CAPSULES

Chapter 7

Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems, 9th Edition

Capsules

- **Capsules are solid dosage form in which medicinal agents and/or inert substances are enclosed in a small shell of gelatin. Gelatin capsule shells may be hard or soft, depending on their composition.**

Advantages of capsules

Elegant and Conveniently carried, readily identified, and easily taken.

Easily swallowed .There is no need for spoons or other measuring devices,

Are Tasteless and Odorless when swallowed

Available for many medications in a variety of dosage strengths, providing flexibility to the prescriber and accurate individualized dosage for the patient.

They are packaged and shipped by manufacturers at lower cost and with less breakage

They are also more stable and have a longer shelf life than their liquid counterparts.

Hard gelatin capsules

- **Hard gelatin capsule shells are used in most commercial medicated capsules.**
- **They are also commonly employed in clinical drug trials to compare the effects of an investigational drug with those of another drug product or placebo.**
- **The community pharmacist also uses hard gelatin capsules in the extemporaneous compounding of prescriptions.**

Hard Gelatin

- **The empty capsule shells are made of gelatin, sugar, and water. As such, they can be clear, colorless, and essentially tasteless.**
- **They may be colored with various dyes and made opaque by adding agents such as titanium dioxide.**
- **Most commercially available medicated capsules contain combinations of colorants and opaquants to make them distinctive, many with caps and bodies of different colors**

Gelatin

- Gelatin is obtained by the partial hydrolysis of collagen obtained from the skin, white connective tissue, and bones of animals.
- It is available in the form of a fine powder, a coarse powder, shreds, flakes, or sheets.
- Gelatin is stable in air when dry but is subject to microbial decomposition when it becomes moist. Normally, hard gelatin capsules contain 13% to 16% of moisture.
- However, if stored in an environment of high humidity, additional moisture is absorbed by the capsules, and they may become distorted and lose their rigid shape. In an environment of extreme dryness, some of the moisture normally present in the gelatin capsules is lost, and the capsules may become brittle and crumble when handled.
- Therefore, it is desirable to maintain hard gelatin capsules in an environment free from excessive humidity or dryness.

Effect of moisture on gelatin

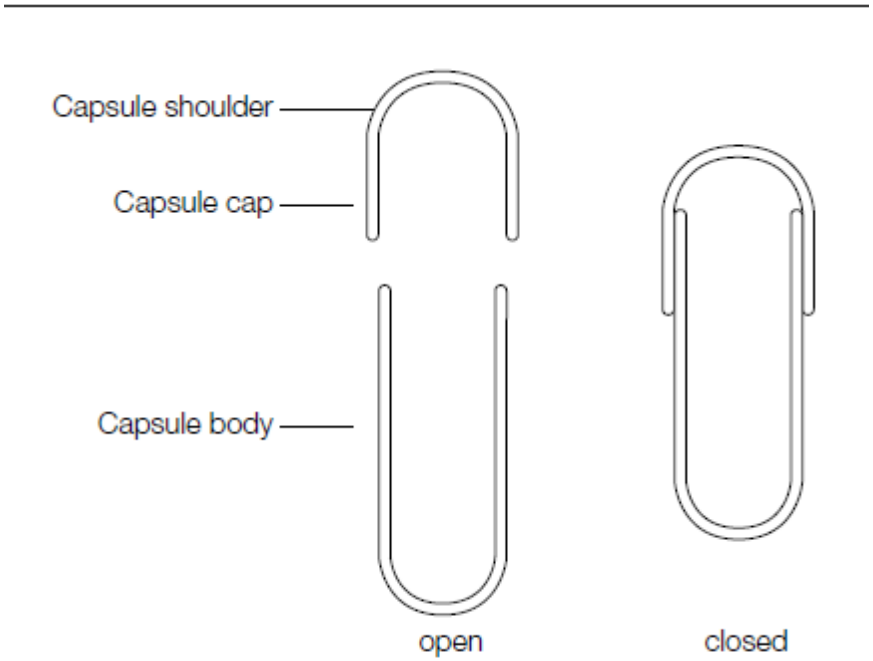
- **Because moisture may be absorbed by gelatin capsules and may affect hygroscopic agents within, many capsules are packaged along with a small packet of a desiccant material to protect against the absorption of atmospheric moisture.**
- **The desiccant materials most often used are dried silica gel, clay, and activated charcoal.**
- **Prolonged exposure to high humidity can affect *in- vitro* capsule dissolution. Such changes have been observed in capsules containing tetracycline, chloramphenicol, and nitrofurantoin. Because such changes could forewarn of possible changes in bioavailability, capsules subjected to such stress conditions must be evaluated case by case.**

