Capsules

University of Pécs

Institute of Pharmaceutical Technology and Biopharmacy

Capsules

Definition

Capsules are solid preparations with hard or soft shells of various shapes and capacities, usually containing a single dose of active substance. They are intended for oral administration.

Capsules

Advanteges

1) Unpleasant drug tastes and odors can be masked by the tasteless gelatin shell,
2) Easy to swallow – form, good wettability, softnesses,
3) They are attractive in appearance
4) As compared to tablets less excipients are required,
5) The shells are physiologically inert and easily and quickly digested in the gastrointestinal tract,
6) Encapsulation of pharmacies can be performed manually or semi-automated devices,
7) Avoiding compression disorders,
8) They are easy to handle and carry,
9) The shells can be opacified (with titanium dioxide) or colored, to give protection from light,
10) Capsules are available in many sizes to provide dosing flexibility,
11) The administration of liquid and solid drugs enclosed in hard gelatin capsules is one of the most frequently utilized dosage forms.

Capsules

Disadvanateges

1) Expensive technology,
2) Volume is limited,
3) During storage hard gelatine capsules require a 45-65% moisture content,
4) The drugs which are hygroscopic absorb water from the capsule shell making it brittle and hence are not suitable for filling into capsules,
5) Gelatine capsule contains 8-10% moisture, which can result degradation of moisture-sensitive drugs,
6) The concentrated solutions which require previous dilution are unsuitable for capsules because if administered as such lead to irritation of stomach.

Materials of shell

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Materials of shell

The aqueous solution of the capsule shell gelling materials made

1) animal protein (commonly used: gelatine)

2) plant polysaccharides and derivatives eg.
   starch,
   cellulose,
   chitosan (tiny crabs found skeletons of the polysaccharide)
   HPMC (hydroxy-propyl-methylcellulose)

3) poly-vinyl-alcohol (PVA) copolymers

The capsules manufacturing, packaging, storage and distribution in the appropriate manner to ensure the microbial quality.

Materials of shell

The gelatine is particularly suitable for the preparation capsules because of :

1) tasteless
2) non-toxic,
3) easily formable,
4) transparent,
5) flexible, shape-retaining,
6) dissolves in the GI fluids at body temperature, reversible sol-gel transformation capable of swelling in the GI tract in a few minutes, and then disintegrates, allowing release of the drug,
7) controlled liberation with cross-linking of shell material

Materials of shell

Gelatine

For capsule shells generally a mixture derived from pork (beef and fish) skin and bones is used.
Pork skin gelatine contributes plasticity while bone gelatine gives firmness.

One important reason for the exclusive use of gelatine for making hard and soft capsules is its solubility characteristics in stomach fluids. It absorbs cold water readily, though the rate of absorption depends upon moisture content of gelatine.

The capsules manufacturing, packaging, storage and distribution in the appropriate manner to ensure the microbial quality.

Materials of shell

Additives

1) Plasticizers - preserve the moisture content of the capsule wall, and the flexibility of the capsule wall strength (eg glycerin, sorbitol),
2) Cross-linkers (pl.formaldehid) - to influence of dissolution,
3) Surfactants,
4) Opacity enhancers,
5) Coloring materials,
6) Flavor improving agents,
4) Preservatives (eg, methylparaben, propylparaben).

Materials of shell

Gelatine QC

Controles	Unit	E xigences	Results
Jelly Strength	Bloom g	≥240	246
Viscosity	mpa.s	≥4.7	4.72
Moisture	%	≤14	11.4
Ash	%	≤1.0	0.8
Transparency	mm	≥280	296
PH		4.0-7.0	5.8
SO2	mg/kg	≤100	18
Insoluble Material	%	≤0.2	0.1
Heavy Metal (pb)	mg/kg	≤50	14
Arsemic	mg/kg	≤1.0	0.09
Cr	mg/kg	≤1.0	0.08
Total Bacterial	cfu/g	≤1000	139
Colibacillus	cfu/100g	absent	0
Salmonella		absent	0
Mesh	mesh	5	5
Conclusion	Pass		

Materials of shell

Gelatine QC

Bloom number

The load, which is needed for a 1/2 inch diameter rod to deflect the surface of the gel 4 mm without breaking it

Bloom Low-Number:	50 - 00
Bloom mid-Number:	100 - 200
Bloom's high-number:	200-300

