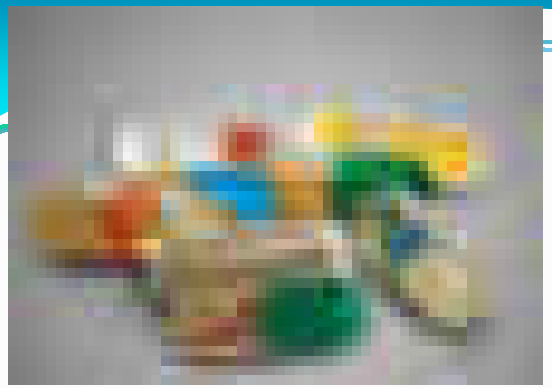
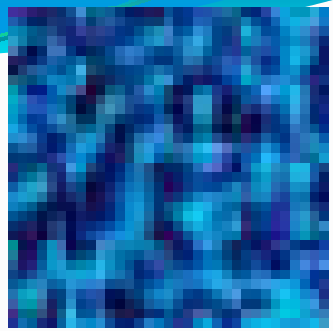




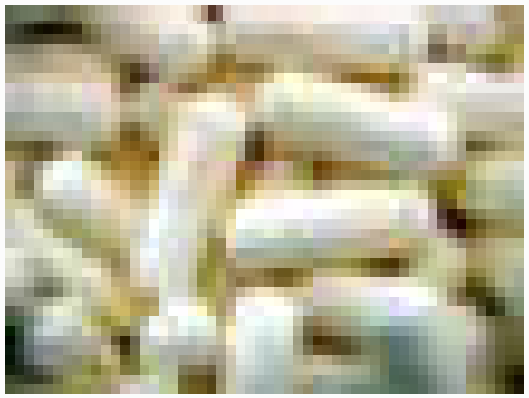
CAPSULES

Capsules are solid dosage forms in which drug substance is enclosed within hard or soft soluble shell. The shells are generally formed from gelatin.

Capsules are of two types

1. **Hard gelatin capsules**

2. **Soft gelatin capsules**



Advantages

- **Capsules are tasteless, odorless and can easily be administered.**
- **Combination of powders we can use**
- **There are attractive in appearance.**
- **The drugs having un-pleasant odor and taste are enclosed in a tasteless shell.**
- **They can be filled quickly and conveniently.**
- **Physician can change the dose and combination of drug according to patient requirement.**
- **They are economical.**
- **They are easy to handle and carry.**

Disadvantages

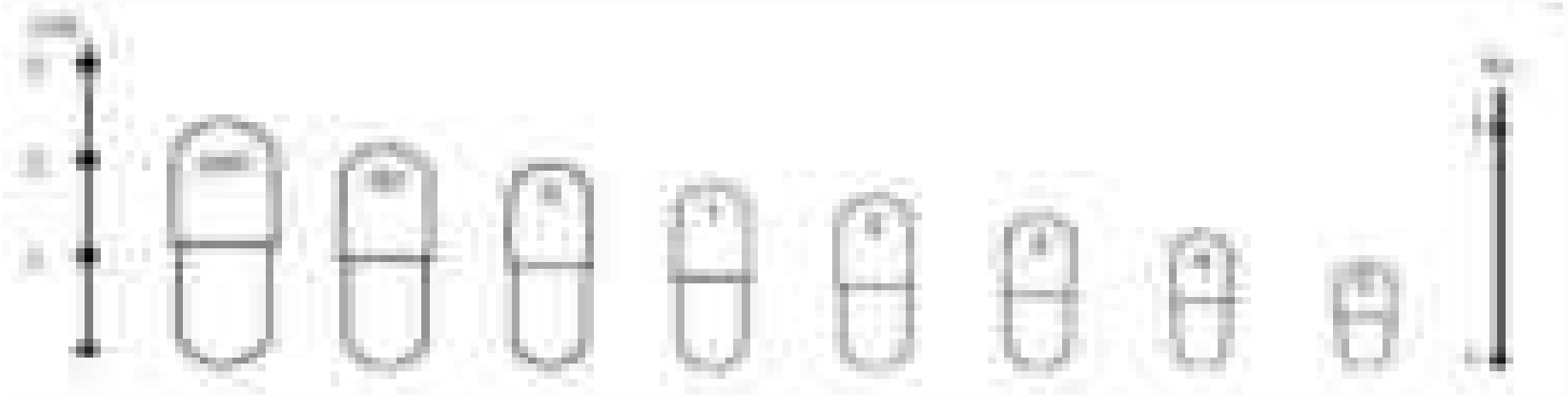
- **Hygroscopic drugs are not suitable for filling into capsules, because they absorb water present in capsule shell makes shell very brittle and ultimately lead to crumble into pieces.**

- **The concentrated solutions which require previous dilution are unsuitable for capsules because if administered as such lead to irritation into stomach**

Capsule size

For human use, empty capsules ranging in size from **000 the largest to 5 the smallest.** Generally, hard gelatin capsule are used to encapsulate between **65 mg to 1 gram.**

Size	Volume in 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	



*The largest size of the capsule is No: 000.

*The smallest size is No: 5.

*The standard shape of capsules is traditional, symmetrical bullet shape.

GELATIN

Gelatin is heterogeneous product derived by hydrolytic extraction of animal's collagen.

The sources of gelatins including animal bones, hide portions and frozen pork skin.

TYPES OF GELATIN

Type A

Type B

There are two basic types of gelatin

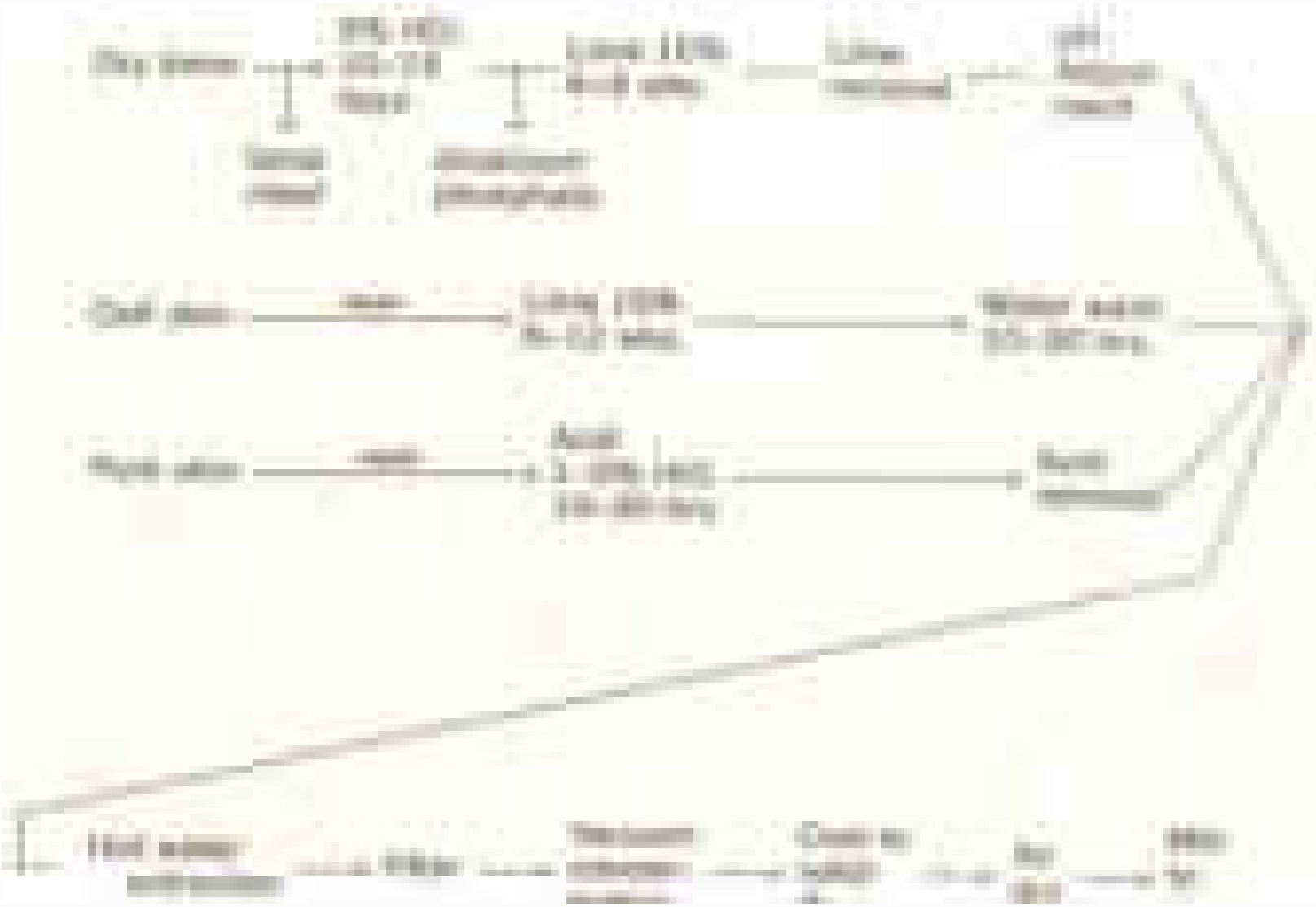
TYPE A

Derived from acid treated precursor that exhibits an iso electric point at pH-9. It is manufactured mainly from pork skin.

