

Capsules



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1

Introduction

- The term "capsule" is derived from latin word capsula means small box.
- It is a unit solid dosage form meant for oral use in which medicament and inert substances are enclosed in a shell or envelope made of gelatin or other suitable material.
- Capsules are formulated for carrying fixed dose of any active pharmaceutical ingredient.

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2

Definition

“Capsule can be defined as solid dosage form in which the drug substance is enclosed in either a hard or soft, soluble shell of gelatin or other suitable material.”

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3

Advantages

1. Capsules are tasteless, odourless and are readily identifiable.
2. They are elegant, attractive in appearance and are comparatively cheaper.
3. Drugs with unpleasant odour or taste can be administered as capsule.
4. Capsules can be filled instantly and congenitally.
5. Physicians have freedom to manipulate the dose for individual patient.
6. Capsule is too easy to handle and carry in ambient environment.
7. They are easily swallowed and quickly dissolved in the stomach,
8. Capsule shells have little or no interaction with GI contents.

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4

Disadvantages

1. Capsules are more expensive than tablets.
2. Some hygroscopic drugs absorb moisture from the capsule shell making it more brittle.
3. Capsules are not air tight thus the shelf life is shorter.
4. Unsuitable for concentrated solutions that require dilution prior to encapsulation.
5. Filling operation is performed without compression and thus occupies more volume.
6. Capsule filling volumes are limited thus limits the dose of the drug.

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5

Classification of Capsules

- A. Hard Gelatin Capsules
- B. Soft Gelatin Capsules
- C. Modified Release Capsules
- D. Enteric Capsules

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6



Hard Gelatin Capsules (HGC)

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7

Hard Gelatin Capsules (HGC)

1. Hard gelatin capsules are used for enclosing solid medicament or dry powders of drug substance.
2. It is also known as dry filled capsule.
3. They are less flexible and consist of cap and body. The cap is short while body is long.
4. It is available in different sizes, shapes and colours.
5. Hard gelatine capsule are hygroscopic in nature.

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8

Primary Ingredients in HGC

☐ Gelatin:

1. Gelatin is a tasteless, odourless protein substance which is extracted by boiling the skin, tendons, ligaments, bones of ox and pig.
2. There are two types of gelatine: Type A which is produced by acid-catalyzed hydrolysis and Type B which is produced by alkali -catalyzed hydrolysis.
3. Due to non toxic nature gelatin is widely used in food industry.
4. Gelatin is readily soluble in biological fluid and it also has good film forming properties.
5. The molecular weight of gelatin is 15000-250000.

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9

Primary Ingredients in HGC

☐ Plasticizers:

1. Plasticizers are additives that increase the plasticity or fluidity of a material.
2. It provides structural integrity to the gelatin so the capsule can maintain its shape.
3. The amount of plasticizers determines the rubbery texture of the capsule.
4. Sorbitol and glycerin are the most commonly used plasticizers in HGC.

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10

Primary Ingredients in HGC

❑ Other components:

1. Other components of HGC are colouring agents, preservatives such as methyl paraben, lubricants such as stearic acid and surface treatment agents.
2. Titanium dioxide (TiO_2) may also be included for opacifying effects.
3. Opaque capsules are used to provide protection against light or to conceal the contents.

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11

Parts of HGC

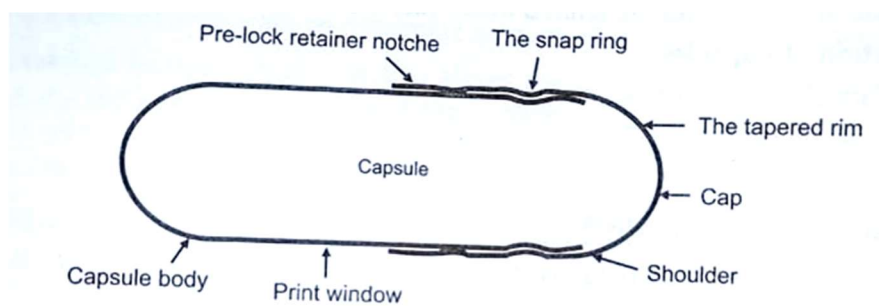
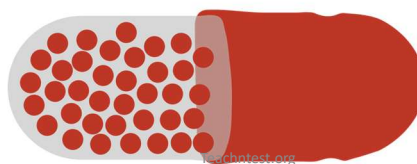