Types of capsules

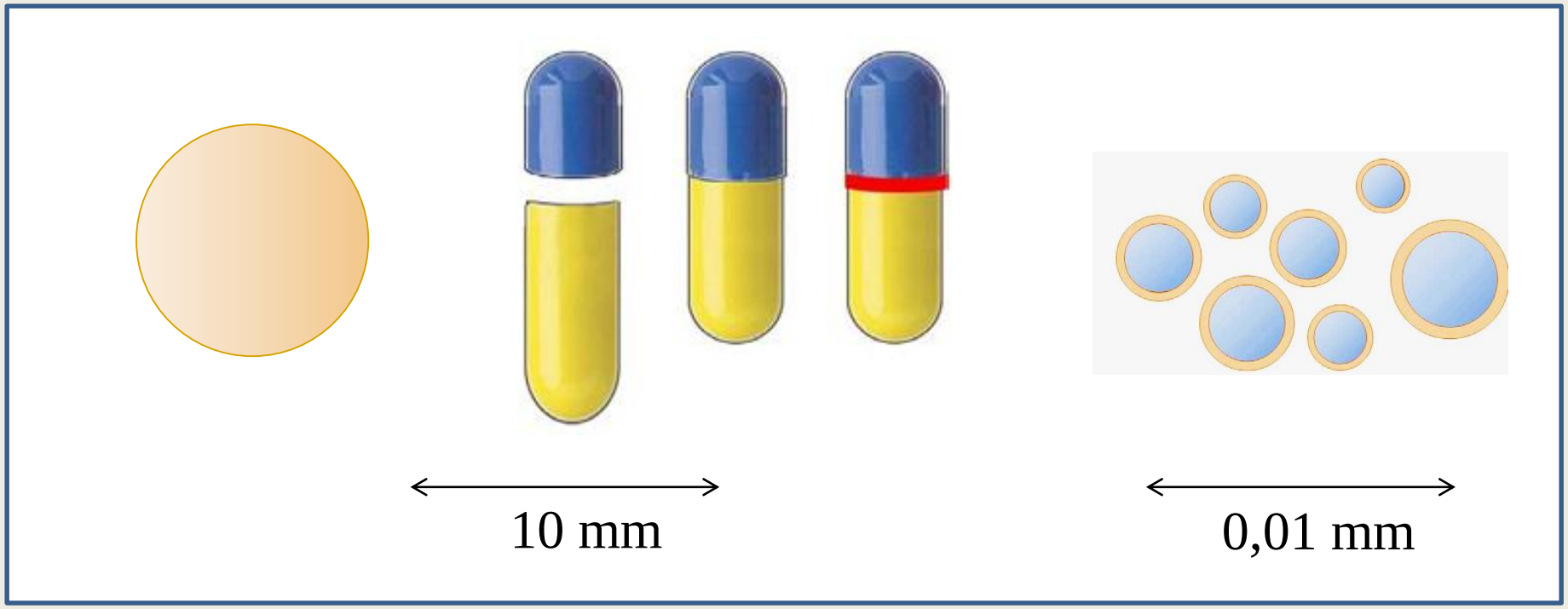
Types of capsules

Several categories of capsules may be distinguished:

1. soft capsules,
2. hard capsules,
3. gastro-resistant capsules,
4. modified-release capsules,
5. cachets,
6. microcapsules,
7. nanocapsules

EUROPEAN PHARMACOPOEIA 5.0

Types of capsules



Soft gelatine capsule

Hard gelatine capsule

Microcapsule

Types of capsules

Soft capsules

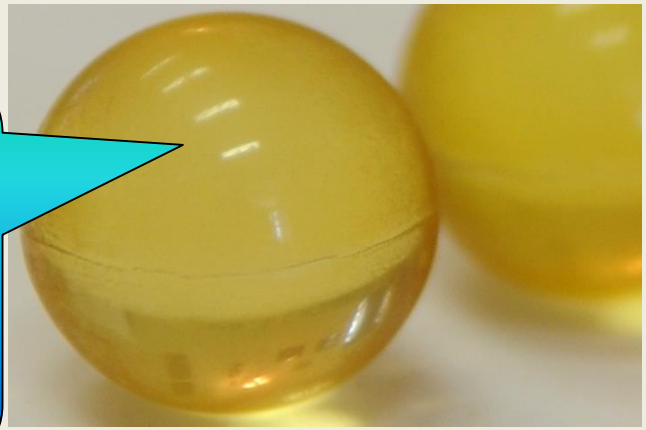
Soft capsules have thicker shells than those of hard capsules.