Gelatin administration

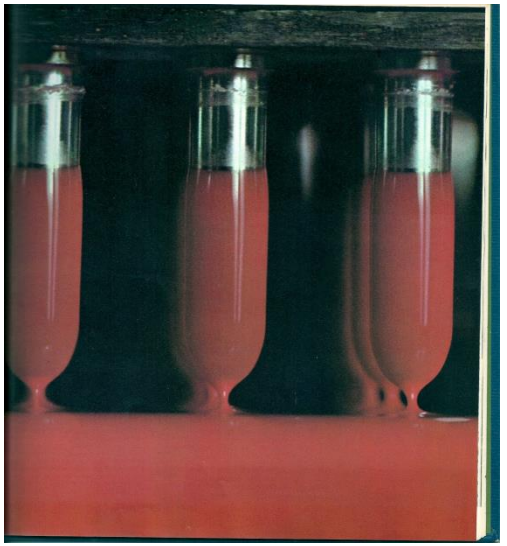
- **Although gelatin is insoluble, it does soften in cold water through the absorption of water up to 10 times its weight of water.**
- **Some patients prefer to swallow a capsule wetted with water or saliva because a wetted capsule slides down the throat more readily than a dry capsule.**
- **Gelatin is soluble in hot water and in warm gastric fluid; a gelatin capsule rapidly dissolves and exposes its contents.**
- **Gelatin, being a protein, is digested by proteolytic enzymes and absorbed.**

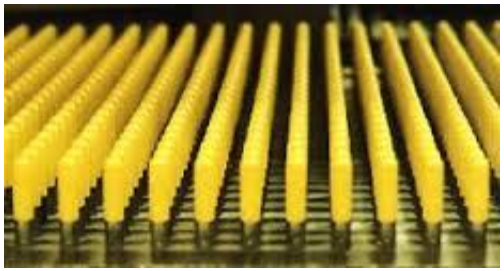
The manufacture of hard gelatin capsule shells

- **Hard gelatin capsule shells are manufactured in two sections, the capsule body and a shorter cap.**
- **The two parts overlap when joined, with the cap fitting snugly over the open end of the capsule body.**



- The shells are produced industrially by the mechanical dipping of pins or pegs of the desired shape and diameter into a temperature-controlled reservoir of melted gelatin mixture.
- The pegs, made of manganese bronze, are affixed to plates, each capable of holding up to about 500 pegs. Each plate is mechanically lowered to the gelatin bath, the pegs submerged to the desired depth and maintained for the desired period to achieve the proper length and thickness of coating.
- Then the plate and the pegs are slowly lifted from the bath and the gelatin is dried by a gentle flow of temperature- and humidity-controlled air.
- When dried, each capsule part is trimmed mechanically to the proper length and removed from the pegs, and the capsule bodies and caps are joined together.





Hard gelatin capsules

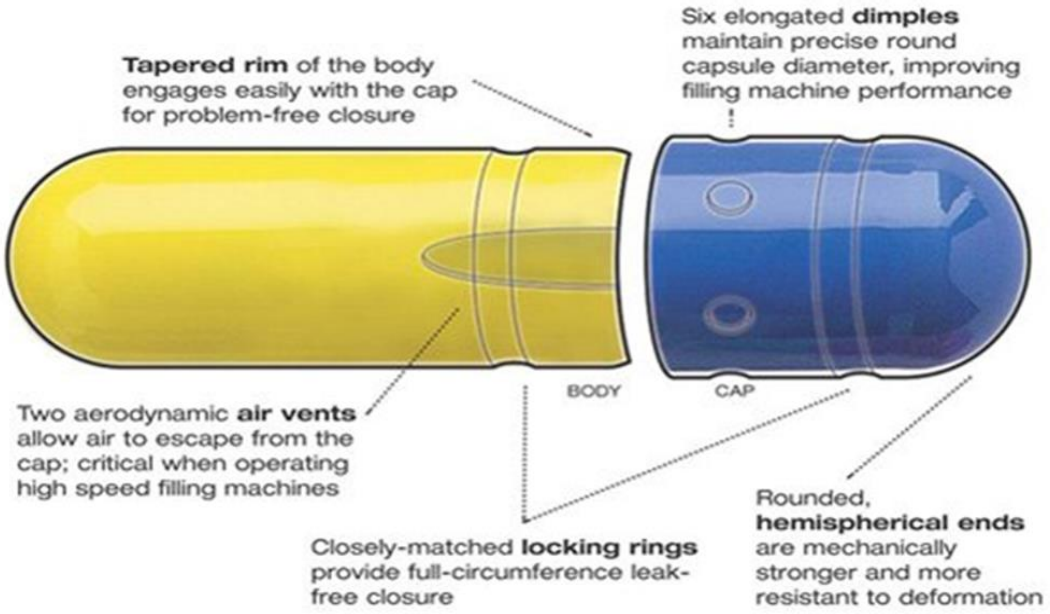
- It is important that the thickness of the gelatin walls be strictly controlled so that the capsule's body and cap fit snugly to prevent disengagement.
- The pegs on which the caps are formed are slightly larger in diameter than the pegs on which the bodies are formed, allowing the telescoping of the caps over the bodies.
- In capsule shell production, there is a continuous dipping, drying, removing, and joining of capsules as the peg-containing plates rotate in and out of the gelatin bath.

