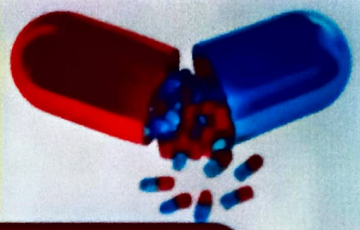
UNIT – III



PART – 1 HARD GELATIN CAPSULES

Points to be covered in this topic

1. INTRODUCTION
2. HARD GELATIN CAPSULES
3. PRODUCTION OF HGC
4. FILLING, SIZE CAPACITY, FORMULATION
5. HAND OPERATED FILLING MACHINE
6. MANUFACTURING DEFECTS

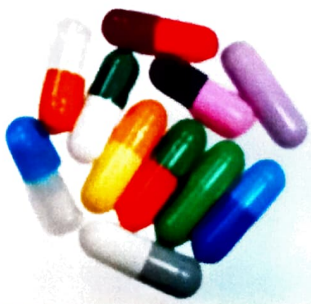
❑ INTRODUCTION

- **"Capsules" are the solid dosage forms** consisting of **single dose of drug** enclosed in a water soluble shell of a **suitable form of gelatin.**
- Capsules may be classified as either hard or soft depending on the nature of the capsule shell.
- Soft gelatin capsules are made from a more flexible, plasticized gelatin film than hard gelatin capsule.

✓ **There are two types of capsules :-**

(a) Hard gelatin capsules

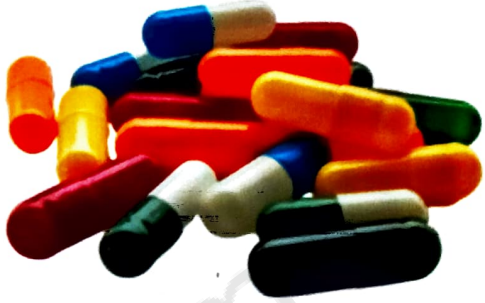
(b) Soft gelatin capsules



HARD GELATIN CAPSULES

❑ INTRODUCTION

- Hard gelatin capsules are used for **administration of powders / solid medicaments.**



✓ It consists of two cylindrical halves:

(a) Body

(b) Cap

- The **diameter of the body is slightly smaller** than the **diameter of the cap** but larger in length and the **cap is slightly larger in diameter and smaller in length**.
- The **drug is filled in the body part** over which the **other half is fitted as a cap.**

❑ ADVANTAGES OF HARD GELATIN CAPSULES

- **Easy to swallow, and masking capacity.**
- **Protection of medicament.**
- **Therapeutically inert & easy to digest.**
- **Easy to handle and carry.**
- **Different sizes are available.**
- **Product Identification.**
- **Provide enteric & sustained release effects.**
- **No need of complicated machinery.**
- **Filling of incompatible substance in the same.**
- Hard gelatin capsules **allow a degree of flexibility of formulation not obtainable with tablets.**

HARD GELATIN CAPSULES

❑ DISADVANTAGES OF HARD GELATIN CAPSULES

- **Hydroscopic drug is not suitable for filling into the capsule.**
- **Chloride are sudden release** such compound in the **stomach cause irritation.**
- **Efflorescent substance may cause to capsule too soft.**
- **Deliquescent material may dry to capsule shell to excessive.**
- **Cross linking can affect hard gelatin.**

❑ PRODUCTION OF EMPTY HARD GELATIN CAPSULE

✓ **Dipping** - **One hundred and fifty pairs** of these **pins are dipped, into a gelatin sol^{n}** of controlled viscosity to form caps and bodies simultaneously.

✓ **Spinning** - The pins are usually rotated to **distribute the gelatin uniformly** during which time the gelatin may be set or gelled by a blast of cool air.

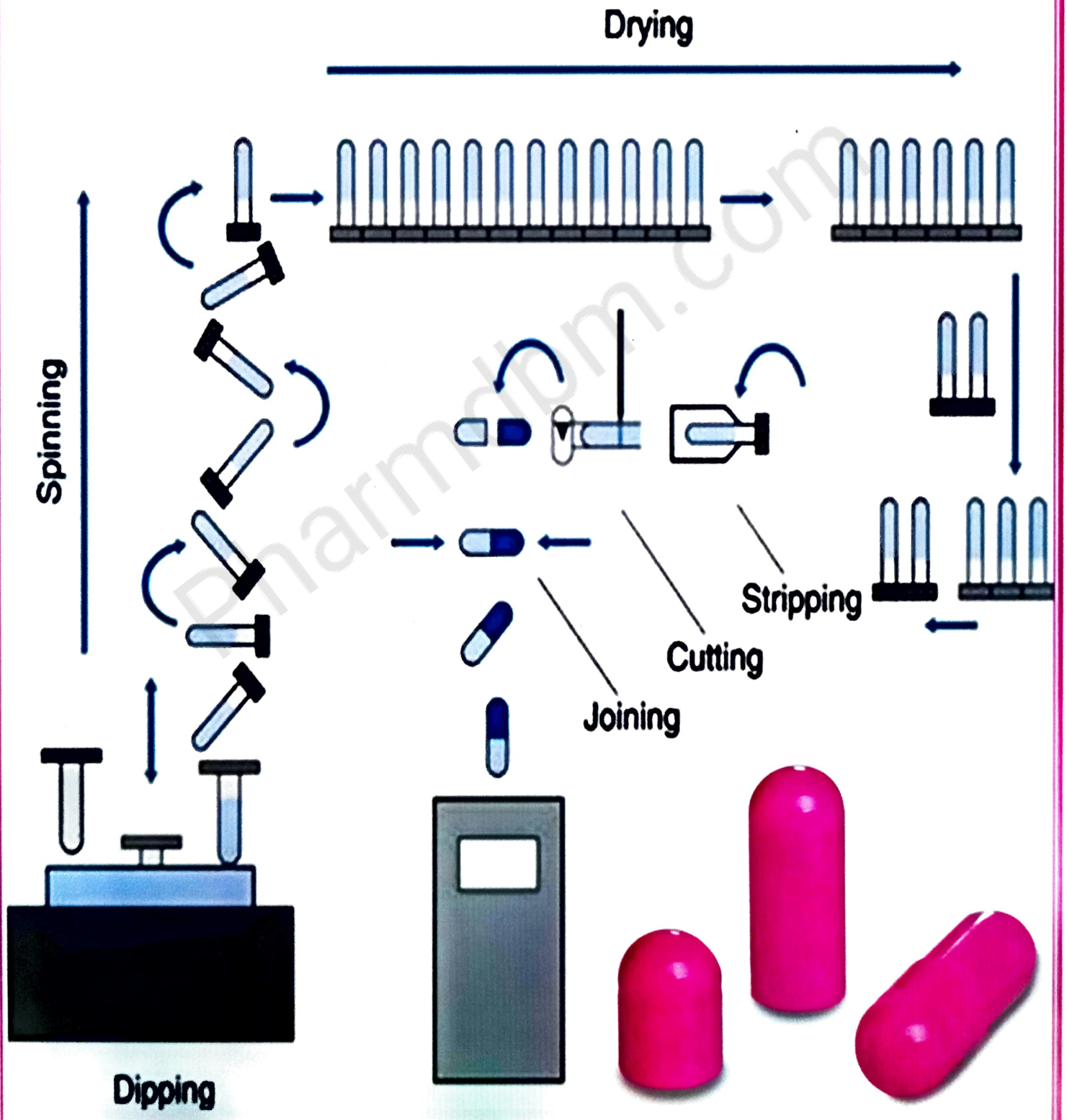
✓ **Drying** - The pins are moved through a series of **controlled air drying kilns** for the gradual and precisely controlled removal of water

✓ **Stripping** - The capsules are **stripped from the pins by bronze** jaws and trimmed to length by **stationary knives while capsule halves are being spun in chucks or collets**

✓ **Trimming** - **After being trimmed to exact length,** the **cap and body sections are joined** and ejected from the machine. The entire **cycle of the machine lasts for approximately 45 min.**

HARD GELATIN CAPSULES

- ✓ **Joining** – After trimming the empty capsule shell the cap and body are joined together.
- ✓ **Polishing** - Polishing of capsule shell is done by polymer.



