

CAPSULE: COMPLETE REVIEW

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ABSTRACT

Capsules are Solid Dosage form in which the drug substance is enclosed in a water soluble shell along with its suitable excipients. A shell is made of a hard or a soft soluble container or an envelope which usually consist of a gelatin as a main ingredient. Capsules are available both as hard capsule and soft capsule in different shapes and sizes in the markets.

KEYWORDS: Capsule, gelatin, advantages of capsule, disadvantages of capsules, types of capsules, hard gelatine capsules, soft gelatine capsules, method of filling of soft gelatin capsule, method of filling the hard gelatin capsule, difference between hard gelatin and soft gelatin capsules, Evaluation of capsules, packing and storage.

^[1]The word “capsule” is derived from the Latin word “capsula” which means a small box or a container. They are a solid dosage form made up by using gelatin. An active ingredient may be incorporated into the outer, the inner or both. Lots of ingredients are used in making a shell such as gelatin (type A and B), plasticizers, sugars, preservatives, colourants, opacifying agents etc. Excipients such as diluents, absorbents, glidants and

antidusting compounds etc. are included in the formulation of capsules.

^[2]Capsules are easier to swallow and are used by manufacturers when the drug cannot be compacted into a solid tablet. They are also useful when the drug needs to be mixed with oil or other liquid to aid absorption in the body. It is normally a shell or container made of gelatin that contains the drug.

CAPSULE



Figure 1: laboratory made hard gelatin capsule with granules and PCM as active ingredient.

GELATIN

^[3]The word gelatine or gelatin is derived from Latin word “gelatus” meaning stiff or “frozen”. Gelatin is a translucent, colourless, flavourless food ingredient, derived from animal body parts. It is brittle when dry and gummy when moist. It may also be referred to as hydrolysed collagen, collagen hydrolysate, gelatin

hydrolysate, hydrolysed gelatine, and collagen peptides after it has undergone hydrolysis. It is commonly used as gelling agent in food, medications, drug and vitamin, photographic films and papers and cosmetics.

Gelatin is an animal protein made by boiling the collagenous material from animal bones, hides, skins etc.

In pharmaceutical industry, gelatin is used primarily to make hard and soft gelatin capsules. Other uses include tablets, emulsions, suppositories and syrups.

^[4]There are two types of gelatin, namely:

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 acid treated precursor that exhibits an ISO electric point at pH-4.7. It is manufactured mainly from animal bones.

ADVANTAGES OF CAPSULE^[5]

- Bitter drugs and drugs having unpleasant odour can be administration by enclosing them in a tasteless shell
- They are smooth and become very slippery when moist that makes it easy to swallow
- They are attractive in appearance
- Children and elderly patients can swallow easily
- It reduces gastrointestinal irritation
- It can be transported easily
- It protects any sensitive ingredients
- They are economical
- They are easy to handle and carry
- They are therapeutically inert since they are made from gelatin

DISADVANTAGES OF CAPSULE

- Bulky materials can result in large capsule size
- Ingredients can interact with capsule shell
- The concentrated preparations which need previous dilution are unsuitable for capsules because it may lead to irritation in stomach
- The hygroscopic drug cannot be filled in capsules as they absorb water present in the capsule shell which makes it very brittle and ultimately breaks into pieces.
- ^[6]Not suitable for highly soluble substances like potassium chloride, potassium bromide, ammonium chloride, etc.
- Not suitable for highly efflorescent or deliquescent materials.
- Special conditions are required for storage.

TYPES OF CAPSULES

Capsules are mainly of two types, they are:

1. Soft gelatin capsule
2. Hard gelatin capsule

SOFT GELATIN CAPSULE

^[7]Soft capsules are formed in a single piece and are more suitable for oils e.g. fish oils, or the drugs that need to be dissolved in oil or other liquid that aid the drug to be absorbed in the stomach.

^[8]A soft gelatin capsule is an oral dosage form consisting of a gelatin based shell surrounding a liquid fill. Softgel shells are a combination of gelatin, water, opacifier and plasticizers such as glycerine and sorbitol. The gelatin is plasticized by the addition of glycerine and sorbitol etc. A soft gelatin shell may contain preservatives to prevent the growth of fungi. Softgel shelled capsules are primarily used for oils and for active ingredients that are dissolved or suspended in oil. They are used to enclose liquid medicaments-oils, suspensions, food concentrates and ophthalmic products. They are available in different shapes such as round, oval and tube like shapes.