Capsule shapes

- A manufacturer also may prepare distinctive-looking capsules by altering the usual rounded shape of the capsule-making pegs.
  - By tapering the end of the body-producing peg while leaving the cap-making peg rounded, one manufacturer prepares capsules differentiated from those of other manufacturers (Pulvules, Eli Lilly).
  - Another manufacturer uses capsules with the ends of both the bodies and caps highly tapered (Spansule Capsules, SmithKline Beecham).

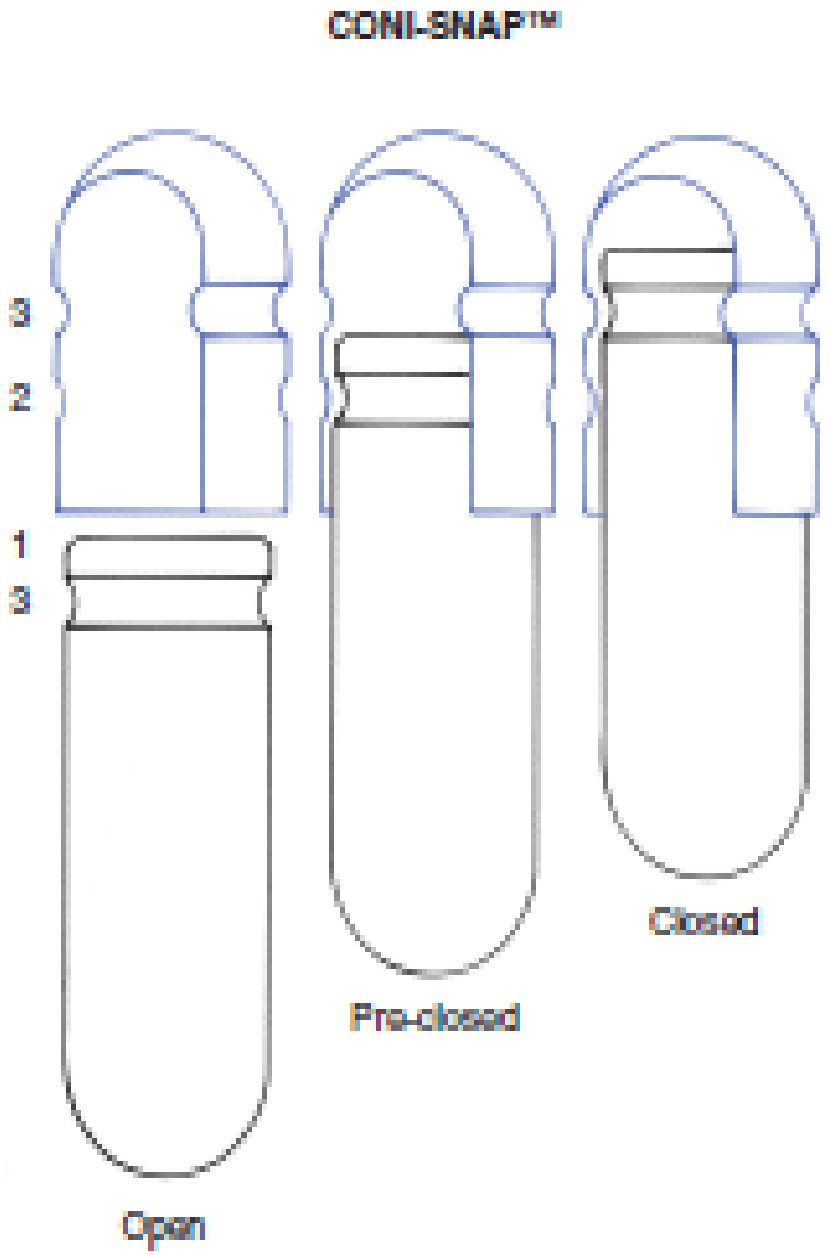
- Another innovation in capsule shell design is the Snap-fit, Coni-snap and Coni-snap Supro hard gelatin capsules