The shells consist of one part and are of various shapes.
The soft gelatin capsule is also called as “one piece”.

Types of capsules

Soft capsules

liquid (!)



Liquids may be enclosed directly; solids are usually dissolved or dispersed in a suitable vehicle to give a solution or dispersion of a paste-like consistency.

Types of capsules

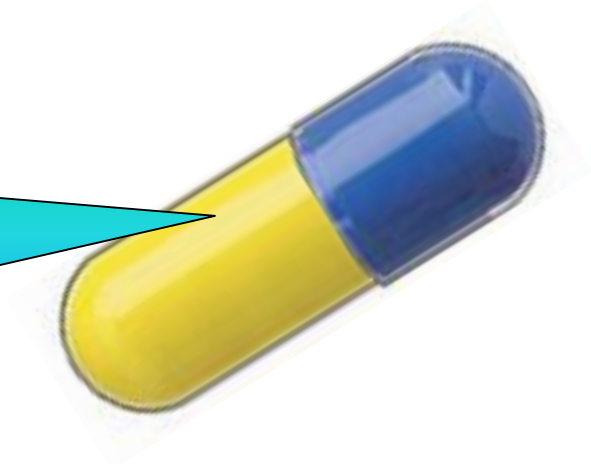
Hard capsules

Hard capsules have shells consisting of two parts, two prefabricated cylindrical sections one end of which is rounded and closed, the other being open.

