

Capsules dosage

form



Topics

- **General description**
- **Advantages and disadvantages**
- **Types**
- **Manufacturing of capsules (Materials, methods and equipment)**
- **Quality control**

Capsules

- Are solid dosage forms that are most commonly composed of gelatin shells or containers designed to contain one or more medicinal agent and inert ingredients (powder, semisolid or liquid).

Advantages: ?? Related to (manufacturing and biopharmaceutical considerations)

Disadvantages: ??? Related to (Stability problems, content properties and weight variation)

Types

- According to the type of capsule shell : **Gelatin and non gelatin capsule or called vegetarian capsules (starch, PVA, seaweed and HPMC types)**
- According to gelatin shell composition: **hard (two-piece) and soft gelatin capsules (softgels)= (single piece). (H.w Compare??)**
- According to the release pattern: **modified released capsules (enteric, sustained or extended) and plain capsules.**
- According to the route of administration: **oral and non oral capsules.**
- According to the shape: **oblong, oval, tube and round.**

Manufacturing of capsules

- Is varied with variation of capsules type (hard or soft).
- For hard gelatin capsule (HGC) type, in general we have some similarities with tablet formulations, while in softgels, we have similarities with oily solutions.

HGC

Materials:

Involves :

- a) **The empty gelatin capsule shells**
- b) **The fill content (Mainly bulk powder, semisolid or liquid in state).**

The capsule shells:

- Mainly with oblong shape.
- Consist of cap and body.
- Found into different sizes



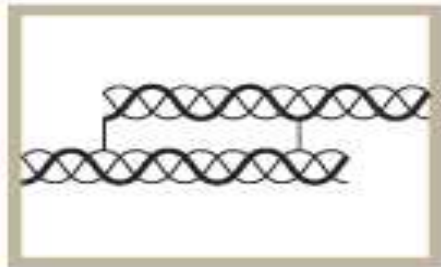
Size	Volume	Fill weight(g) at 0.8 g/cm ³ powder density
000	1.37	1.096
00	0.95	0.760
0	0.68	0.544
1	0.50	0.400
2	0.37	0.296
3	0.30	0.240
4	0.21	0.168
5	0.13	0.104

- The capsules size depend on the properties of the powder to be filled (the density and compressibility), but generally certain types of powder may be used for estimation of the capacity (in weight units) of each capsule size like aspirin, sodium bicarbonate and quinine sulphate.
- The gelatin capsule shell is mainly consists of gelatin, water and other additives (preservative, sugar, colorant, opaquant and surfactant).

Gelatin

- A mixture of proteins that is extracted from animal collagen (in skin, bones and connective tissues) by either partial acidic or alkaline hydrolysis, so two types of gelatin are obtained.
- Gelatin has different properties like: safety, solubility, good mechanical properties upon drying, excellent rheological properties at high temperature (sol form) and then forming (gel form) at low temperature.

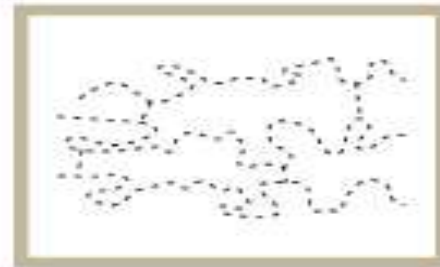




COLLAGEN
(COLD EXTRACTION)



GELATIN
(HEAT EXTRACTION)



**COLLAGEN
HYDROLYSATE**
(HEAT - ENZYNE EXTRACTION)



Bone, Skin, Scale



Collagen
molecular weight :
300,000



Heating (Denaturation)



