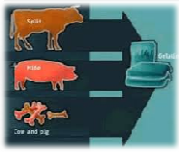
CAPSULES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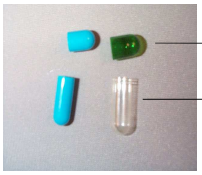
CAPSULES

- **DEFINITION:-**

These are solid dosage form of medicaments, in which drug is enclosed within the shells made up of gelatin.

PARTS OF CAPSULE



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CAPSULE SHELL

- Gelatin
- Water
- Opacifying agents
- Plasticizer
- Preservatives

Certified Dyes
Colour approved by D & C act.

Opacifiers
Titanium dioxide.

Plasticizers
Sorbitol, Glycerin.

Preservatives
Propyl and Methyl Parabens.

GELATIN CAPSULE SHELLS

Hard | Soft

Depending on their composition


HARD GELATIN CAPSULES

Advantages

- Tasteless and odorless
- Swallowing is easy
- Flexibility in formulating

Disadvantages

- More expensive to produce than tablets
- Not suitable for highly soluble salts

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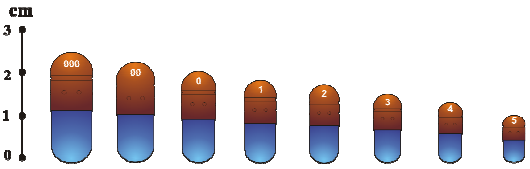
GELATIN


CAPSULE SIZES

- For human use, empty capsules ranging in size from 000 (the largest) to 5 (the smallest) are commercially available



Hard Gelatin Capsules

It contains 12 - 16 % moisture typically filled with dry solids
- powders
- granules
- pellets
- tablets

also contain
- colorant
- preservatives

SIZE	VOLUME (cm^3)
000	1.37
00	0.95
0	0.68
1	0.50
2	0.37
3	0.30
4	0.21
5	0.13

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MANUFACTURE OF EMPTY GELATIN CAPSULES

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MANUFACTURE OF EMPTY GELATIN CAPSULES

Steps involved in making empty gelatin capsules…

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

Flow Chart

Hard Gelatin Capsule Shells

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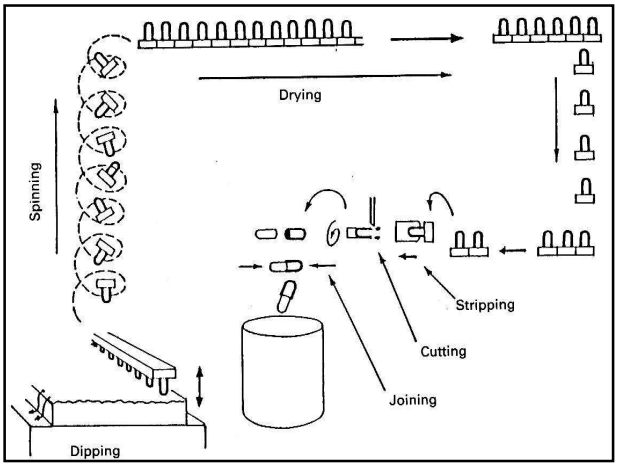


Manufacturing of hard gelatin capsules

1)Once raw materials have been received and released by Quality Control, the gelatin and hot demineralized water are mixed under vacuum in Stainless Steel Gelatin Melting System.

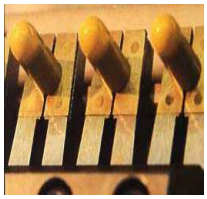
2) After aging in stainless steel receiving tanks, the gelatin solution is transferred to stainless steel feed tanks.

