

INDUSTRIAL PHARMACY - I

UNIT 3 NOTES

CAPSULES

- HARD GELATIN CAPSULES
- SOFT GELATIN CAPSULES

PELLETS

- INTRODUCTION
- PELLETIZATION PROCESS
- EQUIPMENTS



NOTES AVAILABLE AT :



WWW.IMPERFECTPHARMACY.IN

CAPSULES

- Capsules are solid dosage forms in which 1 or more active ingredients along with other excipients are enclosed within a hard or soft gel shell, typically made of gelatin or other suitable material
- It is available in variety of shapes, sizes and materials.
- There are two types of capsules
 - ① Hard Gelatin Capsules
 - ② Soft Gelatin Capsules

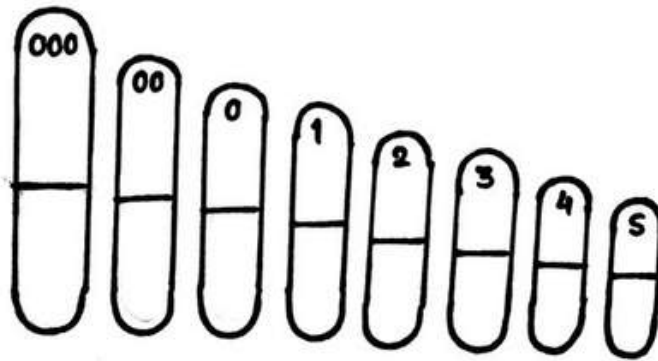
HARD GELATIN CAPSULES

- Hard Gelatin Capsules are type of capsules that consist of a hard, gelatinous shell that encloses a solid or powdered active ingredient
- Hard gelatin capsules consist of two parts :
 - (1) Body
 - (2) Cap
- Body: It is the main part of the capsule that contains the active ingredient.
- Cap: It is the smaller part of the capsule that fits over the body to enclose the active ingredient

Size & Shapes

Hard Gelatin capsule comes in various sizes & shapes including:

- Size: Ranges from 000 (largest) to 5 (smallest)
- Shape: Typically cylindrical or oval.



GELATIN

- Gelatin is a translucent, colorless and flavourless substance derived from collagen, a protein found in animal body parts like skin, bones and connective tissues.
- There are several types of gelatin:
 - (1) Type A: Derived from pig skin
 - (2) Type B: Derived from cow bones & connective tissues.
 - (3) Fish Gelatin: Derived from fish bones & skin

Advantages Of Hard Gelatin Capsules

- Easy to swallow
- Masking unpleasant tastes & odours
- Precise dosing
- Stability & Protection
- Faster drug release
- Patient Acceptability
- Cost Effective

Disadvantages Of Hard Gelatin Capsules

- Not suitable for hygroscopic or highly moisture-sensitive drugs without additional protective measures.
- Incompatibility with certain substances like highly alkaline or highly acidic drugs.
- Gelatin can soften or melt at higher temperatures.
- Slower production rates.

Formulation Of Capsules

Formulating capsules involves a process, where active ingredients, excipients and other necessary components are combined together and ensuring that capsules are stable, effective and easily administrable by the patients.

Key Ingredients

- **Gelatin**: The primary component, derived from animal collagen. It provides structure & flexibility of the capsule shell.
- **Water**: Essential for gelatin solution & maintaining capsule's moisture content
- **Colorants**: Can be used to improve appearance of capsule.
- **Opacifying Agent**: Make the capsule shell opaque, preventing light from affecting the contents
- **Plasticizers**: Improve the flexibility and elasticity of capsule's shell
- **Preservatives**: Inhibit microbial growth and extend capsule's shelf life.

Steps Involved In Formulation Of Hard Gelatin Capsule

Following steps are involved in production of Hard Gelatin Capsule

- Dipping
- Spinning
- Drying
- Stripping
- Trimming
- Joining
- Polishing

• Dipping

Approx 150 pairs of stainless steel moulds pins are dipped in the prepared gelatin solution of controlled viscosity to form caps and bodies simultaneously

• Spinning

The mold pins are rotated so as to provide uniform distribution of gelatin.