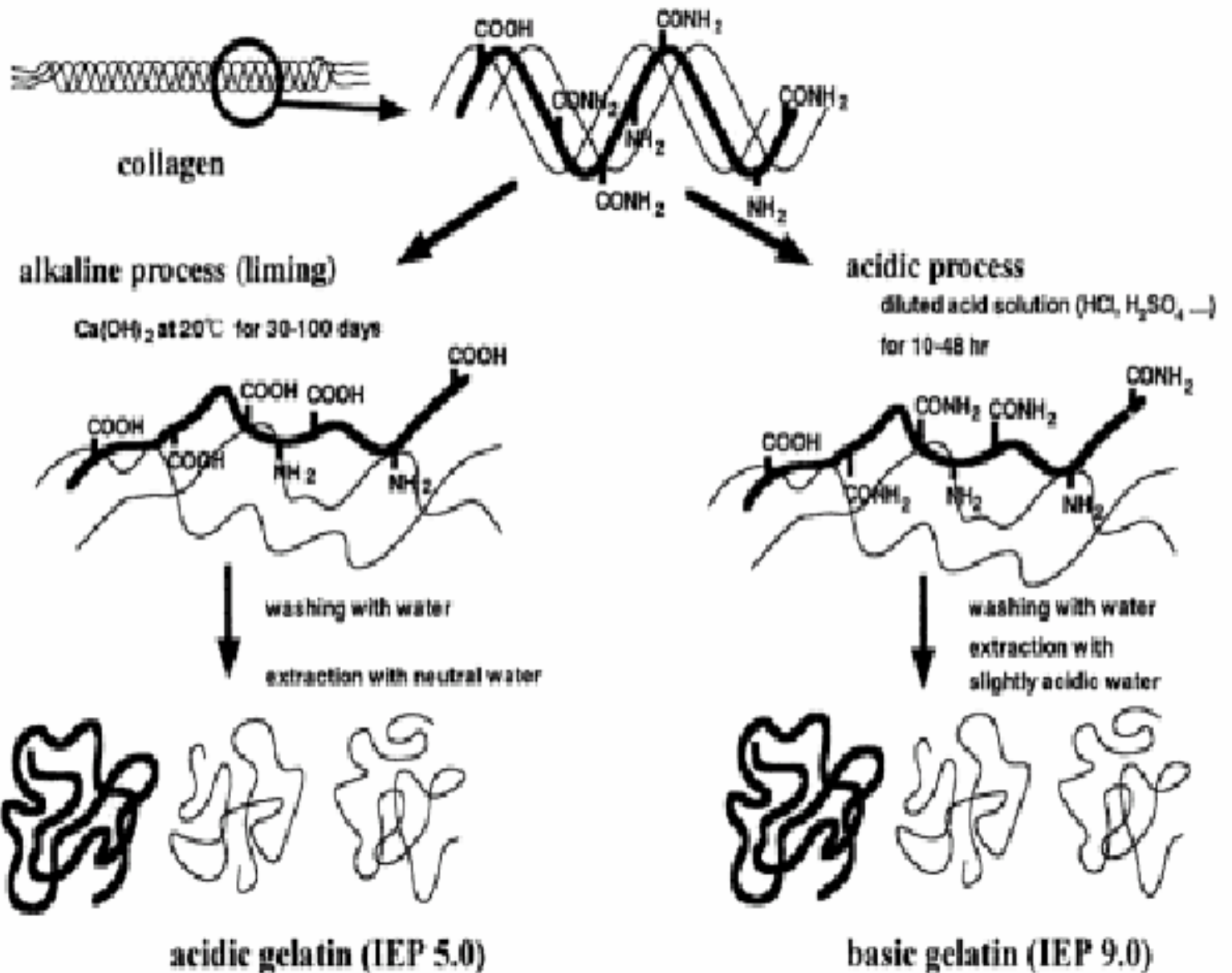
Gelatin
molecular weight :
around 50,000 to 200,000