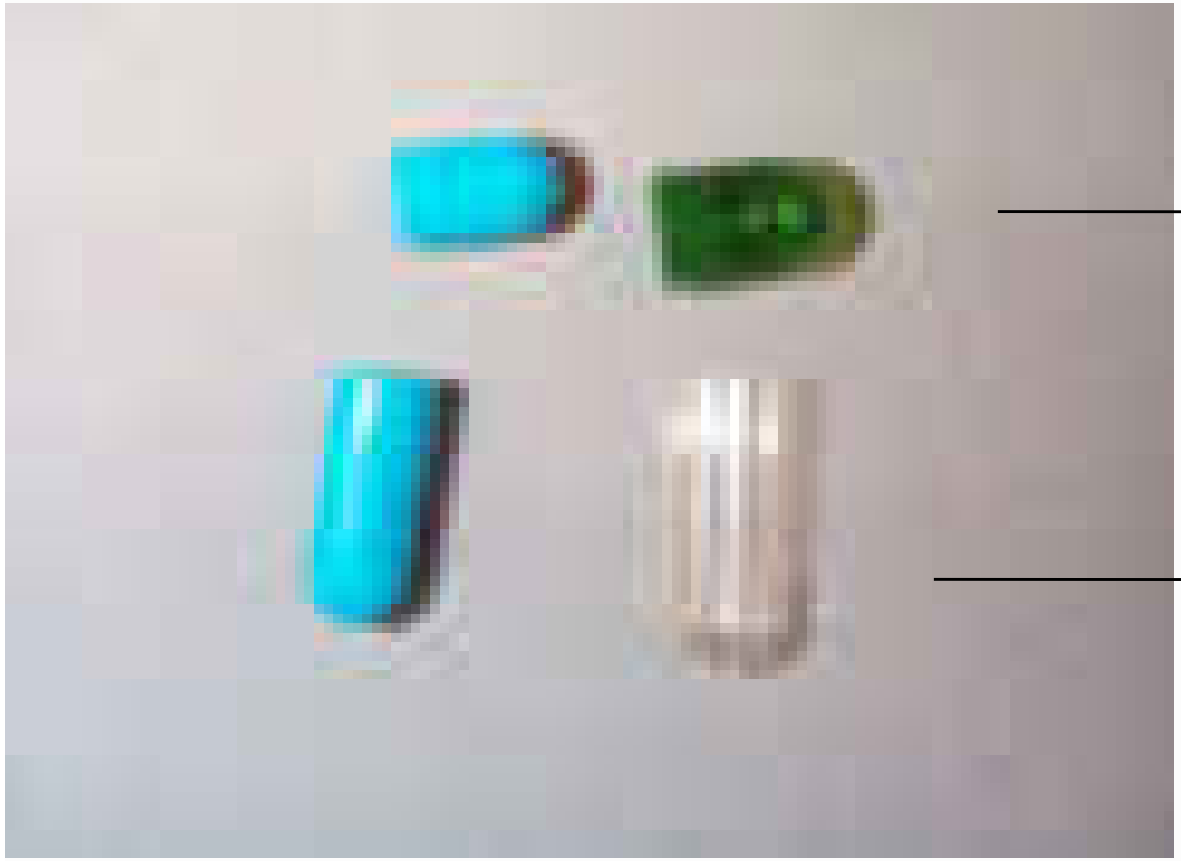
TYPE B

Derived from alkali treated precursor that exhibits an iso electric point at pH-4.7. It is manufactured mainly from animal bones

Preparation Of Gelatin



PARTS OF CAPSULE



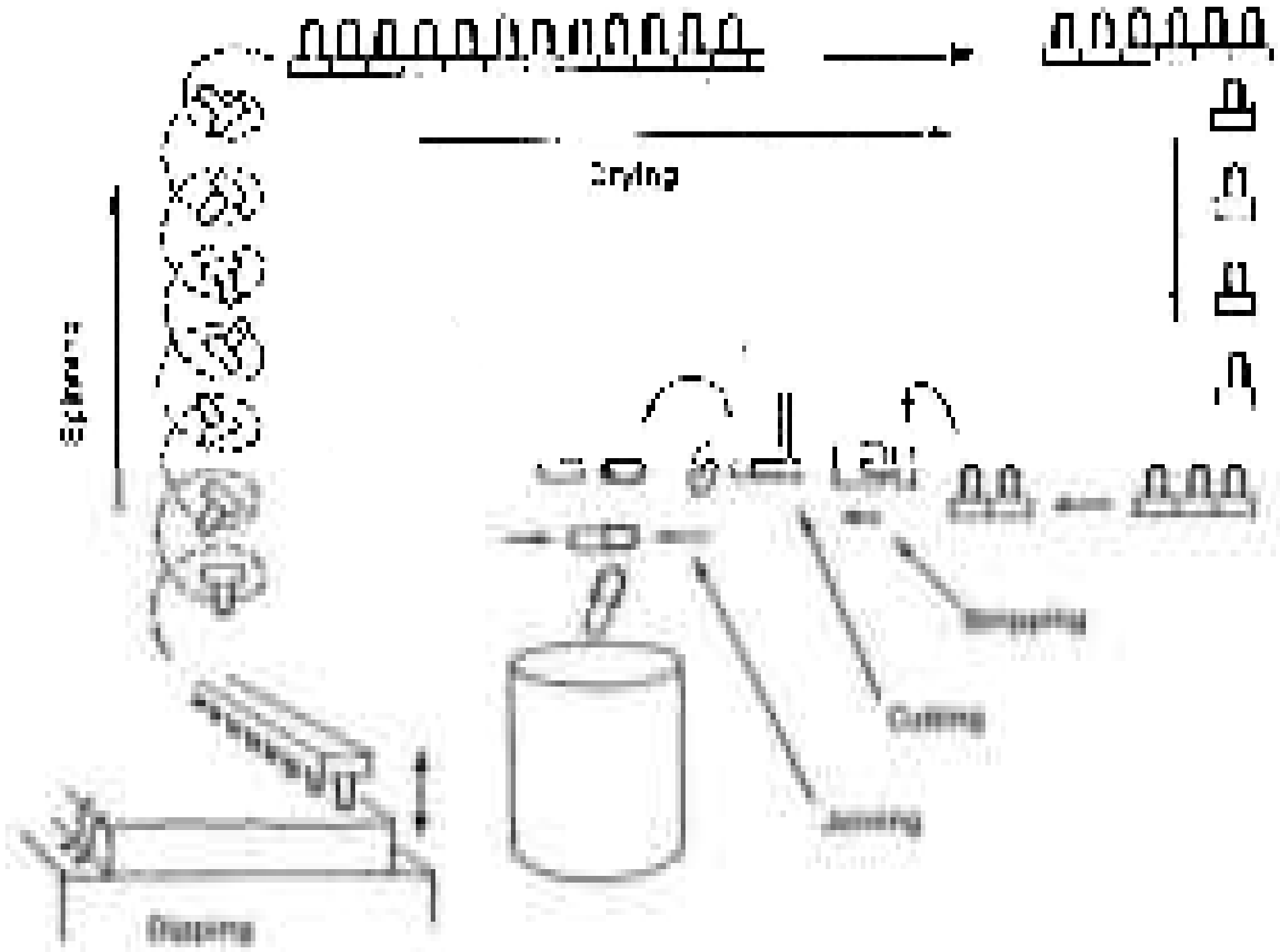
CAP

BODY

Manufacturing of hard gelatin capsules

Steps involved in making empty gelatin capsules…

1. **Dipping**
2. **Spinning**
3. **Drying**
4. **Stripping**
5. **Trimming and Joining**
6. **Polishing**



Dipping :

Pairs of the stainless steel pins are dipped into the dipping solution to simultaneously form the caps and bodies.

The dipping solution is maintained at a temperature of about 50°C in a heated, jacketed dipping pan.

Spinning :

The pins are rotated to distribute the gelatin over the pins uniformly and to avoid the formation of a bead at the capsule ends.

Drying :

The gelatin is dried by a blast of cool air to form a hard shells.

The pins are moved through a series of air drying kilns to remove water

Stripping :

A series of bronze jaws strip the cap and body portions of the capsules from the pins.

Trimming and joining

The stripped cap and body portions are trimmed to the required length by stationary knives.

