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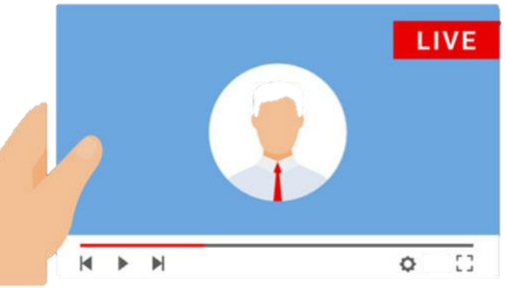

Welcome to "Live online class"

Lecture: Pharmaceutics

Oral solid dosage form: Capsules 1

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Agenda

Today's Topic: **Capsules**

Introduction

Advantages and disadvantages

Gelatin shell

Hard Gelatin Capsule

Solve **6-7 GPAT Questions**

Capsules

- Capsules are **solid dosage form** in which the **drug substance** is enclosed within a **hard or soft soluble shell** generally formed from gelatin.
- Capsules may be classified as either **hard or soft** depending on the **nature of the capsule shell**

Types of capsules

- Soft gelatin capsules (SGC)
    - They are made from a **more flexible, plasticized gelatin film**
    - They are prepared by means of **a plate process or, by a rotary die process,** in which they are formed, filled and sealed in a single operation
- Hard gelatin capsules (HGC)
    - They are manufactured and filled in a completely different operation
- **SGC** are filled with **liquids** that will **not solubilize the shell** while **HGC** typically are filled with **powders, granules or pellets**

Capsules: Advantages

- **Elegant appearance/ Flexibility dosage/ Tasteless and Odorless.**
- Minimum excipients required.
- **Printing and embossing** is easily possible **without** any **defect**.
- The use of capsules **avoids many unit operations** that are associated with the manufacture of tablets, e.g. compression, granulation, drying -> **Easy to make**
- Capsules (generally **soft gelatin capsules**) may be formulated to **increase the oral bioavailability** of poorly soluble therapeutic agents
- Capsules are a convenient method by which **liquids may be orally administered** to patients as a unit dosage form.
- The **stability** of therapeutic agents may be improved in a capsule formulation.

Capsules: Disadvantages

- **Special atmospheric conditions** are required for manufacturing and storage.
    - Eg:-- Capsule filling are 35 %RH and temperature 25°C.
- **HCG are not tamperproof, while SCG are tamperproof.**
- The requirement for **specialised manufacturing equipment**.
- Potential **stability problems** associated with capsules containing liquid fills
- Problems regarding the **homogeneity of fill weight and content** may be associated with capsule formulations.

Common excipients – Gelatin shell

- The capsule shell are made of
  - Gelatin
  - Plasticizers
  - Water
  - Dyes
  - Opacifying agent
  - Flavorings
  - Coloring agents
  - Preservatives

Gelatin

- Gelatin is prepared by the **hydrolysis of collagen** obtained from **animal bones, hide portions, and frozen pork skin**
- Gelatin can vary in its chemical and physical properties depending on the **source of the collagen** and **the manner of extraction**
- **Bone gelatin** → tough, firm film, but hazy and brittle
- **Pork skin gelatin** → provided plasticity and clarity, reducing haze or cloudiness
- **Evaluation using: Bloom strength (gel strength), Viscosity, and iron content**

Type A	Type B
Produced by an **acid hydrolysis**	Produced by **alkaline hydrolysis**
Manufactured mainly from **pork skin**	Manufactured mainly from **green bones**
Isoelectric point near to **pH 9**	Isoelectric point near to **pH 4.7**

Gelatin

Bloom strength (gel strength)

- It is a **measure of the cohesive strength** of the **crosslinking between gelatin molecules**
- It is **proportional to the molecular weight of the gelatin**
- **It is the weight in grams required to move a plastic plunger of 0.5 inches in diameter, 4 mm deep into a 6⅔% (6.67%) gelatin gel that has been held at 10°C for 17 hours.**
- Range of bloom strength: **150 to 250 g**
- **↑ Bloom strength of the gelatin → ↑ physically stable of capsule shell**
- **Cost of gelatin ∝ Bloom strength**

Gelatin

Viscosity of gelatin

- It is a **measure of the molecular chain length**
- It is determined on a **6% concentration of gelatin in water at 60°C**
- Range for viscosity for gelatin: **25 to 45 millipoise**

Low-viscosity (25 to 32 millipoise), high-Bloom (180 to 250 g) gelatins are used in conjunction with the capsulation of hygroscopic vehicles or solids

Iron Content

- It depends on the iron content of the large quantities of water used in its manufacture
- Limit of iron: **not more than 15 ppm (for gelatin used in the manufacture of soft gelatin capsules)**

Plasticizer

- More common for soft gelatin capsules
- **The ratio (w/w) of dry plasticizer to dry gelatin determines the "hardness" of the gelatin shell, assuming that there is no effect from the capsulated material**
- Glycerin, sorbitol, and combinations of these are the most prevalent