HARD GELATIN CAPSULES

❑ FILLING CAPACITY OF HARD GELATIN CAPSULE

- **Empty capsules are sold by sizes.**
- The ones most commonly employed for human use range from **size 0, the largest, to size 5, the smallest.**
- **Size 00 capsules may occasionally** be required because of the volume of material to be filled, **but this size is not used commercially in large volume.**

Capsule	Approx Vol. in ml	Approx. wt. in mg
000	1.35	950
00	0.95	650
0	0.75	450
1	0.55	300
2	0.4	250
3	0.3	200
4	0.25	150
5	0.15	100

❑ PREPARATION OF FILLED HARD GELATIN CAPSULE

- **Development and preparing the formulation** and selection of the size of the Capsule
- **Proper mixing & blending**
  - **Lilly type equipment – Powder must be free flowing.**
  - **Zanasi type equipment – Have cohesiveness**
  - **Add compatible excipients –Microcrystalline cellulose**

HARD GELATIN CAPSULES

❑ PREPARATION OF FILLED HARD GELATIN CAPSULE

❖ Filling the Capsule shells

- Manual punch machine
- Automatic & Semi automatic

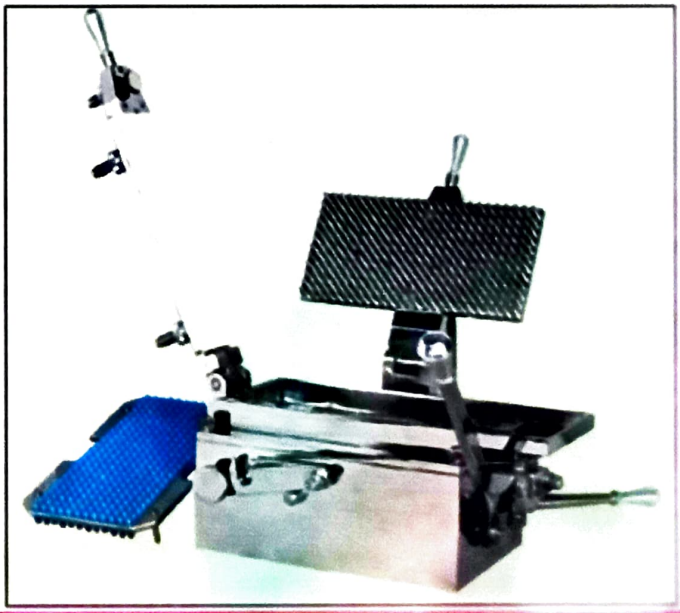
❖ Capsule sealing

- Machine linked with filling machine.
- Banding – Two capsule parts are sealed with gelatin band.
- Contact area seal by water and ethanol and thermally bonded at 40-450°C

❖ **Cleaning & Polishing-** After filling some powder formulation may adhere outside capsule they may be removed by cleaning & polishing.

❑ HAND OPERATED CAPSULE FILLING MACHINE

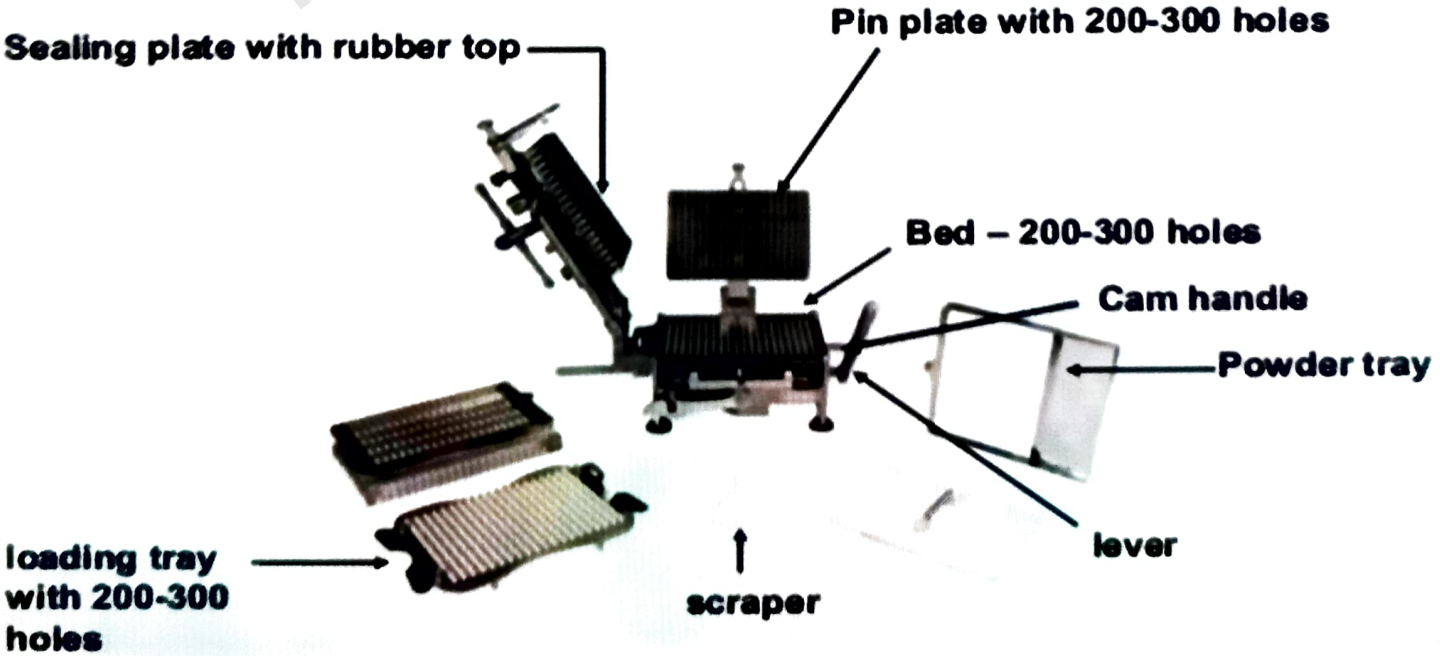
- Place empty capsules onto the loading tray and place tray onto the machine. Check the front knob it should be turned to the right.
- Pull locking lever forward. Push down long handle which will lifts the caps off all the bodies. Set aside the tray containing all the caps.
- Push locking lever back, by which capsule bodies will drop down and become level with filling surface.
- Place powder tray on filler: Keeps powder from spilling.



HARD GELATIN CAPSULES

❑ HAND OPERATED CAPSULE FILLING MACHINE

- Pour & spread the pre-measured powder.
- Move 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. Return the tray containing caps to filler.
- Turn front 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 & all capsules will get out from tray.



HARD GELATIN CAPSULES

❑ MACHINE IN CAPSULE PREPARATION

❖ ROTOSORT

- It is a new filled capsule sorting machine sold by **Eli Lilly and Company.**
- It is a **mechanical sorting device** that removes loose powder, unfilled joined capsules, filled or **unfilled bodies, and loose caps.**
- It can handle up to **150,000 capsules per hour**, and can run directly off a **filling machine or be used separately.**

❖ ERWEKA KEA

- The **Erweka KEA dedusting and polishing** machine is designed to handle the **output from any capsule filling machine.**
- It moves the capsules between soft plastic tassels against a perforated **plastic sleeve, under vacuum.**
- **Any residual powder is removed by the vacuum.**

ROTOSORT

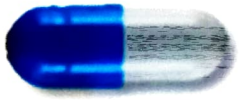
Erweka KEA

HARD GELATIN CAPSULES

❑ CAPSULE MANUFACTURING DEFECTS

➢ Colour deviation

Relative bad stability of selected dyes and pigments, improper amount of the pigment or improper homogenization of the pigment.



➢ Short body/cap

Insufficient entry of the **body/cap into the collet prior to** cutting operation due to wet shell or problem with the collet.

➢ Long body/cap

Caused by a missing knife/broken **knife during cutting operation**.

➢ Dots/specks

Small fragments of shell walls generated during the trimming process **getting into the dipping area**. This happens during the **mold dipping process**. Could also be result of a print.

➢ Double cap

Loose cap fits over the body of another capsule after one of the caps is loose due to insufficient pre-lock position in joining block. **This happens during handling** of capsules.