Fig. 5.1: Parts of Hard Gelatin Capsule



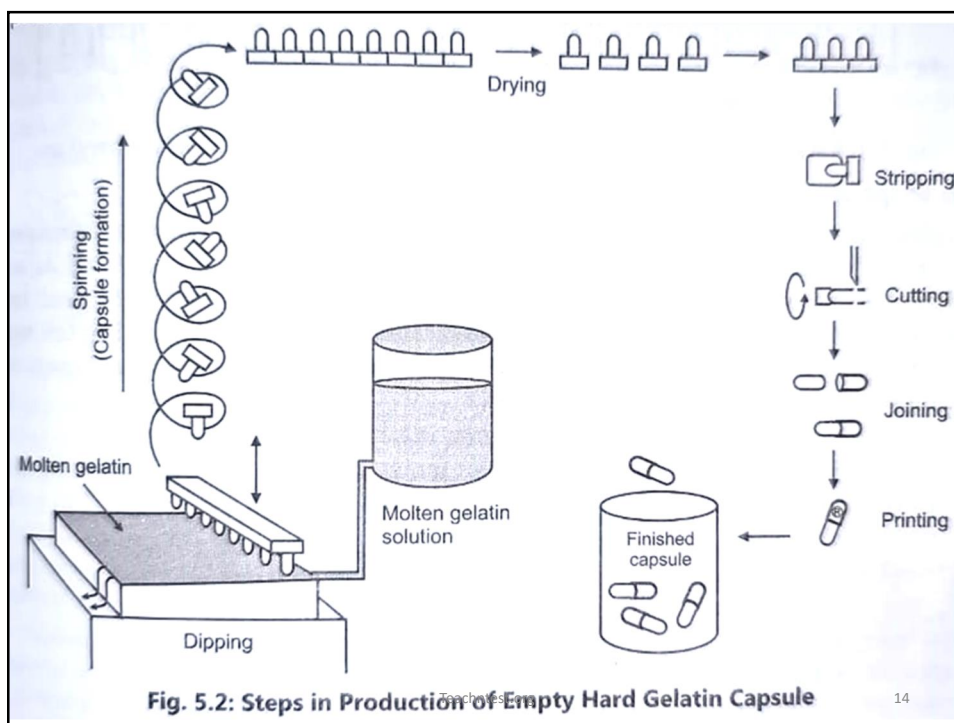
12

Manufacture of HGC


1. The major component of HGC is gelatin.
2. Gelatin manufacturing involves organic reactions and thus its preparation is a time consuming process and may require many weeks to complete the processing.
3. Previously gelatin capsules were fabricated by pharmaceutical manufacturers but currently, capsule shell production is done by third party suppliers.

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13



14




The diagram shows a sequence of steps in capsule production: Gelatin Solution, Dipping, Spinning, Drying, Stripping, Trimming, Joining, Polishing, Brushing, Sorting, and Printing. Each step is represented by a blue box with white text, connected by right-pointing arrows. The 'Gelatin Solution' box is white with blue text, indicating it is the current step.

1. Gelatin solution:

- Capsule production is an automated operation that begins with solubilizing the dry gelatin with a mixture of plasticizer and purified water.
- The gelatin solution is heated and transferred to a dip pan or pot which holds specific amount of hot gelatin at particular temperature.
- The amount of gelatin in pot is maintained automatically by controlling flow from hopper.

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The diagram shows a sequence of steps in capsule production: Gelatin Solution, Dipping, Spinning, Drying, Stripping, Trimming, Joining, Polishing, Brushing, Sorting, and Printing. Each step is represented by a blue box with white text, connected by right-pointing arrows. The 'Dipping' box is white with blue text, indicating it is the current step.

2. Dipping:

- In this process, stainless steel pins are submersed in the heated gelatin solution to simultaneously form caps and bodies.
- The pins are maintained at 20 - 22°C, whereas the dipping solution is maintained at 50°C in a heated, jacketed dipping pan.
- The length time to cast the film is about 12 sec.
- During production, the thickness of the capsule wall is controlled by the viscosity of the gelatin solution, speed and time of dipping.

