



2022/2023

Fifth Stage

First Semester/ Industrial Pharmacy II



Capsules DF

Lecture 18

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Dr. Ahmed Najim Abood
Assistant Professor in
Pharmaceutics

ahmed.abood@uobasrah.edu.iq



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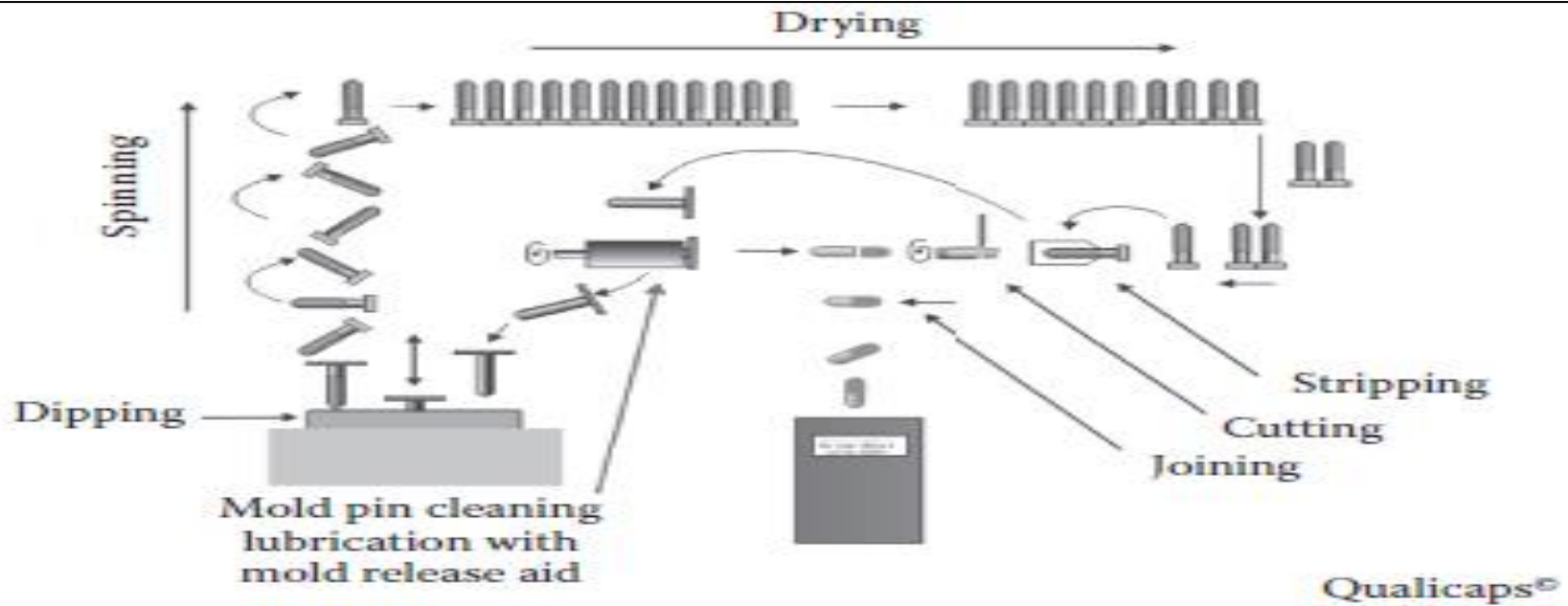
As general specifications for gelatin are :
Bloom strength, viscosity and impurities ratio.

Bloom strength measures the cohesive strength of the cross-linking that occur between gelatin molecules and is proportional to the molecular weight of gelatin (as it is increased as the physical stability and the 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).



3.3 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 (mostly powders or granules)

Active ingredients: Not all drugs can be encapsulated by this type due to incompatibility problems like high solubility, efflorescence, deliquescence and stability.





Formulation materials considerations

- Flowability, particle size, particle shape and density properties
- Compactability
- Compatibility with capsule shell
- API Dose in range (amount in micrograms to 600 mg)
- Solubility and wettability



Excipients

- **Diluents or fillers:** fill the size and improve the flow ability (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
- **Anti-dusting ??**



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.