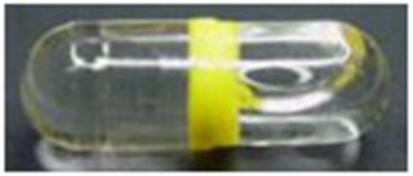
Types of capsules

Hard capsules

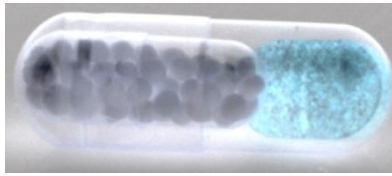
gas
liquid (!)
solid



Hibrid



Liquid



Combined

Powders

Granules

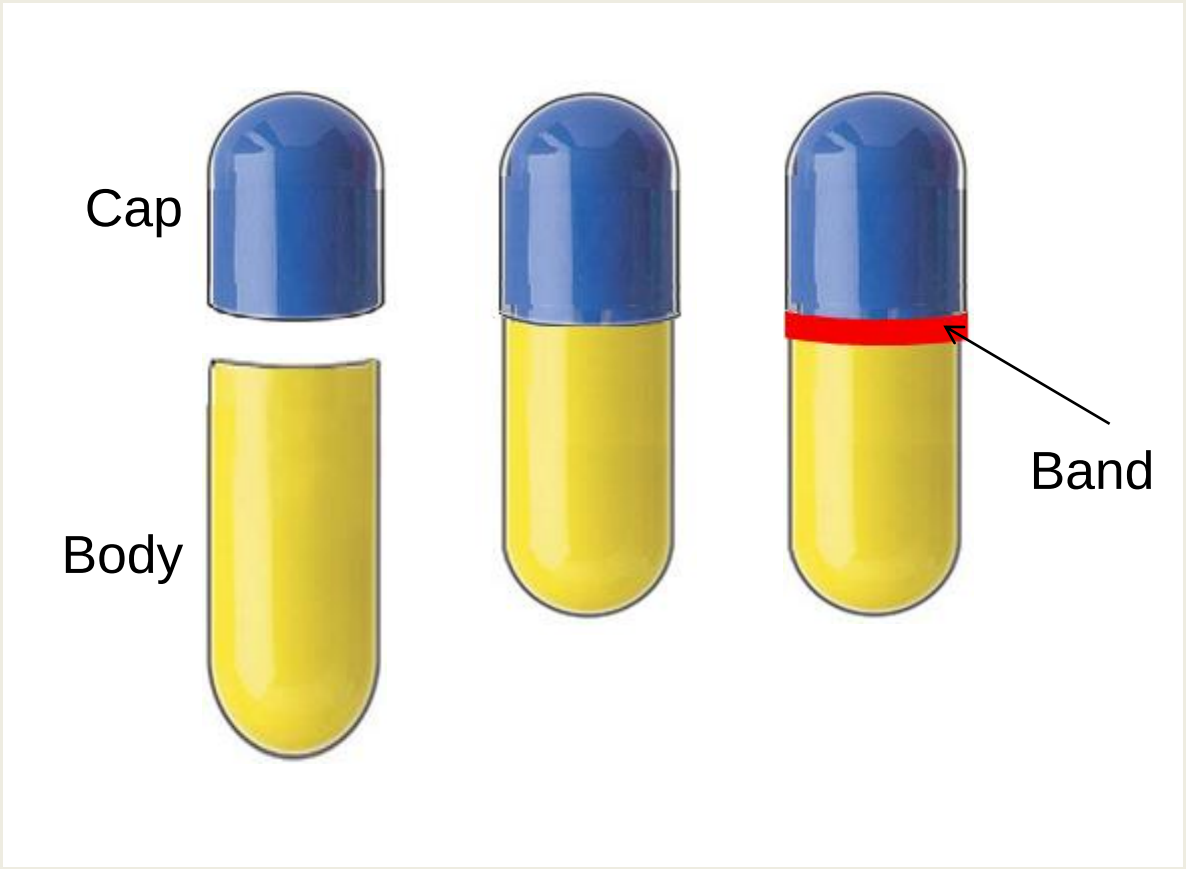
Micropellets

Mini-tablets

Types of capsules

Hard capsules

Conventional

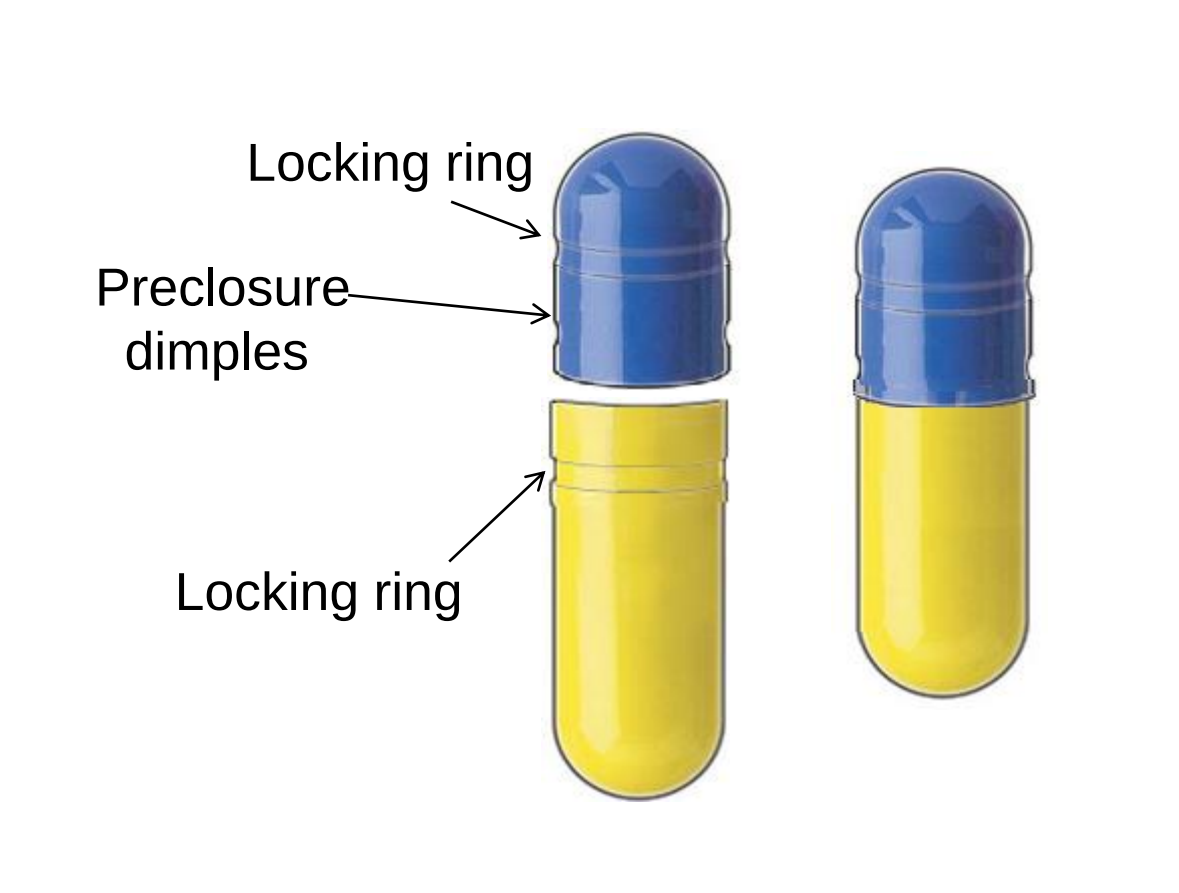


Types of capsules

Hard capsules

Snap-fit

Air to escape

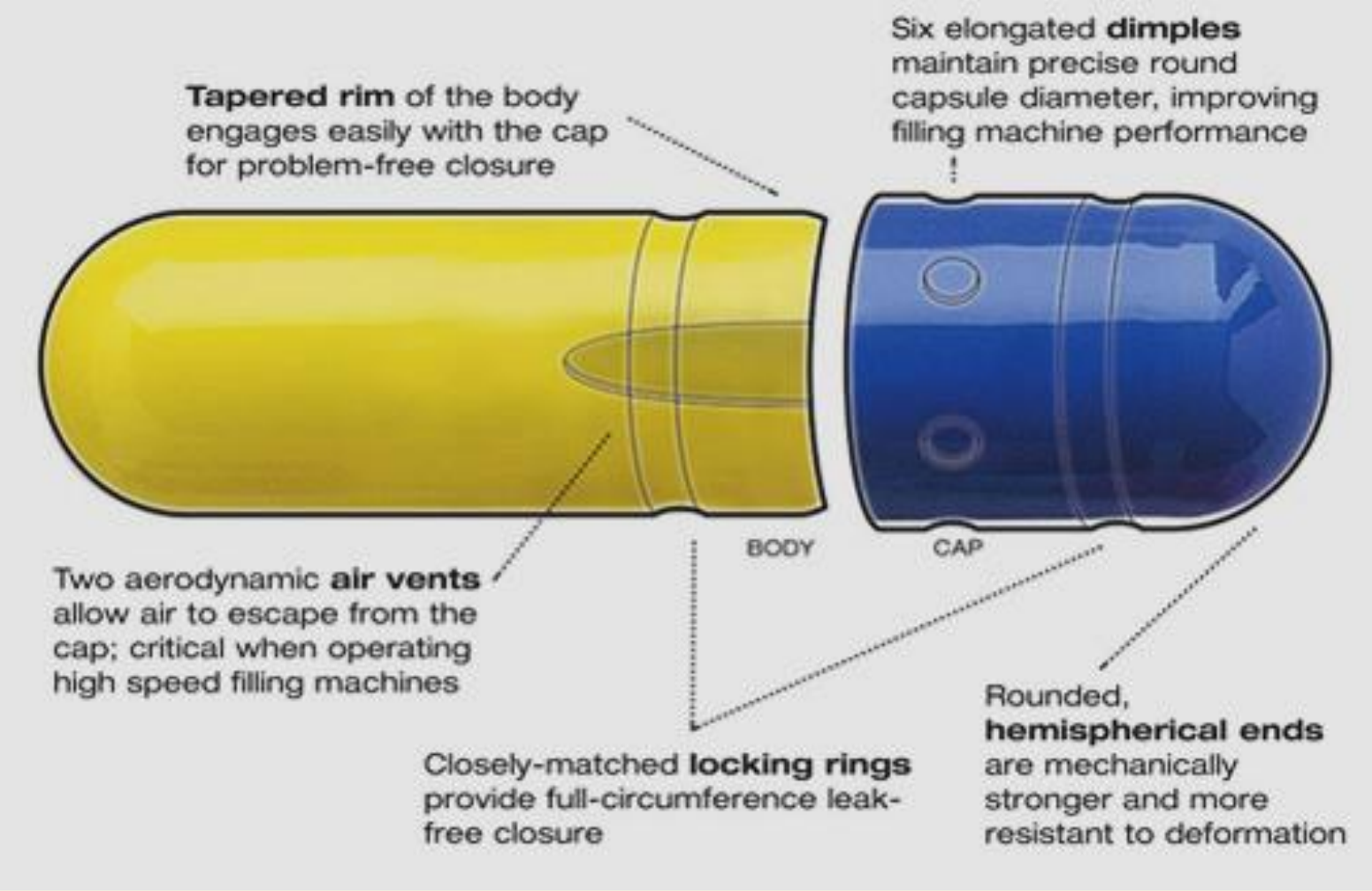


