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COLLEGE OF PHARMACY
2010
AL MUSTAQBAL UNIVERSITY
جامعة المستقبل

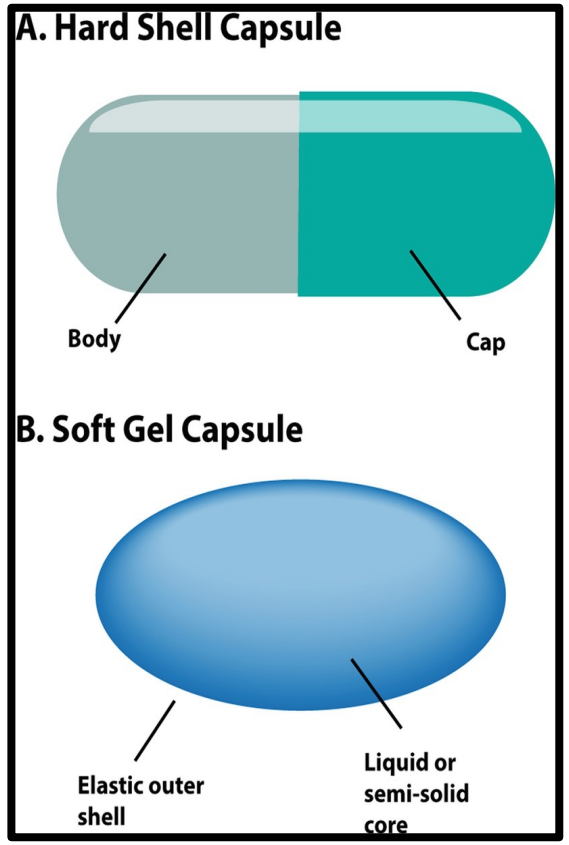
Lec 5: Capsule Dosage Form

Capsules

- A solid dosage form in which the drug substance is enclosed within a hard or soft soluble shell generally formed from **gelatin**.
- **Advantages:**

1. Easier than tables to hide the undesirable test or smell.
2. Elegant looking and easy to swallow.
3. Uses a minimal amount of excipients and little compression is required during formulation.

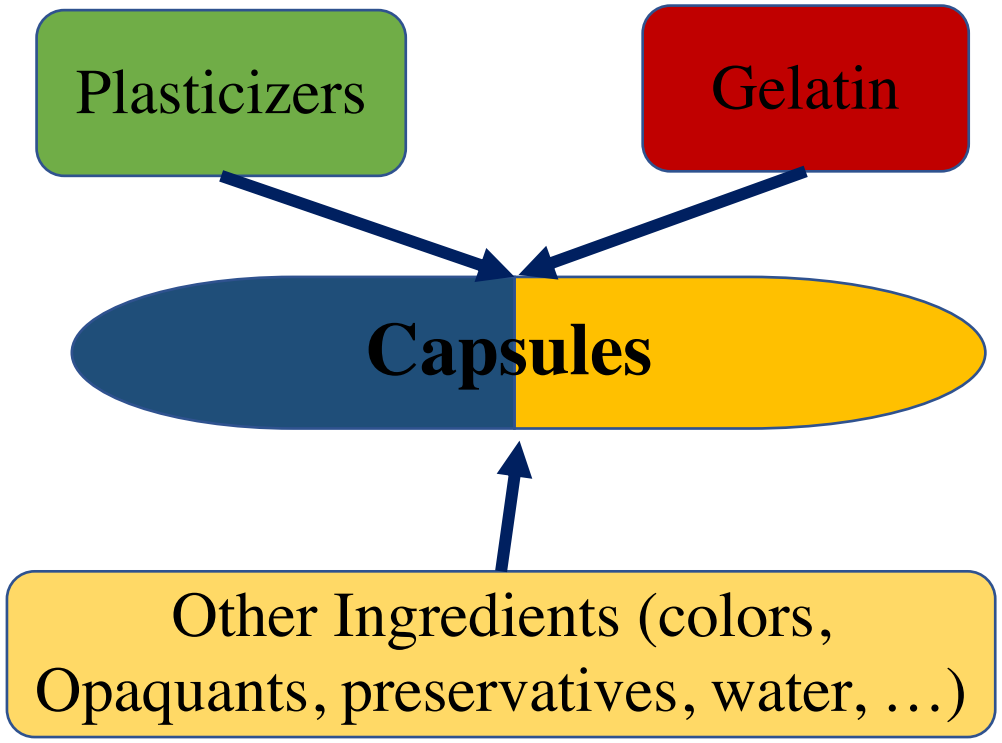
- Capsules are classified into **hard and soft** gelatin capsules depending on the nature of the capsule shell.
- Soft cap. is made of more flexible, plasticized gelatin film than hard gelatin capsules.
- **Difference**: Soft gelatin capsules are made and filled/sealed in **one process** while the hard gelatin cap. are made and filled in **two** separate processes