After trimming to the right length, the cap and body portion are joined and ejected from the machine.

Preparation of filled hard gelatin capsules:

In large scale or small scale the preparation of filled hard gelatin capsule is divided into the following general steps:

1. Developing and preparing formulation.
2. Filling the capsule shell
3. Capsule sealing
4. Cleaning and polishing the filled capsules.

1.Developing and preparing the formulation

Diluent

Generally, hard gelatin capsules are used to encapsulate between about 65 mg and 1 g of powdered material, including drug and any diluent required.

If the dose of the drug to be placed in a single capsule is smaller than 65 mg to produce the proper fill, then the diluents are incorporated. Some ex are lactose, microcrystalline cellulose, and pregelatinized starch. when the amount of drug is large enough to fill a capsule completely, a diluent may not be required.

Lubricant

A lubricant as 1% Magnesium stearate is utilized to prevent adhesion and facilitate the flow of the powder in capsule filling machine.

Glidant

The powder mixture or granules must be free-flowing to allow passage from the hopper. glidant such as 1% silicon dioxide is needed for this.

Lubricant and Glidant are used to improve filling properties.

Wetting agent

Addition wetting agents, as sodium lauryl sulfate, in capsule facilitate the wetting of the drug substance by gastrointestinal fluids to enhance dissolution, and overcome the problem associated with water-insoluble lubricant as magnesium stearate which can delay the dissolution of the drug and its absorption.

Eutectic mixtures

Eutectic mixtures or mixtures that tend to liquefy, may require a diluent or absorbant such as magnesium carbonate, kaolin, or light magnesium oxide to separate physically the interacting agents and to absorb any liquefied material.

Liquids

Gelatin capsules are unsuitable for the encapsulation of aqueous liquids, because water softens the gelatin to produce distortion of the capsules.

However, some liquids such as fixed or volatile oils that do not interfere with the stability of the gelatin shells may be placed in gelatin capsules which then may be sealed to ensure the retention of the liquid (*soft gelatin* capsules)

Semisolids

This system can be used for both liquid and solid active ingredients. Mixtures for filling need only be liquid when filled and should be semisolid after being inside the capsules.

The materials to be filled must be either thermosoftening or thixotropic in nature to be liquefied by heating or shearing forces using heated hopper with a stirrer and revert to the solid state within the capsule shell.

Used for potent drugs to improve uniformity of filling.

Used for safely handling toxic drugs to reduce contamination with filling of powders.

Granules and Pellets

Granules and Pellets are packed in capsules instead of powder to produce modified release patterns.

Granules are produced by granulation and are more irregular than pellets(pellets are spherical and produced by microencapsulation technique)

Capsules within capsules:

If one ingredient must be separated from others in the formulation, a small capsule, such as a No. 5, may be filled with one powder and placed into a larger capsule with the remaining ingredients in the formulation.

Tablets within capsules:

Small tablets are filled into capsules to produce special release forms or to separate incompatible ingredients.

This small tablet can be placed inside the capsule following the addition of a small quantity of the powder and the filling completed.

Filling of Capsules

POWDERS in capsule

GRANULES

BEADS

TABLETS

Selection of capsule size

- The selection of capsule size is best done during the development of the formulation, because the amount of inert materials to be employed is dependent upon the size or capacity of the capsule to be selected.
- The density and compressibility of a powder or a powder mixture will largely determine to what extent it can be packed into a capsule shell.
- The amount may vary according to the degree of pressure used in filling the capsules.

Determination of capsule fill weight:

To determine the size of capsule to be used or the fill weight for a formulation the following relationship is used:

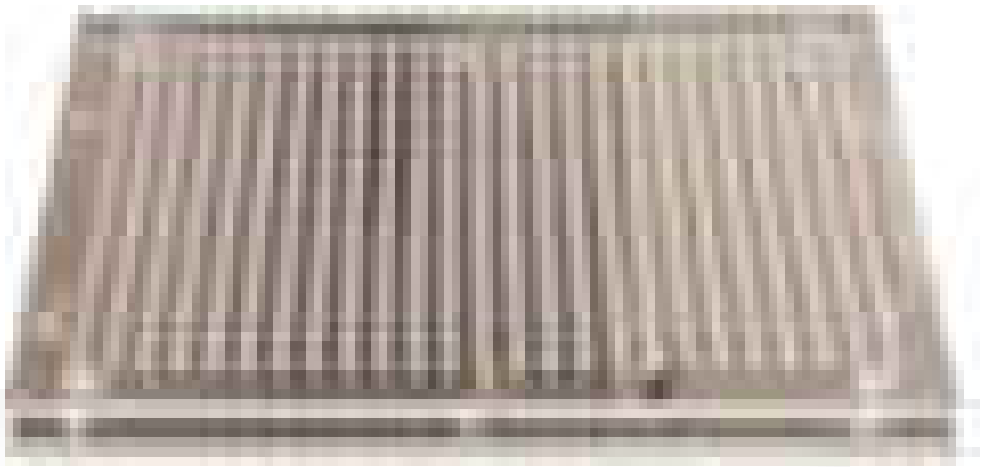
Capsule fill weight =Tapped bulk density of formulation×capsule volume

2.FILLING OF HARD GELATIN CAPSULES

- Hand Operated methods.
- Semi Automatic capsule filling machines .
- Automatic filling machine.

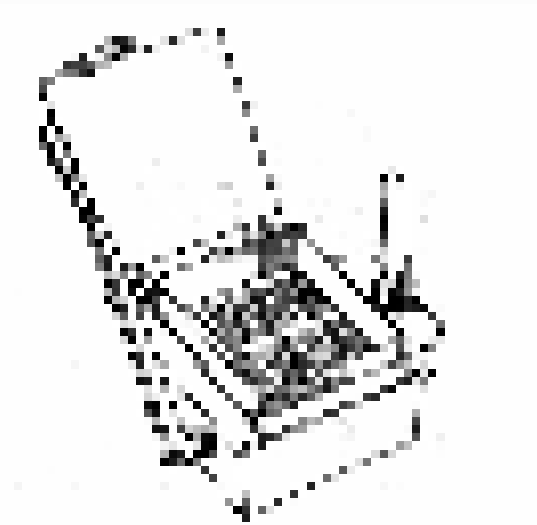
HAND OPERATED CAPSULE FILLING MACHINE

- Hand-operated capsule filling machines or Feton capsule filling machine
- Consist of a couple of plates are capable of producing about 200 to 2000capsules/hr.



A hand operated gelatin capsule filling machine consists of the following parts : -

1. A bed with 200-300 holes.
2. A capsule loading tray
3. A powder filling tray
4. A pin plate having 200 or 300 pins corresponding to the number of holes in the bed and cap holding tray.
5. A lever handle
6. A Cam handle
7. A plate fitted with rubber top.



Punch Method

- Used for filling a small number of capsules in the pharmacy, at the prescription counter.
- The ingredients are triturated to the same particle size and then mixed by geometric dilution.
- The powder is placed on a powder paper or ointment slab and smoothed with a spatula to a height approximately half the length of the capsule body.