HARD GELATIN CAPSULE

^[9]Hard capsules which are commonly seen are made up of ridged shell in two pieces that fit together and is then filled with the drug. This formulation is normally more suitable for drug powders and can only be used if the drug will be easily dissolved in the stomach.

Hard gelatin capsule shell is largely composed of gelatin. Other than gelatin it may contain materials such as plasticizers, opacifiers, colourants and preservatives which either enable capsule formation or improve their performance. Hard shelled capsules which contain dry powdered ingredients or miniature pellets made by eg. Processes of extrusion or spheronization. These are made in two halves: a small-diameter "body" that is filled and then shealed using a large-diameter "cap". They are used for administration of solid medicaments. The empty capsules are available in various sizes. They are numbered according to the capacity of the capsules.^[10] For human use empty capsules ranging in size from 000 (the largest) and goes up to 5 (smallest).

METHODS OF FILLING OF SOFT GELATIN CAPSULES

^[11]The soft gelatin capsules are generally filled mechanically. The manufacturing of the capsule shell and the filling of the medicament take place simultaneously. Rotary machine is being used for this purpose these days. In a rotary die machine, the soft gelatin capsules are prepared and then filled immediately with the liquid medicaments.

The machine consists of two hoppers. Liquid gelatin mixture is placed in one hopper and the liquid medicament in the other hopper. There are two rotating dies that rotate in opposite directions.

Rotary machine

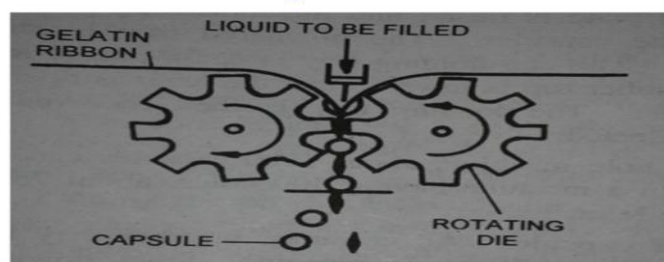


Figure 2: Rotary machine.

METHODS OF FILLING THE HARD GELATIN CAPSULES

^[12]The capsules can be filled either by hand or by a semi-automatic device or by an automatic filling machine. Capsule filling machine (Hand operated) 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 200-300 pins
5. A sealing plate having a rubber top
6. A lever
7. A cam handle

Capsule filling machine (Hand operated)

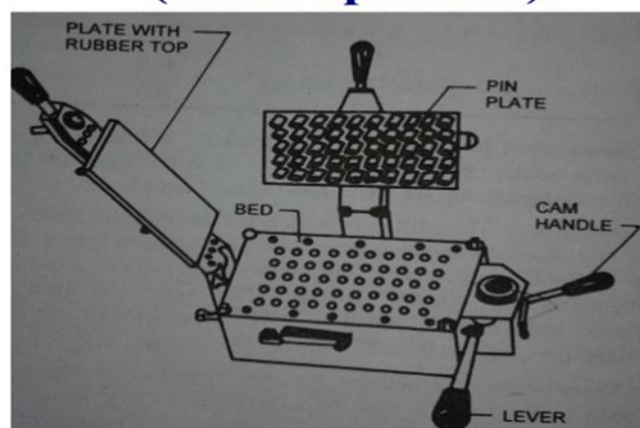


Figure 3: Capsule filling machine

Difference Between Hard Gelatin Capsule And Soft Gelatin Capsule.^[13]

SL.NO.	HARD GELATIN CAPSULES	SOFT GELATIN CAPSULES
1	Consist of two parts i.e a Body and a Cap.	It becomes a single unit after sealing the two halves of the capsules.
2	They are cylindrical in shape.	They are available in oval, round and tube like shapes.
3	The contents usually consist of medicaments or the mixture of medicaments in the form of powder, beads or granules.	The contents usually consist of liquids or solid dissolved or dispersed in suitable excipients to give paste like consistency.
4	These are prepared from gelatin, titanium dioxide, colourants and plasticizers.	These are prepared from gelatin, plasticizer (glycerine or sorbitol) and a preservative.
5	Capsules are sealed after they are filled to ensure that the medicaments may not come out of the capsule due to rough handling.	Filling and sealing of soft gelatin capsules are done in a combined operation on machine.