Types of capsules

Hard capsules

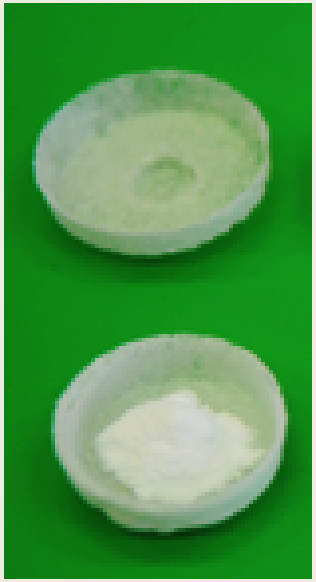
Coni-Snap

Air to escape



Types of capsules

Cachets



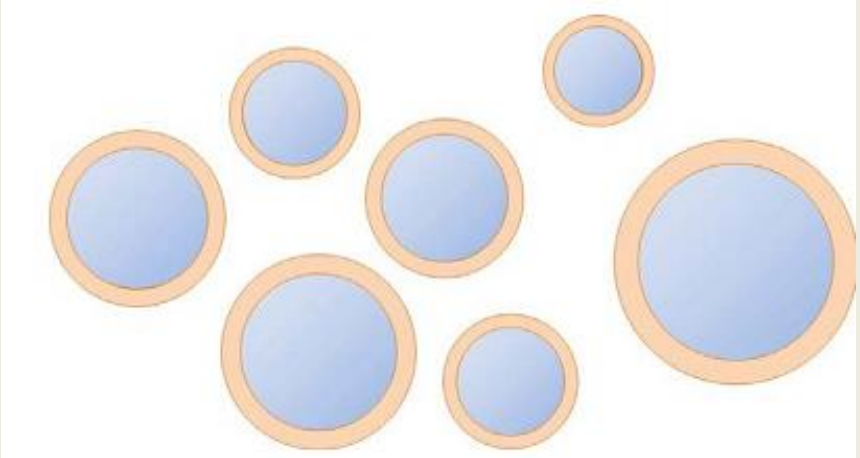
Cachets are solid preparations consisting of a hard shell containing a single dose of one or more active substances. The cachet shell is made of unleavened bread usually from rice flour and consists of 2 prefabricated flat cylindrical sections.