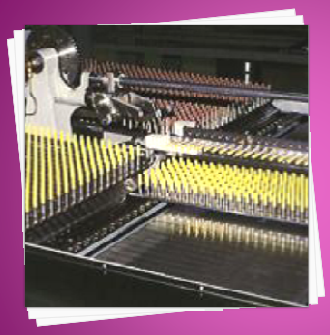
3 Dyes, opacifants, and any needed water are added to the gelatin in the feed tanks to complete the gelatin preparation procedure. The feed tanks are then used to gravity-feed gelatin into the Capsule Machine

4. From the feed tank, the gelatin is gravity fed to Dipper section. Here, the capsules are molded onto stainless steel Pin Bars which are dipped into the gelatin solution

5. Once dipped, the Pin Bars rise to the upper deck allowing the cap and body to set on the Pins.

6. The Pin Bars pass through the upper and lower kilns of Capsule Machine Drying System. Here gently moving air which is precisely controlled for volume, temperature, and humidity, removes the exact amount of moisture from the capsule halves





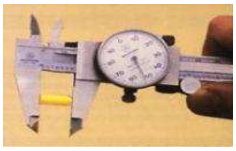
7. Once drying is complete, the Pin Bars enter the Table section which positions the capsule halves for stripping from the Pins in the Automatic section.

8. **In the Automatic section, capsule halves are individually stripped from the Pins.**

9. The cap and body lengths are precisely trimmed to a ±0.15 mm tolerance.

10. **The capsule bodies and caps are joined automatically in the joiner blocks.**

11. Finished capsules are pushed onto a conveyer belt which carries them out to a container.



12. **Capsule quality is monitored throughout the production process including size, moisture content, single wall thickness, and color**

13. Capsules are sorted and visually inspected on specially designed R&D Inspection Stations

FILLING OPERATION OF HARD GELATIN CAPSULES

Filling operation of hard capsules

Manually Filling operation of hard capsules

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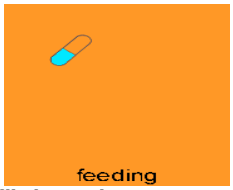
PREPARATION OF FILLED HARD GELATIN CAPSULES

The preparation of filled hard gelatin capsules may be divided into the following steps:

1. Preparing the formulation

2. Selecting the capsule size.

3. Filling the capsule shells.



4. Cleaning and polishing the filled capsules.

FILLING OF HARD CAPSULE SHELLS

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

Polishing

Pan Polishing : Acela-cota pan is used to dust and polish.

Cloth Dusting : Capsule are rubbed with cloth.

Brushing : Capsule are feed under soft rotating brush.

Storage

Finished capsules normally contain an equilibrium moisture content of 13-16%.

To maintain a relative humidity of 40-60% when handling and storing capsules

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FILLING OF HARD GELATIN CAPSULES

Various Filling Machine Available…

- Eli-lily and Co.
- Farmatic.
- Hofliger and Karg.
- Zanasi.
- Parke-Davis.

- These machine differ in there design and output

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ZANASI AUTOMATIC CAPSULE FILLING MACHINE

HOFLIGER KARG AUTOMATIC CAPSULE FILLING MACHINE

Automatic Filling operation of hard capsules

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SOFT GELATIN CAPSULE

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SOFT GELATIN CAPSULE

Definition:-

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

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Soft Capsules

ADVANTAGES

- may contain liquids, suspensions, pastes
- rapid release of contents
- useful for drugs prone to oxidation

DISADVANTAGES

- have a greater tendency to adhere to each other
- more expensive
- increased possibility of interactions between drug and shell

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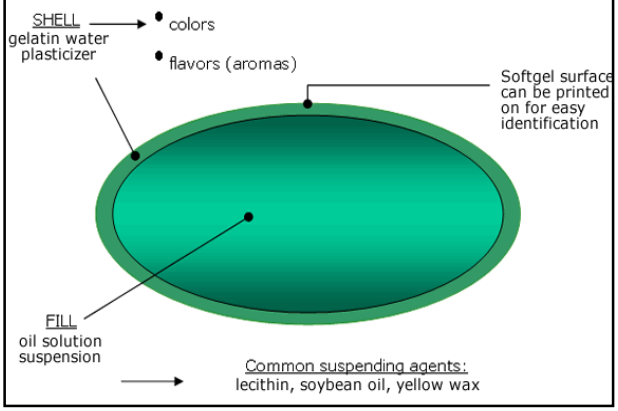
Anatomy of a Softgel



CAPSULE SHELL

The capsule shell is basically composed of

Gelatin, a plasticizer & water, it may contain additional ingredients such as preservative ,coloring &opacifying agents, flavorings, sugars, acids & medicaments to achieve desired effects.