Capsule Shell Compositions

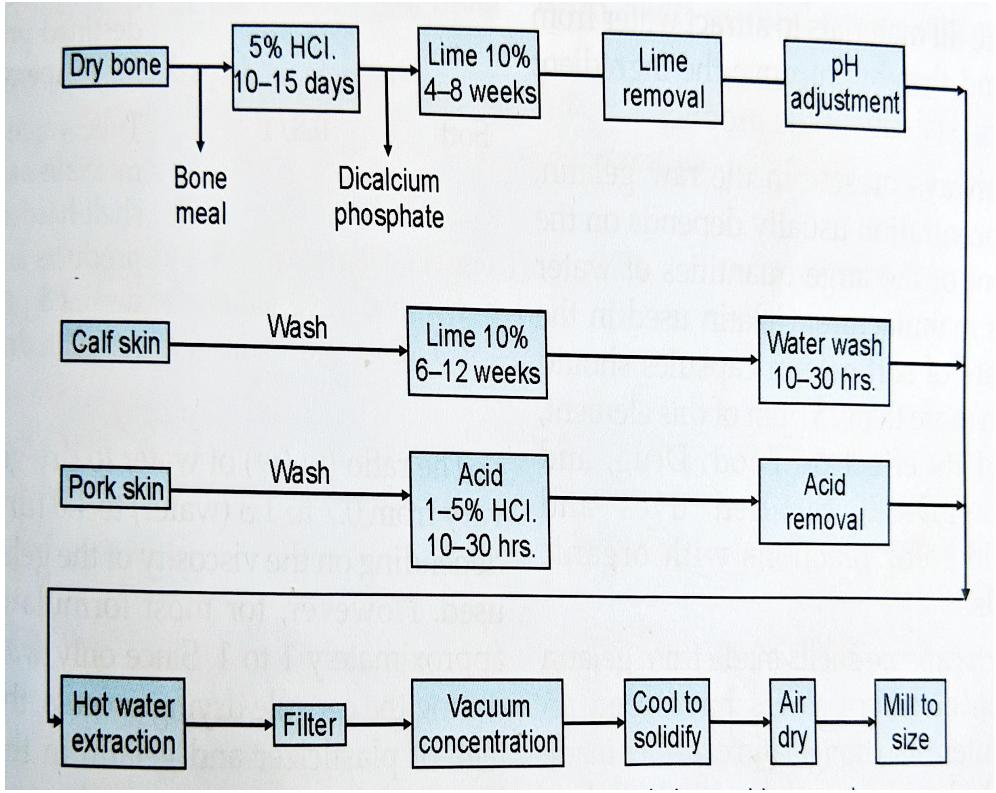
- **Gelatin:**
- Is the main component in the shell of both hard and soft gelatin capsules.
- Gelatin is obtained from hydrolytic extraction of treated animal collagen. → There is **No** natural gelatin.
- Its physical and chemical properties depend on the **parent collagen**, **method of extraction,** and **pH value**.
- Common sources of collagen are animal **bones**, hide portions, and frozen pork **skin.**
- Collagen from bones and skin are readily available in commercial quantities.

Main Ingredients in Capsule Shell



Gelatin Synthesis

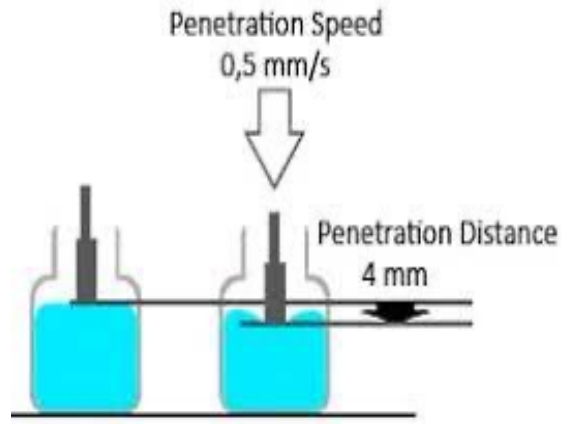
- **Type A** gelatin is derived from acid-treated precursors.
- **Type B** gelatin is from an alkali-treated precursor.
- Capsule shells can be made from either one. However, the **best shell** is the one that is made from a mixture of both.
- A mixture of bone and skin gelatin is used for the production of cap. shell.
- **Bones** gelatin produces tough, firm film, but tends to be hazy and brittle.
- **Skin** gelatin contributes plasticity and clarity to the blend thereby reducing haze or cloudiness in the finished capsules.