Before administration, the cachets are immersed in water for a few seconds, placed on the tongue and swallowed with a draught of water.

The label states the method of administration of the cachets

Types of capsules

Microcapsules

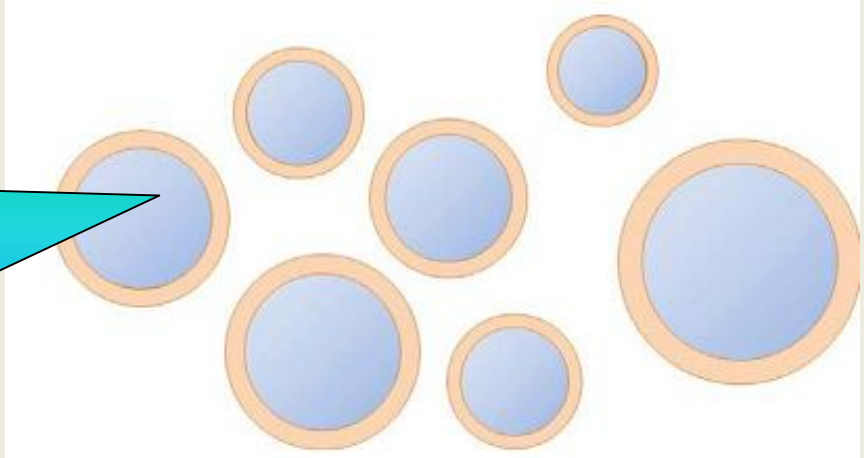


Microcapsules are spherical particles of a diameter of 1-1000 microns, comprising individually coated in the form of solid, liquid or gaseous substance.