• Drying

The gelatin is dried at the blast of cool air to form the hard shell. The pins are moved through air drying, which helps to remove any water content, if present.

- Stripping

A series of bronze jaw strips the cap and body portion of the capsules from mold pins.

- Trimming

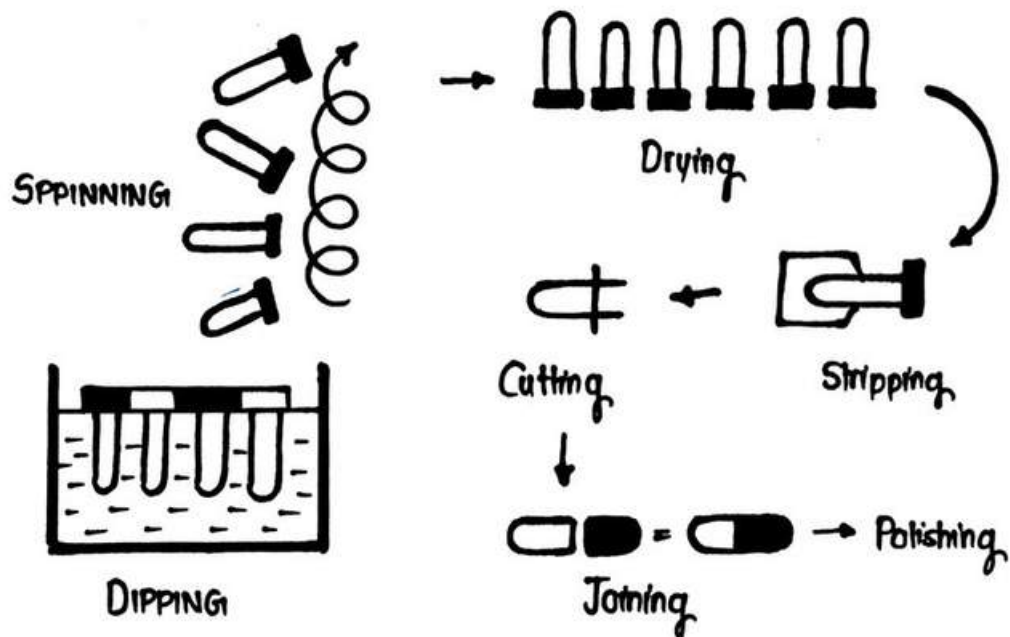
The stripped cap & body portion of the capsules are trimmed to require length using stationary knives.

- Joining

After trimming, the cap & body sections are joined and ejected from machine.

- Polishing

Polishing can be done using Acetate cotra pans and then rubbed with clothes.