Not for save

Gelatin

- The Main Specification required for gelatin is the **Bloom strength.**
- The *bloom* or gel strength of gelatin is a **measure** of the cohesive strength of the cross-linking that occurs between gelatin molecules and is proportional to the molecular weight of the gelatin.
- Bloom test is determined by measuring the **weight in grams** required to move a plastic plunger 4 mm deep into a 6.6% gelatin gel that has been gelled at 10 ˚C for 17 hrs.
  - Bloom ranges from 150 to 250 g are acceptable.
- The **higher** the bloom strength of the gelatin used, the more physically stable the resulting capsule shell.
- The cost of gelatin is directly proportional to its bloom value.



Alternate Capsules

- Capsule shells can be made from materials other than gelatin for various reasons. That includes religious and vegetarian dietary restrictions.

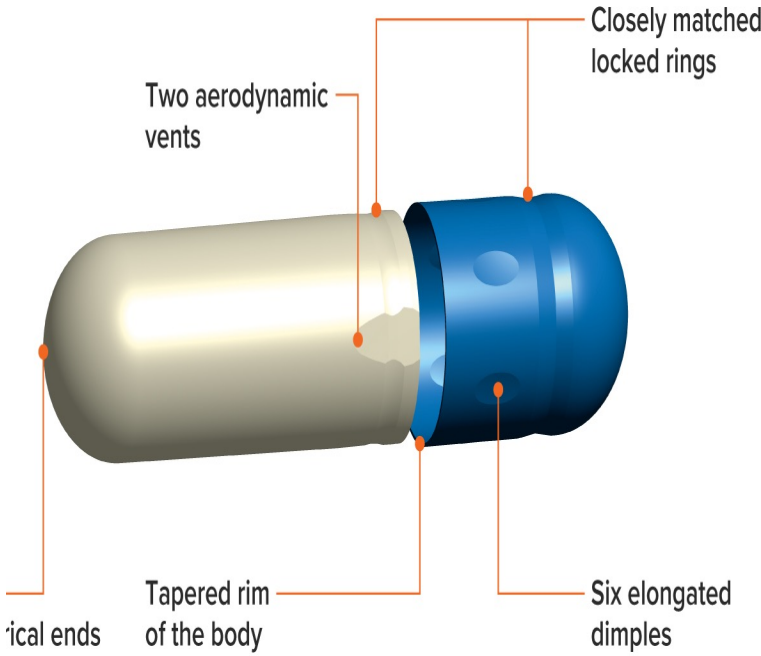
1. **Hydroxypropyl methylcellulose (HPMC):** odorless, and flexible and their appearance corresponds to that of gelatin capsules, except that the surface of HPMC capsules is **matt**. HPMC is plant plant-derived material.
2. **Starch Capsules**: The capsule shell is made of potato starch and represents a direct alternative to hard gelatin capsules.
3. **Pullulan capsules**
   - Biopolymer material. It is a Polysaccharide produced by the fermentation of carbohydrates (like starch/sugar) by the fungus Aureobasidium Pullulan.
   - These are 100% natural vegetable capsules that are edible polymer, odorless & have no identifiable taste.

Capsule Shell compositions

- **Plasticizers:**
- More common for **soft** gelatin capsules.
- The ratio of plasticizers to gelatin **determines** the **hardness of the shell**.
- Examples of materials used as a plasticizer are **glycerin, sorbitol,** and a combination of both.
- **Additional components:**
- Color, Opaquants, or materials such as **methylcellulose** and polyvinyl alcohols have been used to **modify the solubility** of gelatin or to produce an enteric capsule.
  - The color of gelatin is important, especially for soft gelatin capsules.
  - **As a general rule**: clear color is used for clear content and opaque colors are used with suspensions.
  - Darken colors are more appropriate for large-size oral products since they will **not** accentuate the size.

Hard Gelatin Capsules

- **Hard capsules are preferred over tablets due to**:
  1. Easier to formulate **because** there is no requirement that the powders be formed into a coherent compact that will stand up to handling.
  2. The capsule-filling process is easy and requires minimal strength.
  3. Preferred to hide the undesirable taste and odor.
  4. Easier to modify the release profile due to the limited factors involved.