Ratio (Dry Glycerin to Dry gelatin)	Hardness	Usage
0.4/1	Hard	Oral, oil-based, or shell-softening products and those destined primarily for hot humid areas. Oral, tube, vaginal
0.6/1	Medium	Oil-base, water-miscible-base, or shell hardening products and those destined for temperate areas (hot & humid areas) Tube, vaginal
0.8/1	Soft	Water-miscible base or shell hardening products and those destined primarily for cold, dry areas

Additional components

Ingredient	Concentration	Purpose
Methylparaben (4 parts), Propylparaben, (1 part)	0.2%	Preservative
FD&C and D&C water-soluble dyes, certified lakes, pigments, and vegetable colors, alone or in combination	q.s.	Colorants
Titanium dioxide	**0.2 – 1.2%**	**Opacifier**
Ethyl vanillin	0.1%	Flavoring for odor and taste
Essential oils	Upto 2%	Flavoring for odor and taste
Sugar (sucrose)	Upto 5%	To produce chewable shell and taste
Fumaric acid	**Upto 1%**	**Aids solubility; reduces aldehydic tanning of gelatin**

GPAT QUESTION

Ratio of dry glycerin/dry gelatin for hard gelatin capsules is

A. 0.6 : 1

B. 0.4 : 1

C. 0.8 : 1

D. 1 : 0.8

GPAT QUESTION

Isoelectric point for type A gelatin is near _____

A. 4.7

B. 9.0

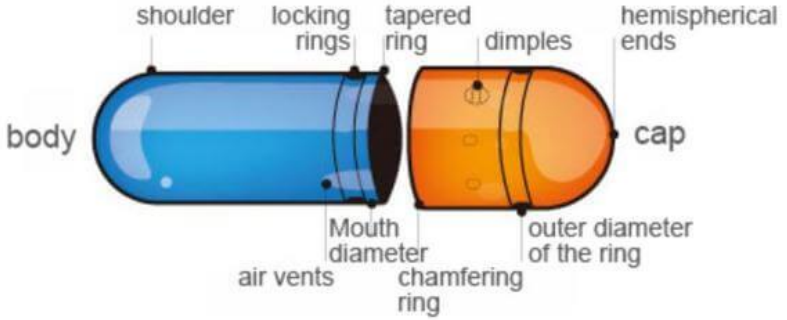
C. 9.7

D. 4.0

Hard gelatin capsule

- The hard gelatin capsule consists of **a base or body** and **a shorter cap**, which fits firmly over the base of the capsule
- It is mainly used for **powder, granules, pellets**

- Hard gelatin capsule not used in
  - administration of extremely soluble materials such as potassium chloride, potassium bromide, or ammonium chloride (sudden release → irritates stomach)
  - Highly efflorescent (soften capsule) or deliquescent materials (makes it brittle)



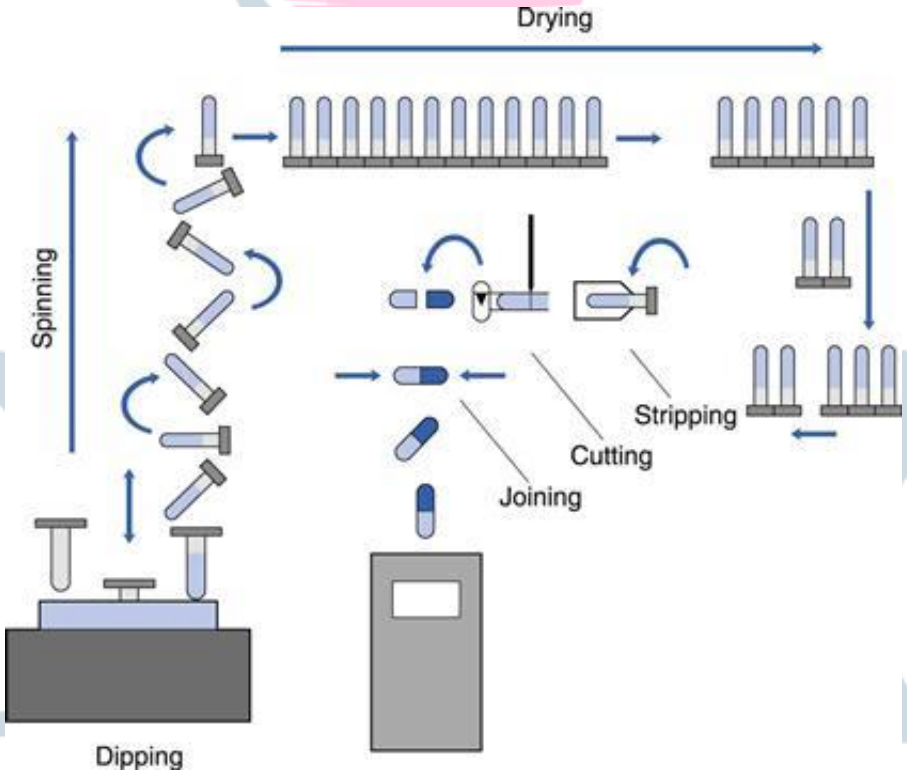
Physical specification hard gelatin capsule shell