EVALUATION OF CAPSULES^[14]

The following test should be carried out for the evaluation of the capsules:

1. Stability tests

- ✓ Shell integrity test
- ✓ Determination of shelf life

2. Invariability test
 - ✓ Weight variation
 - ✓ Content uniformity
3. Disintegration test
4. Dissolution test
5. Moisture permeation test

STABILITY TESTS

- Stability tests for capsules are performed to know the integrity of gelatin capsule shell but not to know the stability of therapeutically active agent and for determining the shelf life of capsules.
- The test helps in improving the quality of contents of capsule shell and for choosing the appropriate retail package.
- The capsule shells are to be stabilized to know atmospheric condition with relative humidity about 20-30% and temperature about 21-24^o c.

A) SHELL INTEGRITY TEST

This test is performed to find out the integrity of capsule shell. The standard capsule shell shells kept at room temperature 40^o c and 80% RH becomes more soft, sticky and swollen.

B) DETERMINATION OF SHELF LIFE

Shelf life or expiry date of packed capsules are determined under normal storage condition.

INVARIABILITY TEST

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

- Weight variation test
- Content uniformity test

DISINTEGRATION TEST

Disintegration 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. The shell pieces after disintegration may agglomerate forming large mass of gelatin taking more time to dissolve and may adhere to the mesh thus blocking the holes. Disintegration tester is a solid state instrument for the accurate estimation of disintegration time.



Figure 4: Disintegration test apparatus.

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 form.

Dissolution test apparatus is an instrument for the determination of active drug ingredient in any pharmaceutical formulation i.e tablet or capsule as per USP,BP,IP specifications. This dissolution testing plays an important role in product development quality control and research. Dissolution test is required to study the drug release from the dosage form and it's in vivo performance. Dissolution test is used to assess the lot to lot quality of drug product. The development and validation of dissolution procedures is of paramount important during development of new formulation and in quality control.

Dissolution examination is the process which is used to measure the release profile of the drug from formulations which are commonly solid oral dosage forms like tablets and capsules.

Dissolution mainly takes place in two steps:

- 1) Liberation of drug from the formulation,
- 2) Dissolution of drug in the liquid medium.

Dissolution is expressed in terms of rate process. If the rate increases, the dissolution process also increases. Dissolution test apparatus consist of many types such as rotating basket, paddle, flow through cell etc for in vitro testing models.



Figure 5: Dissolution test apparatus.

MOISTURE PERMEATION TEST

This test is carried out to assure the suitability of containers for packaging of capsules. The moisture permeating feature of capsules packaged in:

- a) Single unit containers-blister pack or strip pack
- b) Unit dose containers glass or plastic bottle is to be determined.

PACKAGING OF CAPSULE

^[15]Capsules should be packed in well closed glass or plastic containers and stored at a temperature not exceeding 30⁰ C. They should comply with such additional storage requirements as are specified in the individual monographs given in the pharmacopoeia. Capsules can be individually protected by enclosing them in a strip or blister packs. In strip packing the capsules is hermetically sealed within the strips of an aluminium foil or plastic film. The contents are removed from the strip packs by tearing or cutting to separate the capsules. In case of blister packs, a press on the blister forces the capsules through the backing strip. Generally, capsules have a long shelf life in the unopened glass bottles than in strip-packs but this is reversed, once a bottle has been opened.^[16] Another type of blister packs made by cold forming use lidding material such as aluminium foil as double-web component to create a cavity by cold stretching which holds the capsules. Blister packs are commonly used as unit dose packaging for pharmaceutical capsules.

^[17]There are several different ways to package pills and capsule supplements. The most effective method is a trap blister with a foil barrier. Using this technique, supplement pills and capsules are first pre-packaged in "foil" blisters, before the packages are completed with rigid trap card blisters.

CONCLUSION

In a view of above facts, we have learned that the capsules are solid dosage forms in which the shells are made of gelatin and other materials where the active ingredient is dispersed in the oily substance as in soft gelatin capsules or a granules or pebbles are stuffed in the body of the shell that is covered with cap as in hard gelatin capsule. And underwent the treatment tests processes for quality control tests to meet the demand.

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