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The diagram shows a sequence of steps in capsule manufacturing: Gelatin Solution, Dipping, Spinning, Drying, Stripping, Trimming, Joining, Polishing, Brushing, Sorting, and Printing. The 'Spinning' step is highlighted with a yellow background.

3. Spinning:

- After dipping, pins are elevated and spinned to uniformly distribute the gelatin over the surface to avoid the formation of a bead at the capsule ends.
- This operation is performed until pins are facing upward.

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The diagram shows a sequence of steps in capsule manufacturing: Gelatin Solution, Dipping, Spinning, Drying, Stripping, Trimming, Joining, Polishing, Brushing, Sorting, and Printing. The 'Drying' step is highlighted with a yellow background.


4. Drying:

- Blasts of cool air, which dry and solidify the capsules, is the next operation.
- The viscous gelatin is allowed to dry on the pins (about 100 pairs of pins/mould) and when dry these are removed from the pins.

5. Stripping:

- A series of bronze jaws are used to strip the cap and body capsules from the pins.
- Capsules are rotated on a fixed clamping device to keep them in parts of the place.

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A horizontal process flow diagram at the top of the slide. It consists of a sequence of blue rectangular boxes with white text, connected by right-pointing arrows. The steps are: Gelatin Solution, Dipping, Spinning, Drying, Stripping, Trimming, Joining, Polishing, Brushing, Sorting, and Printing. The 'Trimming' box is highlighted with a yellow border.

6. Trimming:

- Once the capsules are dry, they are separated from the pins by a set of mechanical jaws.
- The stripped cap and body parts are further trimmed to the required length using stationary knives.
- The stripped cap and body parts are delivered to a collector where they are firmly held together.
- As collector rotate, knives trims shells to the required length.

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A horizontal process flow diagram at the top of the slide. It consists of a sequence of blue rectangular boxes with white text, connected by right-pointing arrows. The steps are: Gelatin Solution, Dipping, Spinning, Drying, Stripping, Trimming, Joining, Polishing, Brushing, Sorting, and Printing. The 'Joining' and 'Polishing' boxes are highlighted with a yellow border.


7. Joining:

- After trimming to the right length, the cap and body are aligned concentrically in channels and the two portions are slowly pushed together to join them.
- The joined whole empty capsule is ejected from the machine.

8. Polishing:

- Empty capsules are polished in pan. Acela-cota pan is used to de-dust and polish.
- Capsules are rubbed with cloth to make surface smooth.

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9. Brushing:

- Capsules are fed under soft rotating brush to make them free from adsorbed particles.

10. Sorting:

- The capsules moving on conveyor are examined visually for sorting defective units by the automated systems or by inspectors .

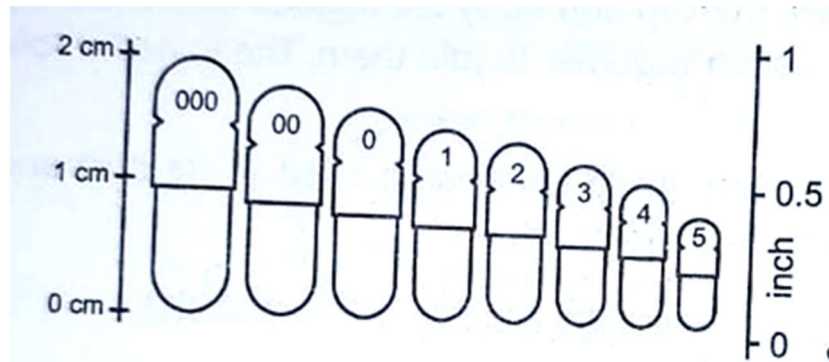
11. Printing:

- Often capsules are printed before filling operation
Printing is done on offer rotary printing machines having capacities of about 7.5 to 8 lakh capsules per hour.