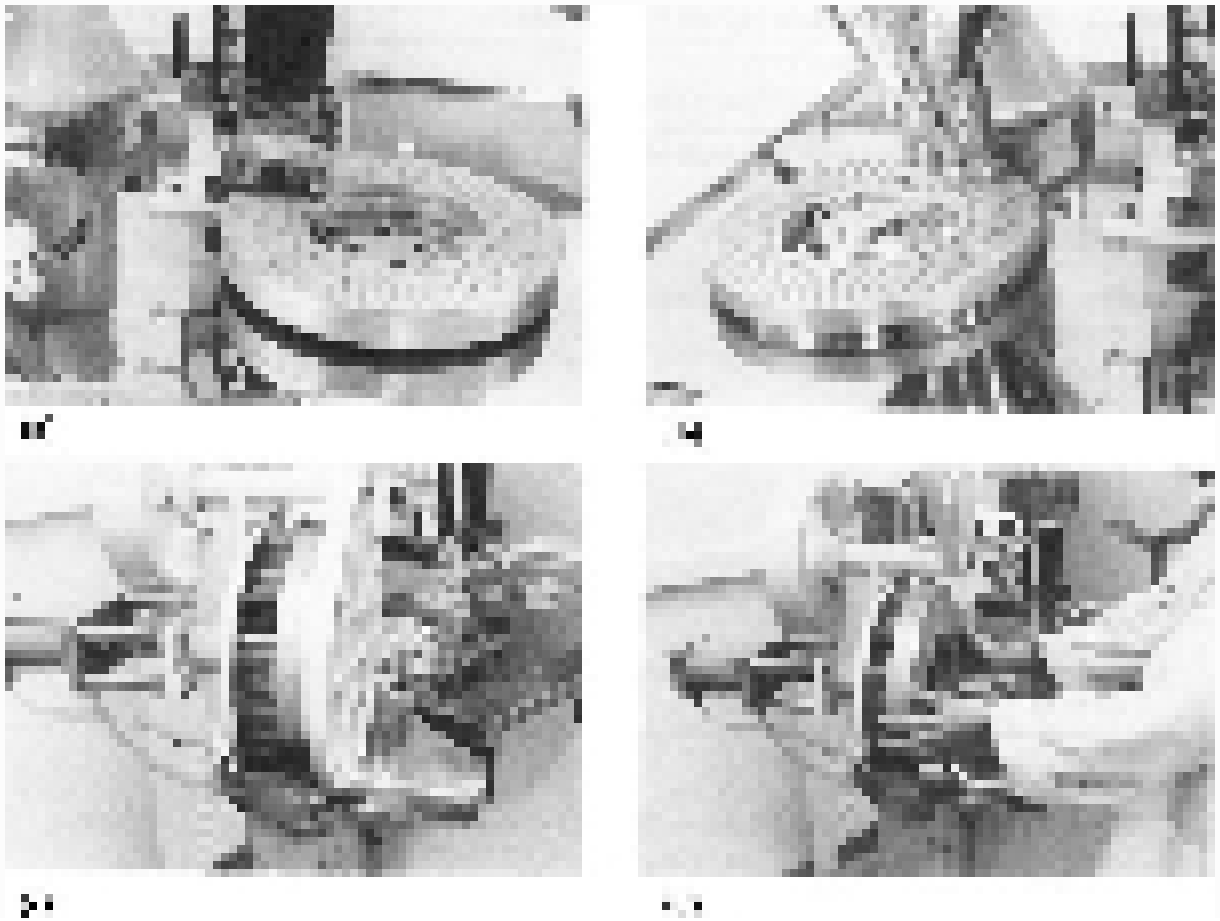
❑The base of the capsule is held vertically and the open end is repeatedly pushed or "punched" into the powder until the capsule is filled;

❑The cap is then replaced to close the capsule. Each filled capsule is weighed using an empty capsule as a counterweight.

❑Powder is added or removed until the correct weight has been placed in the capsule.

❑The filled capsule is tapped so that no air spaces are visible within the contents.

Semiautomatic capsule-filling machine. (a)``Sandwich'' of cap and body rings positioned under rectifier to receive empty capsules. Vacuum is pulled from beneath the rings to separate caps from bodies. (b) Body ring is positioned under foot of powder hopper for filling. (c) After filling the bodies, the cap and body rings are rejoined and positioned in front of pins. These pins push the bodies to engage the caps. (d) The plate is swung aside and the pins are used to eject the closed capsules



SEMI AUTOMATIC MACHINE

Various Filling Machine Available…

- **Eli-lily and Co- Indiana polis**
- **Farmatic SNC-Italy**
- **Hofliger and Karg- Germany**
- **Zanasi- italy**
- **Parke-Davis- Detroit**
- **Perry industries- WI**
- **Osaka- Japan**
- **MG2- Italy**
- **Macofar SAS- Italy**

These machine differ in there design and output

Filling hard capsule shells

The process of working:

- Rectification
- Separating the caps from empty
- Filling the bodies
- Scraping the excess powder
- Replacing the caps
- Sealing the capsules
- Cleaning and polishing of filled capsules

Rectification

- The empty capsules are oriented so that all point the same direction i.e. body end downwards
- In general, capsule pass one at a time through a channel just wide enough to provide grip at cap end
- The capsules will always be aligned body end downwards, regardless of which end entered the channel first with the help of specially designated blades

Separation of caps from body

- This process depends on the difference in diameters between body and cap
- The rectified capsules are delivered body end first into the upper portion of split bushings or split filling rings
- A vacuum applied from below pulls the body down into the lower portion of the split bushing
- The diameter of the cap is too large to allow them to follow bodies into the lower bushing portion
- The split bushings are separated to expose the bodies for filling

- **Auger fill principle**:
- The empty capsule bodies are held in a filling ring that rotates on a turn table under the powder hopper. The fill of the capsule is primarily volumetric
- Because the auger mounted in the hopper rotates at a constant rate, the rate of delivery of the powder to the capsules tend to be constant.
- Major control over fill weight is the rate of rotation of the filling ring under the hopper
  - Flat blade auger
  - Screw auger- provides greater fill weight and smaller co.eff of weight variation.

  E.g. Capsugel type 8 filling machine

Flow properties powder blend should be adequate
Glidants- colloidal silica is used in capsugel type 8 machine
The optimum conc of glidant for lactose capsules is 0.5% and
for corn capsules is 1 %
Lubricants –mg stearte & stearic acid are helpful

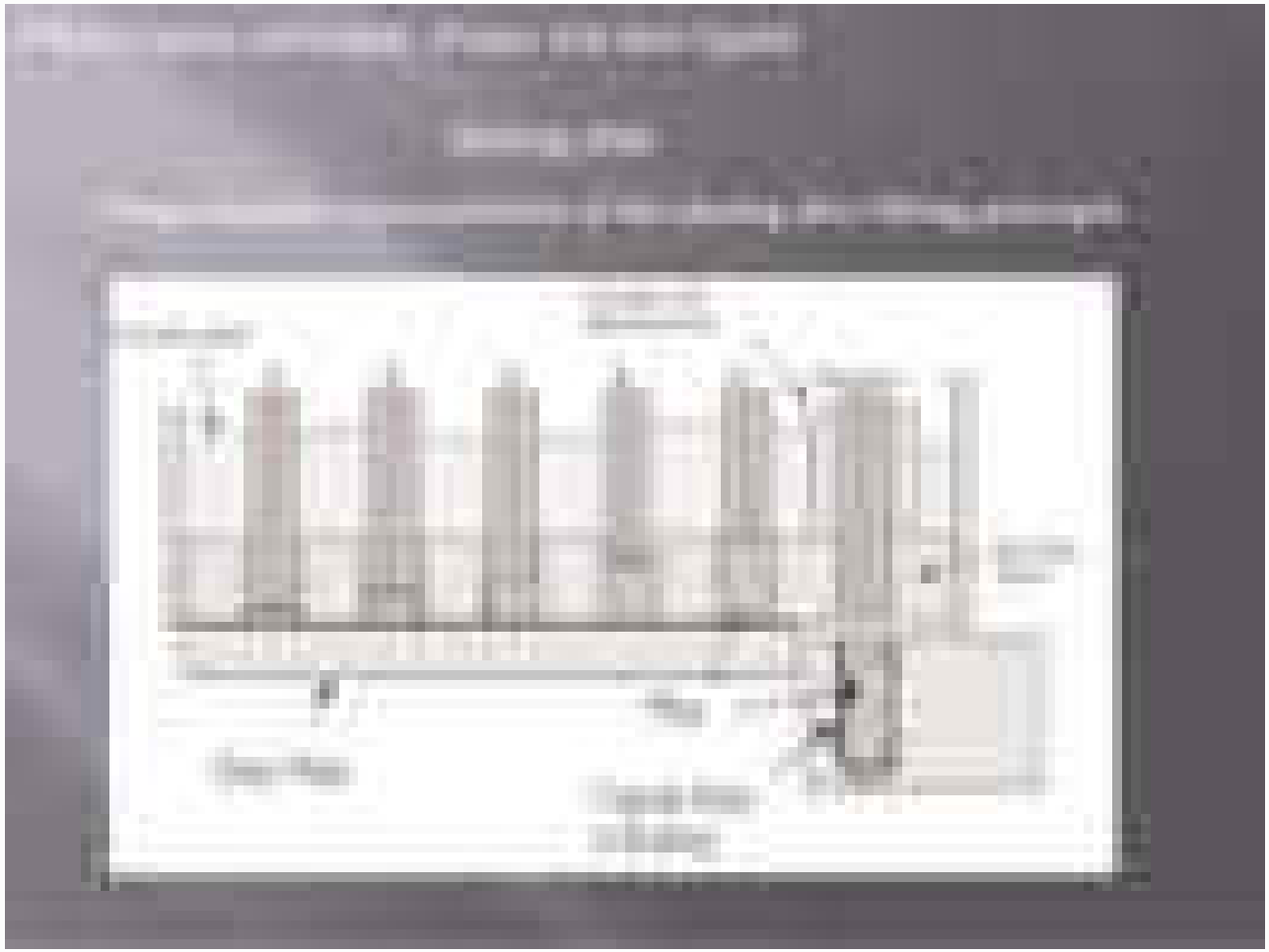
- **Vibratory fill principle**:
- The osaka machine works based on this principle. Here the capsule body passes under a feed frame that holds the powder in the filling section
- In the powder, a perforated resin plate is positioned and it is connected to a vibrator
- The powder blend tends to be fluidized by the vibration of plate and assists the powder to flow into the bodies through the holes in resin plate
- The fill weight is controlled by the vibrators and by setting the piston of the body under the feed frame

