

## Unit-3<sup>rd</sup>

### ☺ Capsule ☺

Introduction: → Capsule is a solid unit dosage form.

- The capsule is made up of the Gelatin covering in side the drug molecule are filled.
- When it goes inside the stomach the layer of Gelatin is ruptured drug removes out and goes inside the systemic circulation.
- The term capsule is derived from latin word "capsula" which means packet.
- Capsule is prefer over the tablet because it can be use for the amorphous powder and it can be mask bad taste of powder (Tablet).
- In the capsule dosage form it is made up of two part cap and body.
- The body is long in size and the cap is small in size and the drug material is filled inside the body.



Latin  
↓  
capsula  
↓  
Packet



## Types of capsule

It is of two types :-

- (1) Hard Gelatin Capsule.
- (2) Soft Gelatin Capsule.

### Advantages of capsule

- It can be used for the amorphous powder.
- It can be used for the bad taste.
- Minimum excipients required.
- Protection for sensitive ingredients.
- Reduced gastrointestinal irritation.
- Little pressure required to compact the material.
- Oil and fat-soluble nutrient delivery.
- Easy to store and transport.

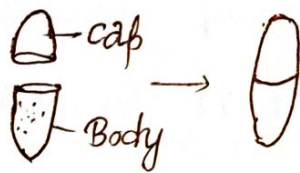
### Disadvantages of capsules

- Bulky materials can result in large capsule size.
- Ingredients can interact with the capsule shell.
- Not suitable for highly efflorescent or deliquescent materials.
- Limited fill weight based on capsule volumes.
- Special conditions are required for storage.
- Variation in fill volume is known to occur.
- Soft gel contents restricted to a tight pH range.



## Hard Gelatin Capsule

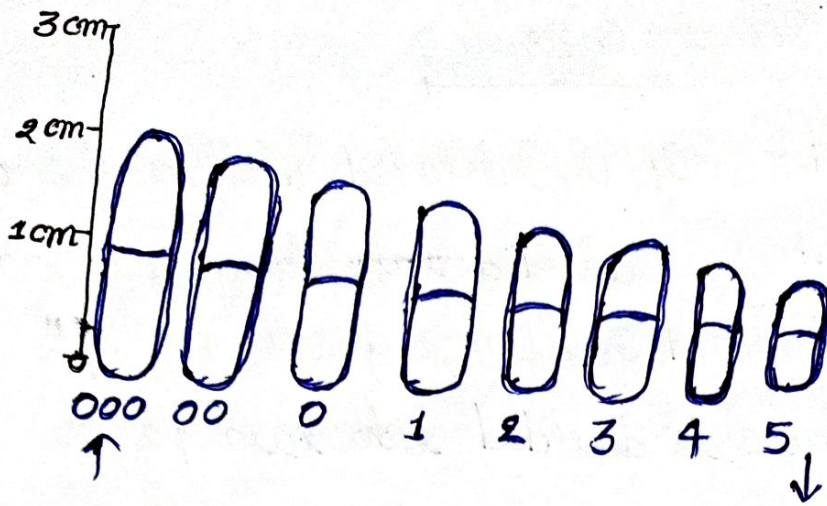
- When the powder drug is enclosed within the shell of Gelatin which is divided into two parts cap & body this is called hard Gelatin capsule.
- Hard gelatin capsule is divided into two parts cap & body.
- The body is elongated cylindrical structure and the cap is half cylindrical structure and the drug is filled inside the body and then cap is fitted above the body. this is called hard Gelatin capsule.



### Properties of hard Gelatin Capsule

- (i) Capsule Size: Hard gelatin capsule is available total eight sizes in the market.
- ⇒ If the size is vary from triple zero to 5.
- ⇒ The triple zero capsule size is the largest size.
- ⇒ of the capsule which is used for the veterinary product
- ⇒ And the capsule no five is the smallest size of the hard gelatin capsule





(2) Moisture Content :- Moisture content in the hard gelatin capsule is about 13%. but it is available in to the dry form due to it is maintain under the 25 to 40% humidity condition.

(3) Solubility :- The solubility of hard gelatin capsule can be dissolve in any <sup>kind of</sup> medium in the 30°C.  
 → When we take the hard gelatin capsule the temp of body is 37°C so immediately this is dissolve and the drug release in to the gastric media. and started to absorb.

### :- Composition of Hard Gelatin Capsule Shell :-

→ The hard Gelatin shell is composed of following five parts.

- |              |                  |                    |
|--------------|------------------|--------------------|
| (1) Gelatin  | (3) Preservative |                    |
| (2) Colorant | (4) Plasticiser  | (5) Wetting Agent. |



## ∴ Gelatin:

- Gelatin is the main composition of the <sup>outer</sup> covering of the hard Gelatin capsule shell.
- It is obtained from the Bone, muscle, skin and connective tissue part of the animal body, so it is natural in origin.
- Basically some ~~non~~ vegetarian capsule are also available which is made up of Hydroxy propyl methyl cellulose (HPMC)
- The Gelatin is obtained by the hydrolysis of the collagen protein which is obtained from the connective tissue.

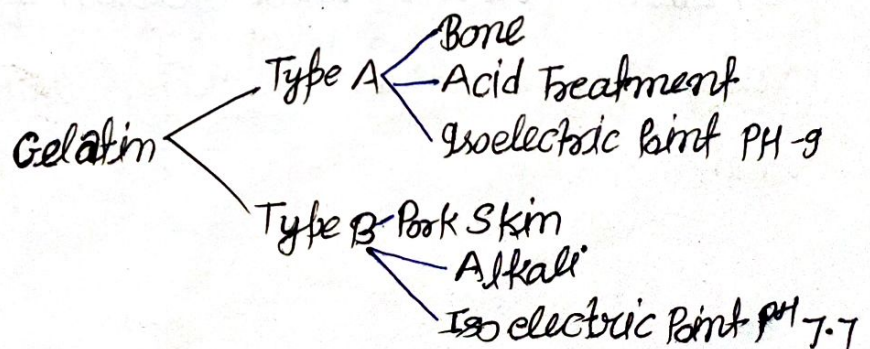
## ∴ Characteristics of Gelatin:

- It should be non toxic and accepted world wide.
- It should be soluble protein.
- It should be melt at high temp and it should be again convert into the solid form after cooling
- When the hard gelatin is soluble in water then they form the semi-solid colloidal gel.