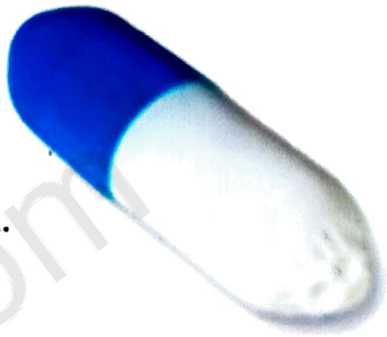
HARD GELATIN CAPSULES

❑ CAPSULE MANUFACTURING DEFECTS

➢ Points/damaged edge/rough cut

Caused by a blunt knife during cutting operation.

➢ Star ends



Uneven distribution of **gelatin on dip-coated pins or an** excessive amount of gelatin solution on the end of the pin.

➢ Bubbles

Improper vacuum or duration of the **gelatin bubbles extraction process.**

➢ Damaged print

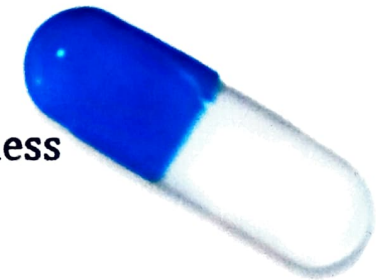
Improper ink viscosity **and applying pressure,** uneven flow of the ink, clogged ink jets, incomplete drying of ink etc.

➢ Thin/thick wall

Uneven distribution of **gelatin on dip-coated pins (thin wall).**

Pins are dipped **twice or are in gelatin too long (thick wall).**

➢ Split



Caused by uneven drying or an uneven film thickness at the **point of split.**

UNIT – III

PART – 2 SOFT GELATIN CAPSULES

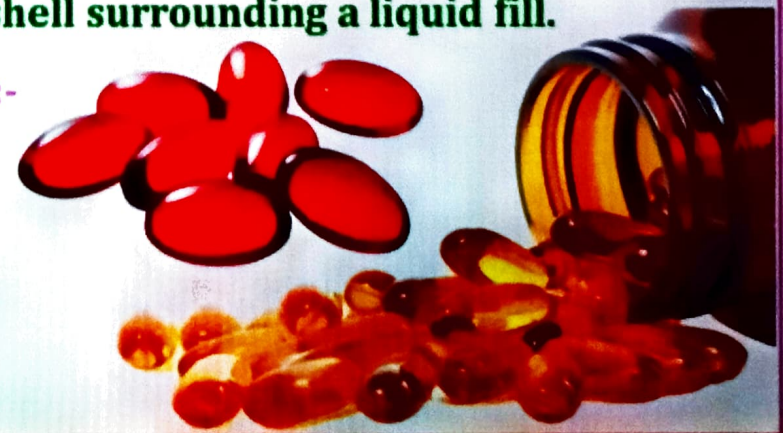
Points to be covered in this topic

1. INTRODUCTION
2. CONTENTS OF SOFT GELATIN CAPSULE
3. PHYSIOCHEMICAL PROPERTY
4. PREPARATION OF SGC
5. EVALUATION OF CAPSULES
6. PACKAGING, STORAGE & APPLICATION

❑ INTRODUCTION

➢ **SOFT GELATIN CAPSULES**

- A softgel is an oral dosage form for **medicine in the form of a specialized capsule.**
- They **consist of a gelatin based shell surrounding a liquid fill.**
- Softgel shells are a **combination :-**
  - ✓ **Opacifier –**
    - Gelatin, Water
  - ✓ **Plasticizer –**
    - Glycerin, Sorbitol



❖ ADVANTAGES OF SOFT GELATIN CAPSULES

- They permit liquid drugs to be presented as solid dosage forms
- Problem encountered during mixing of solids & during compression are avoided
- Stability of sensitive drugs may be enhanced by encapsulating as softgel
- Bioavailability of certain drug is improved when administered in the form of soft gelatin capsules.
- Provide a patient-friendly dosage form for peroral administration of nonpalatable.

❖ DISADVANTAGES OF SOFT GELATIN CAPSULES

- Moisture-sensitive drugs may not be stable in soft gelatin capsules due to relatively higher water content in soft gelatin shell (20–30% w/w).
- Soft gelatin capsules are not an inexpensive dosage form, particularly when compared with direct compression tablets.

- There is more intimate contact between the shell and its liquid contents than exists with dry-filled hard gelatin capsules, which increases possibility of interactions.

❑ CONTENTS OF SOFT GELATIN CAPSULE

❖ **Preservative** – Preservatives are added to prevent the growth of bacteria and mould in the gelatin solution during storage.

Methyl paraben: Propyl Paraben Cholesterol - 4 : 1

❖ **Opacifiers** - An opacifier is a substance added to a material in order to make the ensuing system opaque. Ex :- TiO_2 (0.2-1.2%)

❖ **Sugar** - To produce chewable shell and taste.

❑ CONTENTS OF SOFT GELATIN CAPSULE

- **Essential Oil**- Essential oils are also known as volatile oils, ethereal oils, aetheroleum, or simply as the oil of the plant from which they were extracted, such as oil of clove. 2% for odor & taste.
- **Coating Material**- A coating is a covering that is applied to the surface of an object, usually referred to as the substrate. The purpose of applying the coating may be decorative, functional, or both. E.G. - Salol, CAP, Shellac

- **Formaldehyde**-

  Retards dissolution of gelatin shell (Formalin).

- **1% Fumaric acid**-

  To increase acid solubility & reduce the aldehyde tanning of gelatin.

❑ PHYSIOCHEMICAL PROPERTY OF GELATIN

- **Bloom or Gel Strength**– Measure cohesive strength of capsule cohesive strength between gelatin molecule ∝ Molecular weight of gelatin
  - Higher the bloom strength stable the gelatin shell. 6.66% w/v gelatin kept at 100° C for 17 hour.
  - A plastic plunger having diameter 0.5 inch.
  - Bloom strength – The weight in gram required t plunger in gelatin mass upto 4mm.

- **Viscosity** - Determined by using 6.66% w/w of gelatin solution in water at 60°C using capillary pipette. Range must be in 25-45 millipoise.

❑ PHYSIOCHEMICAL PROPERTY OF GELATIN

❖ **Base adsorption**– Defined as the **minimum amount of base or vehicle** in grams required per gm of solid drug to form a mixture when **easily can be encapsulated in SGC.**

$$\text{Base Adsorption} = \frac{\text{Weight of base}}{\text{Weight of Solid}}$$

BA is number of grams of liquid base required to **produce a capsutable** mixture with 1 gram of solid. Minim per gram

$$(M/G)=(BA+S) \times V/w$$

- M/G is volume in minim that is **occupied by one gram of solid(S)** plus weight of **liquid base required** to **produce a capsutable mixture.**
- **Lower the BA of solid, higher the density of mixture** and **thus smaller the capsule size.**

❑ PREPARATION OF SOFT GELATIN CAPSULES

Preparation of Soft Gelatin Capsules

- **Plate Process**

- **Rotary Die Process**

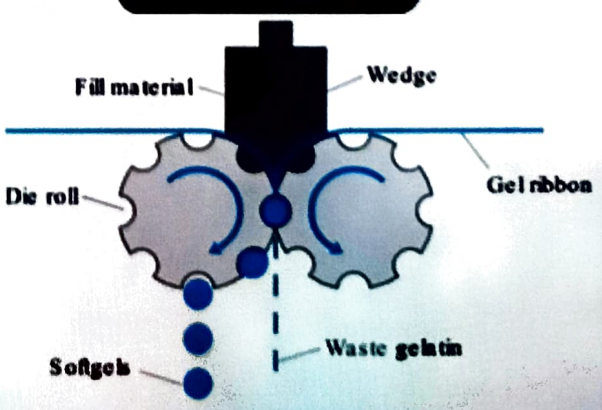
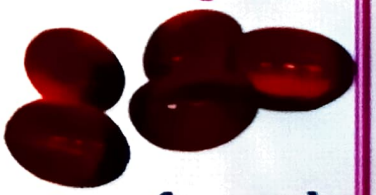


PLATE PROCESS

❑ PLATE PROCESS

- The plate process is the **oldest commercial method of manufacture**, but today this **equipment can no longer be purchased**, and consequently, only a few companies still use this process.
- **Plate process—a batch process**— involves pressing two sheets of wet gelatin together between two molds, **provided with depressions.**

