dusting powder
    D) Granular **Ans: A**

3. **What is the standard size of a '000' capsule?**

    A) The smallest
    B) The largest
    C) Medium size
    D) Pediatric size **Ans: B**

4. **'Diluents' in tablet formulation are used to:**

    A) Increase the weight and bulk of the tablet
    B) Improve the flow of the powder
    C) Help the tablet break up in the stomach
    D) Provide a shiny coating **Ans: A**

5. **Which of the following is a 'Glidant'?**

    A) Starch
    B) Talc
    C) Lactose
    D) Gelatin **Ans: B**

6. **The main component of a hard gelatin capsule shell is:**

    A) Cellulose
    B) Gelatin
    C) Plasticizer
    D) Sorbitol **Ans: B**

7. **A 'Eutectic mixture' is formed when:**

    A) Two solids liquefy when mixed at room temperature
    B) A solid turns into a gas
    C) Two liquids form a precipitate
    D) A powder catches fire **Ans: A**

8. **Which of the following is an example of a 'Disintegrant'?**

A) Magnesium Stearate
B) Sodium Starch Glycolate
C) Sucrose
D) Acacia **Ans: B**

9. **The process of shifting a powder through a mesh to ensure uniform particle size is:**

A) Trituration
B) Levigation
C) Sifting
D) Spatulation **Ans: C**

10. **Hard gelatin capsules are usually filled with:**

A) Liquids
B) Dry powders or granules
C) Semi-solids
D) Volatile oils **Ans: B**

Level 2: Understand (Comprehension)

11. **Why are 'Enteric-coated' tablets designed to bypass the stomach?**

A) To prevent the drug from being destroyed by gastric acid
B) To prevent gastric irritation
C) To delay the drug action until it reaches the intestine
D) All of the above **Ans: D**

12. **What is the primary function of 'Binders' in tablet manufacturing?**

A) To ensure the tablet breaks down in water
B) To promote adhesion of particles to form granules
C) To make the tablet taste sweet
D) To prevent the tablet from sticking to the punches **Ans: B**

13. **Dusting powders should be 'Impallpable' to prevent:**

A) Excessive absorption
B) Local irritation of the skin
C) Change in skin color
D) Evaporation **Ans: B**

14. **What is the difference between a 'Tablet' and a 'Pill'?**

A) Tablets are compressed; Pills are made by rolling a mass into a sphere
B) Tablets are only for animals; Pills are for humans
C) There is no difference
D) Tablets are always liquid-filled **Ans: A**

15. **How does 'Hygroscopic' powder differ from 'Deliquescent' powder?**

A) Hygroscopic absorbs moisture but remains solid; Deliquescent absorbs enough to dissolve
B) Hygroscopic is for internal use; Deliquescent is for external use
C) Hygroscopic releases water; Deliquescent absorbs it
D) They are the same thing **Ans: A**

Level 3: Apply (Application)

16. **When preparing an 'Effervescent powder', why must the environment be dry?**

    A) To prevent the powder from becoming too heavy
    B) To prevent the premature reaction between acid and base
    C) To keep the pharmacist's hands clean
    D) To speed up the mixing process **Ans: B**

17. **Which capsule size would you select for a dose requiring 200mg of a medium-density powder?**

    A) Size 000
    B) Size 0
    C) Size 4
    D) Size 5 **Ans: B** (Note: Size 0 typically holds ~300-500mg, Size 1 holds ~200-300mg)

18. **A pharmacist is mixing Menthol and Camphor. What technique should be used to prevent liquefaction?**

    A) Mix them vigorously
    B) Add an inert adsorbent like Light Magnesium Carbonate
    C) Mix them in a hot mortar
    D) Add water **Ans: B**

19. **If a tablet is "capped" (the top separates from the body), what should be adjusted?**

    A) Increase the lubricant
    B) Reduce the compression force or check moisture content
    C) Change the color
    D) Add more flavoring **Ans: B**

20. **Which method of preparation is most suitable for a drug that is sensitive to moisture and heat?**

    A) Wet Granulation
    B) Dry Granulation (Slugging)
    C) Direct Compression
    D) Both B and C **Ans: D**

Level 4: Analyze (Analysis)

21. **Analyze the role of 'Plasticizers' (like Sorbitol) in Soft Gelatin Capsules:**

    A) To make the shell hard
    B) To keep the shell flexible and elastic
    C) To act as a preservative
    D) To provide the color **Ans: B**

22. **Compare 'Effervescent granules' and 'Effervescent powders'. Why are granules preferred for use?**

    A) Granules are cheaper
    B) Granules have a smaller surface area and react more slowly/controllably
    C) Powders are too difficult to swallow
    D) Granules are only for vitamins **Ans: B**

23. **Identify the 'Disintegrant' mechanism:**

    A) It coats the drug to prevent it from dissolving
    B) It swells or creates capillary action to break the tablet apart in contact with fluid
    C) It melts at body temperature
    D) It reacts with oxygen to explode the tablet **Ans: B**

