

PHB



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Topic Name : Capsules

Capsules are solid dosage forms in which the drug substance is enclosed within either a hard or soft soluble shell, usually formed from gelatin. The medication may be a powder, a liquid or a semisolid mass. Capsules are usually intended to be administered orally by swallowing them whole. Occasionally, capsules may be administered rectally or vaginally.

Type of Capsule:

1. Hard gelatin capsule
2. Soft gelatin Capsule

Advantages of Capsule dosage form:

- Capsules are tasteless, odorless and can easily be administered.
- Combination of powders can be used.
- There are attractive in appearance.
- They are economical.
- They are easy to handle and carry.
- The drugs having un-pleasant odor and taste are enclosed in a tasteless shell.
- They can be filled quickly and conveniently.
- The ready solubility of gelatin at gastric pH provides rapid release of medication in the stomach.

Disadvantages of Capsule dosage form:

- Capsules are not suitable for liquids that dissolve gelatin, such as aqueous or hydro alcoholic solutions.
- Not useful for efflorescent or deliquescent materials. Efflorescent cause capsules to soften & deliquescent may dry the capsule shell to brittleness.

Raw materials:

1. Gelatin
2. Sugar
3. Water - 12 to 16 % (may vary depending on the storage condition)
4. Sulfur dioxide (15%) - prevent decomposition during manufacture
5. Colorants / Opacifying agent: There are two types
 - A) water soluble dyes – e.g. erythrosine
 - B) pigments – e.g. iron oxides, titanium dioxide
6. Preservatives: To prevent microbial growth during manufacture.
7. Diluents: lactose, mannitol, sorbitol, starch, etc

8. Lubricants and Glidants: talc, magnesium stearate & calcium stearate

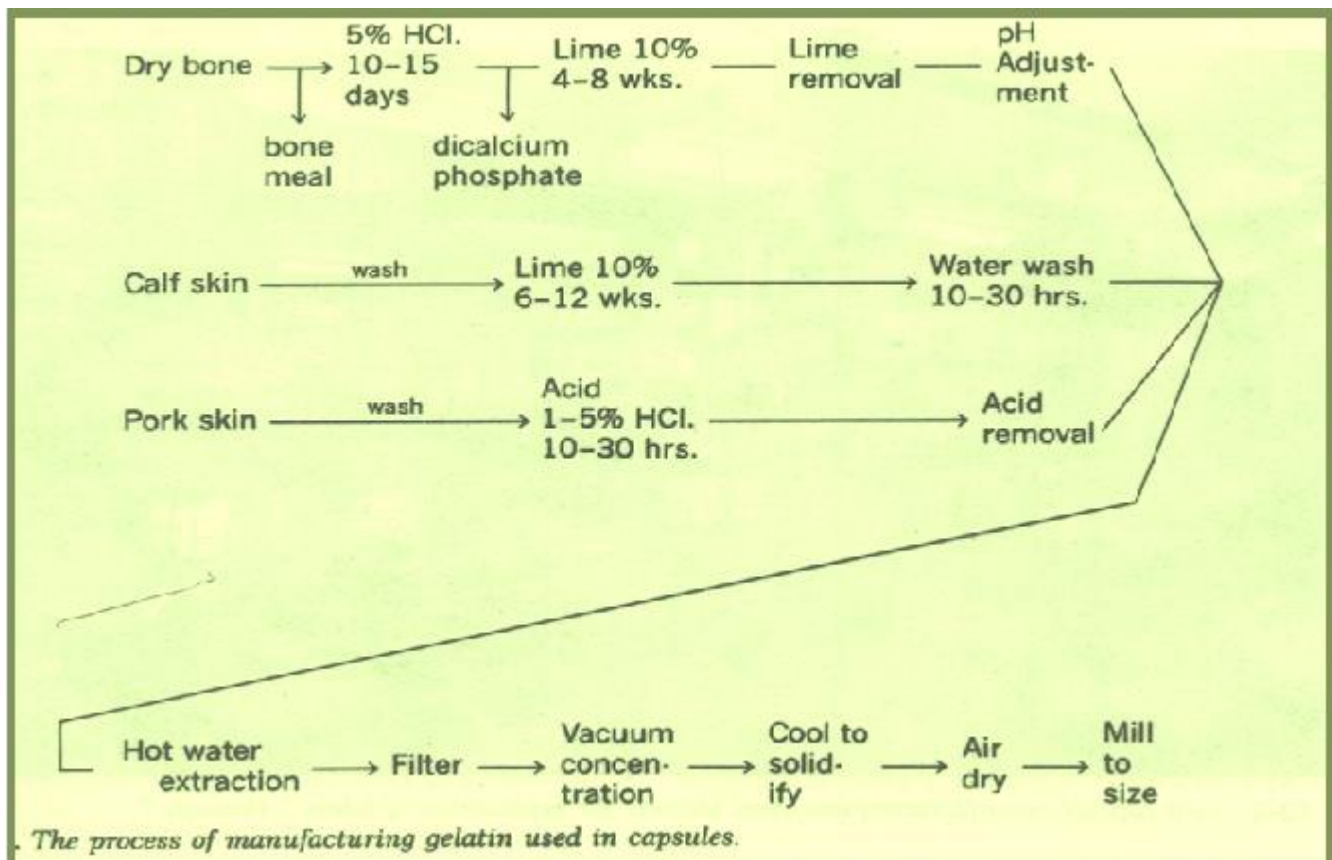
9. Wetting agents: sodium lauryl sulphate