OSAKA MODEL R-180
SEMI AUTOMATIC CAPSULE FILLING MACHINE

- **Piston tamp principle**:
- In this pistons or tamping pins lightly compress the individual doses of the powders into plugs(also called as slugs) which resembles a soft tabletin consistency and eject the plugs into empty capsule bodies
  - DOSATOR PRINCIPLE
  - DOSING DISC PRINCIPLE

DOSING DISK PRINCIPLE:

- Ex of this type are Hofliger –karg GKF & Harro hofliger KFM models
- The dosing disk, which forms the base of the dosing or filing chamber has a no of holes bored through it
- a solid brass ‘stop’ plate is sliding down the dosing disc to close off the hole there by forming openings similar to the die cavities of a tablet press. Five sets of pistons compress the powder into cavities to form plugs (each plug is compressed five times per cycle)
- Excess powder is scrapped off and the dose is controlled by the thickness of the dosing disc, powder depth and the tamping pressure
- The flow of powder from the hopper to the disk is auger assisted
- A capacitence probe senses the powder level and activates an auger feed if the level falls below the preset level
- Powder is distributed over the dosing disk by the centrifugal action
- Baffles are provided to help maintain a uniform level
- Lubrication is required for efficient pug ejection and to prevent filming on pistons



DOSATOR PRINCIPLE:

- Ex: Zanasi,MG2,DOH Bonapace and Macofer machines
- It consists of cylindrical dosing tube fitted with movable piston.

The position of the piston is preset to a particular height to define a volume that would contain the desired dose of the powder. Powder enters the open end of dosator and is slightly compressed against the piston into a plug.

- The plug is withdrawn from the powder hopper and is moved over to the empty capsule body where the piston is pushed downward to eject the plug

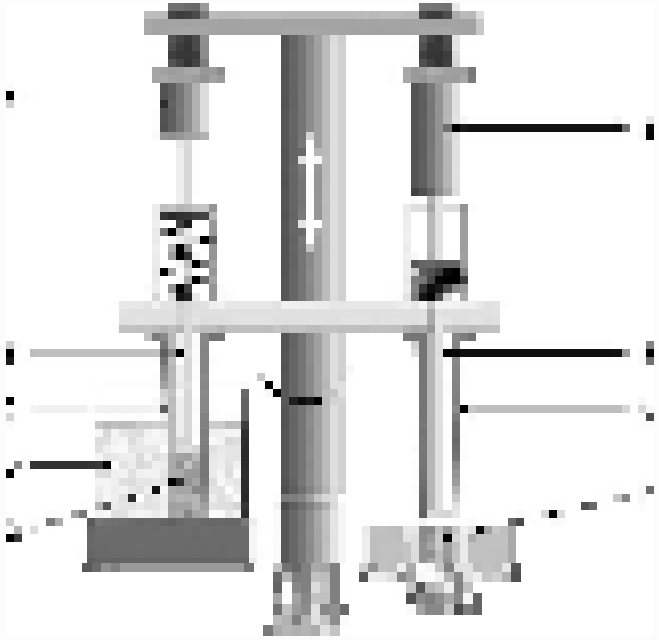


Diagram of a dosator or dosing tube system (Zanasi RM63): (A) compression force platen; (B) piston; (C) dosing tube; (D) powder hopper; (E) plug ejection (F) capsule body in bush; and (G) powder plug...

HOFLIGER KARG AUTOMATIC
CAPSULE FILLING MACHINE

ZANASI AUTOMATIC
CAPSULE FILLING MACHINE

Filling of hard gelatin capsules

✓ Equipment used are: -

- **Hofliger-Karg machine:**

➢ Formation of compacts in a die plate using tam ping pins to form a compact.

- **Zanasi or Martelli encapsulator:**

➢ Forms slugs in a dosator which is a hollow tube with a plunger to eject capsule plug.

Capsule Sealing

1. Tamper evident capsules by sealing the joint between the 2 capsule parts
2. Capsules are sealed through a heat welding process that fuses the capsule cap to the body through the double wall thickness at their juncture. This results in a distinctive ring around the capsule where heat welded
3. Another process utilizes a melting point lowering liquid wetting agent in the contact areas of the capsule cap and body and then thermally bonds the two parts using low temp.
4. Lightly coating the inner surface of the cap with a warm gelatin solution immediately prior to placement on the filled capsule body.

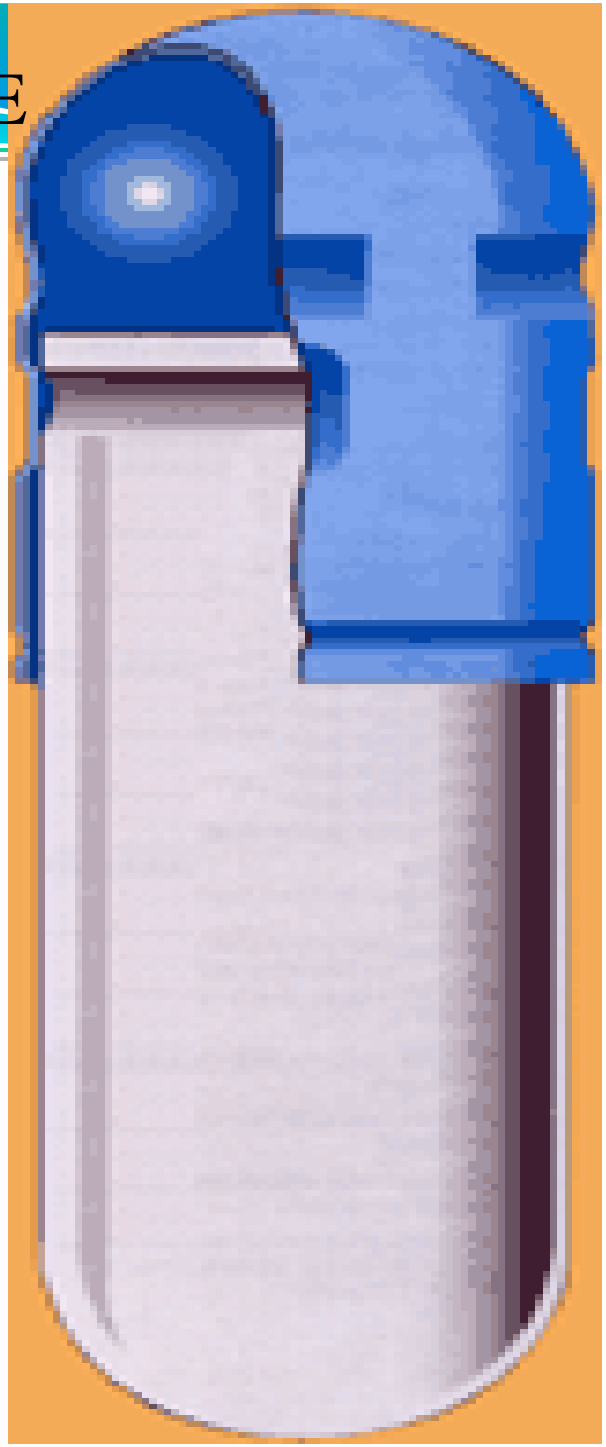
SEALING OF GELATIN CAPSULES

In this process, the two capsule parts are sealed with a gelatin or polymer band at the joint of the cap and body.

A tamper-resistant seal on hard gelatin capsules was developed in which the contact areas of the cap and body are wetted with a mixture of water and ethanol to soften the gelatin and then thermally bonded at 104° to 113°F to form the seal.

CONI-SNAP HARD GELATIN CAPSULE

- A recent innovation in capsule shell design, where the two halves of the capsule shells are enable to be positively joined through locking grooves in the shell walls.
- The two grooves fit into each other and ensure reliable closing of the filled capsule.
- Opening of such capsule is difficult with increasing security of the contents of the capsule.



Cleaning and polishing capsules

Small amount of powder may adhere to the outside of capsules after filling.

1) Salt Polishing- NaCl
2) Cloth Dusting- filled capsules are rubbed with a cloth that may or may not be impregnated with inert oil
3) Brushing- Capsules are fed under rotating soft brushes
4) Pan Polishing- Acela-cota pan is used to dust and polish th capsules. A polyurethane or cheese cloth is placed in the pan

Some commercially available capsule sort / polish equipments are

1.ROTOSORT- capsule sorting machine sold by elilily&company
Removes loose powder, unfilled joined capsules, filled or unfilled bodies and loose caps

2. ERWEKA. KEA- handles output from any capsule filling machine

3.SEIDENADER EQUIPMENT- It has a belt that presents the capsules for visual inspection and vaccum system to automatically remove unfilled capsules

4.PM 60- A cleaning and polishing machine

Storage, packaging, and stability

- Finished capsules normally contain an EMC of 13-16%.
- < 12% MC, the capsule shells become brittle
- >18% make them too soft
- To maintain a relative humidity of 40-60% when handling and storing capsules.
- QUALI-V, developed by Shionogi Qualicaps, is the first HPMC capsule developed for eventual use in pharmaceutical products.