24. **In 'Wet Granulation', what is the purpose of the 'Drying' step?**

    A) To remove the flavoring
    B) To remove the granulating liquid (solvent) to achieve stable moisture levels
    C) To kill all bacteria
    D) To make the granules turn white **Ans: B**

25. **Why are 'Lubricants' added at the last stage of mixing before compression?**

    A) Because they are expensive
    B) To prevent them from over-coating the granules and interfering with disintegration
    C) Because they are liquid
    D) To ensure they stay on the outside of the tablet **Ans: B**

Level 5: Evaluate (Evaluation)

26. **Evaluate the advantage of 'Capsules' over 'Tablets' for a drug with a very bitter taste:**

    A) Capsules are easier to make
    B) The gelatin shell provides a physical barrier that masks the taste entirely
    C) Capsules dissolve faster
    D) Tablets cannot be flavored **Ans: B**

27. **Why is 'Direct Compression' considered the most economical method of tablet manufacturing?**

    A) It uses fewer excipients
    B) It involves the fewest processing steps (no granulation or drying)
    C) It requires no machinery
    D) It can be done by hand **Ans: B**

28. **Assess the impact of 'Particle Size' on the bioavailability of a solid dosage form:**

    A) Larger particles dissolve faster
    B) Smaller particles have a higher surface area, leading to faster dissolution and absorption
    C) Particle size has no effect on absorption
    D) Only the color of the particle matters **Ans: B**

29. **Judge the suitability of 'Soft Gelatin Capsules' for delivering liquid oils:**

    A) Poor; liquids will leak out
    B) Excellent; they are specifically designed to hermetically seal liquids
    C) Only if the liquid is water-based
    D) Only for external use **Ans: B**

30. **Evaluate the necessity of 'Sustained-release' tablets for a drug with a very long half-life:**

    A) It is highly necessary

B) It is unnecessary as the drug stays in the body a long time anyway
C) It is used only for marketing
D) It is dangerous **Ans: B**

Level 6: Create (Synthesis)

31. **Propose a formula for an 'Antacid Effervescent Powder':**

A) Sodium Bicarbonate + Citric Acid + Tartaric Acid
B) Starch + Lactose + Talc
C) Gelatin + Glycerin + Water
D) Magnesium Stearate + Menthol **Ans: A**

32. **If you were to design a tablet for a patient who has difficulty swallowing (Dysphagia), which would you choose?**

A) Enteric-coated tablet
B) Effervescent or Mouth-dissolving tablet
C) Large compressed pill
D) Sugar-coated tablet **Ans: B**

33. **Develop a strategy to prevent 'Sticking' during tablet compression:**

A) Increase the binder concentration
B) Increase the lubricant concentration or polish the punches
C) Decrease the compression speed
D) Change the color of the tablet **Ans: B**

34. **How would you formulate a drug that is oily and needs to be given in a solid dosage form?**

A) Compressed into a tablet
B) Absorbed into a powder and filled into a hard capsule
C) Encapsulated in a Soft Gelatin Capsule
D) Both B and C **Ans: D**

35. **Create a quality control test for tablets to ensure they won't break during transport:**

A) Disintegration test
B) Friability test
C) Dissolution test
D) Weight variation test **Ans: B**

Mixed Bloom's Levels (36-50)

36. **Which of the following is used as a 'Plasticizer' in capsules?**

A) Sorbitol
B) Glycerin
C) Propylene Glycol
D) All of the above **Ans: D**

37. **'Lactose' is most commonly used in tablets as a:**

A) Binder
B) Diluent
C) Disintegrant
D) Lubricant **Ans: B**

38. **‘Bloom Strength’ is a parameter used to measure the quality of:**

    A) Tablets
    B) Gelatin
    C) Powders
    D) Syrups **Ans: B**

39. **The ‘Angle of Repose’ is used to determine the:**

    A) Solubility of a drug
    B) Flow properties of a powder
    C) Hardness of a tablet
    D) Melting point **Ans: B**

40. **‘Trituration’ involves:**

    A) Grinding a powder in a mortar with a pestle
    B) Mixing with a spatula
    C) Using a sieve
    D) Boiling the powder **Ans: A**

41. **Which of the following is an ‘Internal’ dusting powder?**

    A) Talc
    B) Kaolin
    C) Effervescent salt
    D) Zinc Oxide **Ans: B**

42. **‘Sub-coating’ in sugar coating is done to:**

    A) Provide a smooth surface
    B) Increase the bulk and round the edges
    C) Add color
    D) Prevent moisture entry **Ans: B**

43. **The ‘IP’ limit for friability of tablets is usually not more than:**

    A) 5%
    B) 1%
    C) 10%
    D) 0.1% **Ans: B**

44. **Which test measures the time required for a tablet to break into small particles?**

    A) Dissolution test
    B) Disintegration test
    C) Hardness test
    D) Friability test **Ans: B**