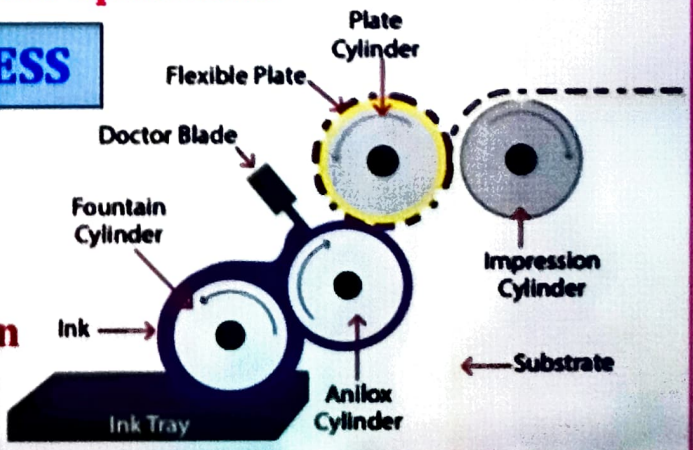
- One of **gelatin sheet is placed over mold** & application of vacuum produce depressions in the gelatin sheet into **which active fill was then placed.**
- A **second gelatin sheet** was laid over the first and both were pressed together with fill **material sandwiched in between.**
- The **pressure of the plate** sealed the top and **bottom sheets of gelatin together.**



- **Softgels were produced by cutting followed by drying.**
- The **plate process that requires** two or three **operators for each machine** has given way to the more modern continuous processes, **which require considerably less manpower for operation.**

➢ ADVANTAGES OF PLATE PROCESS

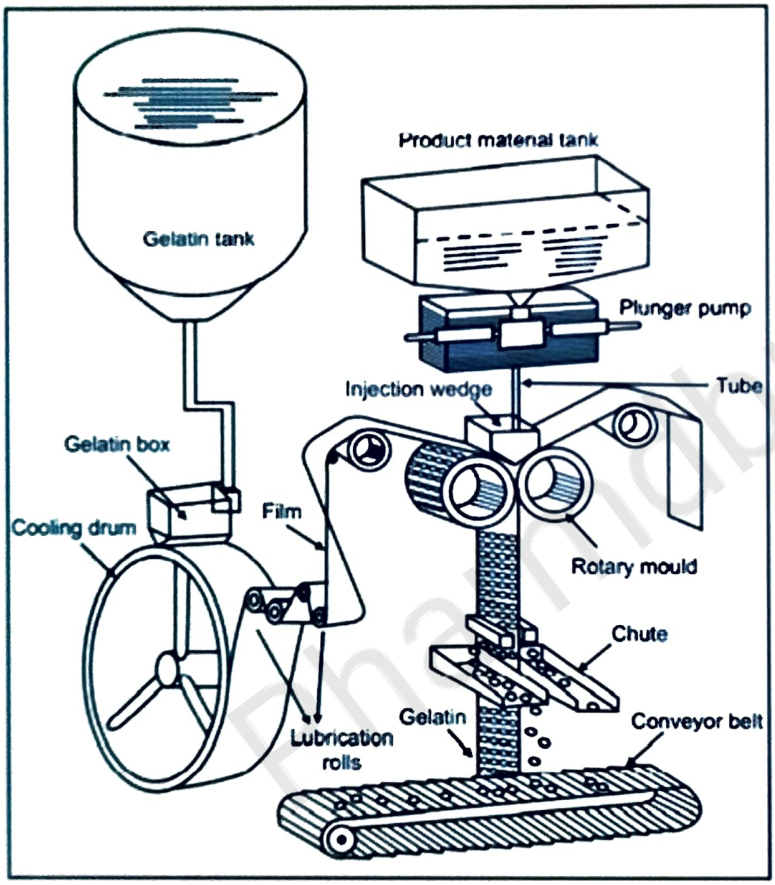
- **Easy to undertake.**
- **Easy to operate.**
- **Doesn't requires a very skilled person for operating this machine.**



ROTARY DIE PROCESS

❖ INTRODUCTION

- Rotary die process is the process of **making a soft gelatin capsule** using a **Rotary Die machine.**
- A rotary die machine is an equipment that is used in **filling gelatin shells with liquids, suspensions or semisolids.**



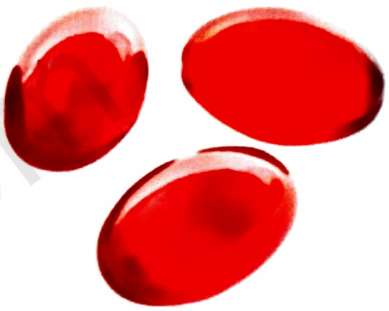
❖ CONSTRUCTION

- The machine used for the **process contains two hoppers, one for the hot liquid gelatin mix** while the **other for the semi-solid or liquid fill.**
- There are **two rotating dies** containing **cavities of desired shape and size** which **rotate in opposite directions.**
- In a rotary die machine, the **soft gelatin capsules are prepared** and **then filled immediately with the liquid medicaments.**

ROTARY DIE PROCESS

❖ WORKING

- Liquid gelatin mixture is placed in one hopper and the liquid medicament in the other hopper.
- There are two rotating dies which rotate in opposite directions.
- When fluid gelatin mixture enters into machine, it produces two continuous ribbons
- These ribbons come over the rotating dies from opposite directions & enter in between dies.
- Thus, half shell of the capsule is formed.
- At this stage measured quantity of medicament is filled into it with stroke of pump.
- With the subsequent movement of the dies.
- The other half of the capsule is formed.
- Two halves of capsules are sealed together by heat & pressure of rotating dies.



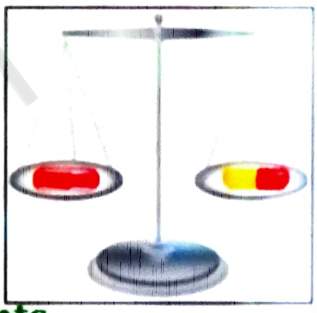
❑ EVALUATION OF CAPSULES

1. Content of active ingredient
2. Uniformity of Weight
3. Uniformity of content
4. Disintegration test
5. Dissolution test

❑ EVALUATION OF CAPSULES

❖ Content of active ingredient :-

- The content of active ingredient is **determined on a sample of 20 capsules** by following assay procedure as **indicated in individual monograph.**
- The result of the assay gives the average drug content of the **20 capsules** which must lie within the range for the **content of active ingredient stated** in the **monograph (which is usually 90 to 110 % of the label claim).**



❖ Uniformity of Weight :-

- In **these test 20 intact capsules** are **first weighed individually** & **then weighed after removing their contents**
- **Difference between two weights gives weight of contents.**
- **Not more than two capsules** should deviate from **average weight of the contents**
- This **test is not applicable to capsules** that are **required to comply with the test for Content uniformity of active ingredients.**

❖ Uniformity of content :-

- This test is applicable to capsules which have a **drug content of less than 10 mg** or when the active ingredient **comprises less than 10% of the total capsule content.**
- This test is however **not applicable to capsules containing multivitamins & trace elements.**
- In this test, **ten capsules are assayed individually** by the method specified in the individual monograph.