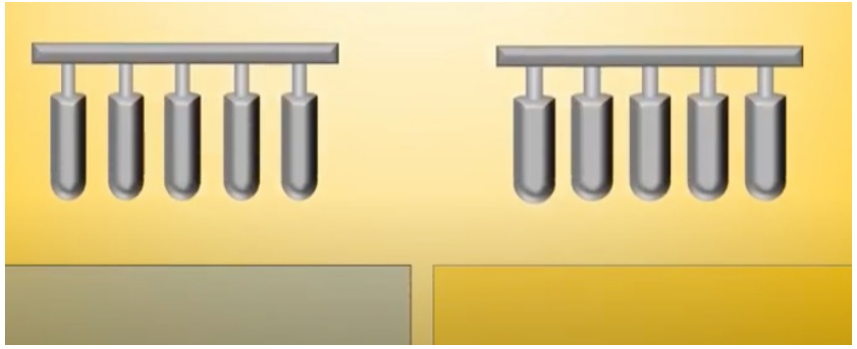


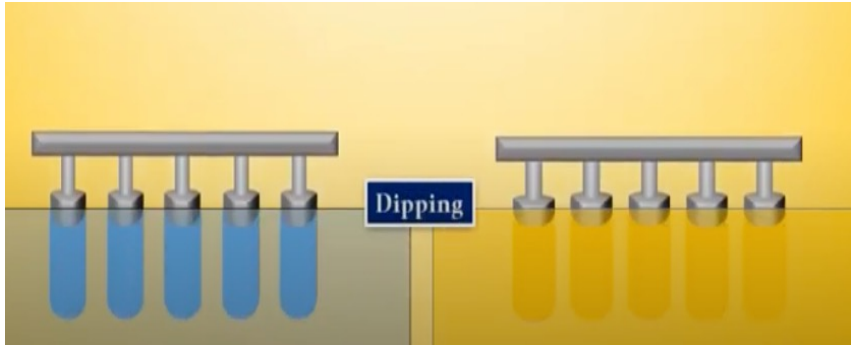
- **Disadvantage:**

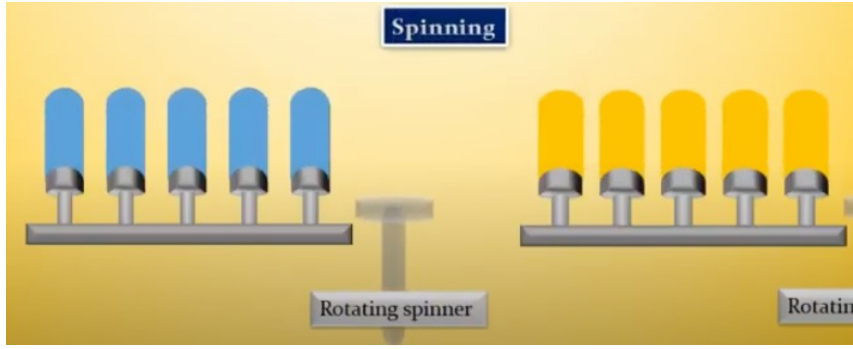
1. Capsule filling is much **slower** than the tablet press process.
2. Some drugs **may cause irritation** when suddenly released in the stomach (especially for extremely soluble compounds)

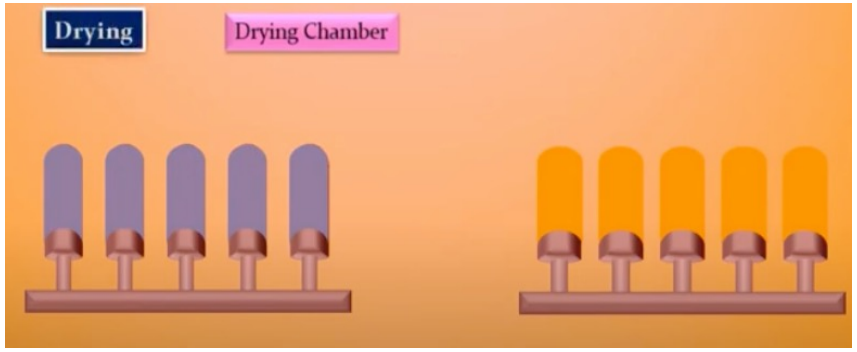
Hard Capsule Shell Synthesis

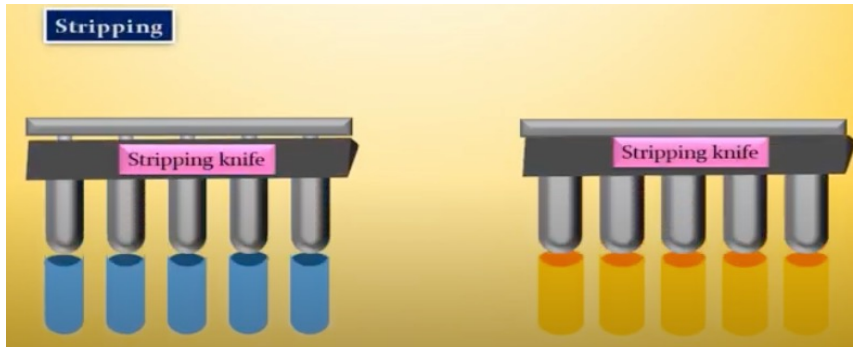
- Include different steps:
- Dipping ➔ Spinning ➔ Drying ➔ Stripping ➔ Trimming ➔ Joining