Enzymatic Hydrolysis



Collagen Peptide
molecular weight :
around 2,000 to 5,000



**Alkaline Process
Type B Gelatin**

**Acid Process
Type A Gelatin**

Split

Bones

Pig Skins

Washing

Grinding

Washing

Grinding

Defatting

Grinding

Liming Process

Washing

Hydrolysis

Washing

Macerating

Washing

Neutralizing

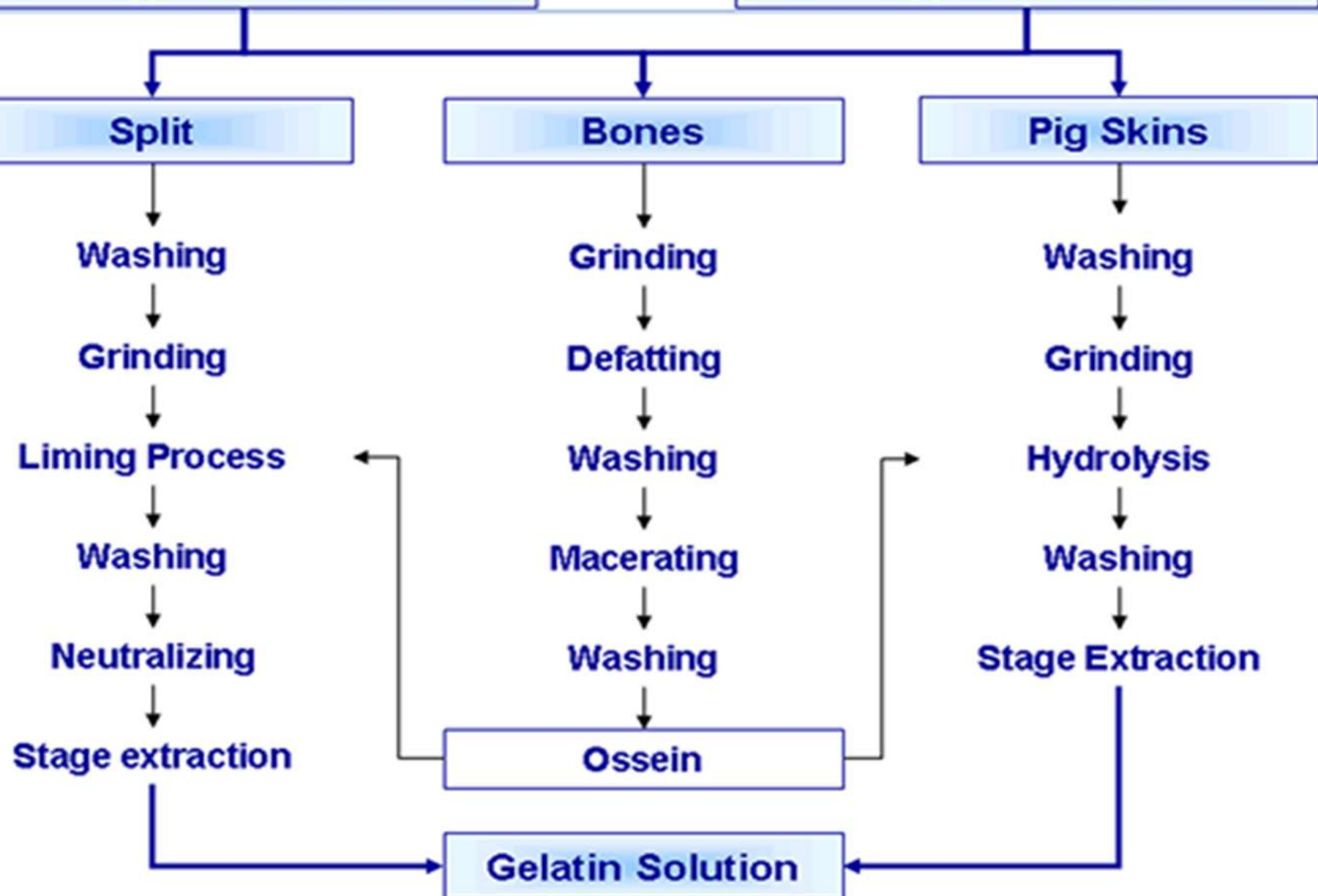
Washing

Stage Extraction

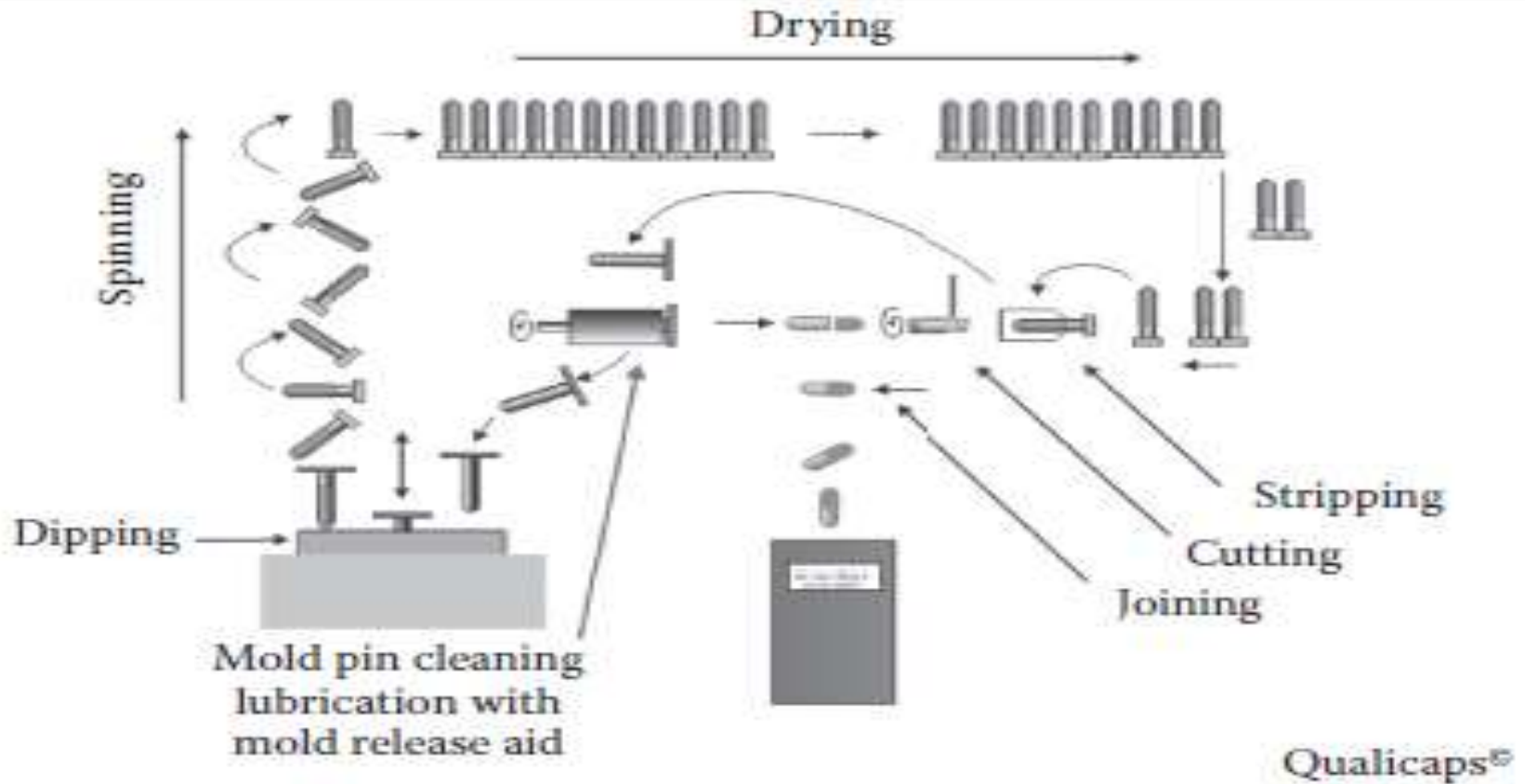
Stage extraction

Ossein

Gelatin Solution



- As general specifications for gelatin are : **Bloom strength, viscosity and impurities ratio.**
- **Bloom strength** measures the cohesive strength of the cross-linking that occur between gelatin molecules and is proportional to the mol.wt. of gelatin. As it is increased as the physical stability and cost are increased.
- Now, how the gelatin capsule shells are manufactured?? Are manufactured mainly by **dipping method** (**mechanical dipping of pins or pegs about 500 of the desired shape and diameter into a temperature controlled reservoir of melted gelatin mixture**).