Manufacturing 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

Types of fills

- 1) Powders
- 2) Granules
- 3) Pellets
- 4) Minitablets (round in shape with a typical diameter of 2.0–3.0 mm)
- 5) Tablets
- 6) Liquids, paste and semisolids



Filling methods

1) Manual filling = *a- Punch method*

PUNCH METHOD*

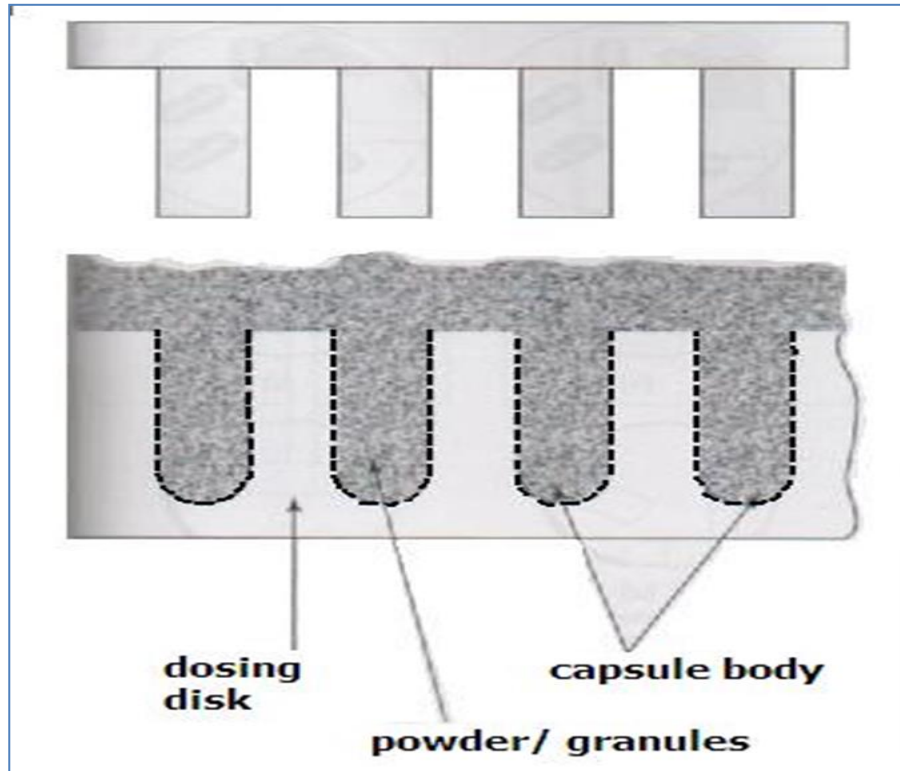


**used when filling a small number of capsules*

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b- Hand operated filling machines