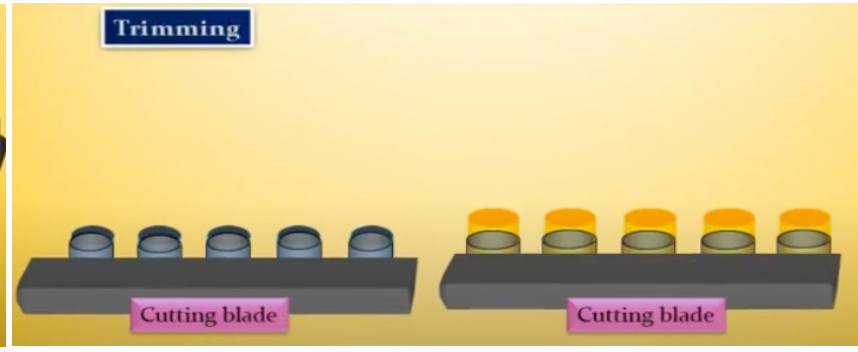








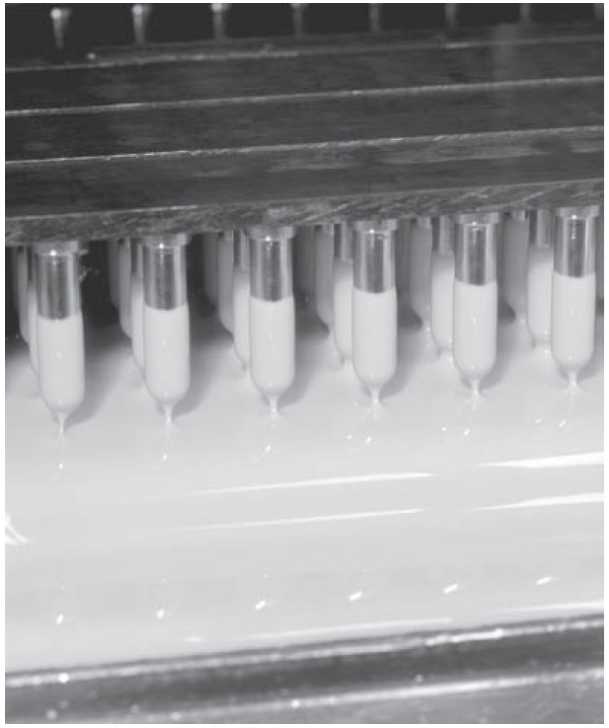




- https://youtu.be/IDtNhL7z06M

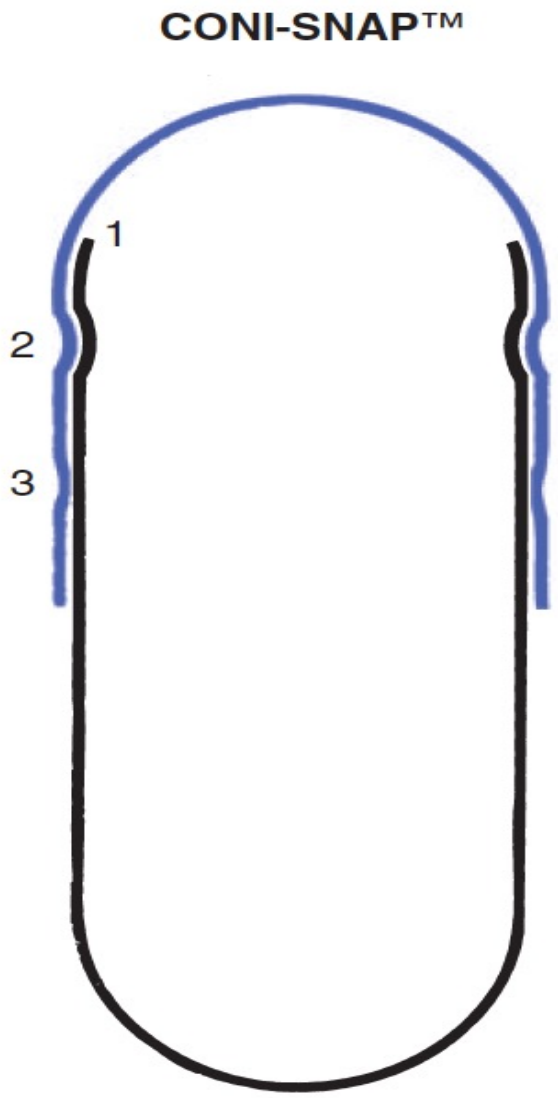
Hard Capsule Shell Synthesis

- **Dipping**: Cold pins of a **specified size** are dipped into a hot gelatin solution of a controlled viscosity.
  - Solution **viscosity**, **rate, and time** of dipping will **determine** the shell **thickness**.
  - Both the cap and body are dipped at the same time into a solution of similar viscosity.
- **Spinning**: Pins are rotated to distribute the gelatin uniformly during which time the gelatin bay be set or gelled by a blast of **cool air**.
- **Drying:** The pins are moved through a series of controlled air drying kilns (oven) for the gradual and precisely controlled removal of water.