## Types of Gelatin

It is of two type:

- (i) Type A
- (ii) Type B





## (2) Colorant

- Different-2 color are used to color the hard Gelatin capsule shell to increase their attractiveness and their acceptability.
- Basically two types of colorants are used which one is water soluble dye and other is water insoluble pigment.
- On the basis of diazonium compound colorant is of further two types - (i) Diazo color (ii) Non diazo color.
- Ex- Erythrosin (E127) (Red)  
Indigo Carmine (E132)  
Quinoline Yellow (E104)
- $TiO_2$  →
- We also acts as some amounts of Titanium dioxide ( $TiO_2$ ) as a opacifier which produce shining to the hard Gelatin capsule shell

## (3) Preservative

- Because the Gelatin is obtained from the natural sources so there is a more chances of contamination with the microbes.
- So ~~from~~ prevent these gelatin<sup>shell</sup> from microbes we are using preservatives Ex Methyl Parabene, & Propyl Parabenzic Acid.



#### (4) Plasticiser:

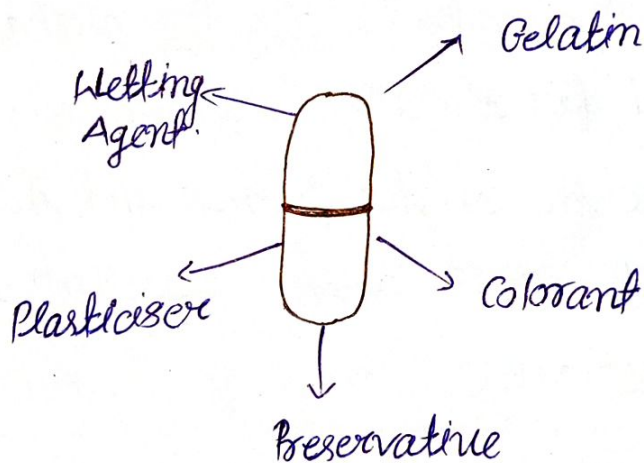
→ Plasticiser are used to make hard Gelatin capsule remaining hard during the use.

Ex- Sorbitol & Glycerine.

#### (5) Wetting Agent:

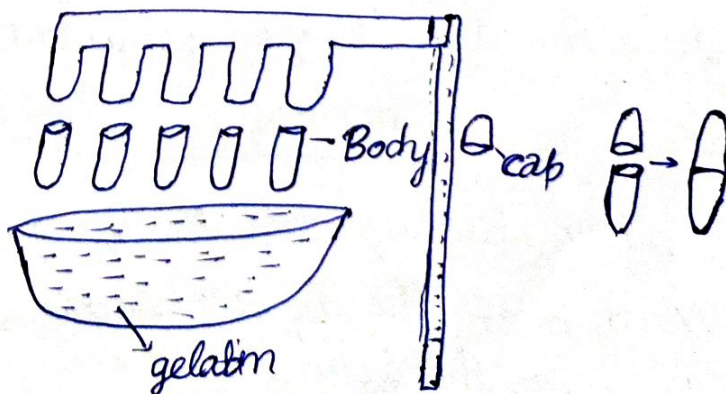
→ Wetting Agent are used to mix in the solvent for filling the hard Gelatin capsule. the basic example of wetting agent is Sodium Lauryl Sulphate.

→ It will be use 0.15% conc.



#### Manufacturing of Hard Gelatin Capsule:

- (1) Dipping
  - (2) Spinning
  - (3) Drying
  - (4) Stripping
  - (5) Joining
  - (6) Polishing
- Polishing is further detailed with three sub-steps: Pan, Cloth, and Brushing.





- For the manufacturing of hard Gelatin capsule.
- First of all we have to make a colloidal solution of Gelatin in a container.
- And we have to choose the purchase "frame" as per the capsule size.
- First of all choose frame for the capsule shell as per their size.
- Now hard gelatin capsule can be prepared in following steps:-

### (1) Dipping:-

- In<sup>the</sup> first of all the capsule can be prepared in two step for body and for the cap.
- First of all choose the right frame and this frame dip into the freshly prepared Gelatin solution. This is called dipping.

### (2) Spinning:-

- After dipping the frame into the gelatin solution, remove the frame and by the spinning or rotating into the air it goes upward. This is called spinning.

### (3) Drying:-

- After spinning lift the frame to be remain in <sup>the</sup> dry air
- And passes the dry air so the gelatin layer is completely dry over the frame



∴ Limitations of Formulations:

(4) Stripping:

→ In the stripping with the help of knife cut the capsule cap & body.

(5) Joining

→ After stripping or cutting separately body and cap now we join the body and cap with the help of machine.

(6) Polishing:

After this polishing for increasing the shining of the capsule shell. this is a last step polishing. it is of three type - (i) Pan Polishing (ii) cloth Polishing (iii) Bussing Polishing

∴ Manufacturing of Hard Gelatin capsule:

→ The hard Gelatin capsule is prepared into following four steps.

- (1) Development and preparing formulation along with size.
- (2) Filling.
- (3) Sealing.
- (4) Clearing / Polishing.



## (1) Development and Preparing formulation along with size

→ First of all select the appropriate size of capsule shell as per their formulation.

### ∴ Capsule size ∴

(Size)	Volume (ml)	Size in (mm)
↑ 000	1.37	26.3
00	0.95	23.7
0	0.68	21.8
1	0.50	19.2
2	0.37	18.3
3	0.30	15.3
4	0.21	14.7
↓ 5	0.15	11.9

### ∴ Formulations ∴

- After selecting the capsule size now prepare the formulation for the capsule in which the main API and excipient are added.
- In the excipient diff. types of excipient are used like
  - Diluent
  - Glidant
  - Lubricant
  - Disintegrating
  - Preservative



## Limitations of Formulations:

- The formulations should be dry otherwise it can destroy the gelatin layer
- The powder should not be hygroscopic because they absorb the moisture and gelatin capsule may be destroy.
- It should be not sticky with the gelatin layer.
- It should be non toxic.
- And the formulation should not be interacted with the gelatin cover or it should be compatible with gelatin cover.

## (2) Filling:

### (A) Loading of Empty capsule shell:

First of all we fill the empty capsule shell with body and cap inside the filling machine.

→ It should be keep remind that the body should be below side and the cap beyond the upper side.

### (B) Rectification of capsule shell:

→ After filling the capsule shell. the largest size and smallest size or defected size can be removed by the visual inspection this is called rectification of capsule shell.



### (3) Separation of body and cap.

→ In this step the cap is removed goes upward size and the body and cap is separated.