GELATIN:-Obtain from partial hydrolysis of collagen derived from the skin, connective tissue & Bones of animals. may have viscosity of 38 mpa

Bloom strength:-150-250

cost of gelatin α Bloom strength

Plasticizer and Gelatin ratio

In soft gelatin capsule the amount of plasticizers used is more

In soft gelatin capsule the plasticizer and gelatin ratio is

0.8 : 1

In hard gelatin capsule the plasticizer and gelatin ratio is

0.4 : 1

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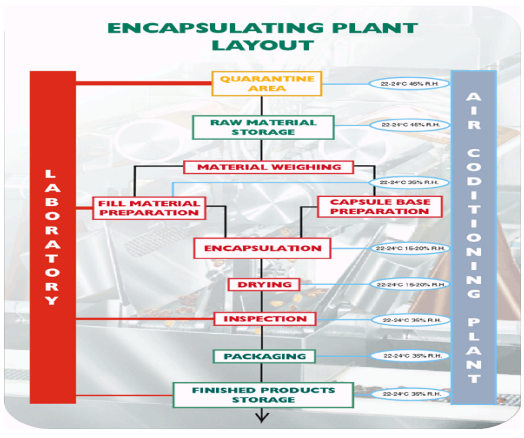
Typical formula for gelatin sheet

▶ Glycerin	I.P.	52.0 Kg
▶ PropMethyl Paraben	I.P.	0.512Kg
▶ Methyl Paraben	I.P.	0.128Kg
▶ Gelatin 120 Bloom	I.P.	152.000Kg
▶ Brilliant Blue Ponceau 4R		0.300Kg
▶ Sunset Yellow	I.P.	0.300Kg
▶ TiO2	I.P.	16.000Kg
▶ Water	I.P.	120.00Ltr
▶ Sorbitol Liq.	I.P.	16.00Kg



Gelatin Mass Manufacture

The gel is prepared in a 300-litre stainless steel vessel.

↓

Gelatin powder is mixed with water and glycerine.

Heating ↓ Stirring

The molten gelatin mass is formed.

↓

It is decanted into 200-kg mobile vessels.

Turbine mixing ↓

where colours and flavours can be added.

It ensures consistency of gelatin mass.

This mass is kept at a constant temperature until it is needed for the next stage of the process.

Content of Gelatin Capsules

Soft gelatin capsules are prepared to contain a variety of liquid, paste, and dry fills.

Use of soft gelatin capsules

POWDERS w/ capseal

GRANULES

Use of soft gelatin capsules

BEADS

TABLETS

Use of soft gelatin capsules

PASTES

LIQUIDS w/ capseal

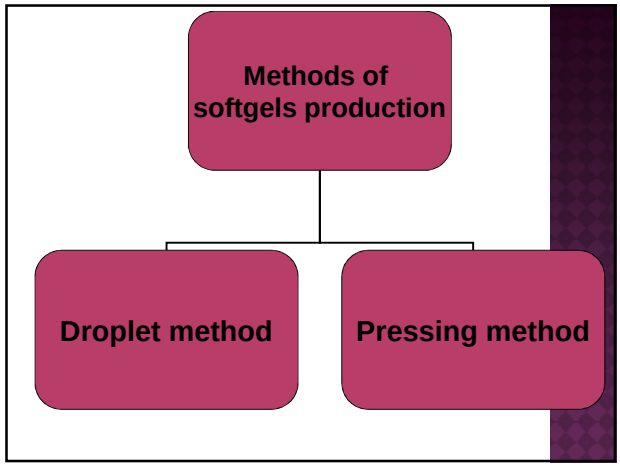
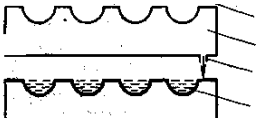


Plate process:

- 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.



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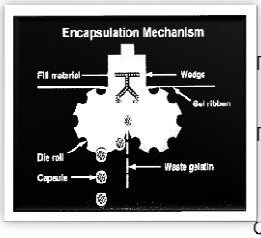
Pressing (rotate die) method



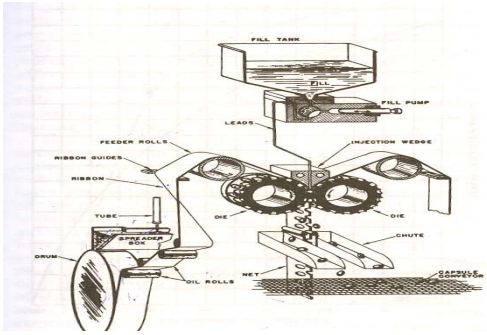
The glycerol – gelatin solution is heated and pumped onto two chilled drums-1 to form two separate ribbons-2, which form each half of the softgel.