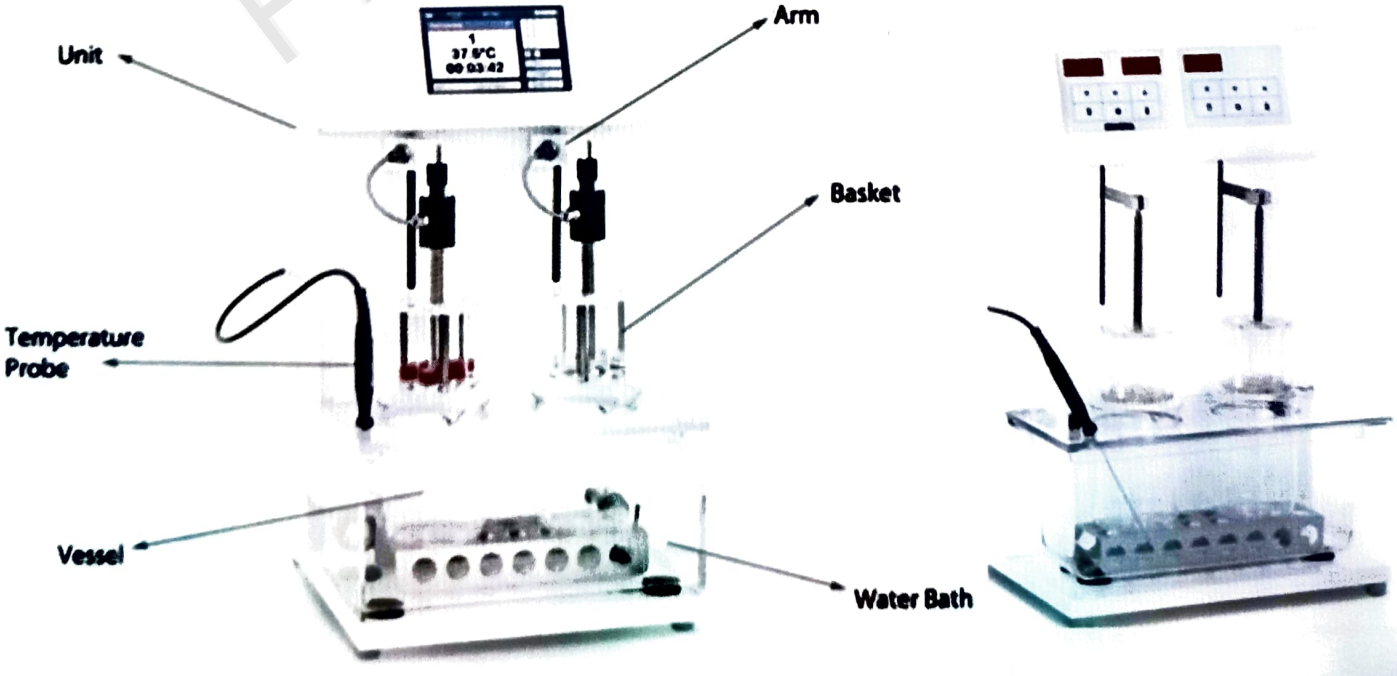
❑ EVALUATION OF CAPSULES

❖ Disintegration test :-

- The disintegration test for **capsules is similar** to that used for **testing of tablets.**
- Test is **not applicable to modified release capsules** & capsules for which **dissolution test is prescribed.**
- The **hard gelatin capsules** are expected to disintegrate within **30 minutes** while the **soft gelatin capsules** in **minutes unless otherwise specified**, when water is used as the testing fluid.

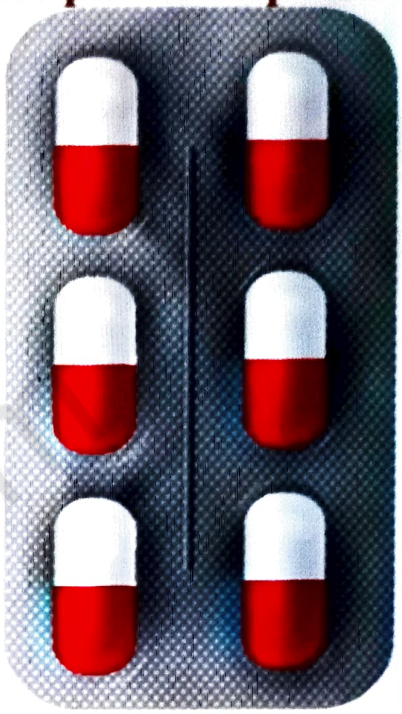
❖ Dissolution test :-

Dissolution test for capsules is essentially **similar to that followed for tablets** with the acceptance **criteria also being the same as that for capsules.** However, where the capsule shells are found to interfere with the analysis. Necessary correction can be made by dissolving the empty shells of **not less than 6 capsules** in the specified **volume of dissolution medium.**



PACKING AND STORAGE OF CAPSULES

- **Capsules should be packed in well-closed glass** and stored at a **temperature not exceeding 30°C.**
- They should comply with **storage requirements in the pharmacopoeia of India.**
- Capsules can be individually **protected by enclosing them in a strip or blister packs.**
- In strip packing, capsule is hermetically sealed within strips of an **aluminum foil/plastic film.**
- The contents are removed from the strip packs by **tearing / cutting to separate capsules.**
- **In case of blister packs,** a press on blister forces the capsule through the backing strip.



- Generally, capsules **have a longer shelf life** in unopened **glass bottles than in strip-packs** but this is reversed, **once a bottle has been opened.**

Criteria	Hard Gelatin Capsules	Soft Gelatin Capsules
Shell	**Not plasticized**	**Plasticized (Glycerin, Sorbitol, PEG)**
Moisture	**12-16%**	**6-10%**
Sizes	**Limited**	**Many**
Shapes	**Two-piece**	**One-piece**
Content	**Usually dry solids**	**Usually liquids or suspensions**
Closure	**Traditional friction-fit; mechanical interlock, banding**	**Hermetically sealed (inherent)**

APPLICATION OF CAPSULES

Enteric coated capsules

- Enteric coated capsules are hard or soft capsules prepared in such a manner that shells
- resist the action of gastric fluid but are attacked by the intestinal fluid to release the contents.

Chewable capsules

- Chewable soft gelatin capsules are soft gelatin capsules designed to release the active ingredients in the mouth.
- Some of the capsules dissolve completely in the mouth while some others leave a residue of a water-insoluble gum

Modified release capsules

- Modified release capsules are hard or soft capsules in which the contents or the shell, or both.
- Contain auxiliary substances or are prepared by a special process designed to modify rate at which active ingredients are released.

Rectal and vaginal capsules

- Soft gelatin capsules provide a good substitute for rectal and vaginal suppositories.
- Various shapes and sizes are used for the purpose with the oval shape being most popular because of the ease of insertion.

Ophthalmic capsules

- Soft gelatin capsules provide a useful and economical unit dosage pack for ophthalmic ointments.

UNIT – III

PART – 3 PELLETS

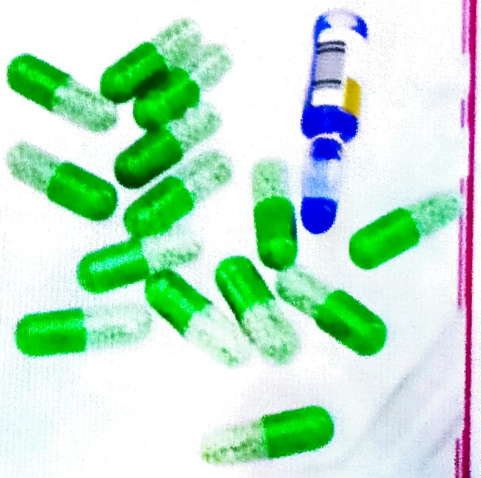
Points to be covered in this topic

1. INTRODUCTION
2. ADVANTAGES OF PELLETS
3. DISADVANTAGES OF PELLETS
4. FORMULATION REQUIREMENTS
5. METHODS OF PELLETIZATION PROCESS
6. EQUIPMENTS FOR MANUFACTURING

❑ INTRODUCTION

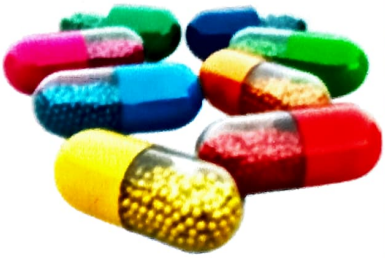
➢ **PELLETS**

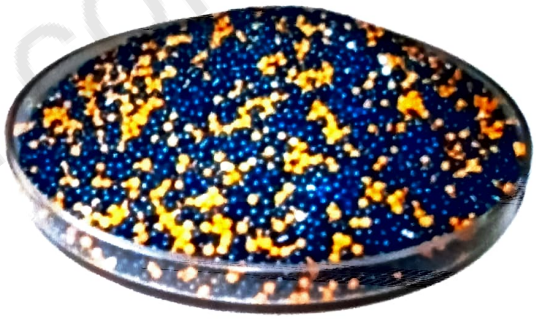
In pharmaceutical industries, **pellets are multiparticulate dosage form** which was formed by the **agglomeration of fine powdered excipient** and drugs together that leads to the formation of **small free flowing spherical** or **semi spherical particles.**



❑ ADVANTAGES OF PELLETS

- **Uniformity of dose.**
- **Pellets composed of different** drugs can be blended and formulated in **single unit dosage form.**
- **Excellent flow properties**
- Prevention of contamination **due to dust formation.**
- Pellets are recommended for **patients with difficulty in swallowing.**
- **Improves aesthetic appearance of products.**
- Bitter taste masking can be obtained.
- **Pellets disperse freely in the GIT** and hence greater **absorption of the active drug occurs.**
- **Reduced risk of dose dumping (Premature release of drug)**