### (4) Filling up to body:

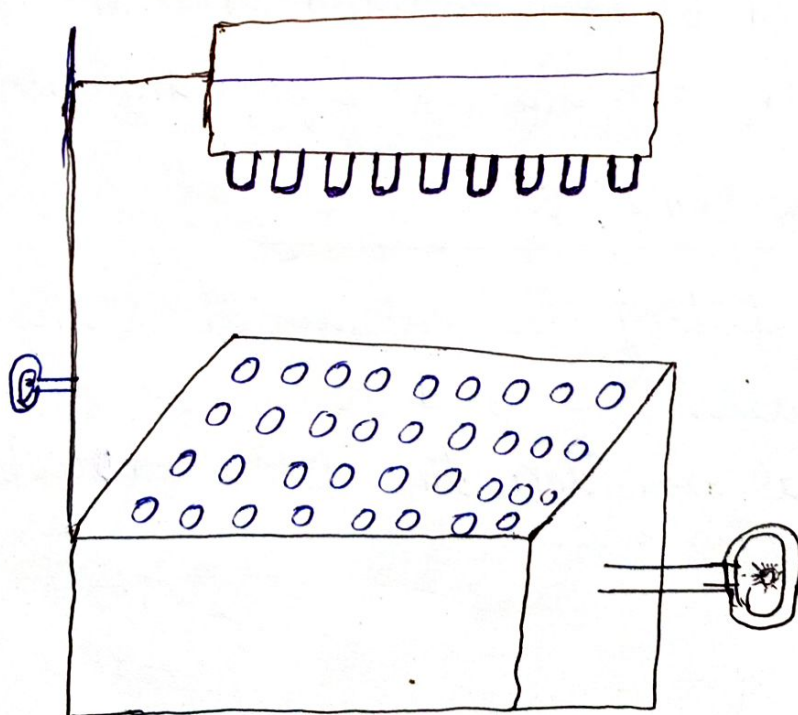
→ Now Pour the packets of the formulating Product and with the help of plate fill the each and every capsule with the powder.

### (5) Attachment / Joining:

→ After filling the frame is removed and allow to cap fit and fixed in body.

### (6) Ejection:

→ After filling and fixing the cap and body the capsule are ejected from the filling machine.

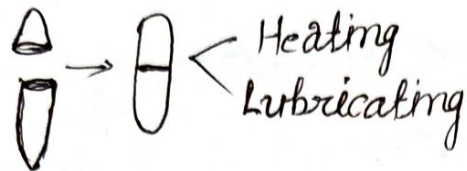


(Semi Automatic Machine)



### (3) Sealing

- The attachment of body and cap is called sealing.  
and it can be performed by the following method -
- by the Heating method.
  - By the lubricating method.



### Hard Gelatin Capsule Filling Machines :

#### Filling Equipment

#### Companies Manufacturing Filling Equipments :

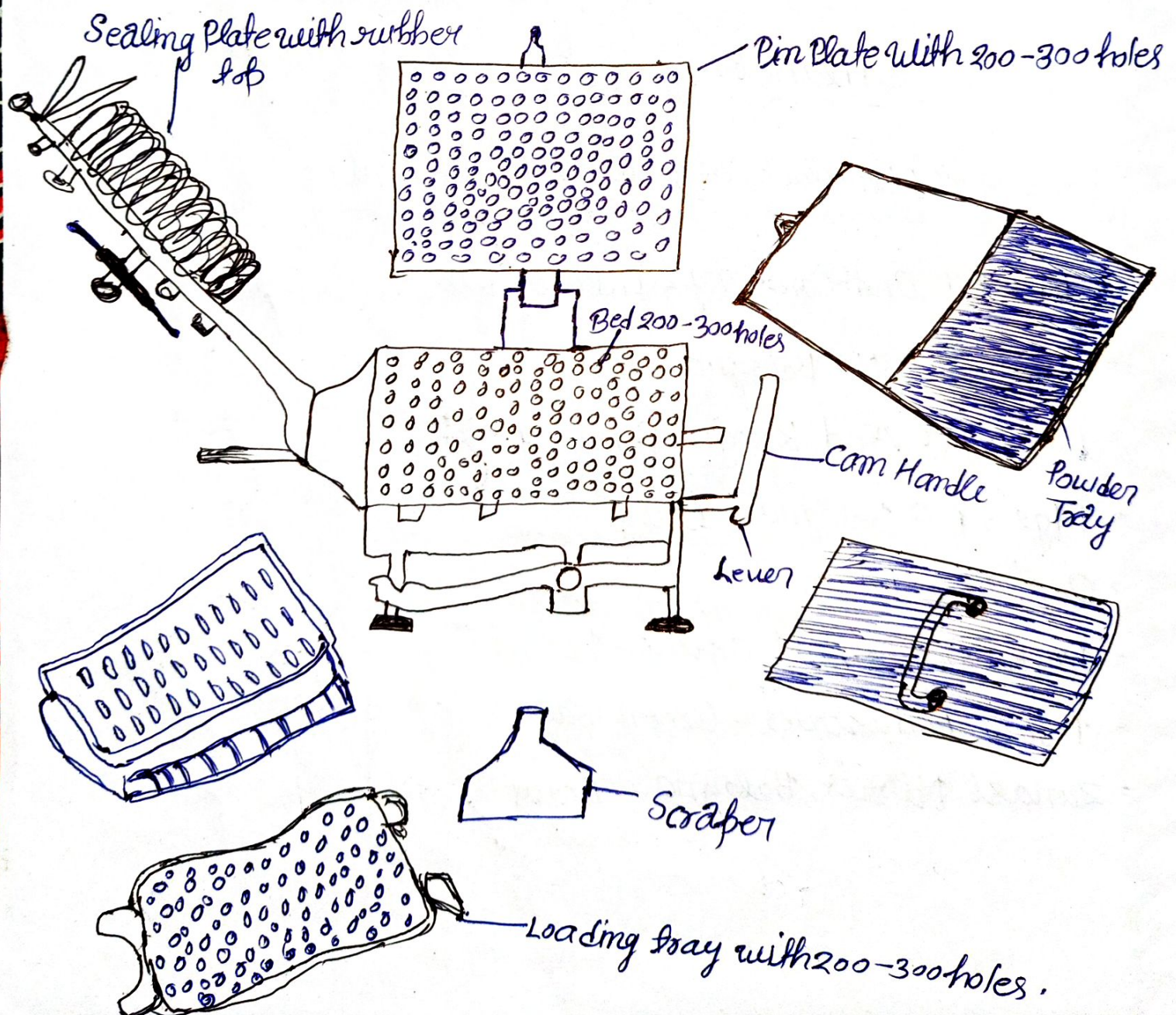
- Elililly and company - Indiana Polis.
- Farmatic SNC Bologna - Italy
- Haflinger And Karg - Germany.
- Mg2 S.P.A Bologna - Italy.
- Osaka - Japan
- Parke Davis And copant - Detroit.
- Perry Industries - Green Bay
- Zanasi Nigri's, Bologna - Italy



# Hard Gelatin Capsule Filling

- (1) Bench scale filling.
  - For small scale filling.
  - Manual Filling Machine.
- (2) Industrial Scale Filling.
  - Comes in varying shapes and sizes.
  - Semi automatic Machine.
  - Fully automatic Machine.