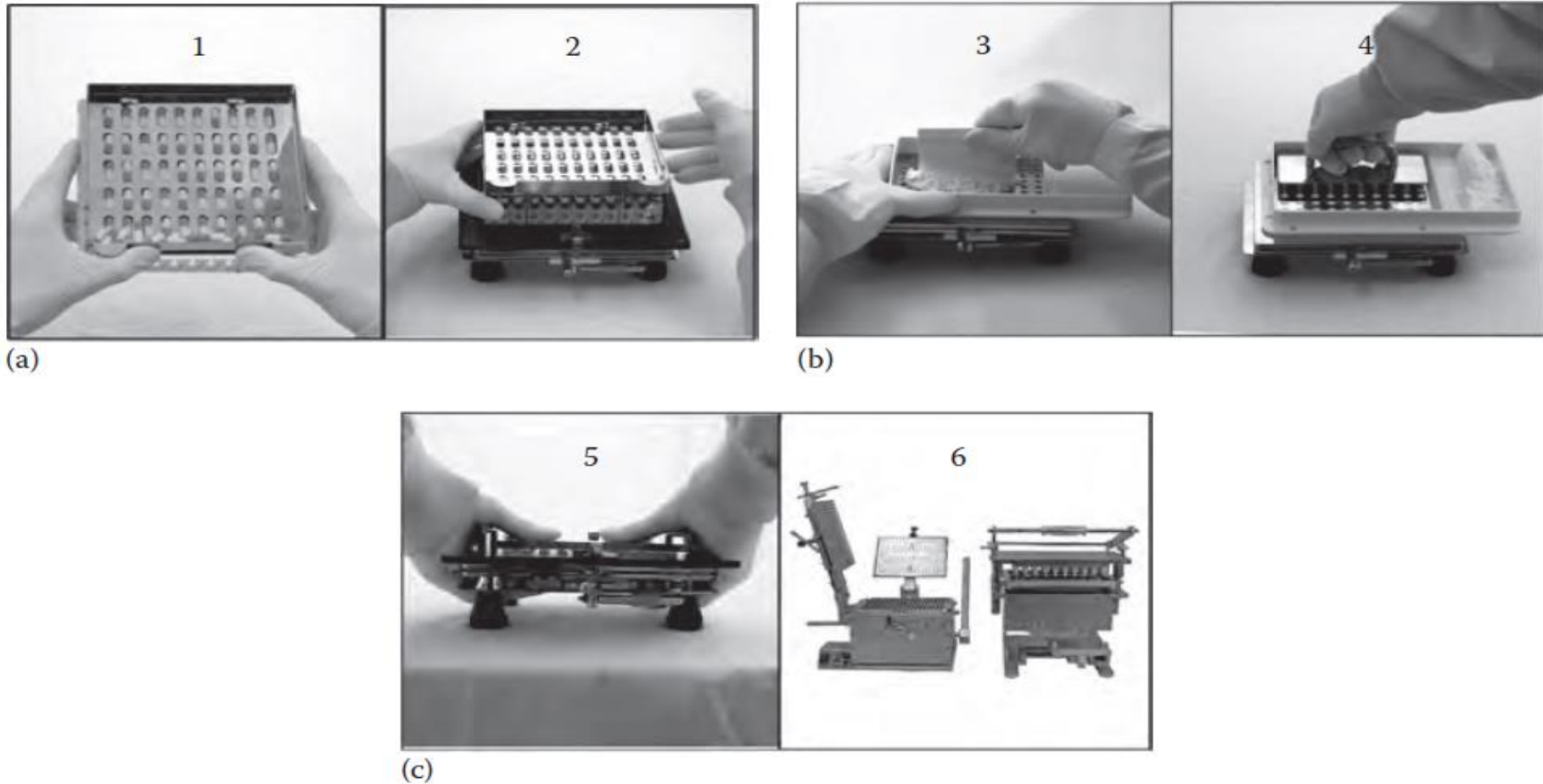


FIGURE 6.14 (a through c) Hand fillers. (Courtesy of Torpac, Fairfield, New Jersey.)

2) *Semi-automatic filling machines*

These machines require an operator to manually transport the capsules through the various machine operations



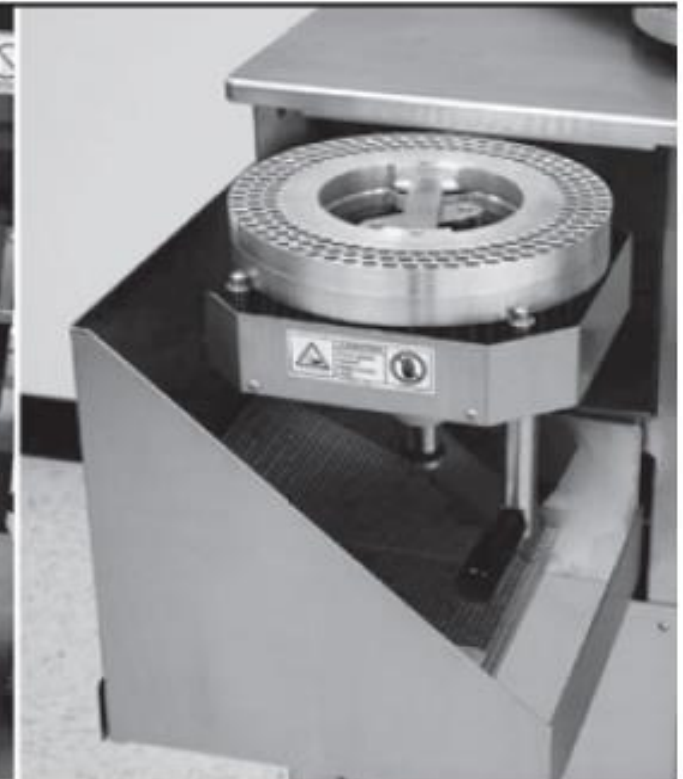
(Courtesy of Capsugel, Greenwood, South Carolina.)