❑ DISADVANTAGES OF PELLETS

- **Preparation of pellets** is a complicated and **time consuming process**.
- **Requires highly specialized equipment.**
- Trained or skilled **personal needed for manufacturing.**
- **Higher cost of production.**
- **Lack of manufacturing reproducibility and efficacy.**

❑ FORMULATION REQUIREMENTS OF PELLETS

- **Formulation aids or excipients are added to pharmaceutical dosage forms for satisfactory delivery of the drug to the target site, to impact favorable features to the dosage form, and to facilitate product manufacture.**
- **Since pellets are meant for oral administration the excipients used are same as those used in the formulation of tablets or capsules.**

❖ Excipients used during manufacture are

- **Fillers** :- Are used to add bulk or weight to the products.
  - E.G. -Microcrystalline cellulose (MCC) , Starch, Sucrose.
- **Binders** :- Added to bind powder & makes the pellet integrity.
  - E.G. - Hydroxypropyl methylcellulose (HPMC), Hydroxypropyl cellulose (HPC), Gelatin.
- **Lubricants** :- Added to reduce friction between particles and surface of equipment.
  - E.G. Glycerine, Polyethylene glycol(PEG), Magnesium or Calcium stearate.
- **Separating agents** :- During manufacture, pellets may develop surface charge and get attracted to each other. Separating agents promote separation of pellets into separate unit.
  - E.G. Kaolin, Talc, Silicon dioxide.
- **Disintegrating agents** :- Break down of pellets when ingested.
  - E.G. Alginate, Cross carmellose sodium.
- **pH adjuster** :- A pH adjuster is a chemical used to alter the pH or Potential Hydrogen level.
  - E.G. Citrate, Phosphate

❑ PELLETIZATION PROCESS

❖ PELLETIZATION TECHNIQUES

- Palletization is an agglomeration 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.
- Palletization is often referred to as a size-enlargement process that involves the manufacture of agglomerates or pellets having a relatively narrow size range (Mean size from 0.5-2.0mm).

❑ METHODS OF PELLETIZATION PROCESS

a. DIRECT PELLETIZATION

b. AGITATION

c. CRYOPELLETIZATION

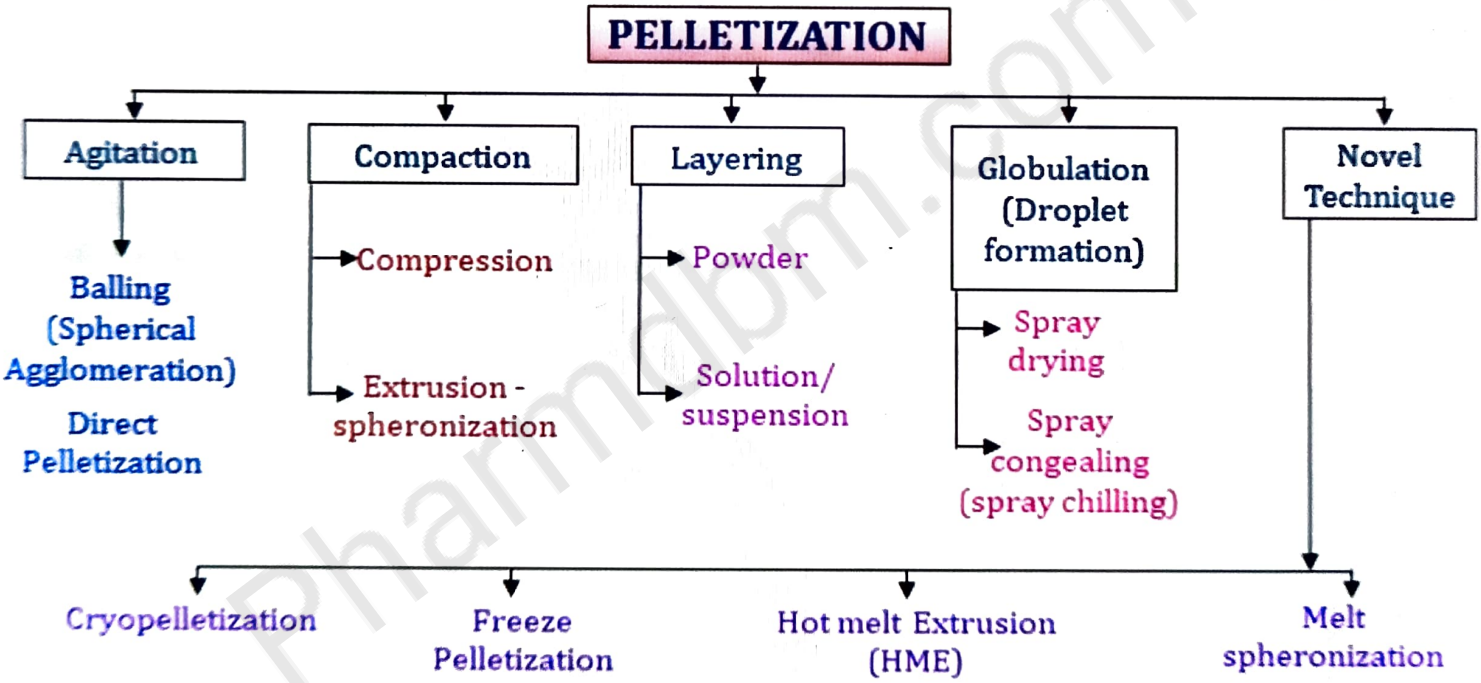
d. POWDER LAYERING

e. SOLUTION / SUSPENSION LAYERING

f. EXTRUSION – SPHERONIZATION

g. GLOBULE / DROPLET FORMATION

h. FREEZE PELLETIZATION



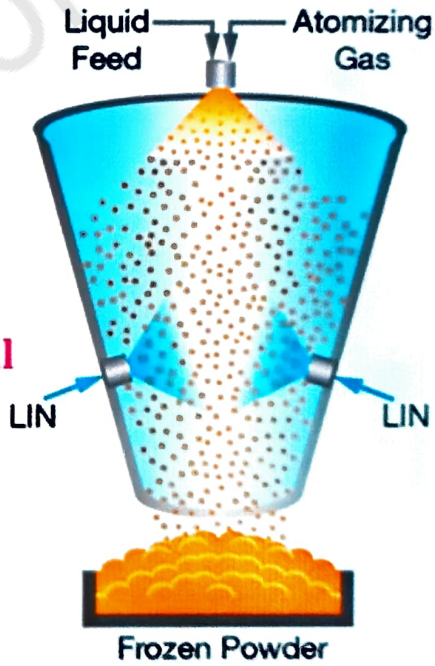
❖ DIRECT PELLETIZATION

- In **direct pelletization technique,** pellets am manufactured directly from powder **with a binder or solvent.**
- This process is fast and **requires less auxiliary materials.**
- **By this technique,** compact and round pellets of **diameter between 0.2-1.2mm are obtained.**
- Such pellets am ideal for automatic **dosing and uniform coating.**
- **Pellets have a density higher** than the spray **granulates and agglomerates.**

❖ AGITATION

- Agitation is also known as spherical agglomeration.
- In **spherical agglomeration process**, suitable quantity of liquid is added **before or during agitation** to the finely divided **particles to convert into** spherical particles by a **continuous rolling or tumbling action**.
- Spherical agglomeration can **be divided into liquid-induced** and melt **induced agglomeration.**
- Since many years spherical agglomeration is carried out in horizontal drum **pelletizer, inclined dish pelletizer,** and **tumbling blenders.**