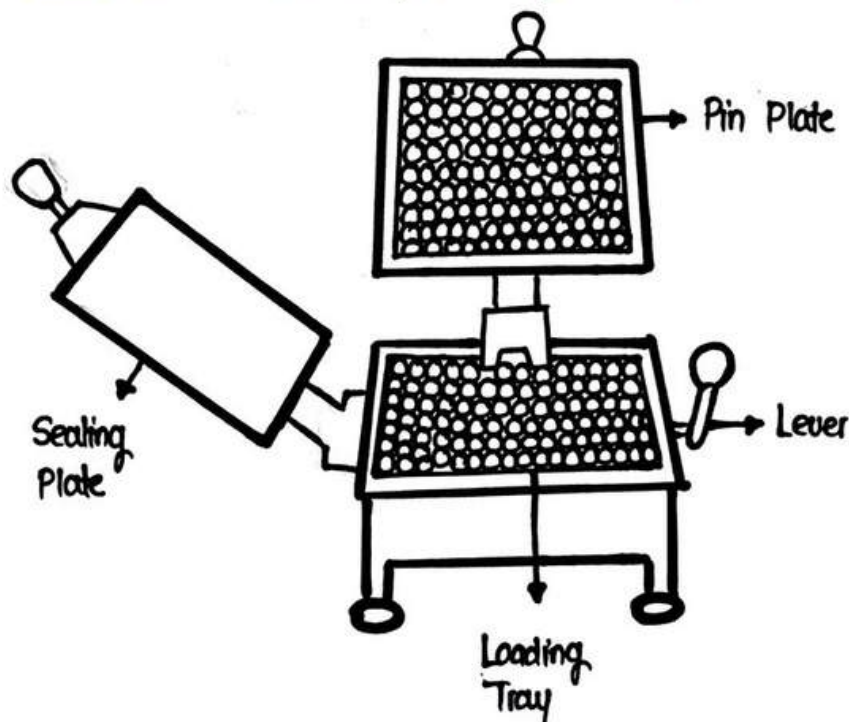


FILLING OF CAPSULES

- Filling of capsules involves precise and consistent encapsulation of powders, granulations, liquids or semi-solids
- The capsule filling process varies depending on whether it's done manually or with a machine

① Manual Filling Machine

- This is the most basic method, where capsule bodies are filled with powder manually
- This method is suitable for small scale production
- It involves following steps:
 - Separate the capsule into its body & cap.
 - Place the body into a capsule holder or tray
 - Fill the body with the prepared material using spatula or funnel.
 - Reassemble the capsule by pressing the cap onto the body.



Semi Automatic Filling Machine

- These machines are more advanced than manual machines and can handle larger production volumes.
- They automate most of the filling process, including powder filling and capping.
- The operators need to manually load the powder hopper & empty capsules.

Fully Automatic Filling Machine

- These machines are highly automated and can handle large production volumes.
- They can automatically load empty capsules, fill them with powder, cap them & sort the filled capsule.

EVALUATION TEST FOR CAPSULES

- Evaluation Test for capsules are essential test performed to ensure their quality, safety and efficacy
- These tests are conducted during the development and manufacturing stages to meet regulatory standards and ensure the safe and effective delivery of the drug
- Below are main evaluation test for capsules

① Weight Variation Test

- Purpose : To ensure that capsule contains a consistent amount of fill material, as variability in weight
- Procedure: A sample of capsules ~~is~~ are weighed and the average weight is calculated. Individual capsule weights are also measured and the variability is checked against accepted limits.

② Content Uniformity Test

- Purpose: To ensure that each capsule contains the correct amount of active pharmaceutical ingredient
- Procedure: Capsules are randomly selected and the content is extracted and analyzed (usually via high performance liquid chromatography)
The content of API is compared to the labelled amount to ensure uniformity

③ Disintegration Test

- Purpose: To measure how quickly and completely the capsule dissolves in gastrointestinal tract, ensuring proper release of drug.
- Procedure: Capsules are placed in a disintegration apparatus and submerged in a dissolution medium. The time it takes for the capsule to break apart is measured.
Hard gelatin capsules generally should disintegrate within 30 minutes, but this can vary based on formulations.

④ Dissolution Test

Purpose: To assess the rate and extent to which the drug is released from capsule into a specified dissolution medium, similar to body conditions.

Procedure: Capsules are immersed in a dissolution medium under controlled conditions. Samples are taken at specified time intervals, and the concentration of the drug is measured using a spectrophotometer or chromatography.

SOFT GELATIN CAPSULES

- Soft Gelatin Capsules are one-piece, sealed capsules commonly used for liquid, semi-solid or suspension formulations.
- They are widely used in pharmaceuticals, nutraceutical and cosmetic industries for their easy to swallow design and ability to encapsulate various substances.

Advantages Of Soft Gelatin Capsules

- Easy to swallow
- Precise dosing
- Better Bioavailability
- Masking Taste and Odor
- Rapid Absorption

Disadvantages Of Soft Gelatin Capsules

- Moisture sensitivity
- Limited Fill Materials
- Higher Cost
- Production complexity

FORMULATION OF SOFT GELATIN CAPSULES

- The formulation of soft gelatin capsules is mainly done by Rotary die process.
- It involves several key steps from preparation of gelatin shell to the encapsulation of filling material :

① Preparation of Gelatin Shell

- Gelatin powder is mixed with purified water, plasticizers and other excipients.
- The mixture is heated and homogenized to form a viscous gelatin mass.
- The gelatin mass is then cast onto cooled drums to form thin, continuous gelatin sheets.