SOFT GELATIN CAPSULES

Definition

Soft Gelatin capsules are one piece, hermetically sealed, soft gelatin shells containing a liquid, a suspension, or a semisolid.

Soft gelatin is mainly composed of gelatin, plasticizers, preservative, colouring and opacifying agents, flavoring agents and sugars.

APPLICATIONS OF SOFT GELATIN CAPSULE

The pharmaceutical applications of soft gelatin capsules are:

- as an oral dosage form
- as a suppository dosage form
- as a specialty package in tube form, for human and veterinary use, single dose application for topical, ophthalmic, and rectal ointments.

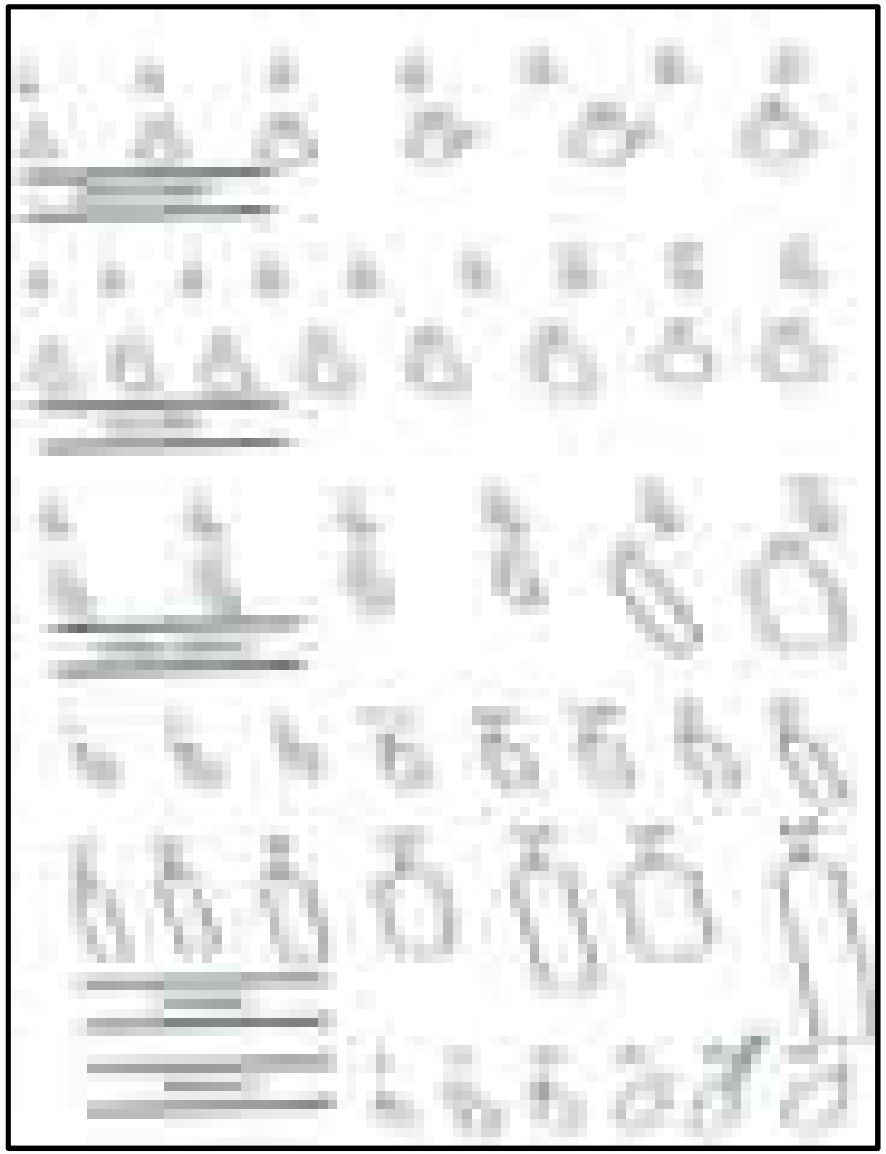
- **ADVANTEGES**
- Easy to administer
- Easy to Manufacture
- Liquids can be encapsulated (non water soluble)
- Small to large sizes possible
- Elegance
- Portability
- Odour and taste masking
- Ready availability of drug hence faster action.
- Specialised dosage forms can be made e.g. chewable, extended release, captabs etc.
- Can be used for ophthalmic preparations e.g. aplicaps, vaginal / rectal suppositories

DISADVANTEGES

- Water soluble material are difficult to incorporate
- Highly Moisture sensitive
- Efflorescent material cannot be incorporated, they may cause softening / leaching
- Deliquescent materials cannot be incorporated, they may cause hardening or brittle capsules.

SHAPE OF CAPSULE

The shape of soft gelatin capsule are round, oval, oblong, tube.



MANUFACTURING SOFT GELATIN CAPSULES

I) Formulation of the shell

The capsule shell is basically composed of Gelatin, plasticizer & water, it may contain additional ingredients such as preservatives coloring and opacifying agents, flavorings, sugars, acids & medicaments to achieve desired effects.

Capsule shell

W ATER:-

Not more than 45% w/w ratio.

weight of water to dry gelatin can vary from 0.7 to1.3(water) to 1.0(dry gelatin) depending on the viscosity of the gelatin being used.

- PLASTICIZER:-Used to make the soft gel shell elastic & pliable.
- Ratio used is between 0.3 to 1.8 for soft to hard shell on dry basis.
- E.g. glycerin , sorbitol

.

Colours may be natural or synthetic.

- OPACIFIER, usually titanium dioxide, may be added to produce an opaque shell ,when the fill formulation is a Suspension or to prevent photo degradation of light sensitive fill ingredients.
- Conc. of opacifier may be up to 0.5%

➢ Chelating Agents:- Iron is always present in raw gelatin, & should not contain iron more than 15 ppm

- Additionally chelating agent may be used for preventing the reaction of iron with materials or colours.

II. Formulation of fill material:

- Formulation for soft gelatin capsules involves liquid, rather than powder technology.
- Materials are generally formulated to produce the smallest possible capsule consistent with maximum stability, therapeutic effectiveness and manufacture efficiency.
- The liquids are limited to those that do not have an adverse effect on gelatin walls.
- Emulsion can not be filled because water will be released that will affect the shell
- The pH of the liquid can be between 2.5 and 7.5.

- Content may be liquid, or a combination of miscible liquids,
- A solution of a solid(s) in a liquid(s) or a suspension of a solid(s) in a liquid(s).
- Ex: Vegetable oils like arachis oil or aromatic or aliphatic hydrocarbons, ethers, esters, or alcohols.

- Vehicles used in soft gelatin capsules are of two main groups :
  1. Water immiscible, volatile or more likely more volatile liquids such as vegetable oils, mineral oils, medium-chain triglycerides and acetylated glycerin.
  2. Water miscible, nonvolatile liquids such as low molecular weight PEG have come in to use more recently because of their ability to mix with water readily and accelerate dissolution of dissolved or suspended drugs.
- All liquids used for filling must flow by gravity at a temperature of 35°C or less.

- The sealing temperature of gelatin films is 37-40°C

BASE ADSORPTION OF SOLIDS TO BE SUSPENDED IN SOFT GELATIN CAPSULES :

➢Base adsorption is expressed as the number of grams of liquid base required to produce a capsulatable mixture when mixed with one gram of solid(s).

➢The base adsorption of a solid is influenced by such factors such as the solids particle size and shape, its physical state (fibrous, amorphous, or crystalline), its density, its moisture content, and its oleophilic or hydrophilic nature.

➢In the determination of base adsorption, the solid(s) must be completely wetted by the liquid base.

➢For glycol and nonionic type bases, the addition of a wetting agent is seldom required, but for vegetable oil bases, complete wetting of the solid(s) is not achieved without an additive.

➢Soy lecithin, at a concentration of 2 to 3 % by weight of the oil, serves excellently for this purpose, and being a natural product, is universally accepted for good drug use.

➢Increasing the concentration above 3 % appears to have no added advantage.

- A practical procedure for determining base adsorption and for judging the adequate fluidity of a mixture is as follows:
- Weigh a define amount of the solid (40g is convenient) into a 150 ml teared beaker.
- In a separate 150 ml beaker tared beaker, place about 100 g of the solid base.
- Add small increments of the liquid base to the solid, and using a spatula, stir the base into the solid after each addition until the solid is thoroughly wetted and uniformly coated with the base.
- This should produce a mixture that has a soft ointment like consistency.
- Continue to add liquid and stir until the mixture flows steadily from the spatula blade when held at a 45-degree angle above the mixture.
- The base adsorption is obtained by means of the folloeing formula
- Weight of the base/ Weight of the solid = Base Adsorption

- The base adsorption is used to determine the “minim per gram” factor (M/g) of the solid(s).