3 Outline of the hard capsule manufacturing process.

As variables affecting the quality of shell are viscosity of gelatin solution, the speed and time of dipping. After that, characterization (sorting) may be needed for the moisture content (15 – 18% w/w), printing and at last, storing at optimum conditions (of humidity and temperature).

Fill contents:

- The components are the active ingredients and excipients
- Active ingredients: Not all drugs can be encapsulated by this type due to incompatibility problems like efflorescence, deliquescence and stability.



Formulation considerations

- Flow, particle size, particle shape and density properties
- Compactability.
- Compatibility with capsule shell
- Dose (amount in micrograms -600 mg)
- Solubility and wettability

Excipients

- Diluents or fillers: fill the size and improve the flowability (free flowing) using as example corn starch or cohesion properties using MCC and lactose monohydrate.
- Disintegrants: as before, ex. Pregelatinized starch, MCC, Sodium starch glycolate, croscarmellose and crospovidone.
- Lubricants/glidants: ex. Mg stearate and colloidal silicone dioxide.
- S.A.A. and wetting agents: ex. SLS, sodium docusate, some hydrophilic polymers

Notes

1- Sometimes the fills may be liquids or semisolid. Like:

A) lipophilic liquids or oils containing dissolved or dispersed drugs may be used like vegetable oil (olive) or fatty acid esters (glyceryl mono stearate).

B) Water miscible liquids containing dissolved or dispersed drug like PEG and Pluronics.

2- As stabilizers for these types. S.A.A., viscosity enhancer and antioxidants may be used.

■ **As limitations for this type of formulation, are:**

- 1) Interaction with capsule shell, like pH effect on gelatin hydrolysis, tanning and hygroscopicity or water effect on shell integrity.**
- 2) Presence of highly hygroscopic excipients that can affect the moisture level of the shell.**

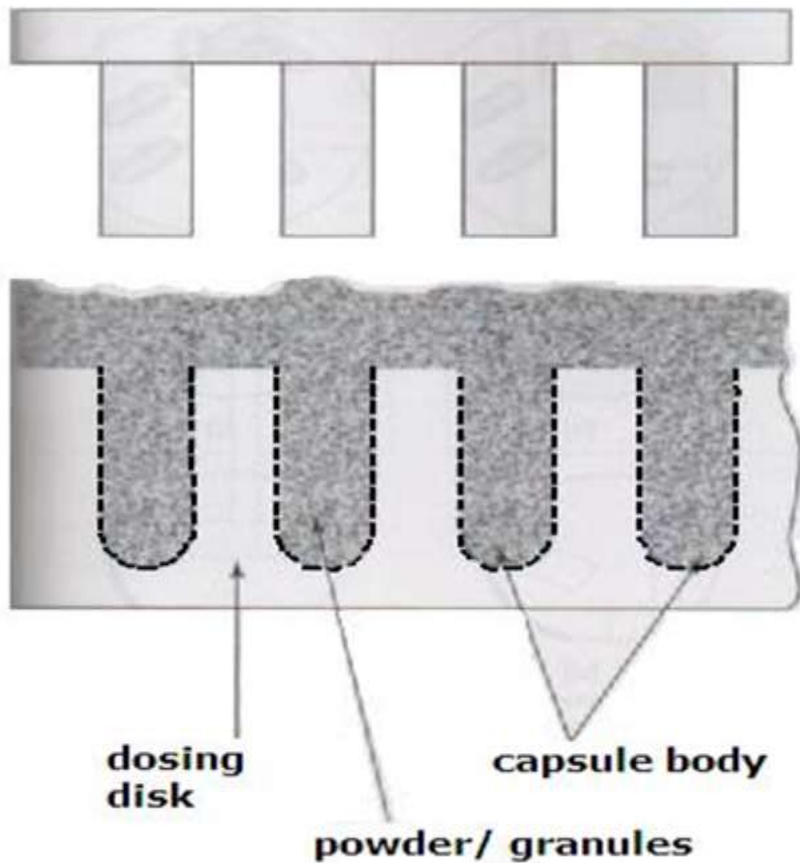
Methods

■ **As general steps involved, we have:**

- 1) Weighing the solid powder or measuring the liquid materials, with selection of an appropriate capsule size.**
- 2) Milling, granulation or microencapsulation may be needed.**
- 3) Mixing {solid-solid (mainly), liquid-liquid or solid-liquid} until get uniform mixture.**
- 4) Filling of the content fill inside the capsule shell.**
- 5) Sealing 6) Cleaning and polishing 7) Imprinting**
- 8) Packaging and labeling**

Filling

1) Manual filling = Punch method and Hand operated filling machines





1. Feeding

2. Orientation

3. Opening

4. Ejection of
non-separated

5. Dosing

6. Closer

7. Ejection

FIGURE 2.3 The basic operational steps of all capsule filling machines.