② Filling Material Preparation

- The active pharmaceutical ingredient is filled mixed with excipients like oils, waxes or other suitable carriers to form a liquid or semi-solid filling material.

③ Rotary Die Encapsulation

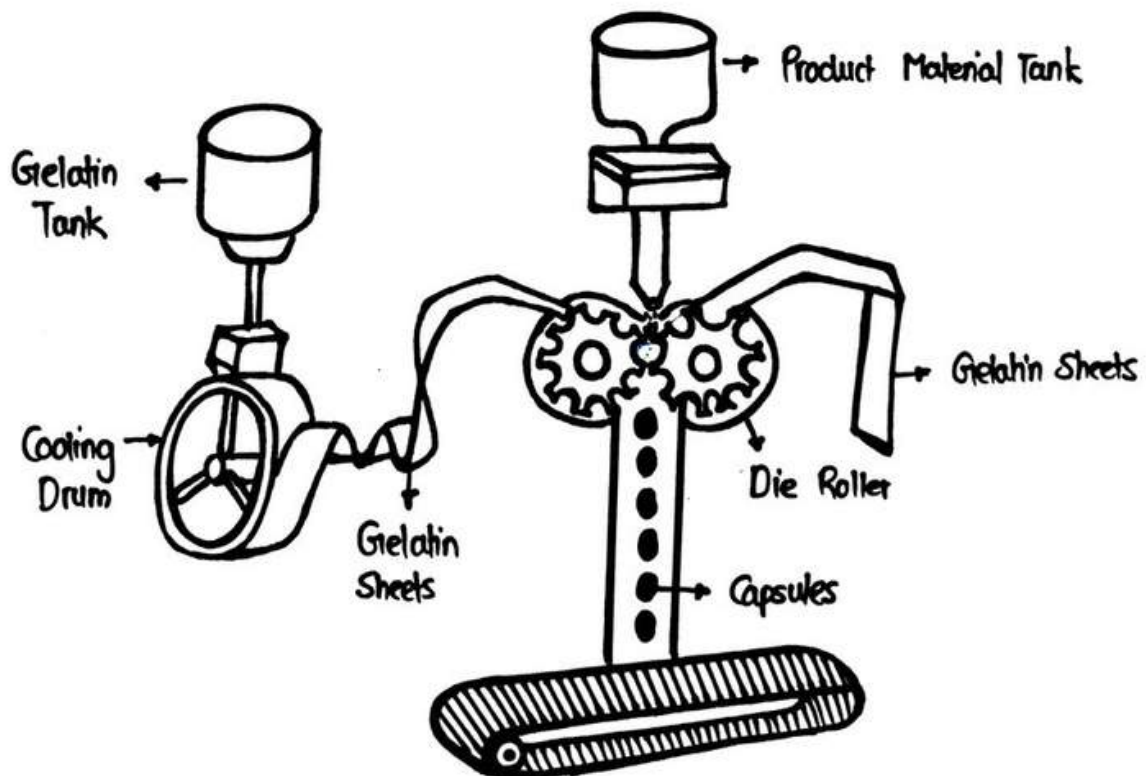
- Two gelatin sheets are fed into rotary die machine, one from each side.
- The fill material is pumped into the die cavity, where it is sandwiched between two gelatin sheets.
- The die rolls apply pressure and heat to seal the capsule and cut it from gelatin sheets.

④ Drying & Polishing

- The freshly formed capsules are dried in controlled humidity and temperature conditions to remove excess moisture.
- The capsules are then polished to improve their appearance & remove any surface imperfections.

Advantages Of Rotary Die Process

- High production capacity
- Efficient use of materials.
- Consistent capsule shape & size
- Accurate dosing of filling material.