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Size of Capsules

1. Capsule consists of a base or body and a shorter cap, which fits firmly over its body (base).
2. Empty HGC are made in a variety of sizes.
3. For human use, eight sizes of capsules are available.
4. The capacity of capsule varies from 0.13 ml to 28 ml.
5. For human use, empty capsules ranging in size from 000 (largest) to 5 (smallest) are used.
6. Generally capsules encapsulate ingredients between 65 mg to 1 g.



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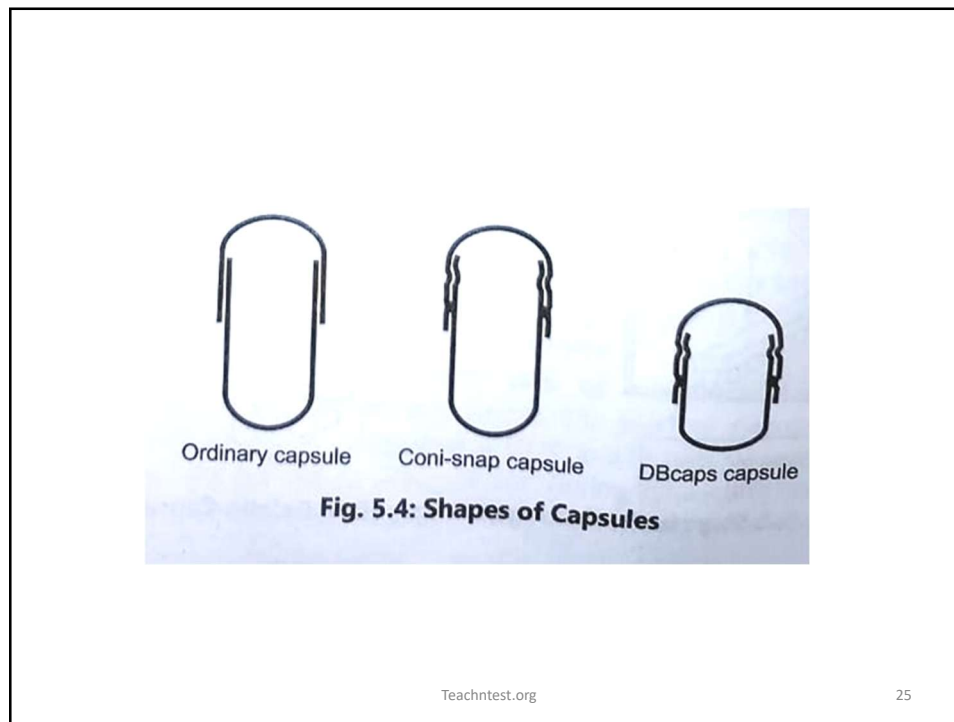
23

Shape of Capsules

1. The standard HGC come in traditional, symmetrical bullet or cylindrical shapes.
2. Capsules are either dot sealed or banded to prevent body and cap separation after filling.
3. As an alternative and to achieve other functionalities self-locking capsules are manufactured, for example, coni-snap and snap fit by Park-Davis, Lo-cap as Posilok by Eli Lilly and Star-Lok and Lox-It by Scherer.

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24



Filling

- Capsule filling is a complex process.
- The HGC can be filled using manual, semi-automatic and automatic capsule filling machines.
- The choice of capsule size and fill weight depends upon the unit dose requirements and the formulation to be filled.
- The product to be encapsulated must be well developed to ensure mass uniformity.

Filling

A. Manual Filling:

1. Punch method:

- In this method precise number and size of capsule to be filled is selected.
- Capsules body and cap is separated. The powder or granules to be filled are taken on a piece of clean paper and filled by holding the capsule body in between thumb and forefinger.
- It is a common technique used by pharmacist but is a slow and laborious.

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27

A. Manual Filling:

- 2. Volume fill method:** This method is based upon the total amount of drug needed based upon the amount per dose per day and total number of dosing days.
- 3. Tamping method:** This method involves compression of contents. The majority of high speed filling machines does capsule filling using tamping method.
- 4. Wax fill method:** This method involves traditional steps of melting wax and mixing of the drugs followed by filling the capsules similar to punch method.