Types of capsules

Microcapsules

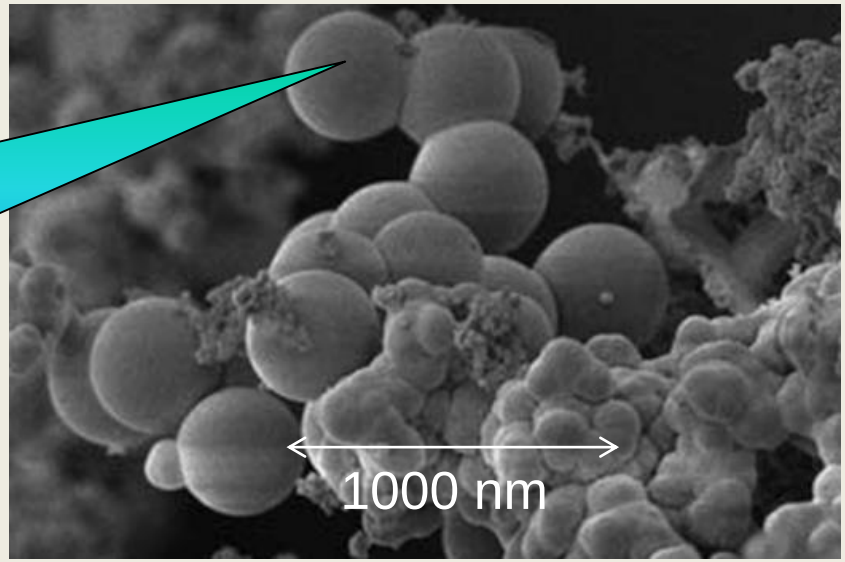
gas
liquid (!)
solid



Types of capsules

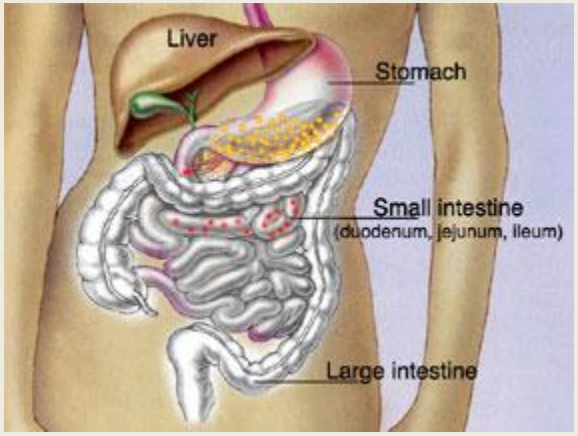
Nanocapsules

gas
liquid (!)
solid



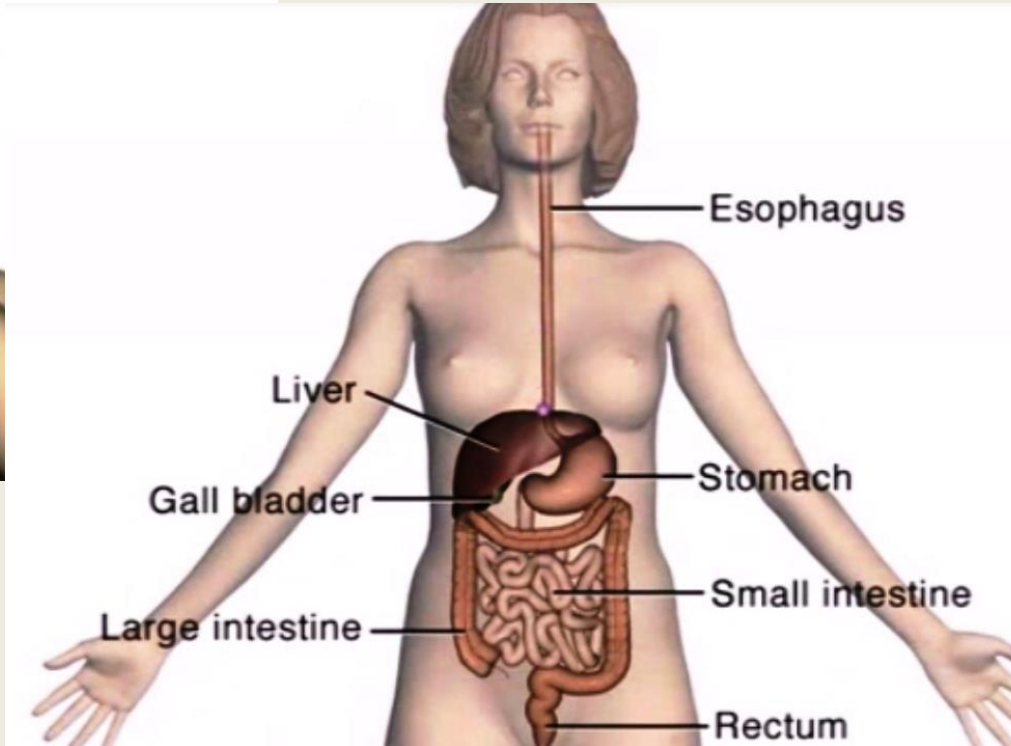
Nanocapsules are 1-1000 nm diameter spherical particles comprising individually coated in the form of solid, liquid or gaseous substance.