Empty
capsule
feed and
separation



Capsule
dosing



Capsule
closing and
ejection

(Courtesy of Schaefer Technologies Inc., Indianapolis,

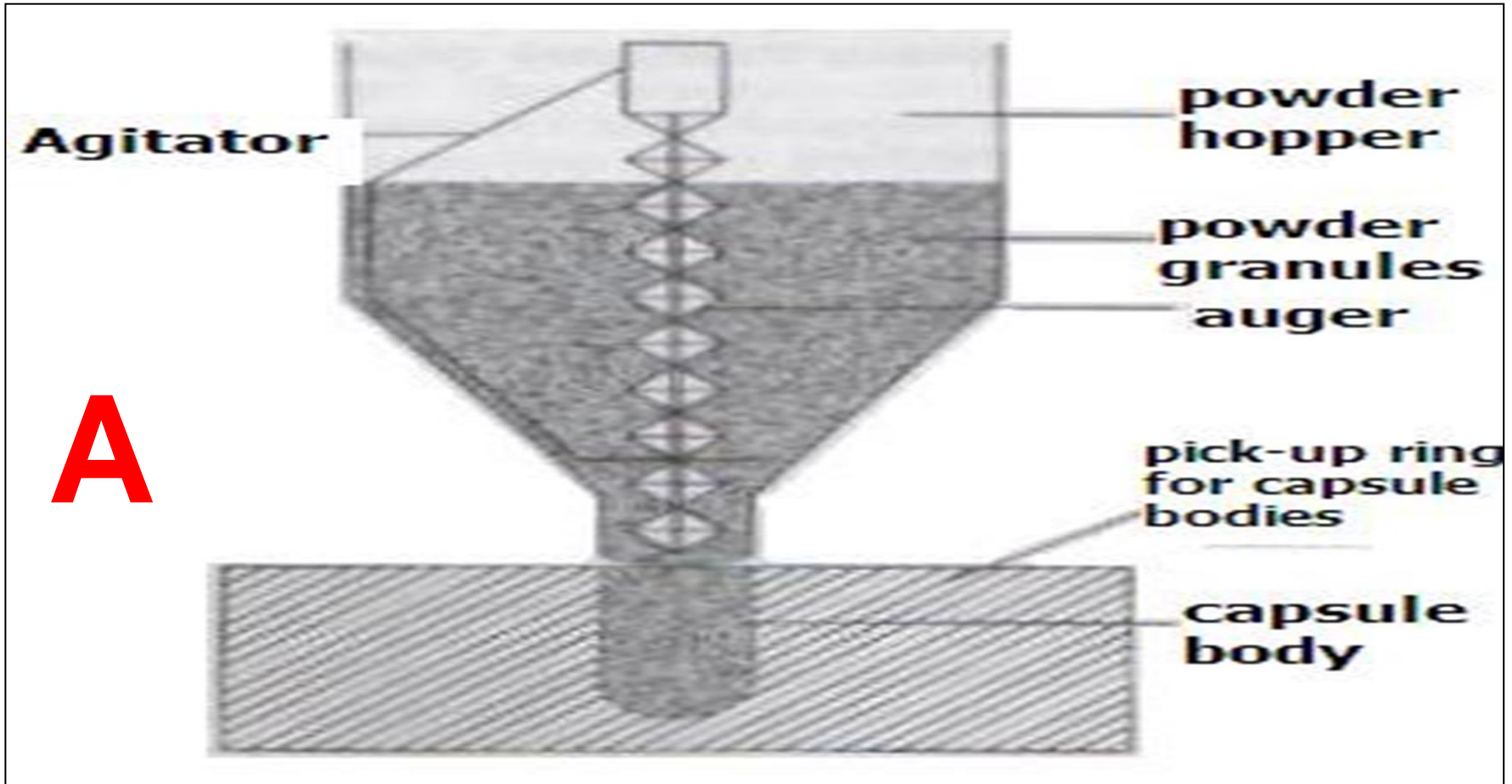


3) Fully automatic filling machines(dosing systems), (dosators)

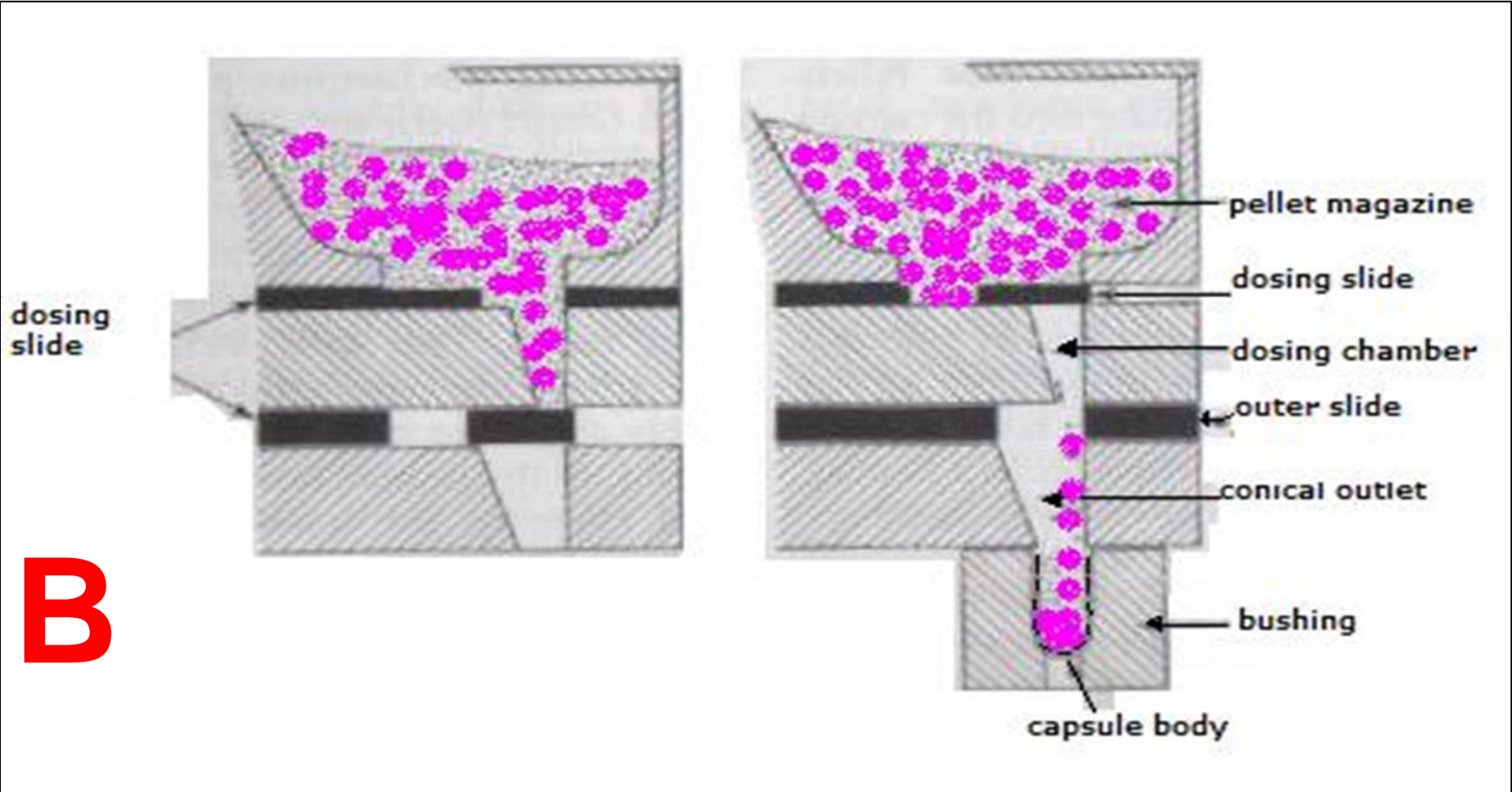
A- Dependent method: use the capsule body directly to measure the powder. Fill uniformity can only be achieved if the capsule is filled completely. (Like fig.A)