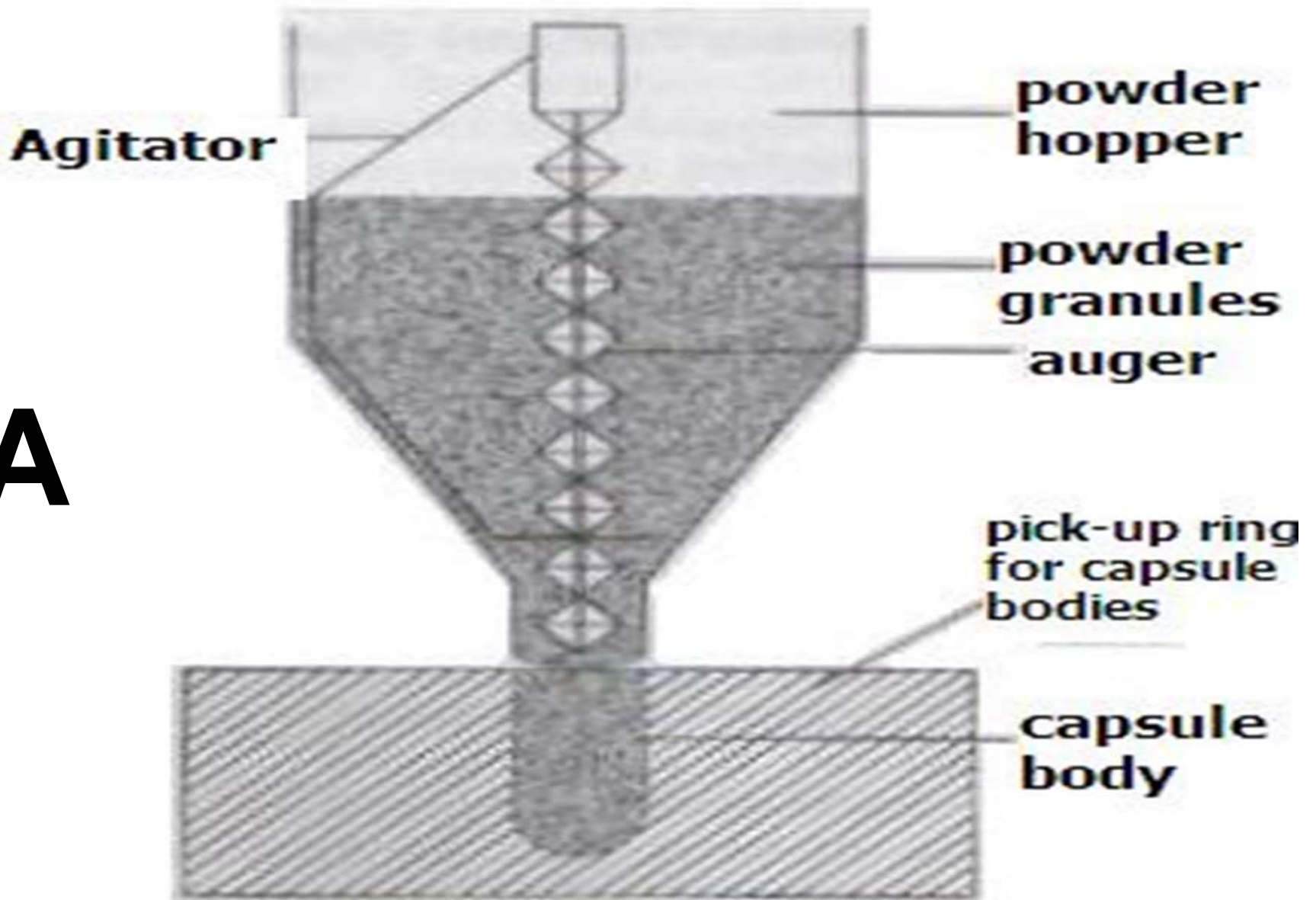
2) Automatic filling machines(dosing systems), (dosators)

A- Dependent method: use the capsule body directly to measure the powder. Fill uniformity can only be achieved if the capsule is filled completely. Like fig.A

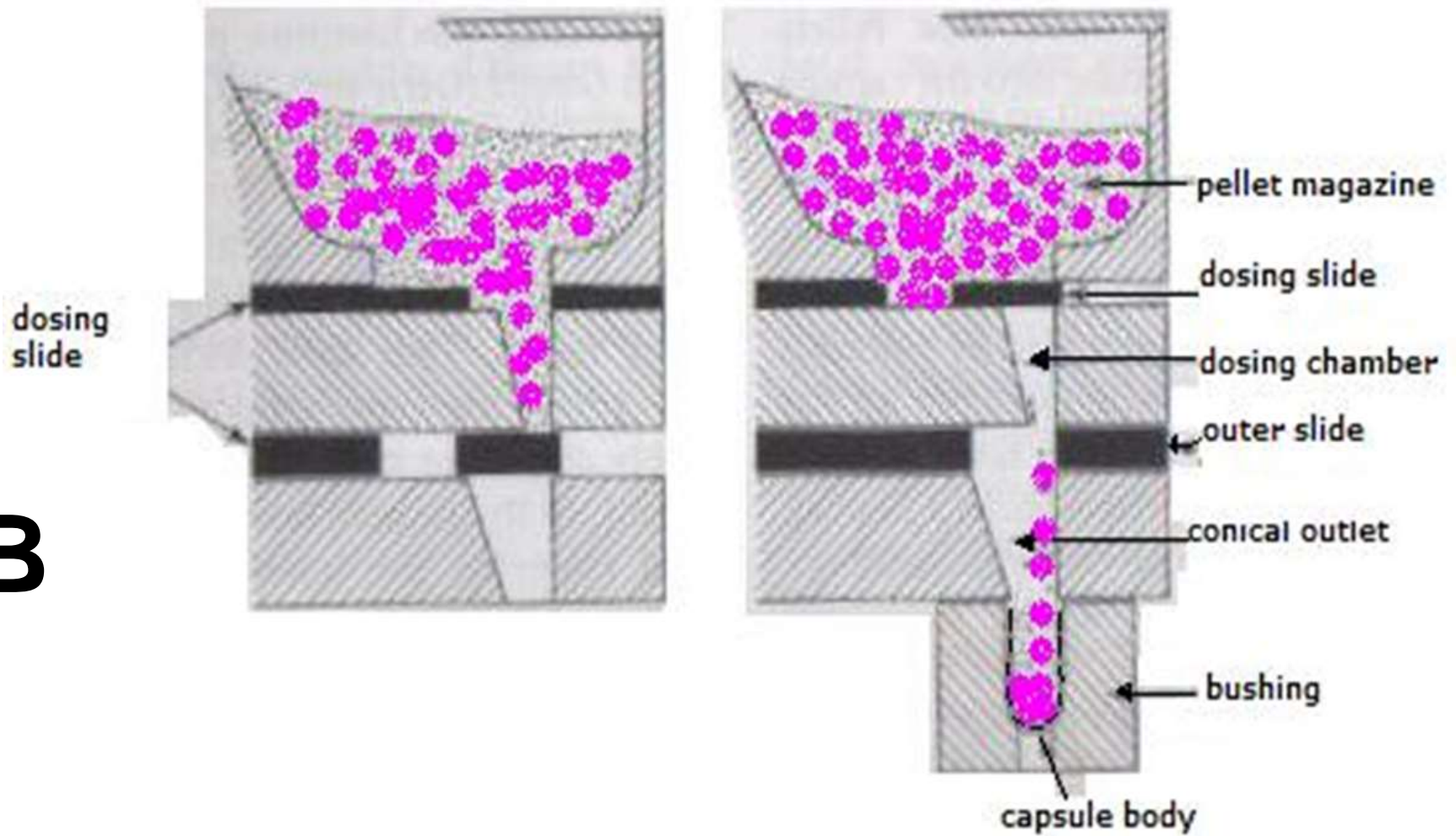
B- Independent method: the powder is measured independently of the body in a special measuring device, no depend on the complete filling. Like fig. B and C