Hard Capsule Shell Synthesis

- **Stripping:** The capsules are stripped from the pins.
- **Trimming:** Capsules halves are trimmed to exact length.
- Finally, the capsule halves are **joined** to each other and ejected from the machine.



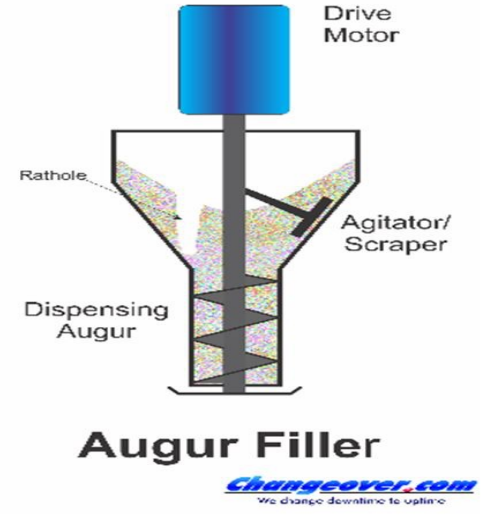
- The thickness of the capsule wall is controlled by 1) the viscosity of the gelatin solution and 2) the speed and time of dipping.
- The capsule body and cap are joined to each other by a coin-snap™ construction through locking grooves in the shell walls.
- This will ensure reliable closing of the filled capsules.

Capsule Filling Machine

- Capsules can be filled with a wide range of pharmaceutical materials including powders, granules, tablets, capsules, paste, and **non-aqueous** and oily liquids.

- Capsule-filling machines work based on **two** feeding mechanisms:

1. **Auger** type (dependent): capsules are filled with **loose powder**.
   - In this type, powder is transferred directly to the capsule body, and the flow of powder is aided by either a revolving auger or by vibrating plate.



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Dosator Type filling machine

- **Dosator** type (independent): compressed the measured amount of powder to form a **plug**.
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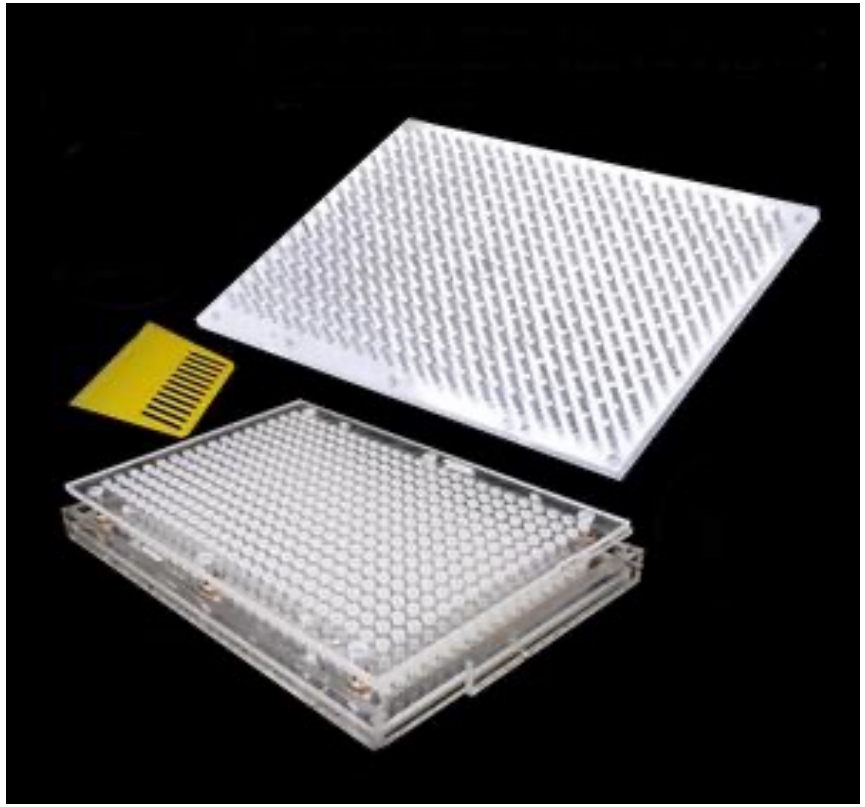
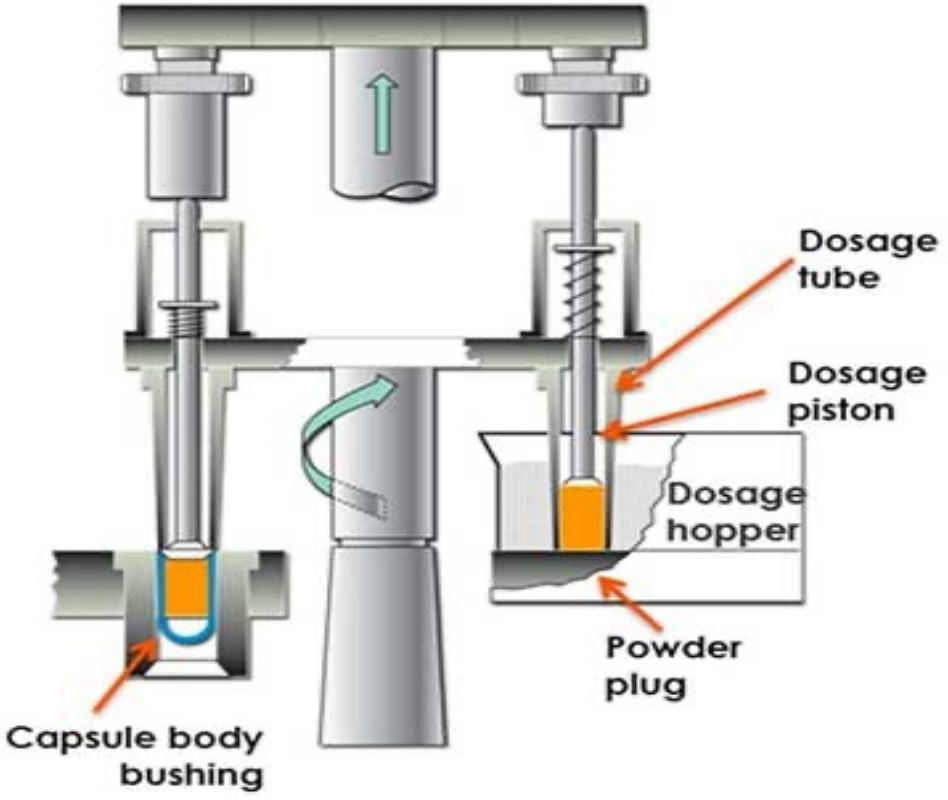