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)

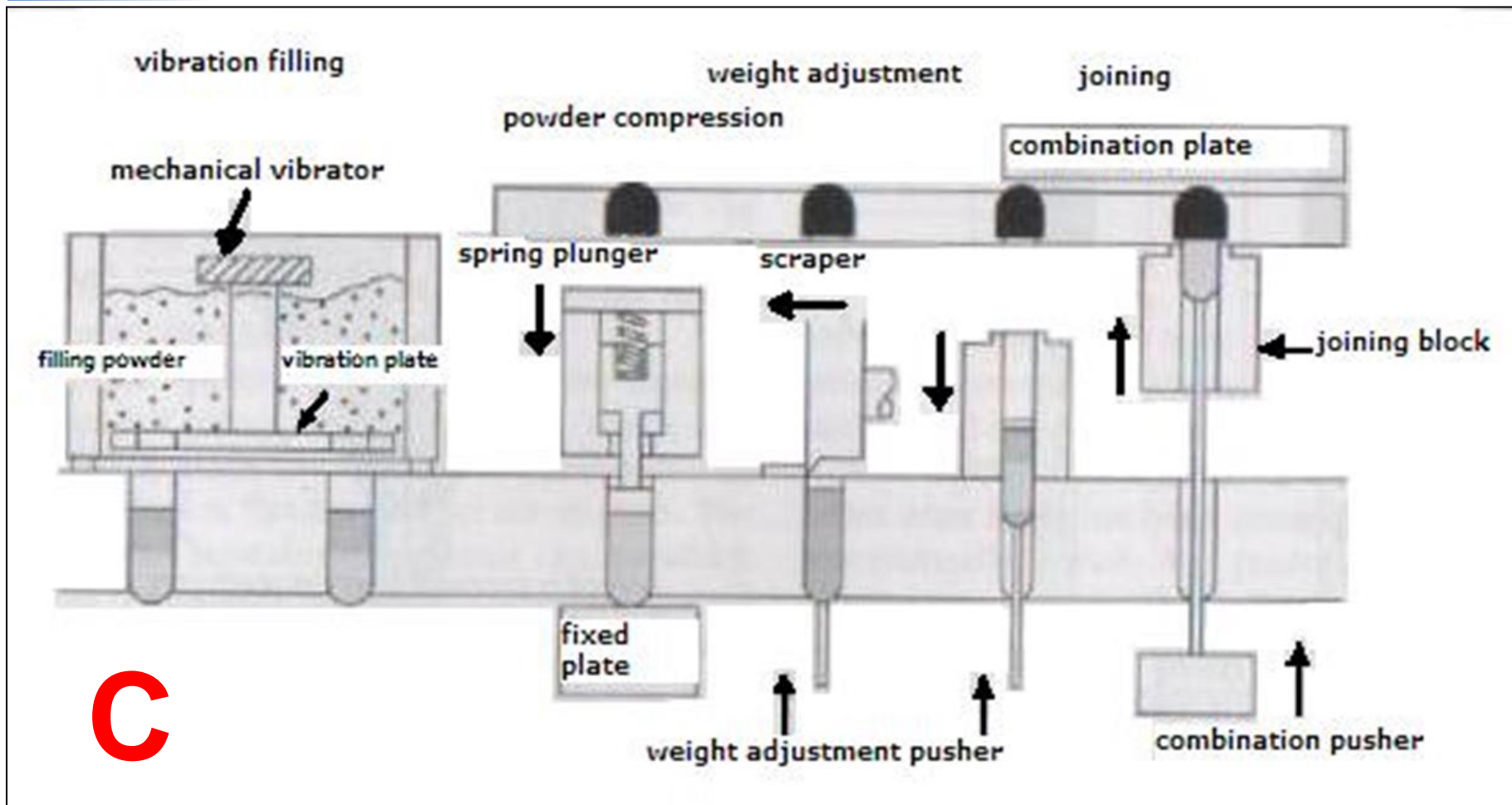
In liquid filling, there is volumetric dosing system which depend on the viscosity. (fig. D)