## ÷ Bench Scale Filling ÷





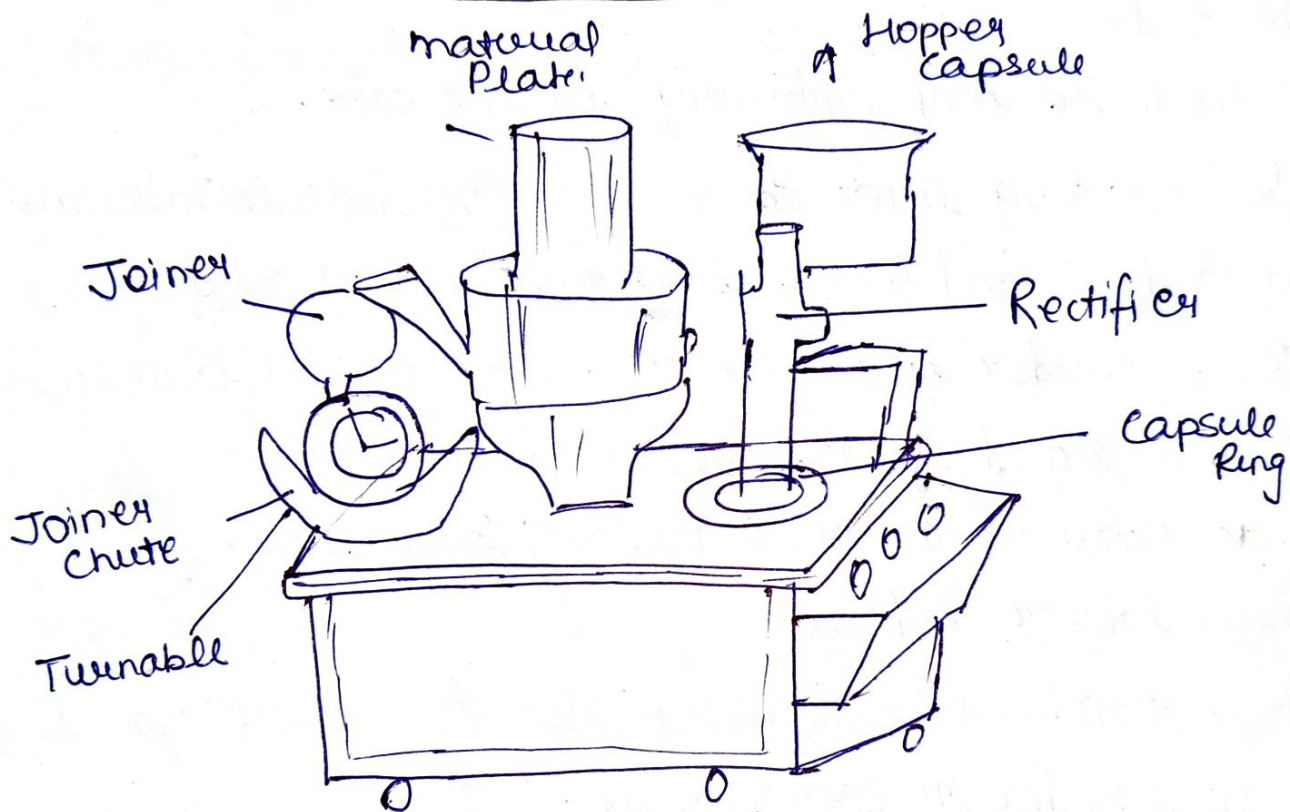
## Process Operation:

- Place empty capsules onto the loading tray and place tray onto the machine.
- Check the front knob it should be turned to the right.
- Pull locking lever forward.
- Push down long handle which will lift the caps of all the bodies.
- Set aside the tray containing all the caps.
  - Push locking lever back by which capsule bodies will drop down and become level with filling surface.
  - Place powder tray on filler keeps powder from spilling.
  - Pour & spread the pre-measured powder.
  - ~~make~~ extra powder onto powder tray's shelf.
  - Lower tamper and lock.
  - Turn handle to compress powder this allows you to fill more powder in each capsule.
  - Raise tamper & spread extra powder from shelf into capsules ensures uniform fill weights.
  - Returns the tray containing caps to filler.
    - Turn knob to the left and lower locking plate.
  - Engage lock for locking plate.
  - Hold tamper handle and push down on long handle.
  - Bodies are pushed up into caps all the capsules are now locked in one step.



- Disengage lock for locking plate.
- Lift locking plate and turn front knob to the right
- Push down long handle and remove tray of completed capsules.
- Capsules are filled now.
- you can turn tray and all the capsules will get out from the tray.

### ∞ Industrial Scale Filling:



### ∞ Semi Automated Capsule Filling Machine:

Features: Suitable for filling capsules of all sizes with powder, granules and pellets.

- Minimizes operator attention and ensures maximum production
- Choice of four auger speed with variable speed of filling table.
- Auto drug hopper in feed mechanism, reduces weight variation and improves productivity



- Easy to maintain and clean.
- Quality and precision manufacturing meets the requirements of GMP.
- Both PLC controlled panel or digital controlled panel with auto capsule loader closing system available to meet customers requirement.
- Feed Empty capsules in the hopper.
- Put on loading ring on loader
- Push the lever to load capsules in loading ring.
- Remove the loading ring and separate its upper and lower part manually (to separate capsule bodies and caps)
- Put the lower part of loading ring on the machine for filling and fill the powder in hopper.
- Press powder filling button to fill powder in capsule bodies.
- Join upper and lower parts of loading ring and send them for sealing.
- Loading ring will come with sealed capsules and it will turn upside down for ejection.

### ÷ Fully Automated Capsule Filling Machine ÷

- |                           |                                      |
|---------------------------|--------------------------------------|
| (1) Empty Capsule hopper. | (7) Unopened Capsules rejection unit |
| (2) Rectifying roller.    | (8) Joining station.                 |
| (3) Magazine              | (9) Discharge chute. (+50)           |
| (4) Cap Segment           | (10) Segment cleaning                |
| (5) Body disc             | (11) Weight Control unit             |
| (6) Powder filling hopper | (12) Control station                 |
|                           | (13) Auger Motor                     |
|                           | (14) Auxiliary Powder hopper.        |



- Empty capsules are fed in the hopper one row of capsules released in rectifier track.
- The direction of capsules is rectified and they are pushed into the hole with caps on upper side.
- The capsules are sent to different workstations with the help of a turntable.
- Capsules are separated with the help of a vacuum
- Capsules bodies are filled with the powder and pins push the powder.
- Capsule bodies and caps are rejoined.
- Non-separated capsules are ejected.
- The holes are cleaned for the next operation cycle.