Capsule Capacity

- The empty capsules are sold by size.
- The most commonly employed for human use range from **size 000** (the largest) to size 5 (the smallest).
- **Size 00** capsules may occasionally be used if the amount to be filled is large (capacity ~ 960 mg).
- Powder weights listed are approximate and vary with the amount of pressure employed in hand filling, or with the type of equipment utilized in machine filling.

Size	Overall Capsule Lenght (in)	Average Mg Capacity	Volume Capacity
000	1.029	800 -1600 mg	1.37 ml
00E	0.996	600 - 1200 mg	0.90 ml
00	0.921	600 - 1100 mg	1.00 ml
0E	0.909	462 - 924 mg	0.78 ml
0	0.85	400 - 800 mg	0.68 ml
1	0.764	300 - 600 mg	0.48 ml
2	0.693	200 - 400 mg	0.36 ml
3	0.618	162 - 324 mg	0.27 ml
4	0.563	120 - 240 mg	0.20 ml

Finishing and Polishing

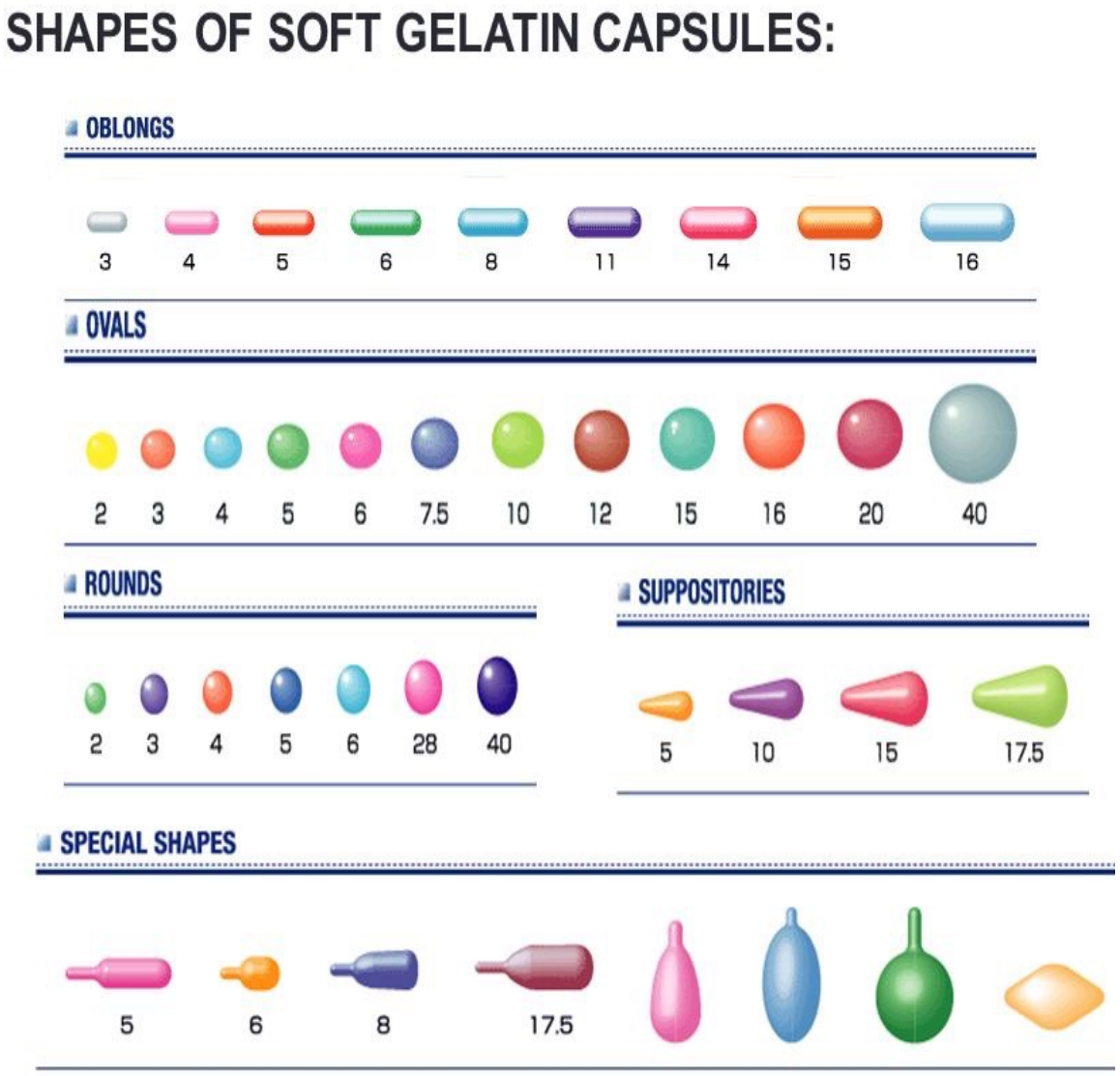
- Finished capsules from filling equipment require some type of dust removal and/or polishing before the remaining operations of inspection, bottling, and labeling are done.
- The following equipment is commonly used for this purpose:

1. **Pan polishing**: A piece of cloth is placed in the pan, and this cloth is used to trap the removed dust as well as to impart a gloss to the capsules.
2. **Hand polishing**: the capsules are rubbed with a cloth manually. This procedure imparts a somewhat improved gloss to the capsule.
3. **Brushing**: capsules are fed under rotating soft brushes, which serve to remove the dust from the capsule shell.


SGcaps
Soft Gelatin Capsules

Soft Gelatin Capsules (SGcaps)

- Solid dosage form containing **liquid** medication.
- They are formulated for oral, suppository, topical, and for cosmetic uses.
- As in a hard gelatin capsule, the shell of the capsule is composed of **gelatin**, water, and plasticizer.