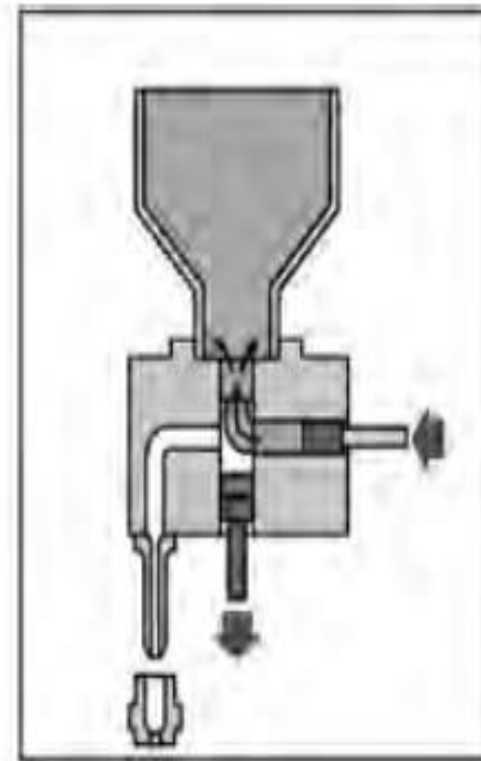
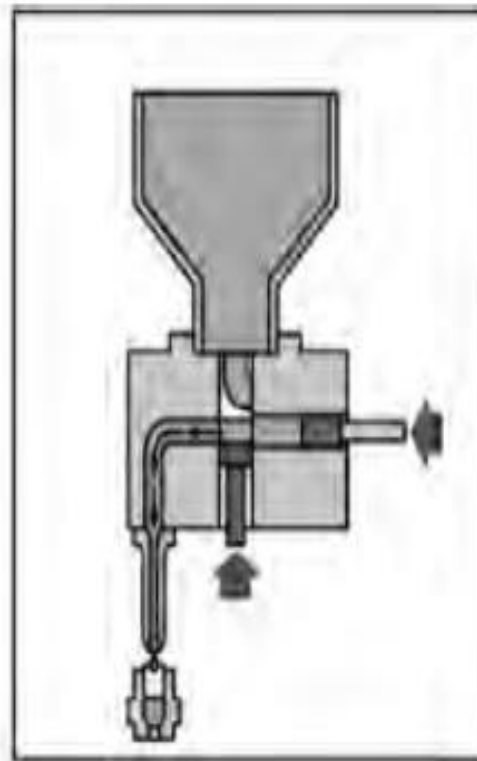
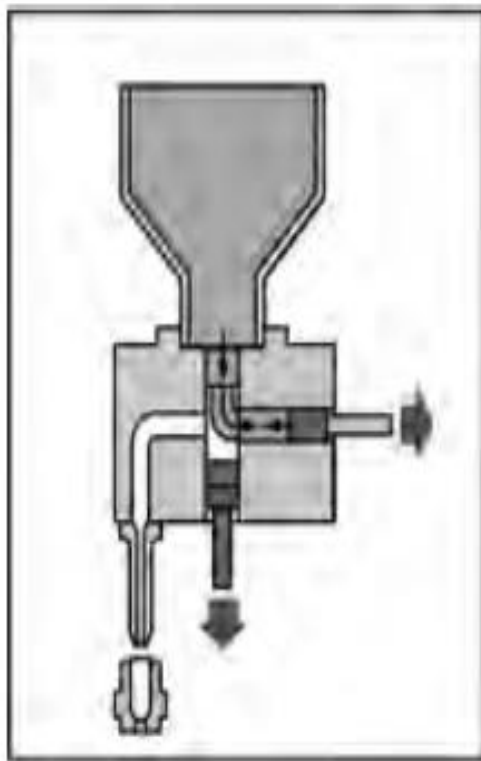
Auger dependent filling