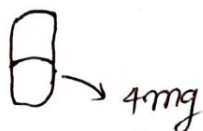


## ∴ Evaluation of hard Gelatin Capsule ∴

→

### (1) Content of Active Ingredient Potency / Assay ∴

- In this test we determine the exact concentration of API inside the capsule within the excipient.
- By the diff-2 Physical chemical and biological Method the drug content can be assayed.
- And this content will be equal to the as per label.
- And it is acceptable as the range of 90 to 110%.



Pantoprazole

⊖ → 4 mg

x 3 mg

x 2 mg

x 5 mg (3.6 mg - 4.4 mg)

x 4.5 mg

x 6 mg

### (2) Weight Variation Test ∴

- In this method first of all we can calculate the weight of twenty empty capsule shells and then calculate the twenty filled capsule shells.
- And by dividing the empty shell weight the filled capsule we calculate the average weight of each and every capsule.
- Then by using this formula we can calculate the Percentage weight variation of each and every capsule.



- Then after we decide the range from lowest to highest category.
- Then after checking we can calculate the either it is pass or fail.

$$\text{○ } 485 \text{ mg} \rightarrow 485 \text{ mg}$$

20 Empty Capsules → Weight → 300mg

20 Filled Capsule → weight → 10 gm.

$$\text{Exact Weight} = 10 \text{ gm} - 0.3 \text{ gm}$$

$$= \boxed{9.7 \text{ gm}}$$

1 — 510 +5.15%

2 — 515 +6.18%

3 — 495 +2.06%

4 — 485 +0.206%

5 — 460 -5.15%

⋮

20 +8%

$$\text{Average Weight} = \frac{9.7}{20} = 485 \text{ mg}$$

$$\% \text{ Weight Variation} = \frac{\text{Actual Wt} - \text{Average Wt}}{\text{Average Wt}} \times 100$$

$$\boxed{-5 \text{ to } +8\%}$$

$$(1) \% \text{ Wt variation} = \frac{510 - 485}{485} \times 100 = \frac{25}{485} \times 100 = \frac{2500}{485} = 5.15\%$$

$$(2) \% \text{ Wt variation} = \frac{515 - 485}{485} \times 100 = \frac{30}{485} \times 100 = 6.18\%$$

$$(3) \% \text{ Wt variation} = \frac{495 - 485}{485} \times 100 = \frac{10}{485} \times 100 = 2.06\%$$

$$(4) \% \text{ Wt variation} = \frac{485 - 485}{485} \times 100 = \frac{0}{485} \times 100 = 0.206\%$$

$$(5) \% \text{ Wt variation} = \frac{460 - 485}{485} \times 100 = \frac{-25}{485} \times 100 = -5.15\%$$



- If the capsule size is less than 300mg then wt. variation is  $-10$  to  $+10\%$ .
- If the capsule size more than 300mg then wt. variation is  $-7.5\%$  to  $+7.5\%$ .
- If the capsule size is more than 500mg then wt. variation is  $-5\%$  to  $+5\%$ .
- If the capsule size is more than 1000mg then wt. variation is  $-2.5\%$  to  $+2.5\%$ .

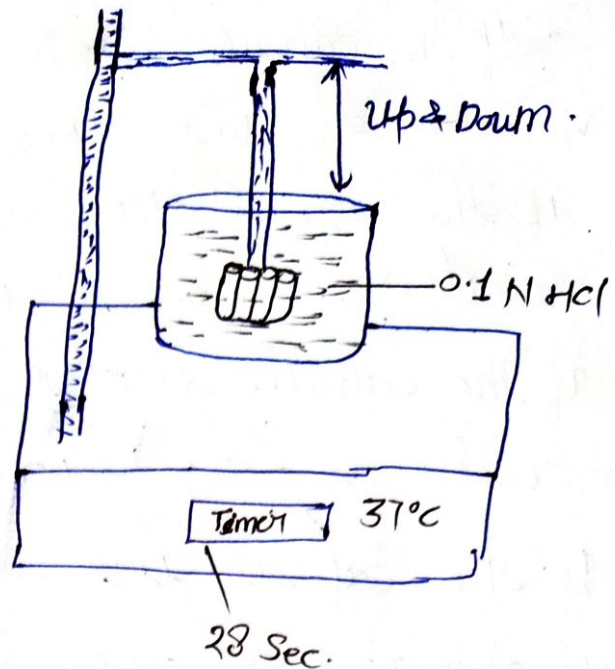
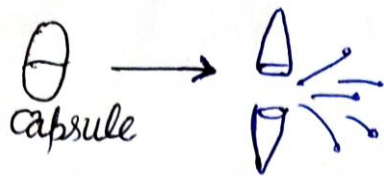
### ∴ (3) Content Uniformity Test ∴

- ⇒ In this test we actually calculate the <sup>range of</sup> content in the capsule.
- First of <sup>all</sup> we select the 30 capsule and calculate the content each by each individually.
- ⇒ And then after calculate the range of the content uniformity if the range is in the limit of 90 to 110%. it means the capsule testing is pass.

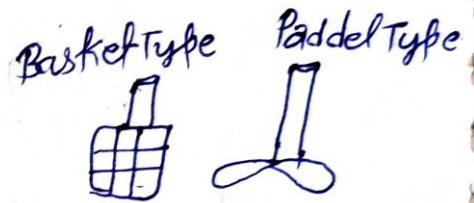
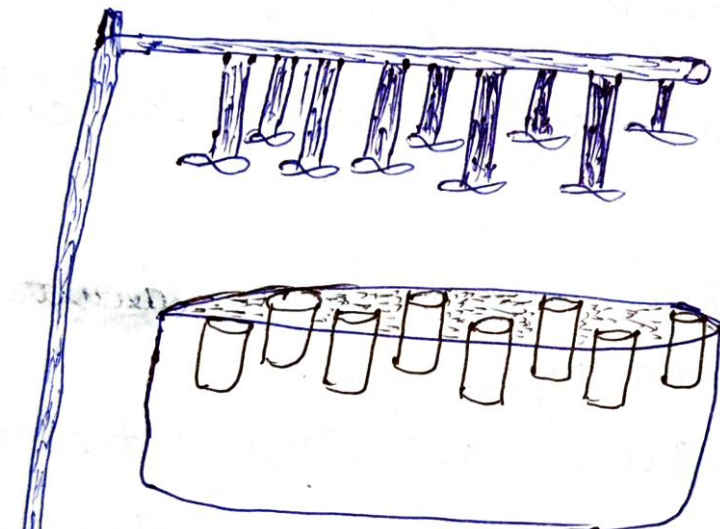
### (4) Disintegration test ∴

- ⇒ In this test we actually perform the or determine the rupture of gelatin shell and the release of drug from the capsule inside the gastric medium.
- For this use 0.1N HCl solution or water maintain the temp  $37^{\circ}\text{C}$ .
- And with the help of disintegration test we perform the test and calculate the actual time when drug is release from the capsule shell this is called disintegration time.