10. Disintegrates

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. It is the major component of the capsule. The reason for this is that gelatin possesses five basic properties:

1. Non-toxic.
2. Soluble in biological fluids at body temperature.
3. It is a good film-forming material.
4. Solutions of high concentration, 40% w/v, are mobile at 50°C.
5. A solution in water changes from a sol to a gel at temperatures only a few degrees above ambient

Preparation of Gelatin:



Types of gelatin: There are two basic types of gelatin.

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

2.TYPE – B: Derived from alkali treated precursor that exhibits an iso electric point at pH-4.7. It is manufactured mainly from cows' skin.

General Characteristics of Gelatin:

- 1. Bloom value:** It is a measurement of the gelling power and the strength of the resulting gel.
- 2. Gelling power:** The gelling power varies depending on the grade of gelatin.
- 3. Viscosity:** In general, the higher the bloom, the greater the viscosity.
- 4. Foamability:** In general pig skin grades tend to have better foaming properties.
- 5. Melting point:** Lower melting point gelatins dissolve faster in the mouth; therefore, lower bloom grades tend to have lower melting points.
- 6. Color and odour:** The gelatin should be as clear as possible in solution. □Clarity is measured using a turbidimeter. □The gelatin should be without odor.
- 7. Conductivity:** It is a key parameter in photographic applications and grades of the highest purity with minimal or no conductivity are required.
- 8. pH:** It is measured using a pH meter on a 1% solution.

Types of Capsules: Capsules are available in two types:

1. Hard gelatin capsules
2. Soft gelatin capsules.

1. Hard Gelatin Capsules:

- The hard gelatin capsule consists of two pieces in the form of cylinders closed at one end.
- The shorter piece is called the cap. This cap fits over the open end of longer piece called body.
- Hard gelatin capsules are also known as dry-filled capsules or two piece capsules.
- The drug substance placed in the body and the caps are slid over it, hence enclosing the drug substance.



Manufacturing of Hard gelatin capsules Shell: Steps involved in making empty gelatin capsules.

1. Dipping
2. Spinning
3. Drying

4. Stripping

5. Trimming and Joining

6. Polishing

1. 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.

2. SPINNING: The pins are rotated to distribute the gelatin over the pins uniformly and to avoid the formation of a bead.

3. DRYING: The gelatin is dried by a blast of cool air to form a hard shell. The pins are moved through a series of air drying kilns to remove water.

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

5. TRIMMING AND JOINING: The stripped cap and body portions are trimmed to the required length by stationary knives. The cap and body lengths are precisely trimmed to a ± 0.15 mm tolerance. After trimming to the right length, the cap and body portion are joined. Finished capsules are pushed onto a conveyor belt which carries them out to a container.

6. POLISHING:

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

b) Cloth Dusting: Capsules are rubbed with cloth.

c) Brushing: Capsules are fed 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.

Filling machine of Hard Gelatin Capsules:

- Hand Operated methods or Semi-Automatic Capsules Devices.
- Punch Method or Manual Filling.
- Automatic filling machine. ex: osaka capsule filling machine, macofar capsule filling machine.

Hand operated Capsule filling operated method:

It consists of:

1. A bed having 200-300 holes
2. A loading tray having 200-300 holes
3. A powder tray
4. A pin plate having a rubber top
5. A lever
6. A cam handle.



Size of Hard gelatin Capsules

Size	Volume (ml)	Calculated fill weight (g) at powder density of 0.8 g/cm ³
000	1.37	1.096
00	0.95	0.760
0	0.68	0.544
1	0.50	0.400
2	0.37	0.296
3	0.30	0.240
4	0.21	0.168
5	0.13	0.104

Soft gelatin Capsule: 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.



Application 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.
- Easy to administer.
- Easy to manufacture.
- Liquids can be encapsulated (non water soluble)
- Small to large sizes possible.