Double Slide Filling Method

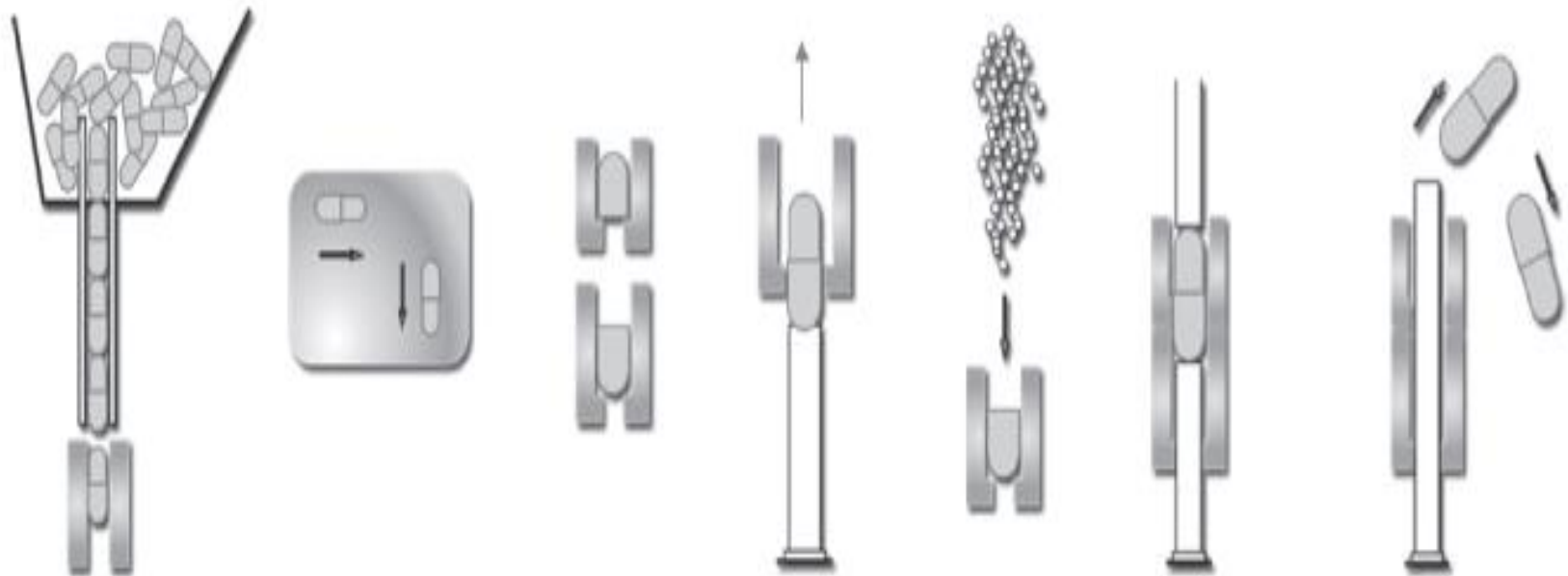


Vibration-assisted Filling



D

6.12 Liquid dosing system. (From IMA ACTIVE Division. ZANASI LAB. 2011. Brochure.)



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.



Powder/pellet
filling



Liquid
filling

STI Model 10. (Courtesy of Schaefer Technologies Inc., Indianapolis, Indiana.)

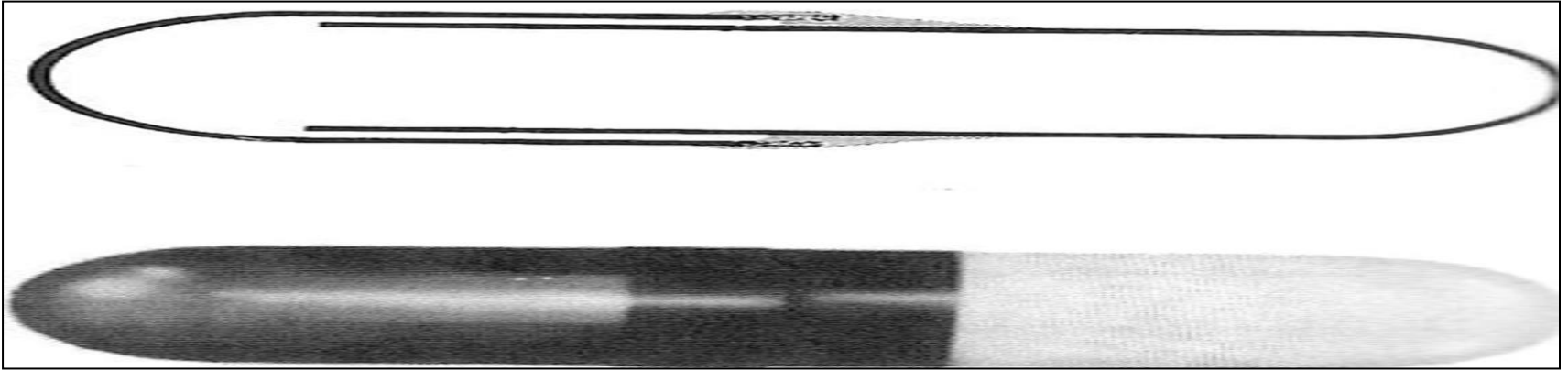


Sealing methods

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® technique)