### (5) Dissolution Test:



USP  $\rightarrow$  Type-I    Type-II

IP  $\rightarrow$  Type-II    Type-I

\* Dissolution Test is performed to determine the absorption rate of capsule. In this method in dissolution chamber 9 tanks are filled with 900 ml of fresh solvent. Now put one capsule each in dissolution chamber & start the machine.

In each 15 min interval take 15 ml of sample from each & add same amount of fresh solvent. & send sample of 10 ml for absorption.

Plot a graph b/w time vs conc and calculate Bioavailability & absorption.



## ÷ Soft Gelatin Capsule ÷

- It is a unit dosage form of a drug in which the liquid semisolid and paste form of the active ingredient is filled inside the Gelatin layer.
- In <sup>this</sup> soft gelatin capsule the composition of opacifier and plasticizer is different than the hard gelatin capsule and it is more soft than the hard gelatin capsule.
- The soft gelatin capsules are available in the different shapes like - oval, rounded, elongated and circular form.
- If the amorphous drug is in solid form or powder form then we use hard gelatin capsule but if the same drug is present in semisolid form, liquid form, paste form or oil form then we use the soft gelatin capsule for their preparation.

### Advantages of Soft Gelatin Capsule ÷

- It has good and better patient compliance.
- It is versatile in nature because different-different dosage forms like semisolid, oil, paste, gel can be used.
- It has improved bioavailability rather than hard gelatin capsule.
- It has improved stability than hard gelatin capsule because the drug is mixed in the oily phase and oil is used as the preservative for long time.
- The dose and conc. is more precise and more accurate than the hard gelatin capsule.



→ Because the flow property of liquid is greater than the flow property of powder.

### Disadvantages:

- It requires special arrangement for manufacturing special devices so it is costly.
- It has stability issue <sup>with the</sup> water soluble drugs.
- It may cause drug interaction with the Gelatin shell.
- These are the highly moisture sensitive in the hygroscopic condition. It can be melt out.

### Composition of the Soft Gelatin Capsule Shell:

#### (1) Gelatin

✓ Same as Hard Gelatin Capsule Shell : ✓

#### (2) Water

- Use water as solvent for dissolving Gelatin Powder and the concentration of Water should not be more than 45%.
- The ratio of water and Gelatin should be 0.7 to 1.3 and decided by 1.

#### (3) Plasticizer:

- The concentration of Plasticizer should be reduced less than hard gelatin capsule.
- Basically the same plasticizer Glycerine or Sorbitol are used.



#### (4) Color:

→ For Improving their organoleptic character we can use different 2 kinds of color.

→ They are exist two form: (i) Synthetic (ii) Non Synthetic  
or Natural color

#### (5) Opacifier.

→ "Same as hard gelatin capsule"

#### (6) Chelating Agent:

→ Chelating agent are used to make complex with the metal, so they can't react with the gelatin layer

→ And the conc. of chelating agent should be less than 15 ppm.

#### ← Manufacturing of Soft Gelatin Capsule →

→ The preparation of soft Gelatin Capsule is very difficult from the hard Gelatin capsule because in this method the soft gelatin shell and filling material are filled simultaneously.

→ For making the soft Gelatin capsule we need two type of material

(i) Gelatin Shell Material

(ii) Filling Material.

#### (i) Gelatin Shell Material

→ It contains Gelatin

→ It contains Water

→ It contains plasticizer like Glycerol or Sorbitol and also contains B. Naphthal.



## (2) Filling Material:

- The filling Material, or Medicament, API which can be filled inside the soft gelatin capsule can be in three form.
- (i) Neat Substance
  - (ii) Solution Form
  - (iii) Suspension Form.

(i) Neat Substance: When the Material is Vitamin A, Vitamin E, Shark liver oil, Cod liver oil, then these material do not contain any kind of solvent they filled alone in the capsule.

(ii) Solution form: When the drug is soluble in oily Nature or Water nature then the medicament is prepare in the solution form.

- The solution form are require as the Soya bean oil as a base.
- They contain diMethyl Iso Soobide as a surfactant.
- They contain Glycerol as a plasticizer and they also contain Polyethyl Glycol as a solubility Enhancer because they increase the solubility.

## (3) Suspension:

- When the drug is not soluble into the oil or base when we use the suspension form and this contain 30 to 70 % ratio of the solute in the solvent.



Method of Preparation: First of all set the two rollers

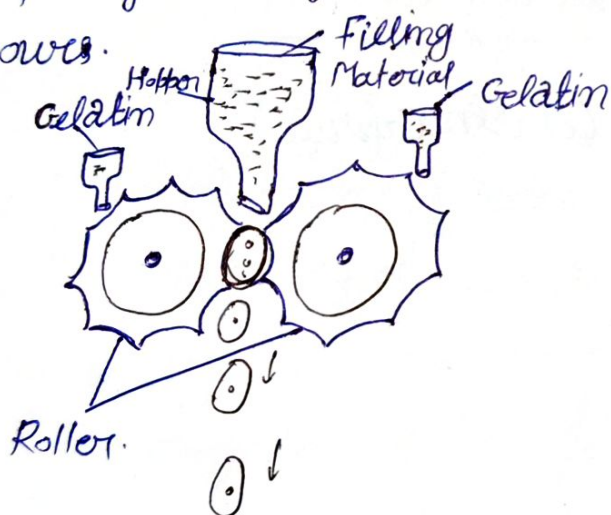
And fill the hopper with Gelatin solution. and set a large hopper of filling material b/w the two rollers.

→ Now start the machine when the gelatin layer is comes into the roller then after rotating and drying.

→ It convert into the seat of the Gelatin.

→ And when the filling material comes into downward then the it included inside the two seats of the gelatin layer and after sealing they converts into the Pellets form and remove out.