Size	Actual Volume (ml)	Typical Fill Weights (mg) 0.70 Powder Density
000	1.37	960
00	0.95	665
0	0.68	475
1	0.50	350
2	0.37	260
3	0.30	210
4	0.21	145
5	0.13	90

Steps of manufacturing of hard gelatin capsule

- Centrifugal Casting method
- Dip-Pin method (**Mostly used on commercial scale**)

1. Gelatin Solution
2. Dipping
3. Setting/Spinning
4. Drying
5. Stripping
6. Cutting/Trimming
7. Joining



Thickness of the capsule wall is controlled by the viscosity of the gelatin solution and the speed and time of dipping

Steps of manufacturing of hard gelatin capsule

1. Gelatin Solution
2. **Dipping:** Pairs of these pins are dipped into a gelatin sol of controlled viscosity to form caps and bodies simultaneously
3. **Setting/Spinning:** The pins are usually rotated to distribute the gelatin uniformly during which time the gelatin may be set or gelled by a blast of cool air.
4. **Drying:** The pins are moved through a series of controlled air-drying kilns for the gradual and precisely controlled removal of water (3 to 6)
5. **Stripping:** The capsules are stripped from the pins by bronze jaws and trimmed to length by stationary knives while the capsule halves are being spun in chucks or collets
6. **Cutting/Trimming:** After being trimmed to exact length, the cap and body sections are joined and ejected from the machine
7. Joining

The entire cycle of the machine lasts for approximately 45 min

Moisture content in hard gelatin capsule

- **Optimum moisture content:** 12% and 15%
- **Below 10% moisture content** → brittle and suffer dimensional changes → handling problems in the filling equipment
- **Above 16%** → problems in the filling and in a loss of mechanical strength → absorb moisture → soften and become tacky
- Exposure to either heat or moisture extremes can distort empty capsules to the extent that they cannot be handled by automatic filling equipment

- **Storage: 30 - 45%RH**

Filling of hard gelatin capsule

1. **Rectification**–Empty capsule are oriented so that all point in same direction i.e., body end downward.
2. **Separation of Body and cap**–Vacuum applied body pull down into lower portion of split bushing or split filling rings.
3. **Dosing of Fill material**
4. **Joining and Ejection** – Capsule are joined by peg rings. it forces the capsule body against the closing plate. Filled capsules are ejected via compressed air.
5. **Collection** – Filled capsule are collected through Chute.

Dosing of Fill Material in hard gelatin capsule

1. Direct filling method:
    1. Auger filling method (Free flowing powder filled): Examples **-- Eli–Lilly, Parke–Devis, Perry**
    2. Vibration assisted filling: Example **-- Osaka**
2. Indirect filling method
    1. Tamp-Filling Method (Dosing disk)–JKF or Bosch or Hoflinger-Karg
    2. Dosator Machine – **Zanasi, Macofar, MG-2, Farmatic**

Finishing

1. **Pan Polishing -** Accela-Cota tablet coating pan is used to dust and polish capsules. A polyurethane or cheese cloth liner is placed in the pan, and the liner is used to trap the removed dust as well as to impart a gloss to the capsules
2. **Cloth dusting – B**ulk-filled capsules are rubbed with a cloth that may or may not be impregnated with an inert oil
3. **Brushing -** Capsules are fed under rotating soft brushes, which serve to remove the dust from the capsule shell. This operation must be accompanied by application of vacuum for dust removal

Finishing

Commercial capsule sort/polish equipment

- **Rotosort:** It is a mechanical sorting device that removes loose powder, unfilled joined capsules, filled or unfilled bodies, and loose caps. It can handle up to 150,000 capsules per hour and can run directly off a filling machine or be used separately.
- **Erweka kea –** Dedusting and polishing machine (Any residual powder is removed by the vacuum).
- **PM60:** offers two units → vacuum system to automatically remove unfilled capsules and cleaning and polishing machine

Imprinting

- It is a method by which **product or company identification** information can be placed upon capsule.
- **Imprinting of filled capsule can damage or contaminate the products. Hence empty capsule are printed**
- **When filled capsules are imprinted, contamination, poor print quality, and actual damage to the imprinting equipment result**
- **Harnett, Markem, Ackley** are imprinting machines based on **Off-Rotagravure principle.**

GPAT QUESTION

Moisture content of empty hard capsule shell should be between _____

A. 12–15%

B. 2–6%

C. 5–8%

D. 20–25%

GPAT QUESTION

Which of the following equipment removes unfilled joined capsules, unfilled bodies, and loose caps.

A. **Erweka kea**
B. **Rotosort**
C. **Both**
D. **None**

THANK YOU