- Snap-fit . The original Snap-fit construction enables the two halves of the capsule shells to be positively joined through locking grooves in the shell walls. The two grooves fit into each other and thus ensure reliable closing of the filled capsule.



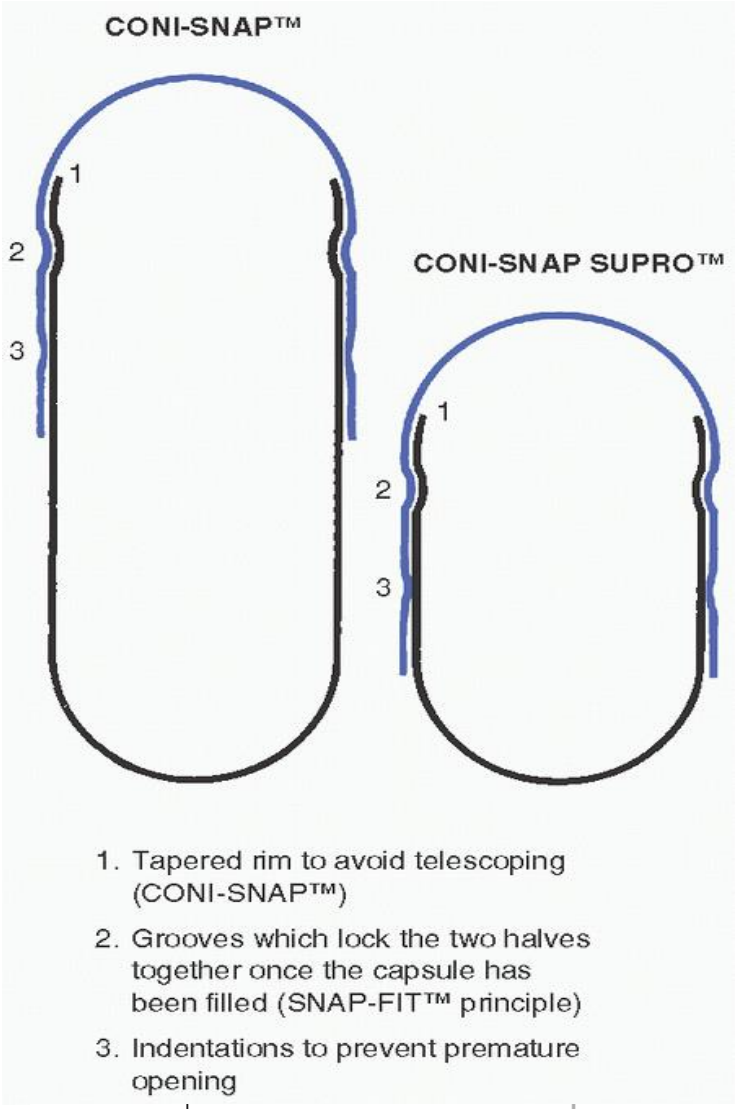
- **Snap-fit**
- **During the closing process, the capsule body is inserted into the cap.**
- **With the high-capacity filling rates of the modern capsule filling machines (more than 180,000 capsules per hour), splitting (telescoping) and/or denting of the capsule shell occur with the slightest contact between the two rims when they are joined.**
- **This problem [splitting (telescoping) and/or denting of the capsule shell] which exists primarily with straight-walled capsule shells, led to the development of the Coni-snap capsule, in which the rim of the capsule body is not straight but tapered slightly.**
- **This reduces the risk of the capsule rims touching on joining and essentially eliminates the problem of splitting during large-scale filling operations.**