- The minim per gram factor is the volume in minims that is occupied by one gram (S) of the solid plus the weight of the liquid base (BA) required to make a capsulatable mixture.

- The minim per gram factor is calculated by dividing the weight of the base plus the gram of solid base (BA+ S) by the weight of the mixture (W) per cubic centimeter or 16.23 minims (V).

convenient formula is-

$$\frac{(BA + S) \times V}{W} = M/g$$

- Thus lower the base adsorption of the solid (s) and higher the density of the mixture, the smaller the capsule will be.

- The final formulation of a suspension invariably requires a suspending agent to prevent the settling of the solids and to maintain homogeneity prior to, during, and after capsulation.

- The nature and the concentration of the suspending agent vary.

- In all instances the suspending agent used is melted in a suitable portion of the liquid base, and the hot melt is added slowly, with stirring, into the bulk portion of the base, which has been pre-heated to 40 degrees prior to the addition of any solids.

- The solids are then added, one by one, with sufficient mixing between additions to ensure complete wetting.

- Incompatible solids are added as far apart as possible in the mixing order to prevent interaction prior to complete wetting by the base.

MANUFACTURE OF SOFT GELATIN CAPSULES

Soft gelatin capsules are manufactured by four methods

1) Plate process
2) Rotary die process
3) Accogel machine
4) Bubble method

1) Plate Process:

- This is the oldest commercial process and it is semi automatic batch process.
- Place the gelatin sheet over a die plate containing numerous die pockets.
- Application of vacuum to draw the sheet in to the die pockets.
- Fill the pockets with liquid or paste.
- Place another gelatin sheet over the filled pockets, and
- Sandwich under a die press where the capsules are formed and cut out.

2) Rotary die process:

Patented by Robert.P.Scherer in 1933

Principle: *Two independent processes take place, often simultaneously yielding two different materials.*

Both are united in the encapsulation process that produces wet soft gels.

Rotary die press

1) In this machine the soft gelatin capsules are prepared & then filled immediately with liquid medicaments it is having two hoppers & two rotating dies

2) Liquid mixture is placed in one hopper & the liquid medicament in other hopper.

3) The two rotating dies rotate in opposite directions when the fluid gelatin mixture enters the machine from the hopper it produces two continuous ribbons .

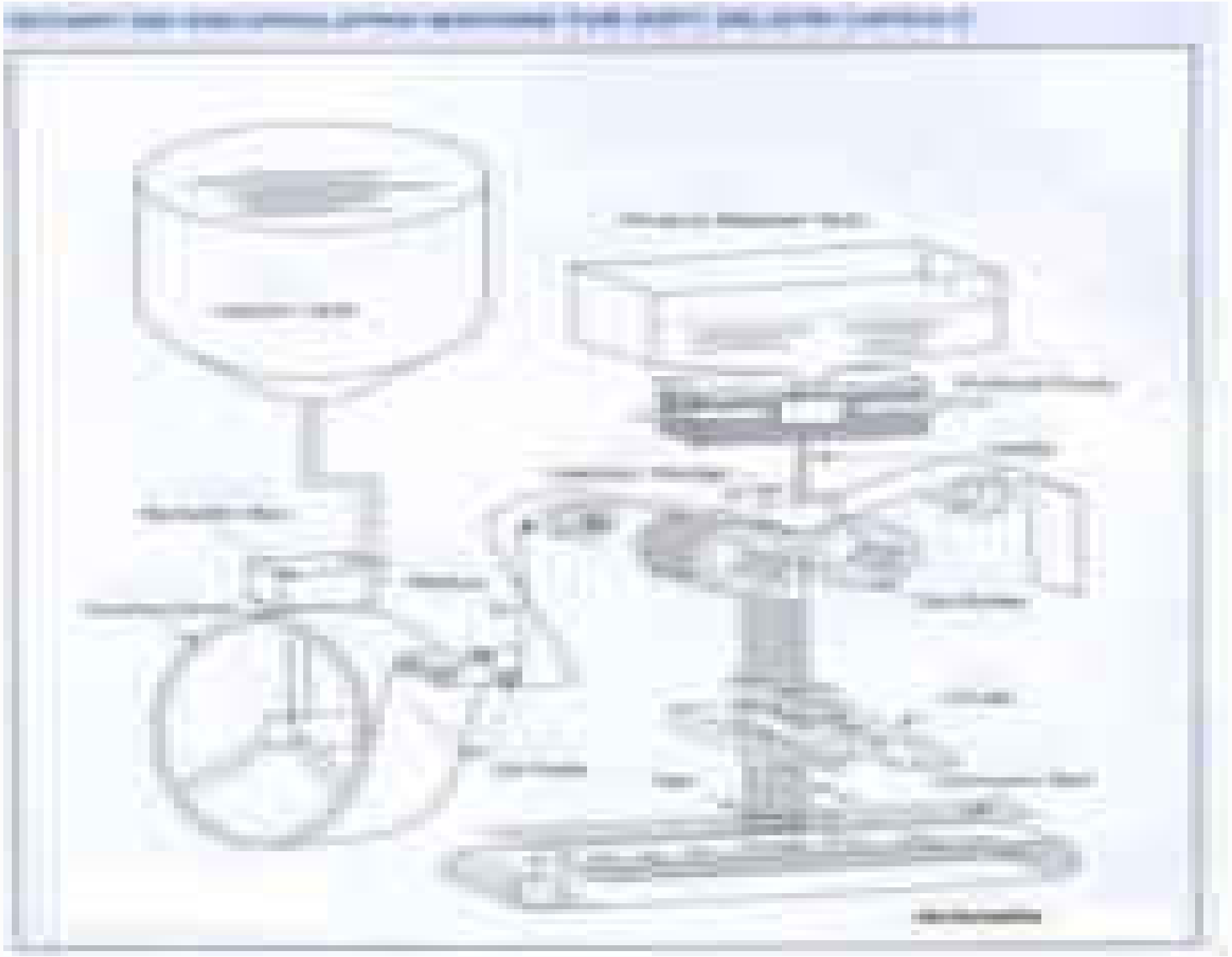
4) Thus half shell of the capsule is formed.

5) At this stage the measured quantity of the medicament is filled in to it with the stroke of a pump with the subsequent movement of the dies the other half capsule is formed.

6) The two halves of the capsules are sealed together by the heat & pressure of the rotating dies.

7) As the die rolls rotate, the convergence of the matching die pockets seals and cuts out the filled capsules

ROTARY DIE MACHINE



3)Accogel process:

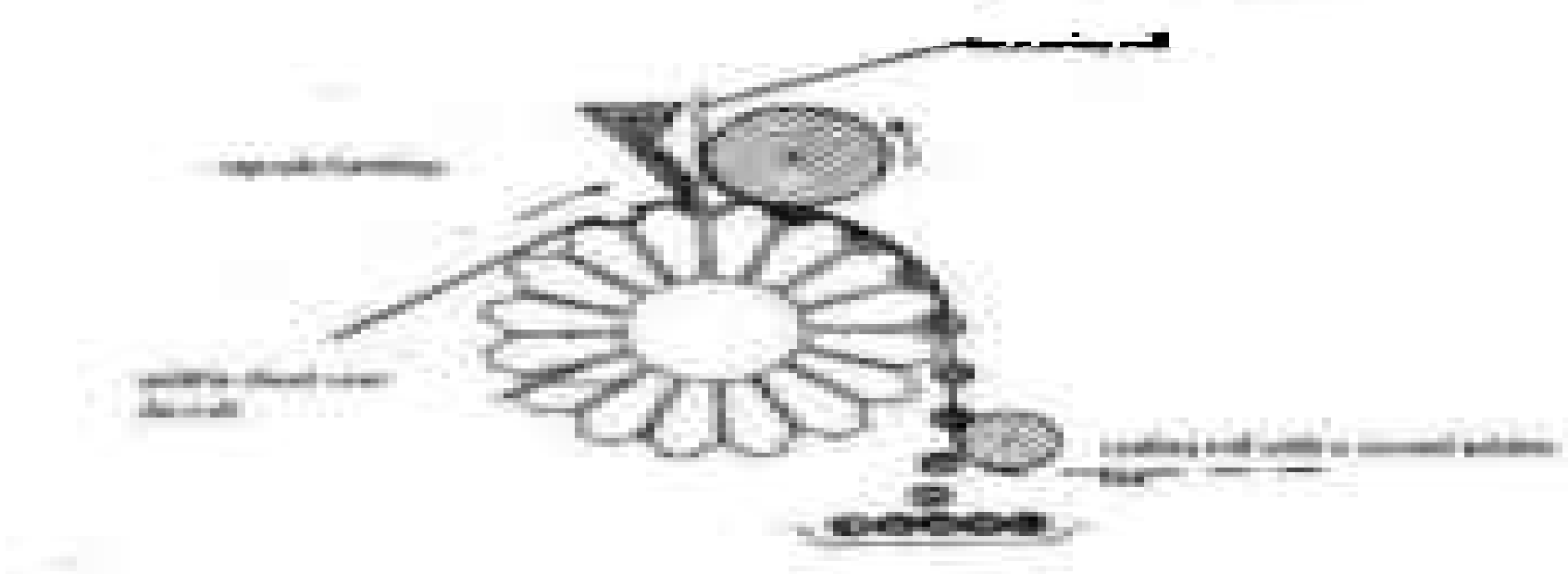
Accogel Capsule Machine Or Stern machine is the only machine that can successfully fill dry powder into a soft gelatin capsule.
Developed by Lederle labs in 1949.