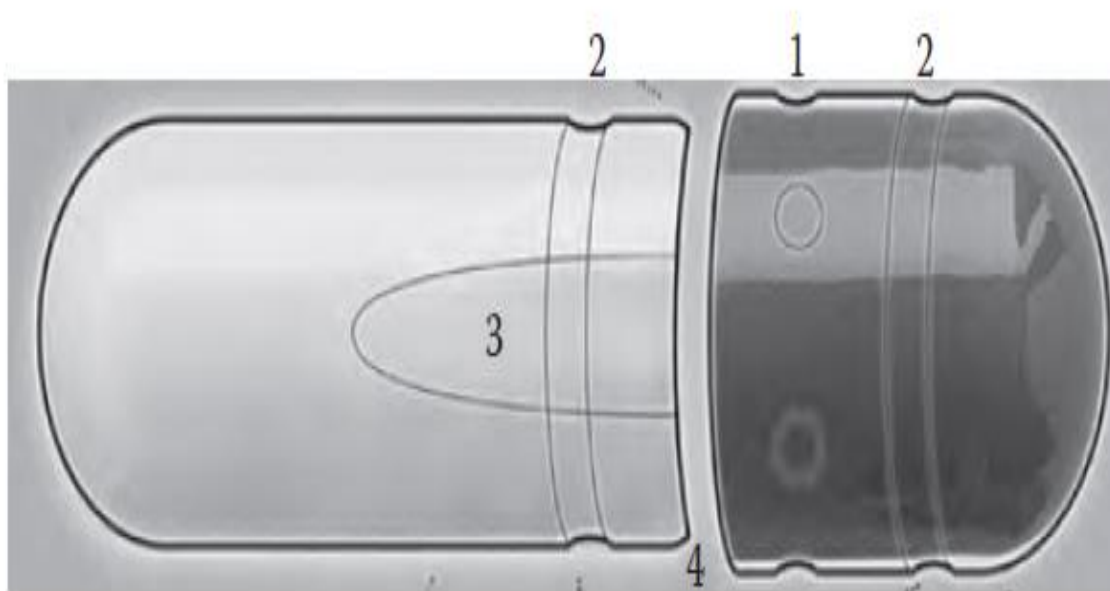


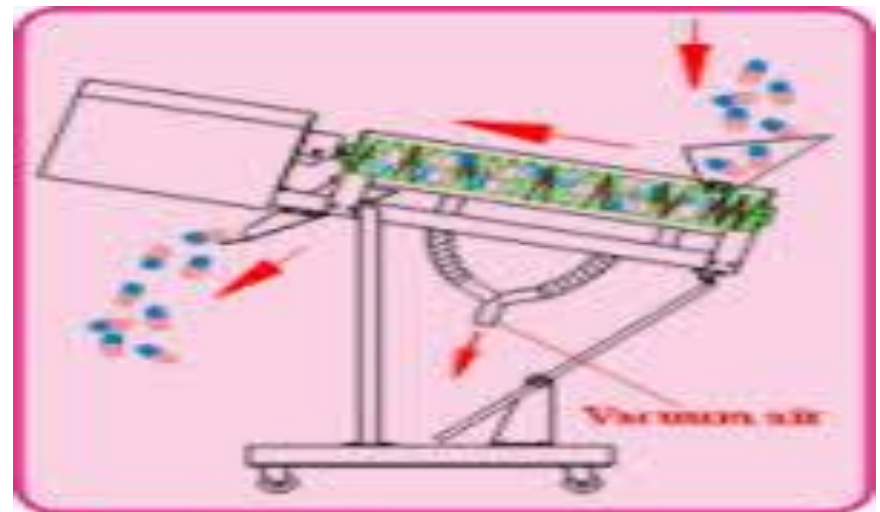
FIGURE 2.4 Capsugel Coni-Snap[®] Capsule: (1) dimples maintain body and cap in pre-joined position; (2) rings lock cap and body together after closing; (3) vents allow air to escape during closing; (4) tapered rim provides additional closing tolerance.

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?
(Optimum conditions =15–25°C and 35–55% RH)
- ❖ What are the advantages of use of HPMC (Hypermellose) capsules (**Vcaps**) over gelatin capsules? (religion, disease transmission, physical properties, MC)
- ❖ How can you make encapsulation for incompatible components?
- ❖ What does **cross-linked dextran** capsule means?