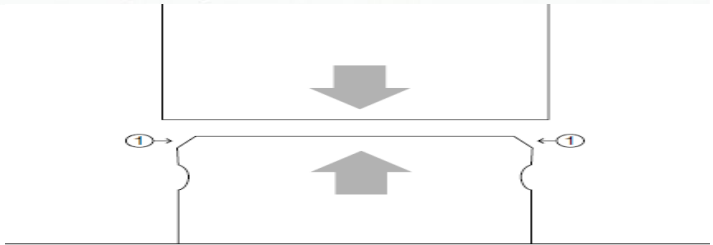
FIGURE 7.4 Line drawings of the CONI-SNAP capsule in open, preclosed, and closed positions. The tapered rims (1) avoid telescoping; the indentations (2) prevent premature opening; and the grooves (3) lock the two capsule parts together after the capsule is filled. (Courtesy of Capsugel Division, Warner-Lambert.)



Coni-snap, and Coni-snap Supro hard gelatin capsules

- **Line drawings of the Coni-snap and Coni-snap supro (right) capsules. The latter is designed to be smaller and to have the lower portion of the capsule shell concealed except for the rounded end. This makes separation of the two parts more difficult and contributes to capsule integrity.**





- **In the Coni-snap Supro capsules, the upper capsule part extends so far over the lower part that only the rounded edge of the latter is visible.**
- **Opening of such a filled capsule is difficult because the lower surface offers less gripping surface to pull the two halves apart. This increases the security of the contents and the integrity of the capsule.**
- **After filling, some manufacturers render their capsules tamper evident through various sealing techniques.**

Capsule sizes

- **Empty gelatin capsules are manufactured in various lengths, diameters, and capacities.**
- **The size selected for use is determined by the amount of fill material to be encapsulated. The density and compressibility of the fill will largely determine to what extent it may be packed into a capsule shell**
- **For estimation, a comparison may be made with powders of well known features and an initial judgment made as to the approximate capsule size needed to hold a specific amount of material.**
- **However, the final determination may be largely the result of trial and error.**

Capsule sizes

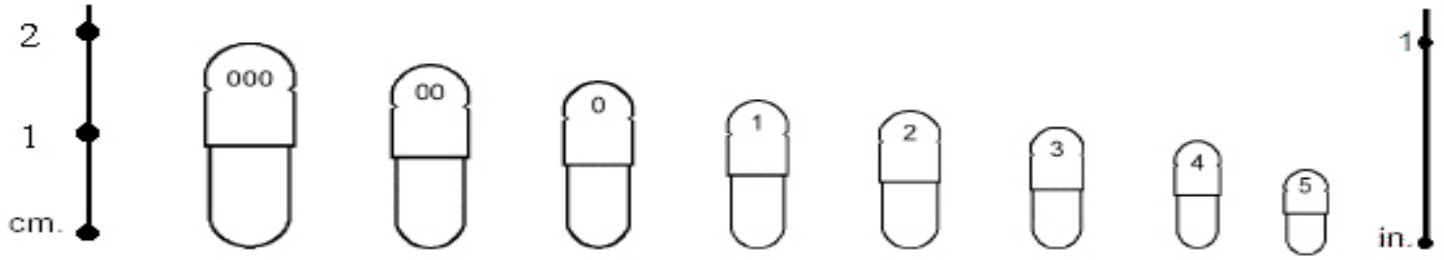
- For human use, empty capsules ranging in size from 000 (the largest) to 5 (the smallest) are commercially available
- Larger capsules are available for veterinary use.
- For prescriptions requiring extemporaneous compounding, hard gelatin capsules permit a wide number of options for the physician.
- The pharmacist may compound capsules of a single medicinal agent or combination of agents at the precise dosage prescribed for the individual patient

Size of capsule	000	00	0	1	2	3	4	5
Capacity	1g	0.65g	0.5g	0.32g	0.25g	0.2g	0.15g	0.1g

Approximate Capacity of Empty Gelatin Capsules

	Capsule size							
Volume (mL)	000 1.40	00 0.95	0 0.68	1 0.50	2 0.37	3 0.30	4 0.21	5 0.13
Drug substance (mg)[a]								
Quinine sulfate	650	390	325	227	195	130	97	65
Sodium bicarbonate	1430	975	715	510	390	325	260	130
Aspirin	1040	650	520	325	260	195	162	97

[a] Amount may vary with the degree of pressure used in filling the capsules



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