Shape of Capsule: The shape of soft gelatin capsule are:-

- ❖ round,
- ❖ oval,
- ❖ oblong,
- ❖ tube.

Capsule sizes and shapes

Shape	Diagram	Size range (number represents the nominal capacity in minims (1 cc = 16.23 minim))
Round		1,2,3,4,5,6,7,9,28,40,90,
		40T,80T
Oval		1,2,3,4,5,6,7.5,10,.12,16,20,30,40,60,80,85,110.
Oblong		3,4,5,6,8,9.5,11,14,16,20,90,360
Tube		55,65,90,160,250,320,480

Soft gelatin capsules composition:

A typical gel mass formula for making soft gelatin capsules would be:

- Gelatin 35-45%
- Plasticizer 15-25% (glycerin or sorbitol)
- Water ~40%
- Dye / Pigment as needed
- Opacifier as needed
- Other (flavour, sugar,) as needed

Manufacturing of soft gelatin capsule: It is manufactured by four methods,

- 1) Plate process
- 2) Rotary die process
- 3) Accogel machine
- 4) Reciprocating die

DIFFERENCE BETWEEN HARD GELATIN CAPSULES AND SOFT GELATIN CAPSULES

Criterion	Soft gelatin capsules	Hard gelatin capsules
Shell	Plasticized (glycerin, propylene glycol, sorbitol)	Not plasticized
Content	Usually liquids or suspensions (dry solids possible)	Usually dry solids (liquids/semi-solid matrices possible)
Manufacture	Formed/filled in one operation	Shells made in one operation and filled in a separate process
Closure	Hermetically sealed (inherent)	Traditional friction-fit; mechanical interlock, banding and liquid sealing possible
Sizes and shapes	Many	Limited

Quality Control of Capsules:

Whether capsules are produced on a small scale or large scale all of them are required to pass through certain tests i.e., quality control tests to test the quality of the finished product. Quality control tests are divided into;

A. Physical Test:

- Disintegration test
- Weight variation

B. Chemical Test:

- Assay
- Dissolution test
- Content uniformity
- Moisture permeation test
- Stability testing

Evaluation of Capsules:

1. Weight variation test
2. Moisture permeation test
3. Content uniformity
4. Dissolution test
5. Disintegration test

1. Weight variation test:

- 20 capsules are taken at random and weighed.
- Their average weight is calculated, then each capsule is weighed individually and their weight is noted.

- The capsule passes the test if the weight of individual capsule falls within 90- 110% of the average weight.
- Moisture permeation test: According to U.S.P the unit dose container is packed along with dehydrated pellets, which have the property of changing color in the presence of moisture. The weight of test capsule is compared with the under-test capsules.

2. Content Uniformity Test:

For this test a sample of the contents is assayed as described in individual monographs and the values calculated which must comply with the prescribed standards.

- 30 Capsules are selected and 10 of these are assayed individually.
- At least 9 of these contain 85-115% of drug and none contain below 75-125% of drug.
- If 1 to 3 of them fall outside of 85 -115% limits, the remaining 20 capsules are individually assayed and the requirements are met if no few than 27 contain 85-115% of drug and none contain less than.

3. Dissolution Test:

- Place 1000 ml of water free from dissolved air having temperature of 36.5°C to 37.5°C. Place specified number of capsules in each basket.
- Start motor and adjust speed 100 rpm as per monograph.
- Withdraw the required volume of solution after 45 minutes or as specified in the monograph Filter and weigh the amount of active ingredients by the method specified in the monograph. Repeat four times.
- The test is said to pass if the amount of active ingredient is not less than 70% of the stated amount given in the monograph.

4. Disintegration Test:

- Place one capsule in each basket.
- Set the temperature of water to 37 +/- 2
- Use disc if Hard Gelatin Capsule floats whereas for soft gelatin use the disc.
- Operate the apparatus for 30 mins for Hard Gelatin Capsule and 60 minutes for Soft Gelatin Capsule.
- The test is said to pass if no residue is left on the screen of the apparatus.
- Repeat the test for 12 capsules if more than 1 or 2 capsules fails to disintegrate
- The test passes if 16 out of 18 capsules disintegrate or else fail.

Packing & Storage of Capsules:

- Capsules should be packed well closed glass & plastic container & stored at temperature not exceeding 30°C. Capsules are individually protected by enclosing in strip & blister packaging.

- In strip packing the capsule is hermetically sealed within the strips of an aluminum or plastic film.
- In blister packs, a press on the blister forces the capsule through the backing strip.
- Capsules have a larger shelf life in unopened glass bottles than in strip pack & but this is reversed.