→ The capacity of this gelatin machine is about 20 to 25 thousand cap. per hours.



∴ Pharmaceutical Application of Soft Gelatin Capsule:

→ It is available in oral unit dosage form and it useful for the human and veterinary dosage form and it is very easy to take and easy to swallow.

→ Different 2 formulations of soft gelatin capsule can also use like suppository they are used as the vaginal Rectal & Nasal suppository for local actions.



- The layer of Gelatin melt at body temperature and drug release and give local action.
- It is available in the special Package tube form. After opening drug is removed and medicament is release. and use for the local action.
- ⇒ Used in cosmetic industry
- It has precise accuracy of dose. chances of weight variation is less than the hard gelatin capsule.
- It has enhanced the stability due to use of oil.

∴ Evaluation of soft Gelatin Capsule:

"(Same as hard Gelatin Capsule)"



## ∴ Pellets ∴

- Pellets is a type of solid multiple<sup>oral</sup> dosage form.
- It is created from the powder or it is manufactured from the powder by the process pelletization.
- In the pellets it is available in the spherical shape.
- The pellets are always usually available in rounded shape and their diameter is 500 to 1500  $\mu\text{m}$ .
- It has better flow property and it has dose accuracy.
- After the incapsulation when pellet is form then they are moisture insensitive.

## Advantages of Pellets ∴

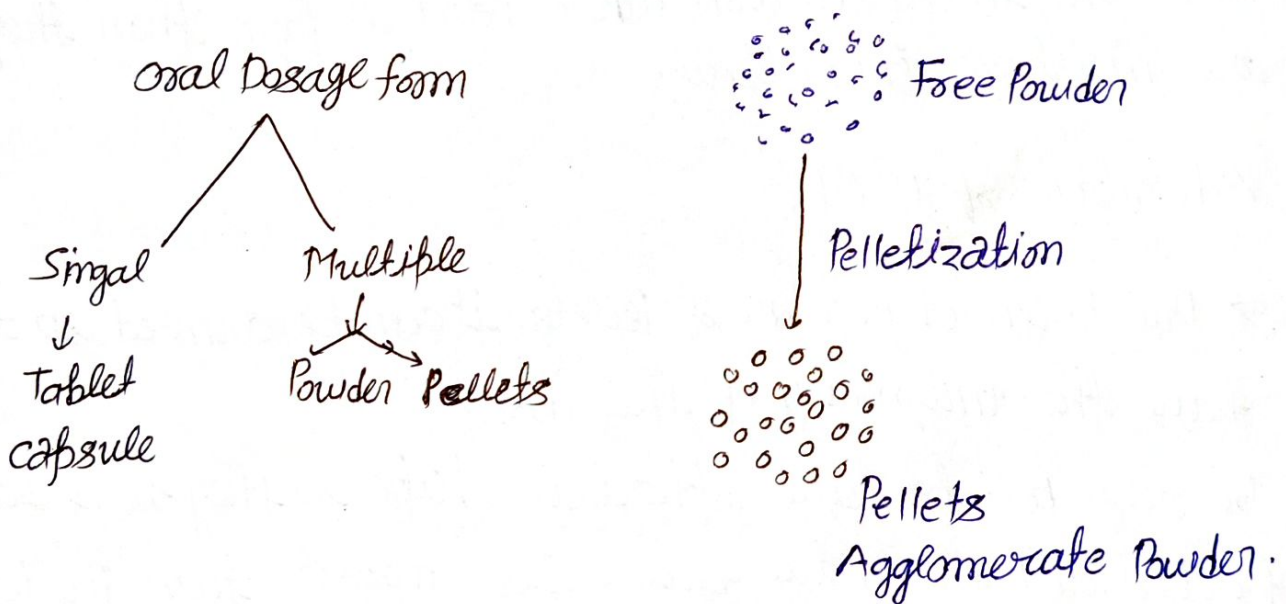
- Due to in character of pellets it can be counted so they have the uniformity of the dose.
- Because pellets have spherical shape so they have less friction and they have better flow property than powder.
- After the formulation of pellets the chances of dust particle is reduce and it helps in the prevention of dust formulation.
- By the incapsulation with polymer coating the drug can be prepared in controlled release or sustained release formulation and their duration of action can be increase.
- The chances of incompatibility of medicament and excipient can be reduced by the formation of pellets.
- It has better drug absorption than tablet or capsule.



→ By using different coating material we can modified their release in intestine and stomach.

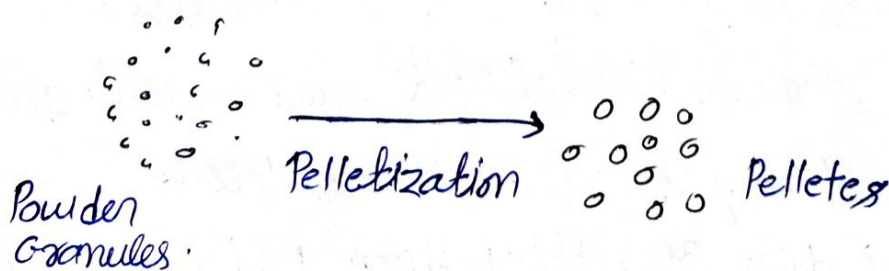
### Disadvantage of Pellets:

- It has high costly. due to diff-2 techniques.
- During the tableting process the film coating of pellets are destroy.
- It has tough.
- It requires special types of Equipment.



### ⊘ Pelletization Techniques ⊘

→ The process of conversion of powder granules into the Pellet this is called Pelletization.





It have different-2 Techniques:

- (1) Drug layering
  - ↳ A) Powder layering
  - ↳ B) Solution / Suspension layering
- 2) Extrusion Spheronization.
- 3) Cryopelletization.
- 4) Compression Pelletization.
- 5) Balling Pelletization.
- 6) Hot Melt Extrusion (HME)

### (1) Drug Layering:

⇒ Drug layering is the most vitally use and easy method for the pellet formation.

⇒ In this method first of all we select the nucleus which is inert material or either the same drug which is in pellet.

⇒ And after this complete into three steps:

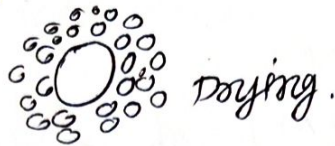
(i) Spraying: In this step the nucleus is taken and the powder drug material or solution / suspension drug material is spray over the nucleus.

(ii) Rolling: Now rotate the nucleus so the proper drug spray around the nucleus.

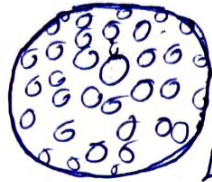




(3) Drying: After spraying let the nucleus to be dry and left for drying.