Evaluation Test For Capsules

Evaluation test for soft gelatin capsules are almost same as Hard gelatin capsules :

- Weight Variation Test
- Content Uniformity Test
- Disintegration Test
- Dissolution Test

PELLETS

- Pellets are small, free flowing, spherical or semi-spherical solid particles typically ranging in size from 0.5 to 2.0 mm.
- They are widely used in formulation of oral dosage forms, such as capsules, tablets or controlled-release drug delivery system.

Advantages Of Pellets

- Uniformity of Dose
- Ease of storage and transport
- Cost Effectiveness
- Controlled Release
- Enhanced Bioavailability
- Versatility in Dosage Forms
- Excellent Flow Properties
- Prevention of Contamination

Disadvantages Of Pellets

- Preparation is complicated and time consuming.
- High Manufacturing Cost.
- Requires highly specialized equipment.
- Requires trained & skilled staff for manufacturing.

PELLETIZATION TECHNIQUES

Pelletization is the process in which the fine powders or particles of bulk drugs and excipients are converted into small, free-flowing, and roughly spherical units called Pellets.

① Direct Pelletization

- Direct pelletization refers to the process of forming pellets directly from a material without the need for intermediate steps such as extrusion or granulation.
- This technique is used for materials that can naturally agglomerate or compact under certain conditions, such as with the addition of a binder, moisture or pressure.
- The goal is to create a uniform, stable pellets that can be used in various applications including pharmaceuticals, agriculture and various other industries.

② Agitation

- Agitation in pelletization refers to the mechanical or dynamic process used to encourage agglomeration (clumping together) of small particles or powders into larger, more stable pellets.
- The process involves applying physical movement to the material to promote the formation of uniform sized pellets, often through mixing with moisture or binders.
- The right level of agitation is essential to control pellet size, quality and uniformity in pellet production.

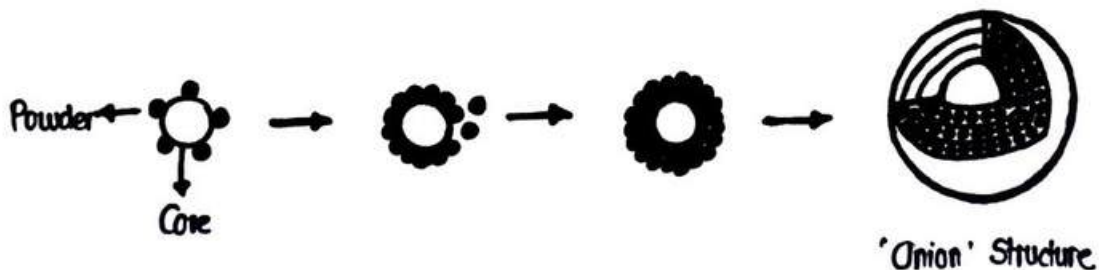
③ Cryopelletization

- Cryopelletization is a specialized technique used to produce uniform spherical pellets by freezing droplets of a liquid formulation.
- In the process of cryopelletization, liquid nitrogen is used as fixing medium to convert the droplets of liquid formulations into solid spherical particles or pellets.
- The process is especially useful for thermolabile drugs and formulations requiring gentle handling.
- The amount of liquid nitrogen required for manufacturing a given quantity depends on the solid content and temperature of the solution or suspension being processed.

④ Layering

- Layering in Pelletization is a process used in the formation of pellets by gradually adding layers of material over a core particle or nuclei.
- There are two different types of layering pelletization.
 - ① Powder layering.
 - ② Suspension or solution layering.