In liquid filling, there is volumetric dosing system which depend on the viscosity.

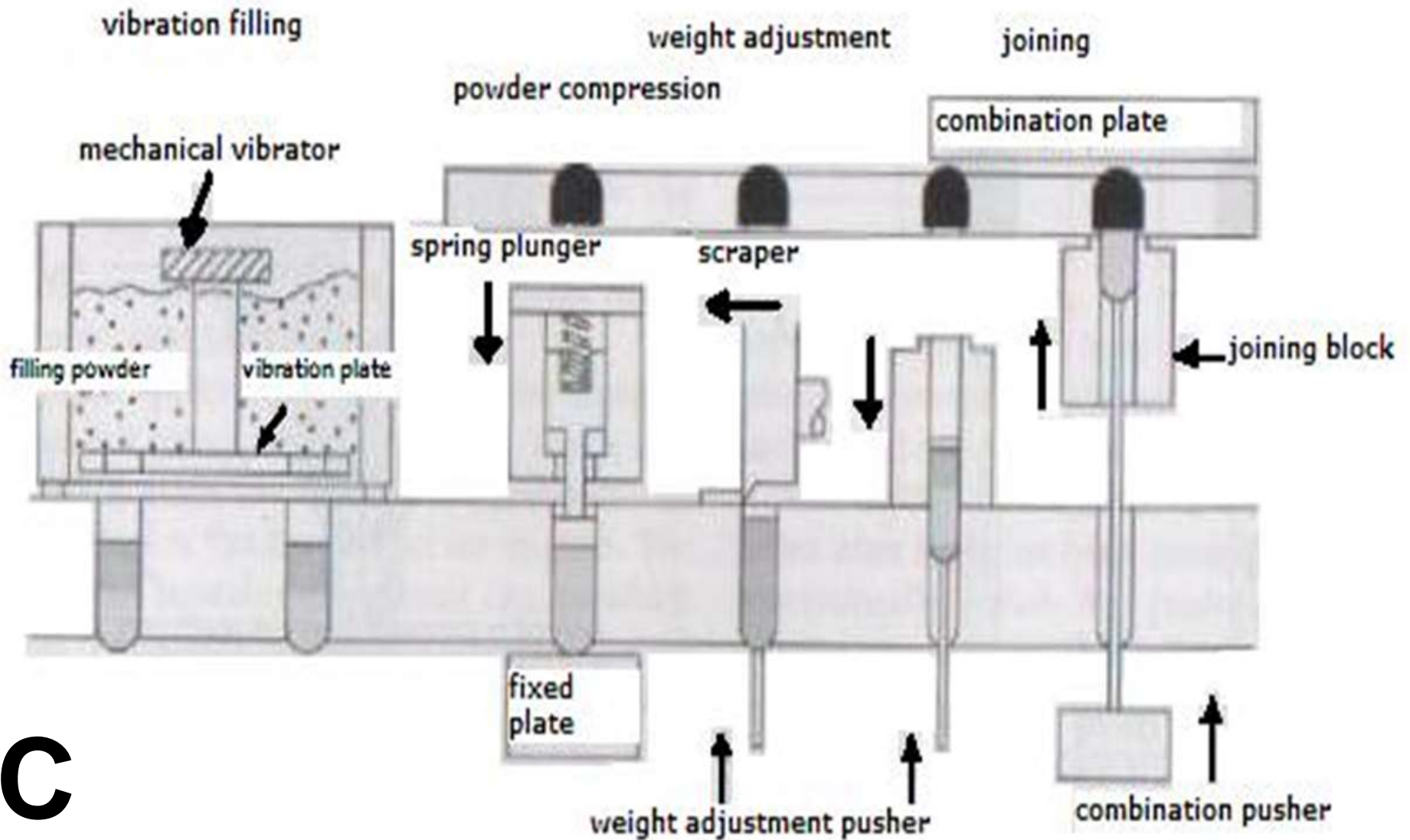
A



B



Double Slide Method

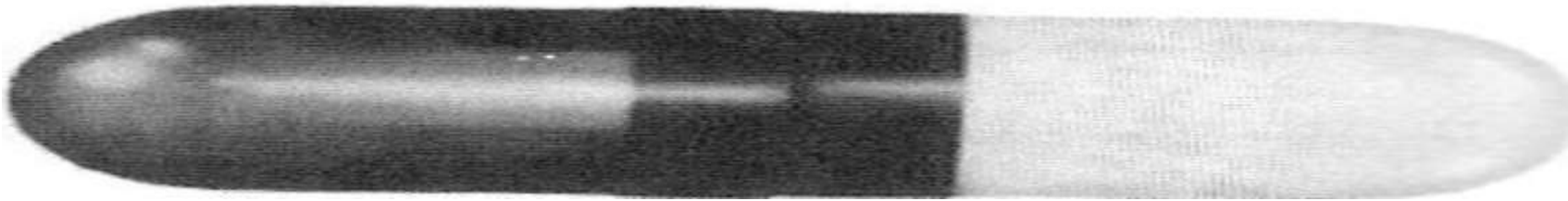
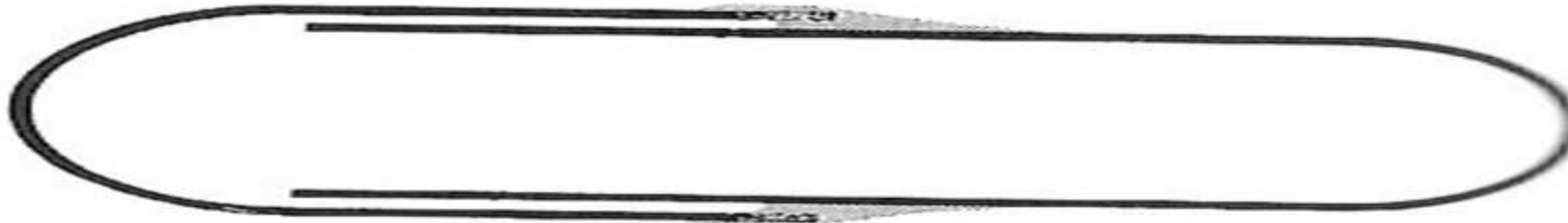