  - In addition, it may contain compounds such as preservatives, colors, and opaquing agents.
- The difference from hard gelatin capsules is the **high amount of water** which may constitute up to 50%.



Advantages

- It offers the following advantages:

1. They permit liquid medications to become **easily portable**.
2. **Uniformity** of dosage because they contain liquid which is more uniform than powder.
3. The **disintegration** and dissolution rates are faster than that of other solid dosage forms.
4. The **bioavailability** of drugs is often improved since these capsules contain the drug in liquid form.
5. Safer handling of **highly potent** or cytotoxic drug compounds.

Disadvantage:

- It does require special equipment and skills to formulate.

Capsule Contents

- The content of soft gelatin capsules may be solution or suspension.
- Only those liquids that are both water-miscible and volatile **cannot** be included as major constituents of the capsule content since they can migrate into the hydrophilic gelatin shell and volatilize from the surface. (**Water** and **ethyl alcohol** fall into this category).
- However, up to **5%**, water and alcohol can be used as minor constituents (e.g., as cosolvents to aid in the preparation of solution).

Capsule Contents

- Preparations for encapsulation should have a pH between 2.5 and 7.5 since preparations that are more **acidic can cause hydrolysis** of the gelatin shell while those that are more **alkaline can tan the gelatin** and thus affect the solubility of the shell.
- Solids are incorporated into the soft gelatin capsules as either a solution or suspension.
- The preparation of a suitable solution of a solid medicament should be the first goal of the pharmacist. Usually, a solution is more easily encapsulated and exhibits better uniformity and *physical* stability than a suspension.