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28

B. Machine Filing:

- Hand filling of small quantities of capsules is employed for small volume fills for controlled drug substances and to minimize and more readily account for product losses.
- For larger quantities up to 3000 capsules/min, automated capsule filling machines are most commonly used.

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29



Fig. 5.5: Process of filling hard gelatin capsule

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30

Finishing

- On a small scale, capsules are cleaned individually by rubbing them with a clean gauze or cloth.
- On a commercial large scale, capsule-filling machines are affixed with a cleaning vacuum that removes any extraneous material from the capsule surfaces as they exit the equipment.

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31

Manufacturing Defects

- Major defects include
 - hard shell formation, cracks, breaks, pinholes or splits,
 - loss of integrity, colour variation,
 - non-uniformity of appearance, surface spots and
 - embedded particles on capsules, non-uniform body and cap, improper fitting,
 - false odour, empty capsule, foreign matter inside the capsules, improper filling etc.
- Whereas minor defects are pits, dents, thin area, specks, spots or blemishes, rough surface with adhering spots, improper opacity, etc.

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32

Storage of HGC

- HGC must be protected against excessive heat and humidity.
- Recommended storage conditions for empty HGC are 15 to 25 °C and a relative humidity (RH) of 35-65 %.

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33

Soft Gelatin Capsules (SGC)

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34

Soft Gelatin Capsules (SGC)

1. SGC, also known as softgels, consist of one-piece hermetically-sealed soft shells.
2. It encapsulates non-aqueous liquids, suspensions, semisolid or pasty materials, or dry powders.
3. Their special application is to deliver volatile drug substances or drugs susceptible to deterioration in the presence of air.
4. The softgels are suitable for non-aqueous solutions and are known to melt within a few minutes in the stomach.

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35

Nature of Shell and Capsule Content

Soft gelatin capsule:

1. The SGC shell is composed of gelatin, plasticizer and water.
2. It also contains additional ingredients like preservative, colouring agent and opacifying agent etc.
3. The basic component of soft gelatin shell is gelatin.
4. The residual shell moisture content of finished SGC is in the range of 6-10%.
5. The ratio of dry plasticizer to dry gelatin can vary from 0.3 - 1.0 for very hard shell to 1.0-1.8 for very soft shell.

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36

Soft starch capsule:

1. Various starches can be used to make soft shell capsules.
2. Moisture content in starch capsule lies between 12 - 14% w/w and more than 50% is tightly bound to starch.
3. The major advantage of starch capsules is its readiness for filling immediately after manufacturing

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37

Primary Ingredients in SGC

Plasticizers:

- Plasticizers are used in the range of 20-30% to make the softgel shell elastic and pliable.
- The most commonly used plasticizer is glycerin but frequently sorbitol and PEG 400 are also used in combination with glycerin.

Water:

- Water is essential component of the soft gel shell that ensures proper processing during gel preparation and softgel encapsulation.
- It usually accounts for 30-40% of the wet gel formulation.

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38

Colourants and/or Opacifiers:

- Colourants can be either natural or synthetic, and are used for product elegance and identification.
- Opacifier is added when the fill formulation is a suspension or to prevent photodecomposition of light-sensitive fill matrix ingredients.
- Ex. titanium dioxide produces an opaque shell.

Preservatives:

- Preservatives are incorporated to preserve the drug medicament from the microbes.
- Methyl paraben and propyl paraben up to 0.2% of the total drug are commonly used.

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39

Flavouring agents:

- Flavouring agents are used to mask the taste of formulation components.
- The commonly used flavouring agents are ethyl vanillin and essential oils whereas sweetening agents such as various sugars, especially sucrose is also used.

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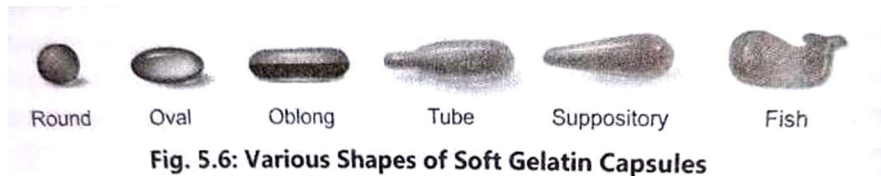
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Size and Shapes

1. SGC are soft, elastic and are one piece hermetically sealed.
2. These are available in different shapes and sizes such as spherical, cylindrical, oval, elliptical, oblong and special tube shapes with and without twist off.
3. The spherical capsules are called pearls.
4. The content in soft gelatin capsules varies from 0.1 to 30 mL.