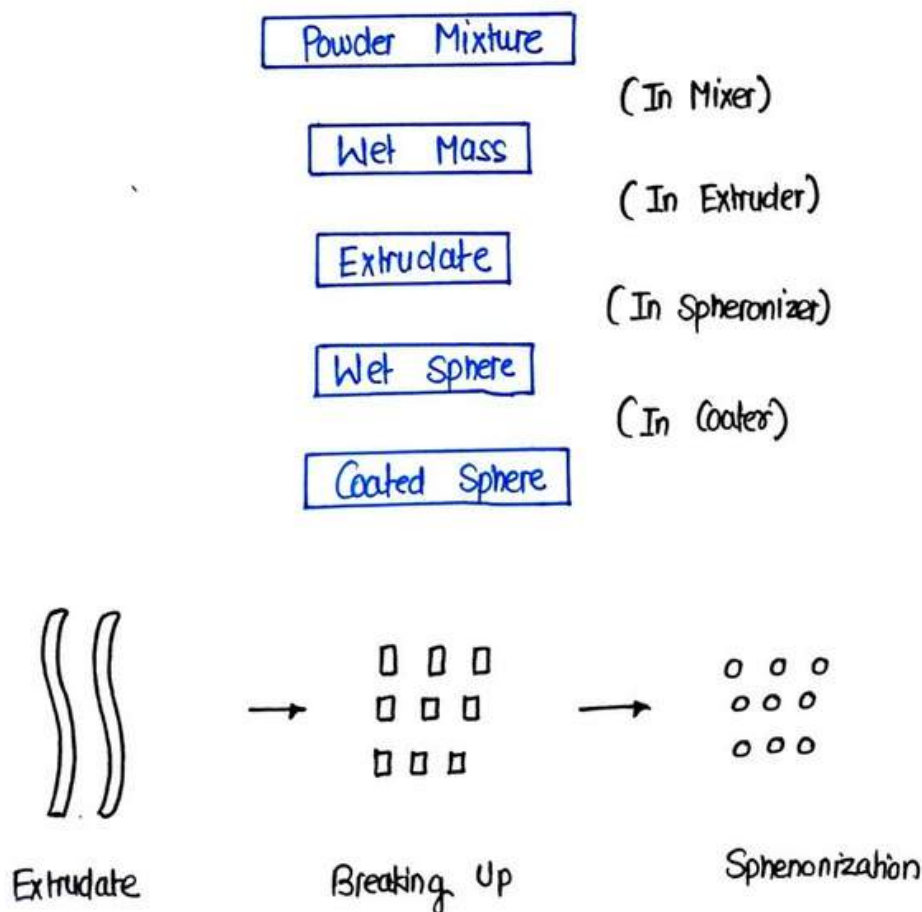
- ④ Powder Layering : • It involves deposition of successive layers of powdered drug and excipients on preformed cores with aid of binding liquid.



⑥ Solution or Suspension Layering : This technique involves deposition of successive layers of solution or suspension of drug substances and binders on starter nuclei

⑤ Extrusion- Spheronization

- Extrusion- spheronization , is a multi step compaction process that produce dense uniformly sized and shaped spheroids roughly 1 mm in diameter.
- This technique is mainly used to produce , pellets with high drug loading capacity.



FORMULATION REQUIREMENTS FOR PELLETS

- Formulation requirements for pelletization are critical to ensure the efficient production of high quality pellets with desired characteristics, such as uniform size, strength and controlled release properties.
- The formulation involves selecting appropriate materials, binders and additives that facilitate the pelletization process and formation of a suitable product.

① Active Ingredient

- The main component that needs to be delivered in the pellet form.
- The particle size of the active ingredient should be fine enough to allow for good agglomeration during pelletization.

② Binders

- Binders are materials added to hold the particles together and give the pellets structure integrity.
- They help the particles stick during the pelletizing process and prevent the pellets from disintegrating after formation.

③ Fillers

- Fillers are inert substances added to the formulation to increase the bulk of the pellet.
- Example: Microcrystalline Cellulose, Starch, Sucrose.

④ Lubricants

- They are added to reduce friction between particles and surface of the equipment.
- Example: Glycerine, Polyethylene Glycol etc.

⑤ Additives

- Colourants or flavouring agents can be added to make the pellet visually appealing or to mask any undesirable odour or taste.

⑥ Disintegrants

- These are used in pharmaceutical pellets to aid in the quick disintegration or dissolution of the pellet in gastrointestinal tract.

EQUIPMENTS FOR MANUFACTURING OF PELLETS

Following equipments are generally used for manufacturing of Pellets :

- Supply Bins
- Pellet Mills
- Coolers
- Crumble Rolls
- Shaker etc.

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