It is a continuous process for manufacturing of soft gelatin capsules filled with powders or granules.
This is another rotary die process involving
a) a measuring roll b) a die roll c) a sealing roll

•Measuring roll rotates directly over the die roll, and the pockets in the 2 rolls are aligned each other.
•Powder or granular fill material is held in the pockets of Measuring roll under vacuum.
•A plasticized sheet is drawn into the die pockets of the die roll under vacuum.
•As the measuring roll and die roll rotates the measured doses are transferred to the gelatin linked pockets of the die roll

The continued rotation of the filled die converges with the rotating sealing roll where a second gelatin sheet is applied to form the other half of the capsule.

Pressure developed between the die roll and sealing roll seals and cuts out the capsule.



4) Bubble method:

- Seamless one piece soft gelatin capsules are produced by bubble method.
- This method of making soft capsules takes the advantage of the phenomenon of drop formation.
- The essential part of the apparatus consists of two concentric tubes (concentric tube dispenser) through the inner tube flows the medicament and, through the surrounding outer tube, the gelatin solution.
- The medicament, therefore, issues from the tube surrounded by gelatin and forming a spherical drop.
- This is ensured by allowing the drop to form in liquid paraffin in which the gelatin is insoluble.
- Regular induced pulsations cause drops of the correct size to be formed, and a temperature of 4°C ensures that the gelatin shell is rapidly congealed.
- The capsules are subsequently degreased and dried.

HARD GELATIN CAPSULES

1) Two piece (large body & short cap)
2) Cylindrical shape.
3) Powder drug or pallets coated with drug are encapsulated.
4) Gelatin in Hard form is used.
5) Capsules are sealed after they are filled to ensure that the medicaments may not come out of the capsule due to rough handling.
6) 8 different type of sizes are available

SOFT GELATIN CAPSULES

1) One piece & hermetically sealed.
2) Available in round , oval & tube like shapes.
3) Liquid & Semi liquid fill & unstable substances are encapsulated.
4) Molten gelatin are used.
5) Filling & sealing of soft gelatin capsules are done in a combined operation on machine.
6) No specific sizes are available.

EVALUVATION OF CAPSULES

1. **STABILITY TESTS.**
   a) **Shell integrity test**
   b) **Determination of shelf life**
2. **INVARIABILITY TESTS.**
   a) **Weight variation**
   b) **Content uniformity**
3. **DISINTEGRATION TEST.**
4. **DISSOLUTION TEST.**
5. **MOISTURE PERMEATION TEST.**

1.STABILITY TESTS

- Stability tests for capsules are performed to know the integrity of gelatin capsule shell (but not to know the stability of therapeuticallay active agent) and for determining the shelf life of capsules.
- The tests helps in improving the quality of contents of capsule shell and for choosing the appropriate retail package.

BEFORE ACTUALLY PERFORMING THE TESTS FOLLOWING FACT:

(i).the capsule shell are to be stabilized to know atmospheric condition with relative humidity about 20-30 % and temperature about 21-24^{0}c .

A) SHELL INTEGRITY TEST :

- This test is performed to find out the integrity of capsule shell.

The standard capsule shells kept at the room temperature 40 ^{0}c and 80% RH becomes more soft ,sticky and swollen .

B) DETERMINATION OF SHELF LIFE :

Shelf life or the expiry date of packed capsules is determined under normal storage conditions.

INVARIABILITY TESTS

The invariabilty in the medicaments packed in the capsule shells can be determined by performing the following tests :

a) **Weight variation test**

b) **Content uniformity test**

DISINTEGRATION TEST

- Disintegration test is a method to evaluate the rate of disintegration of solid dosage forms .

  disintegration is defined as the breakdown of solid dosage form into small particles after it is ingested .

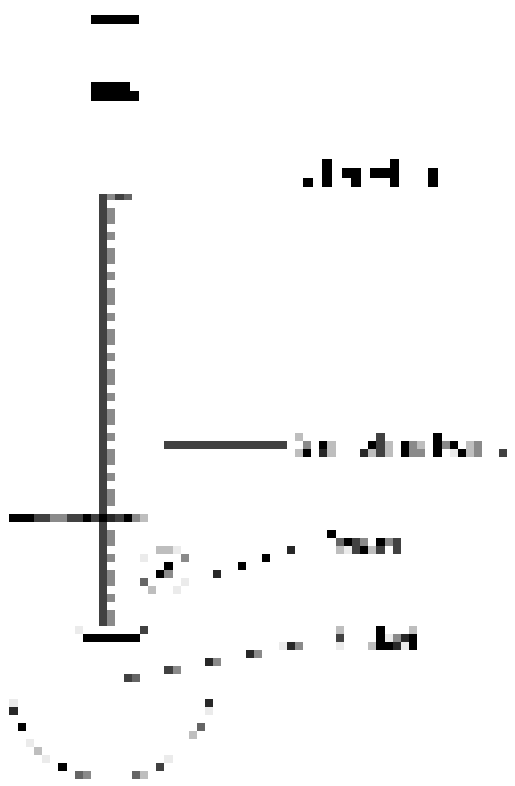
DISSOLUTION TEST

- Dissolution test is an official method to determine the dissolution rate of a solid dosage form .
- Dissolution rate is defined as the rate at which the drug is released into the systemic circulation from the dosage from .

DISSOLUTION TEST APPARATUS

a)Apparatus -1 (rotating basket dissolution apparatus) :-

- Small wire mesh size basket – 22
- Temperature – 37 +/- 5^0c
- Rotated speed – 25 -150 rpm
- Dissolution medium height from the bottom of the vessel :- 23-27 mm

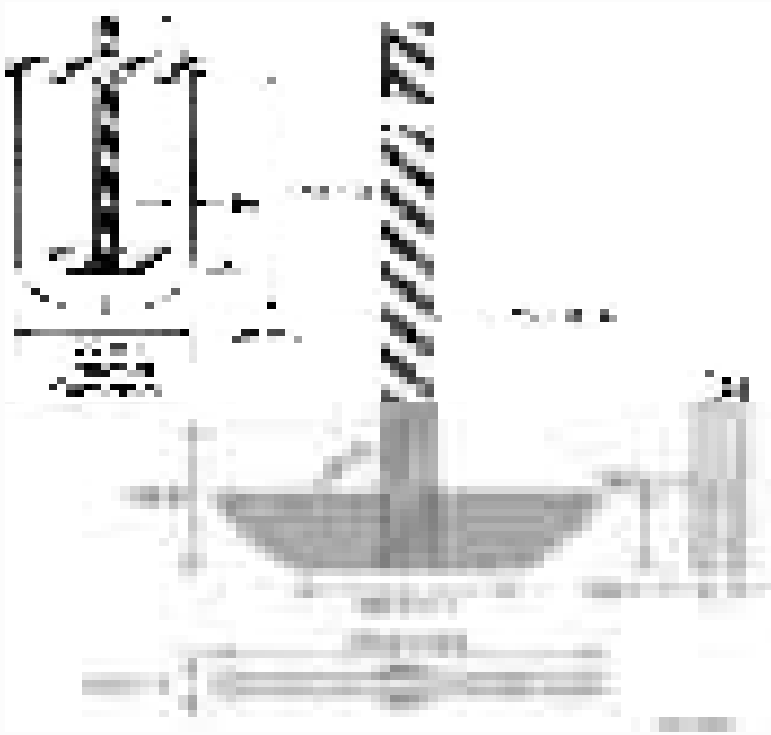


b) Apparatus -2 (rotating paddle dissolution apparatus) :-

Small wire mesh size :- 22

Dissolution medium height from the bottom of the vessel :- 23-27 mm

- Temperature – 37 +/- 5^0c
- Rotated speed – 25 -150 rpm



MOISTURE PERMEATION TEST

To assure the suitability of containers for packaging capsules .

The moisture permeating feature of capsules packaged in

- single unit containers – blister pack or strip pack
- unit dose containers – glass or plastic bottles

are to be determined .

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