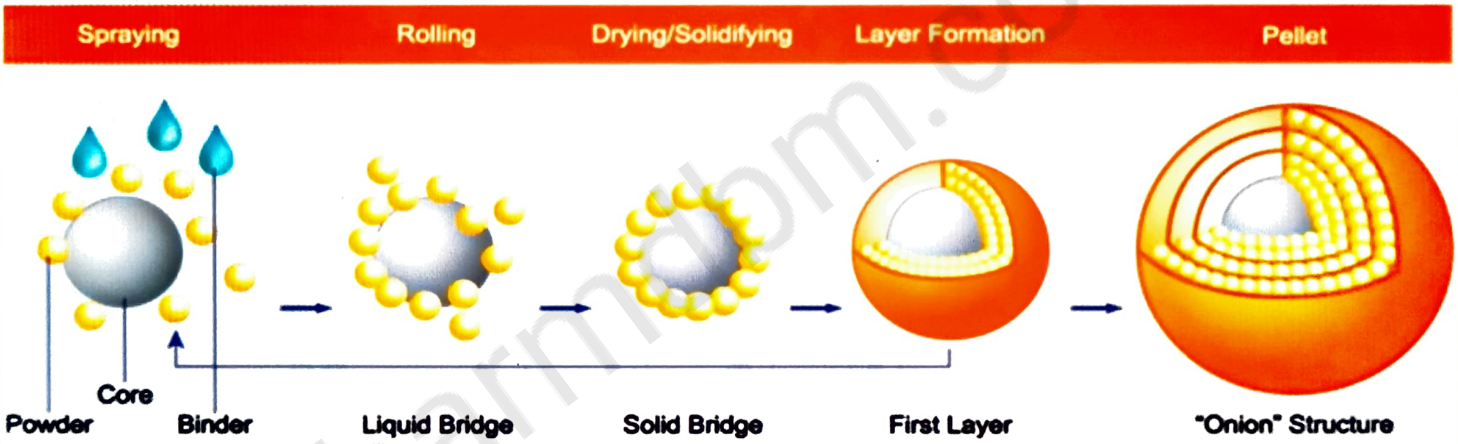
❖ CRYOPELLETIZATION



- In the process of repalletization, **liquid nitrogen is used as a fixing medium to convert the droplets** of liquid formulations **into solid spherical particles or pellets.**
- **Technology initially developed** for **lyophilization can** be used to produce drug-loaded pellets in liquid nitrogen at **160°C temperature**.
- The procedure allows **instantaneous and uniform freezing** of the processed material due to the rapid **heat transfer between the droplets**, and thus the large surface area **facilitates the drying process.**
- 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.

❖ POWDER LAYERING

- Involves deposition of **successive layers of powdered** drug and excipient or both on **preformed cores with the aid of binding** liquid.
- **Both are added simultaneously in a controlled manner.**
- In the initial steps, the drug **particle is bound to the core** to form the pellet **by forming a liquid bridge.**
- These liquid bridges are **solidified to form solid bridges** during solidification.
- **This leads to the formation** of successive layers of a drug and the binder solution until the **desired pellet size is reached.**
- A tangential spray granulator & **centrifugal bed granulator are used.**

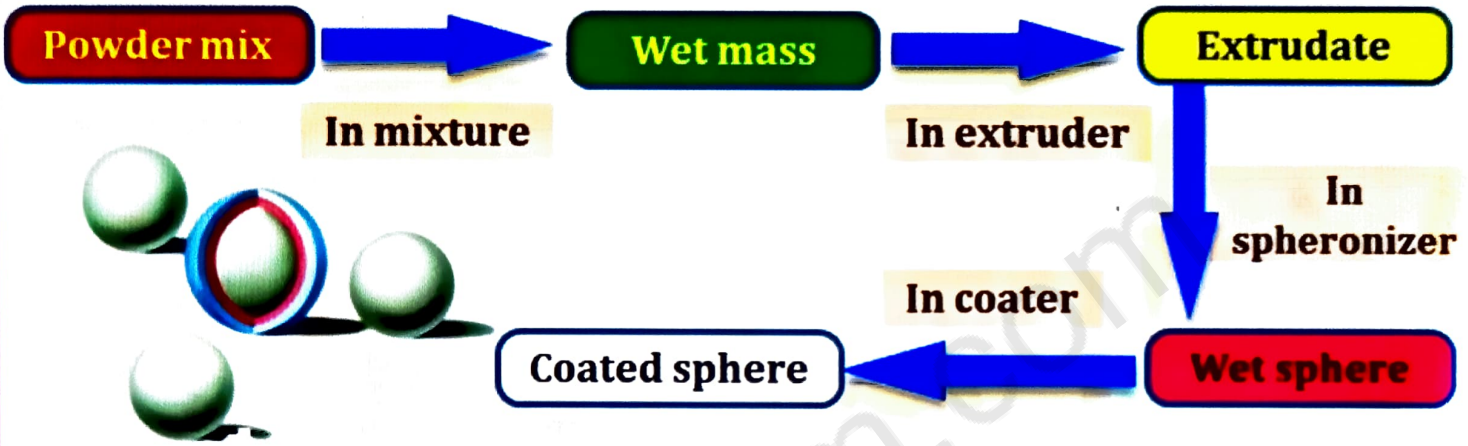


❖ SOLUTION OR SUSPENSION LAYERING

- This techniques involves the **deposition of successive layers** of solution or **suspension of drug substances** and **binders on the starter nuclei.**
- **Which maybe a inert material or granule of the same drug.**
- **Drug particles and other components** are dissolved **or suspended in the binding liquid.**
- Droplets stick on the core and spread **evenly when the solution** or **suspension is sprayed on to the nuclei.**
- **During drying, solid bridges** are **formed between the nuclei and the initial layer** and between the **successive layers of drug substances.**

❖ EXTRUSION – SPHERONIZATION

- **Extrusion — Spheronization, is a multi step** compaction process, to **produce dense uniformly sized** and shaped **spheroids roughly 1mm** in diameter.
- This **technique is mainly used to produce**, pellets with **high drug loading capacity for controlled release** oral **solid dosage form.**



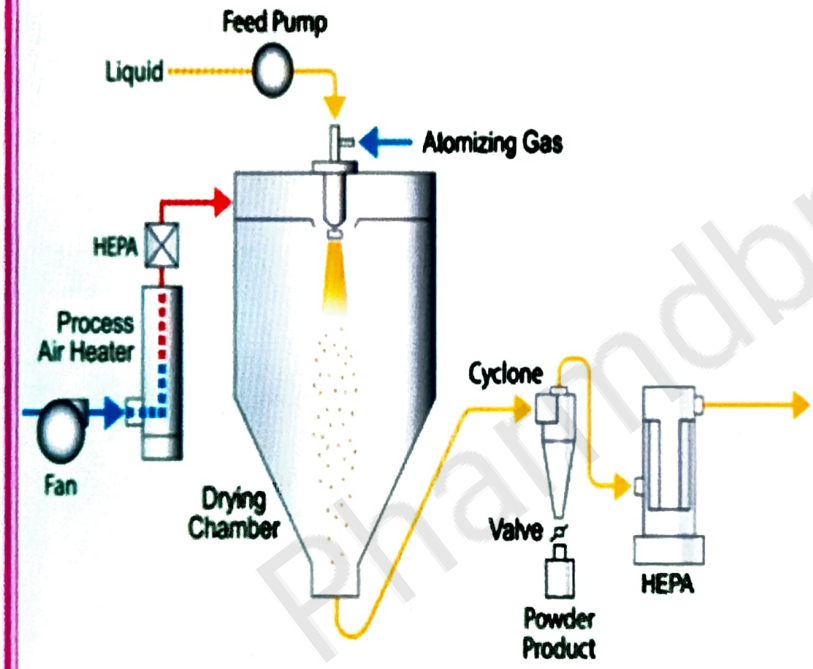
- The **mixture of active ingredients** and excipients are added in to suitable mixture, to get **homogenous powder dispersion**.
- **Conventional wet granulation** method is used to **produce a wet mass in granulators.**
- **In the next step extrusion**, the wet mass passes through the extruder to form rod – shaped **particles of uniform diameter**.
- **The extrudate should have sufficient plasticity** to deform but not so much that the extrudate **particles adhere to other particles.**
- **In the spherization step**, a spheronizer, when **subjected to rotate at higher** speed by friction plate, is **used to break the rod shaped** extrudate in to spherical particle.
- **Pellets are then dried** at room temperature or at **elevated temperature** in a **tray dryer or fluidized bed dryer to retain shape and size.**
- **Then the pellets are finally** screened with the help of sieves, to achieve desired size distribution