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41



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42

Base Adsorption and Minim/Gram Factors

- Base adsorption and minim per gram factor is determined when the SGC shell contains suspension.

“**Base adsorption** is defined as the minimum amount of base or vehicle in grams required per gram of solid drug to form a mixture which easily can be encapsulated in soft gelatin capsule.”

“**The minim per gram factor** is the volume in minims that occupied by one gram (S) of the solid plus the weight of the liquid base (B) required in producing a mixture which can be encapsulated.”

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43

Production of SGC

1. SGC are manufactured by five methods namely, plate process, rotary die process reciprocating die process, accogel process and as a seamless gelatin capsules,.
2. SGC compared to HGC contain more moisture and are prone to microbial decomposition.
3. Gelatin used for making SGC is obtained from the bone and skin of animals that has bloom strength of 150-175 g.
4. All operations of the SGC production take place simultaneously with filling step as the most challenging process.

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44

Finishing of Softgels

- After drying, softgels are sorted, polished, printed, and inspected for their quality.
- The finished softgels are then packed into suitable containers, typically of low density polyethylene (LDPE) bags, high density polyethylene (HDPE) bottles, or blisters.

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45

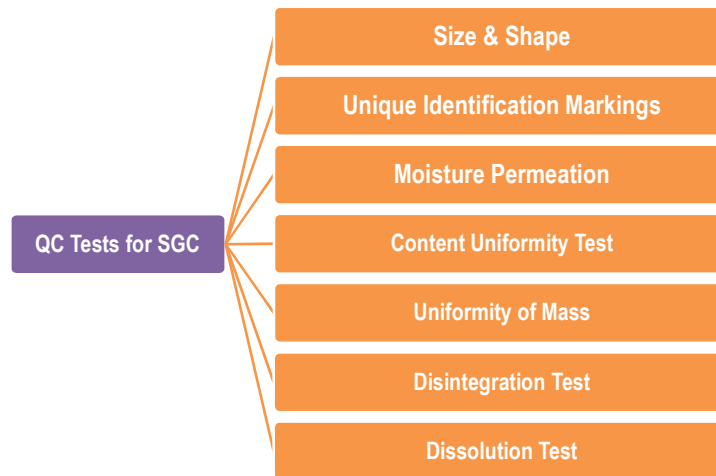
Storage of SGC

The recommended storage conditions for the SGC include a temperature range of 15-30 °C and a RH of not more than 50%.

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46

Quality Control Tests



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47

1. **Size and Shape:** This test encompasses testing capsules for uniformity of size and shape and compared with the standard.
2. **Unique Identification Markings:** Capsule surfaces may bear symbols or other unique identification markings. Inspecting capsule for these features is part of this test. If defective capsules are found, are rejected.

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48

3. **Moisture Permeation:** The degree and rate of moisture penetration are determined by packaging the dosage unit together with a colour revealing desiccant pellet. Any change in colour indicates absorption of moisture.
4. **Content Uniformity Test:** According to BP the content of the active ingredient in each of 10 capsules is taken at random using the method given in the monograph or by any other suitable analytical method of equivalent accuracy and precision.
5. **Uniformity of Mass:** The intact 20 capsules are weighed. Individual capsule is opened without losing any part of its shell and the contents are completely removed. The weight of the contents is the difference between the initial weight and the weight of shell.

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49

6. **Disintegration Test:** To test for disintegration time, one capsule is placed in each. tube of disintegration test apparatus. Capsules comply with the test, if disintegrate, and all particles pass through the 10-mesh screen within the time specified.
7. **Dissolution Test:** The USP or BP dissolution test apparatus (Basket type) is used to determine amount of drug released. A single capsule is placed in the apparatus, and the apparatus is operated at the specified rate. Within the specified time interval, or at each of the times stated, a specimen sample is withdrawn and analyzed using a suitable assay method as directed in the individual monograph.

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50