45. **Soft gelatin capsules are manufactured using the:**

    A) Rotary Die process
    B) Hand filling machine
    C) Punch method
    D) Sifting method **Ans: A**

46. **What is the use of ‘Seal coating’ in tablet coating?**

A) To add flavor
B) To prevent moisture from reaching the tablet core
C) To make the tablet shiny
D) To print the logo **Ans: B**

47. **'Geometrical dilution' is specifically used for mixing:**

A) Large quantities of cheap powders
B) Small quantities of potent drugs with large amounts of diluents
C) Two liquids
D) Powders and oils **Ans: B**

48. **Which of the following is NOT an advantage of Capsules?**

A) Masking unpleasant taste
B) Ease of administration
C) Protection from light
D) Suitability for highly soluble salts (like KCl) **Ans: D** (Highly soluble salts can cause stomach irritation if released too fast from a capsule).

49. **'Sweating' in tablets is a defect related to:**

A) Color migration
B) Moisture absorption in the coating
C) Too much lubricant
D) High compression force **Ans: B**

50. **'Lustre' is provided to tablets during the sugar-coating process by:**

A) Syrup coating
B) Sub-coating
C) Polishing with wax
D) Coloring **Ans: C**

Objective Type (2 Marks - Remember/Understand)

1. Define 'Effervescent Powders'.
2. What are 'Hygroscopic Powders'?
3. Define 'Trituration'.
4. What is a 'Eutectic Mixture'?
5. List two advantages of tablets.
6. What is a 'Moulded Tablet'?
7. Define 'Capsules'.
8. Name two types of capsules.
9. What is a 'Dusting Powder'?
10. Mention one disadvantage of powders as a dosage form.

11. What is the purpose of a lubricant in tablet formulation?
12. Define 'Pills'.
13. What is 'Efflorescent Powder'?
14. State the largest capsule size for human use.
15. What are 'Granules'?
16. Define 'Diluents' in tablet manufacturing.
17. What is a 'Hard Gelatin Capsule'?
18. Give an example of an effervescent salt.
19. Define 'Divided Powders'.
20. What is 'Soft Gelatin Capsule'?

Short Answer (5 Marks - Understand/Apply)

1. Classify powders and explain their advantages and disadvantages.
2. Describe the preparation of Eutectic mixtures.
3. Explain the different types of tablets with examples.
4. Compare Hard Gelatin and Soft Gelatin capsules.
5. Discuss the method of preparation for effervescent powders.
6. Explain the role of various excipients used in tablet manufacturing.
7. Describe the steps involved in the preparation of capsules.
8. Discuss the storage and stability of hygroscopic and deliquescent powders.
9. Explain the classification and use of dusting powders.
10. Describe the advantages and disadvantages of capsules as a dosage form.

Long Answer (10 Marks - Analyze/Create)

1. Discuss in detail the classification and formulation of various types of powders.
2. Explain the manufacturing process of tablets, including common defects and their remedies.
3. Elaborate on the types, sizes, and manufacturing of hard and soft gelatin capsules.
4. Analyze the problems encountered during the dispensing of specialized powders like eutectic and efflorescent powders.

5. Evaluate the role of excipients in the formulation of solid dosage forms.
6. Compare tablets, capsules, and powders in terms of patient compliance and bioavailability.
7. Discuss the formulation and evaluation of effervescent and hygroscopic powders.
8. Analyze the advancements in tablet technology, such as sustained-release and enteric-coated tablets.
9. Detail the various capsule sizes and the criteria for selecting a specific size for a drug.
10. Describe the general methods of preparation and packaging for all solid dosage forms mentioned in the syllabus.

Case-Based Learning (CBL)

Hygroscopic Disaster: A patient leaves their powder paper in a humid bathroom, and it turns into a liquid paste.

Solution: The powder was **hygroscopic or deliquescent**. Patients must be advised to store such powders in air-tight containers in dry areas.

Swallowing Difficulty: An elderly patient is prescribed a large "Size 000" capsule but cannot swallow it.

Solution: Suggest a change to a smaller capsule size (e.g., Size 2) or a different dosage form like a syrup or dispersible tablet.

Eutectic Mixture: A student mixes Menthol and Camphor, and they liquefy.

Solution: This is a **eutectic mixture**. To fix it, the pharmacist should dispense them separately or mix them with an absorbent like light magnesium carbonate.

Problem-Based Learning (PBL)

Effervescent Formulation: Why do effervescent powders fizz?

Solution: The reaction between an organic acid (Citric/Tartaric) and a bicarbonate/carbonate in the presence of water releases CO_2.

Capsule Capacity: You need to fill 500 mg of a dense powder. Which capsule size do you pick?

Solution: Generally, a **Size 0** or **Size 1** depending on the bulk density of the powder.

Tablet Defects: During compression, the top of the tablet separates (Capping). What is the cause?

Solution: Air entrapment or excessive fine powder. Solution: Decrease compression speed or

adjust granulation.