(4) Layer formation: After drying it form a solid tough layer over the nucleus.



Layer formation

(5) Pellet form: After drying and layer formation it is converted into the pellet form.

→ It is may be of two type:-

(A) Powder layering

(B) Solution Suspension layering.

A) Powder layering: If we use the Powder drug for spray this is called Powder layering.

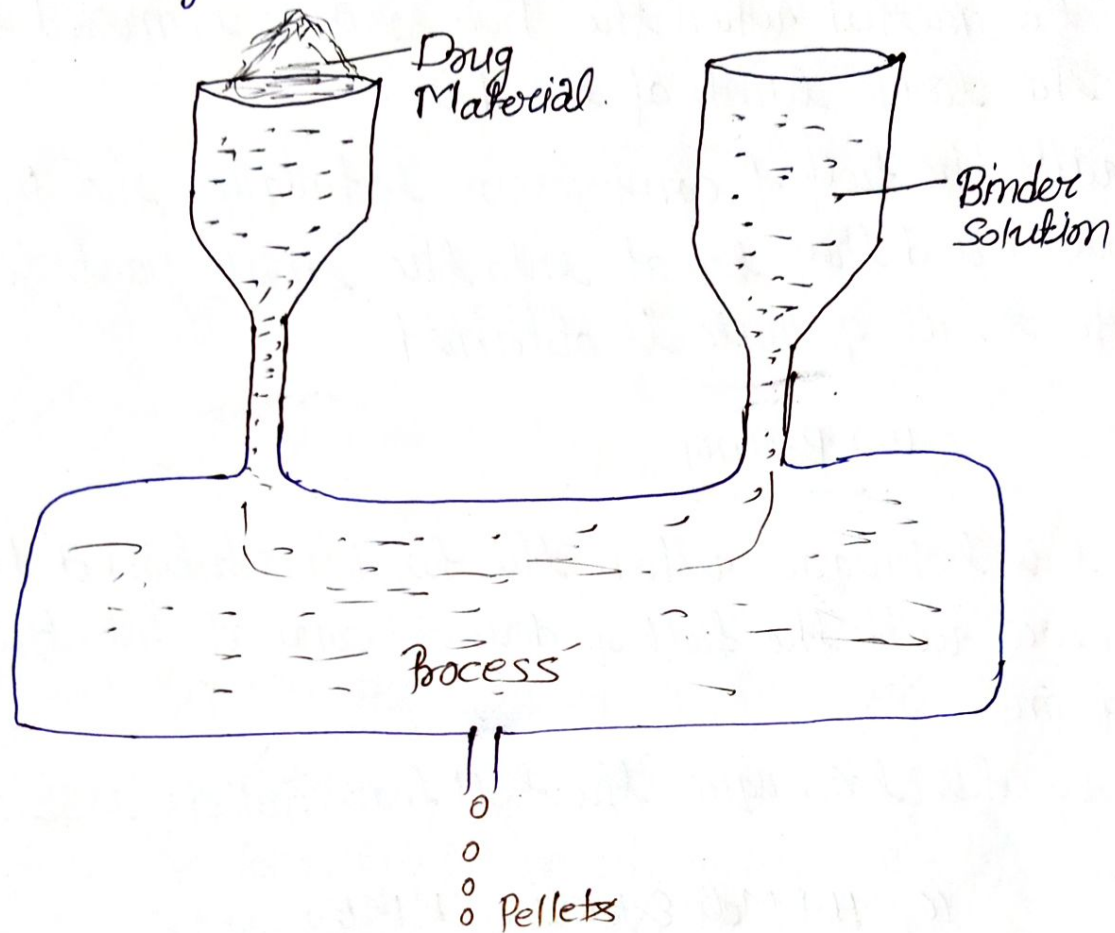
B) Solution Suspension layering: If we use the drug in the form of solution or suspension form then this is called solution or suspension layering.

(2) Extrusion Spheronization:

→ This is the machinery based techniques basically in this techniques. Binder solution and drug material are mixed together and atomize into the small particle and after compression they converts into the pellets form.

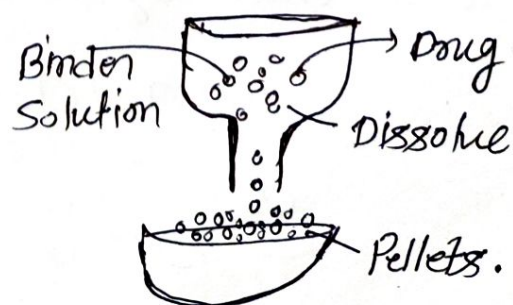


→ They are smooth and uniform in size and very spherically in nature.



### (3) Cryopelletization:

- In this method the formation of pellets is based on the low temperature or below the freezing point.
- In this solution when the drug is mixed in the binder solution and dissolve and they are comes out in the drop form. and this drop is when goes enter the  $-5^{\circ}\text{C}$  then it convert into the solid form and pellets are obtained in the container.





#### (4) Compression:

- ⇒ In this method when the drug solution is mixed they form the large lump of the drug.
- And with the help of compression techniques the pressure is applied and they break into the small particle and the small granule is obtained.

#### (5) Balling

- ⇒ In this techniques when the binder solution and the drug are with the help of devices convert into the ball form.
- ⇒ And by this techniques the ball form pellets is obtained.

#### (6) Hot Melt Extrusion (HME)

- It is based to the balling process the pellets is obtained in the form of ball but in this method the binder is mixed at high temperature.

#### • Evaluation of Pellets & B.C of Pellets:

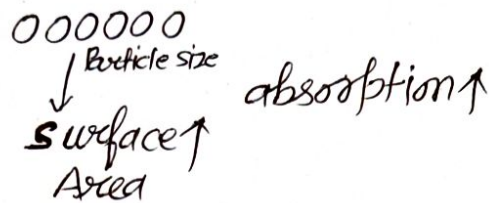
- (1) Particle Size distribution: The particle size of Pellet should be uniform and small in size.
- ⇒ And it is check by the screening method.

○○○○○ - uniform

○○○○○  
○○○ - screening

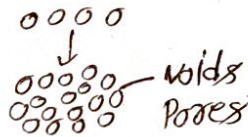


(2) Surface Area: The surface area of Pellets (defined as) besides the absorption rate so the particle size is small the surface area will be large and their absorption rate will be high.  
→ It is determined by the microscopic Method.



(3) Porosity (SEM) The voids space between the Pellets is called Porosity.

→ And the Porosity can be determined by the "Standardized Electronic Microscope"



(4) Density

(5) Hardness and friability