❖ GLOBULE OR DROPLET FORMATION

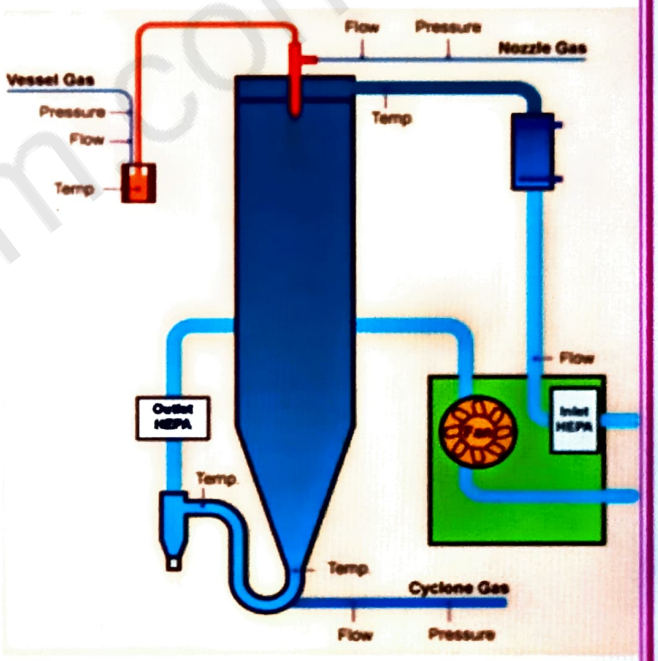
➢ **In the process of globulation, two processes are involved :-**

✓ **Spray drying :- It is a process in which drug** (in solution or suspension), with or **without excipients are sprayed** into a stream of hot air to generate dry, highly spherical particles. **This process is used to enhance the dissolution rates and bioavailability of poorly soluble drugs.**

✓ **Spray congealing :-** It is the process in **which a drug is allowed to melt,** disperse or **dissolve in hot melts of gums,** waxes, fatty acids etc. then it is **sprayed into an air chamber** where the **temperature below** the melting points of the formulation. **No source of heat is used here.**



SPRAY DRYING

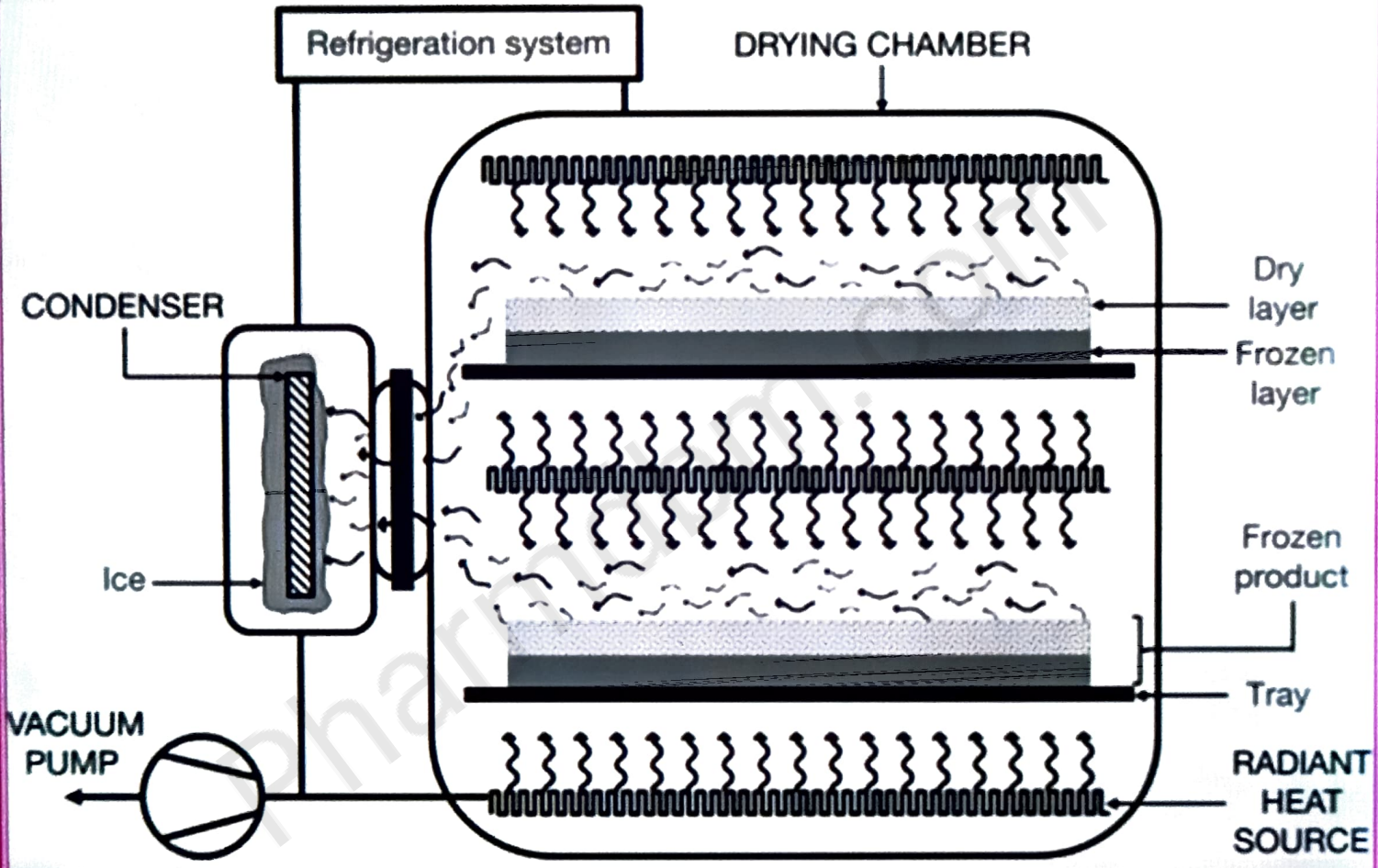


SPRAY CONGEALING

❖ FREEZE PELLETIZATION

- A **molten solid carrier or matrix is introduced in the form of droplets into** an inert column **containing a liquid in which** the molten **solid carrier is immiscible.**
- The molten **solid carrier move upward** or downward in the **liquid column depending** on the density of the **molten solid carrier** with **respect to the liquid in the column, and then solidify into pellets.**

- If the density of the **carrier is less than the liquid,** the carriers are **introduced as droplets from** the top of the **column and the pellets** are **formed at the bottom.**
- If the density of the **carrier is more than the liquid,** the **carriers are introduced as droplets** from the **bottom of the column and the pellets are formed at the top.**



❑ EQUIPMENTS FOR MANUFACTURING OF PELLETS

- ✓ **SUPPLY BINS**
- ✓ **PELLET MILLS**
- ✓ **COOLERS**
- ✓ **CRUMBLE ROLLS**
- ✓ **SHAKER**
- ✓ **PELLET ELEVATING SYSTEMS**

❖ SUPPLY BINS

- The supply bins located ahead of the pellet mill, should store a sufficient quantity of feed to provide a continuous operation of the pelleting unit and also a continuous operation of the mixer which provides mash to the pelleting unit.
- The supply bin constructed from stainless steel should have at least two bins, results in an efficient mixing as well as pelleting.

❖ PELLET MILLS

- The thoroughly mixed ingredients flow into a flow rate regulator called a feeder under gravity.
- It is equipped with speed controlling devices, provides a constant, controlled and uniform flow of feed to the mixing and pelleting operation, and variation in this flow leads to poor conditioning and a variable product.

❖ COOLERS

- The pellets from the pellet mill flow under gravity into a device for cooling and drying.
- When pellets leave pellet mill, they are at very high temp. (190°F) & also have high moisture content (17- 18%).

❖ CRUMBLE ROLLS

- A **crumbling process should** be used for producing pelleted **feed particles smaller than 10/64.**
- In **this process, small pellets are broken** between two powered corrugated rolls, placed below the cooler.
- **A crumbling roll has heavy steel frame and housing.**
- The corrugated rolls are **8-12 inches in diameter and 72 inches** long.

❖ SHAKER

- The product **(either whole or crumblised)** from **crumbling device is passed** to a shaker (screening device) that extracts the **undesirable undersized portions of product from** correctly sized material.
- The **undersized product** is returned to the pellet mill for **repelletisation and is termed recycle or fines.**

❖ PELLET ELEVATING SYSTEMS

- The **correct sized product** in its **finished form is obtained** from the shaker and is ready for **packaging or shipment.**
- **In many mills,** the pellet shaker is **located on the upper floors** of the unit so **that the screened product, the oversize crumbles, and the fines flow under** gravity to **their correct destination.**