C

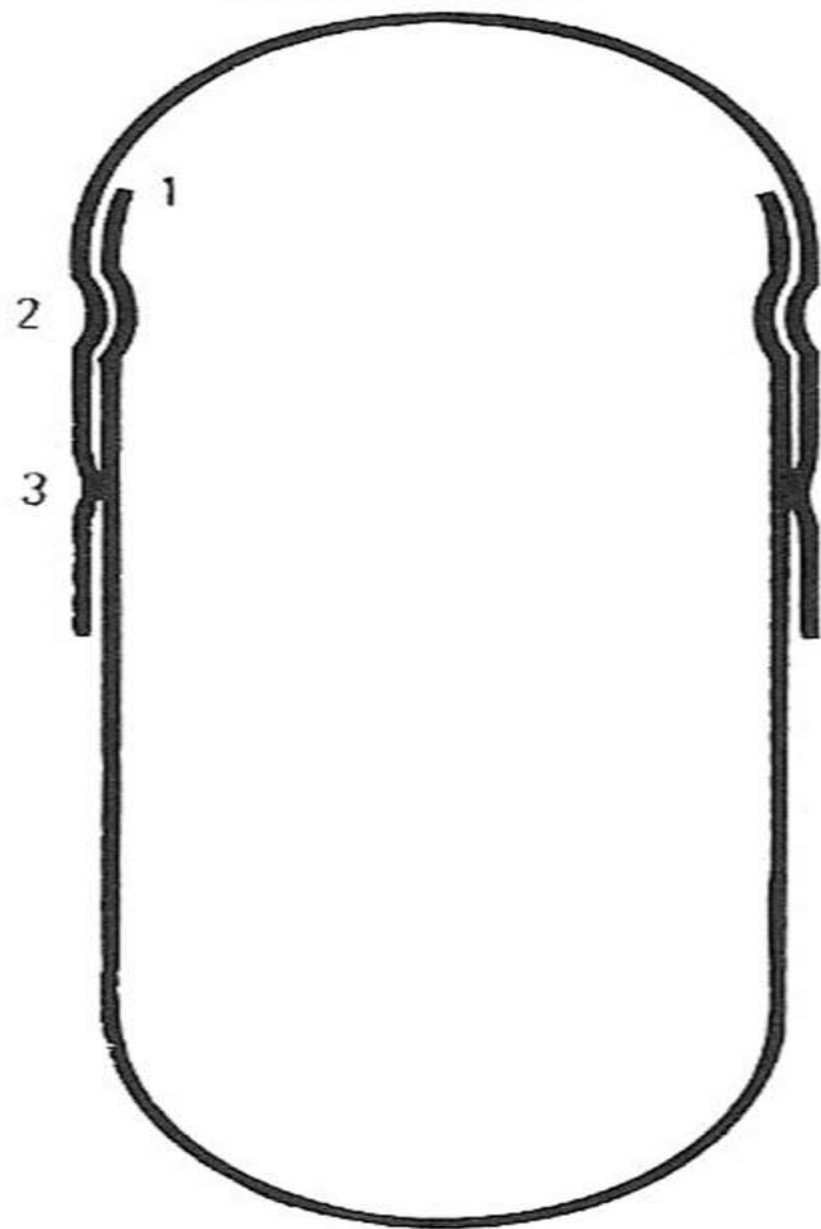
Vibration-assisted Filling

Sealing

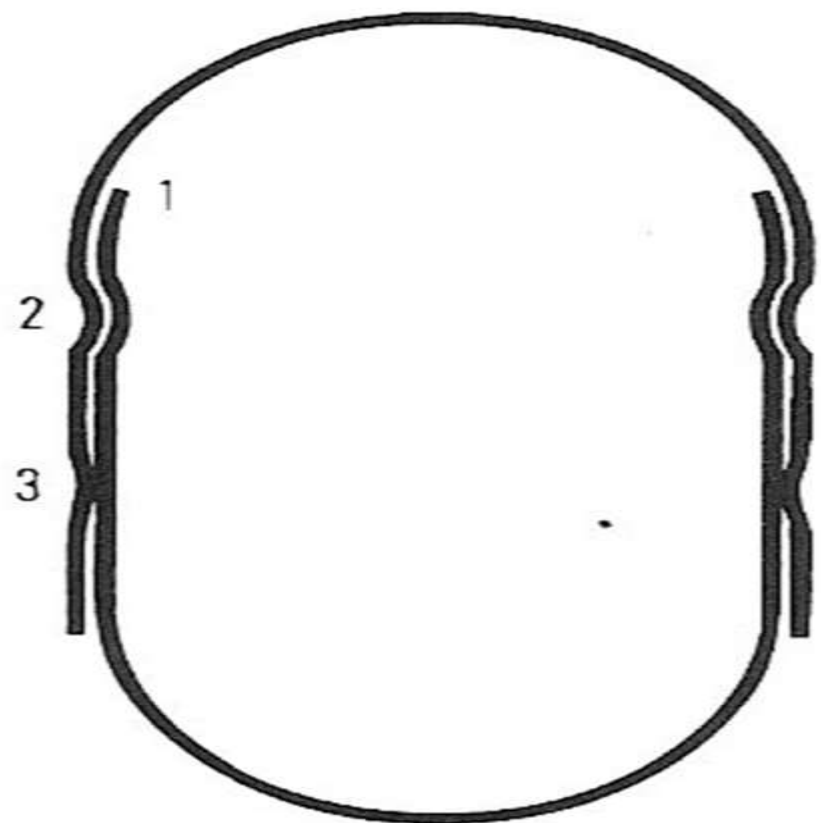
- Used to prevent the splitting of capsules.
- May be preformed into different ways like:
 - 1) Heat welding, give tamper-evident capsules.
 - 2) Use of wetting agent (may be solvent) to decrease M.P. in the contact area between cap and body and then thermally binds the two parts using temperature 40-45°C.
 - 3) Gel-bonding method (colored or non colored) or (Banding)
 - 4) Shell modification



CONI-SNAP™

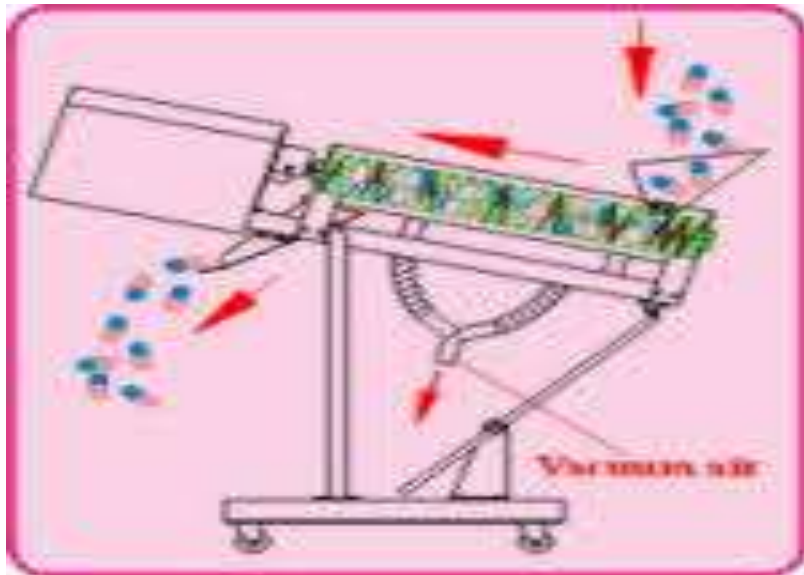


CONI-SNAP SUPRO™



Cleaning and polishing

- Removing of the adhered powder (outside capsules).
- May be preformed into :
 - Small scale (rubbing capsules individually with a clean gauze or cloth).
 - Large scale using (pan polishing or brushing)



Imprinting

- Imprinting of drug or company information



Questions??

- **What are the effects of storage conditions on capsule shells?**
- **What are the advantages of use of HPMC (Hypermellose) capsules over gelatin capsules?**
- **How can you make encapsulation for incompatible components?**