The ribbons are lubricated and fed into the filling machine, forcing the gelatin to adopt the contours of the die.

The fill is manufactured in a separate process and pumped in, and the softgels are sealed by the application of heat and pressure.

Once cut from the ribbon, they are tumble - dried and conditioned at 20 % relative humidity.

The rotary die process



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Examples of Soft Gelatin

Examples of Soft Gelatin CAPSULES

PRODUCT QUALITY CONSIDERATIONS

1. Ingredient specifications

all ingredients of a soft gel are controlled and tested to ensure compliance with pharmacopoeial specifications.

- E.g. Impurities such as aldehydes & peroxides which may be present in polyethylene glycols. Presence of high levels of these impurities gives rise to cross-linking of the gelatin polymer, leading to insolubilization through further polymerization.

2. In-process testing

- During the encapsulation process the four most important tests are:-

a. The gel ribbon thickness;
b. Soft gel seal thickness at the time of encapsulation;
c. Fill matrix weight & capsule shell weight;
d. Soft gel shell moisture level and soft gel hardness at the end of the drying stage.

IMPORTANT SPECIFICATIONS OF GELATIN

Bloom or gel strength: It is a measure of cohesive strength of cross-linkage that occurs between molecules and is proportion to the molecular weight of gelatin.

Bloom is determined by measuring the weight in grams required to move a plastic plunger of 0.5inches in diameter, 4mm into a 62/3% gelatin that has held at 10°C for 17 hrs.

The unit of bloom is grams and it is between 150-250g

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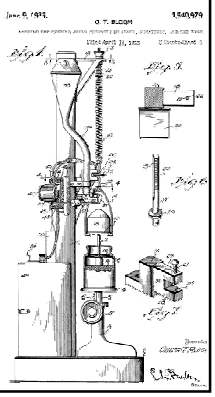
Bloom Strength

- **To make a test, a 112-gram sample of 6.666% w/w gelatin gel is prepared in a standardized container and conditioned following a highly standardized time and temperature regime. After a number of hours the sample is brought to 10°C and an instrument measures the force needed to push a plunger 12.5 millimeters in diameter 4 millimeters into the gelatin. This force is produced by dropping shot into a cup in a controlled manner until the plunger reaches the 4-mm depth. It is the weight of a mass, and that mass, expressed in grams, is the Bloom number. So if it takes 250 grams of shot to depress the plunger 4 millimeters into a sample of gelatin, that is 250 Bloom gelatin.**



Viscosity: Is determined on a 62/3% gelatin of water at 60°C and it is a measure of the molecular chain length.

Standard used: 25-45 milli poise.

Iron content: Iron is always present in raw gelatin, and its concentration usually depends on the iron content of the large quantities of water used in its manufacture .

amount should not exceed 15ppm.

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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.**
6. **Microbiological testing.**
7. **Organoleptic Properties**

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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:

capsule shell are to be stabilized to know atmospheric condition with relative humidity about 20-30 % and temperature about 21-24°c .

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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 °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.

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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

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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 .

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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 .

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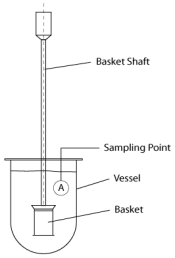
DISSOLUTION TEST APPARATUS

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

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



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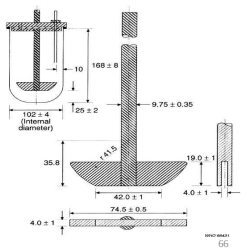
b) Apparatus -II (rotating paddle dissolution apparatus) :-

Small wire mesh size :- 22
Dissolution medium hight from the bottam of the vessel :- 23-27 mm

- Temperature – 37 +/- 5°c
- Rotated speed – 25 -150 rpm
- Dissolution medium hight from the



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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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