Biopharmaceutical aspects



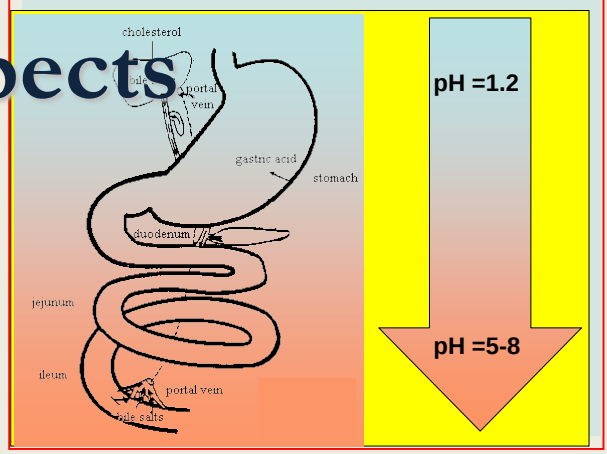
Biopharmaceutical aspects

Peroral administration



Biopharmaceutical aspects

Non-modified capsules

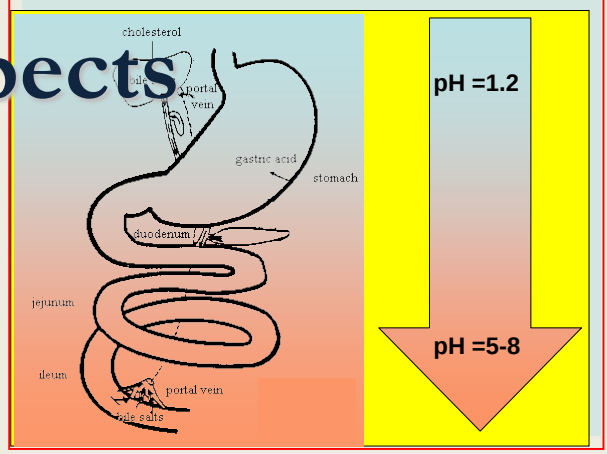


Non-modified capsules made of water-soluble materials uncoated quickly disintegrate in the gastric juice and the active substance is released.

Dosing should primarily serve.

Biopharmaceutical aspects

Modified-release capsules

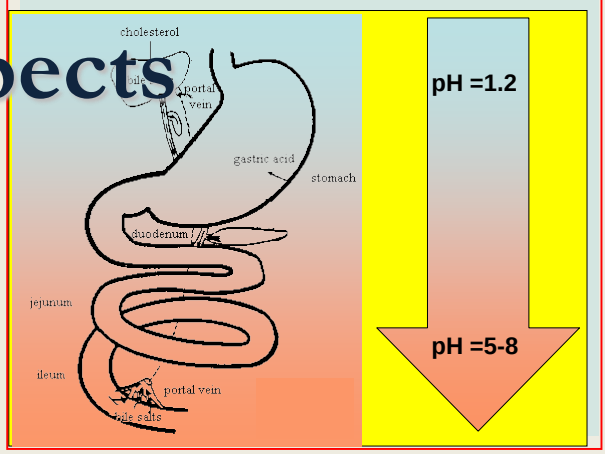


Modified-release capsules are hard or soft capsules in which the contents or the shell or both contain special excipients or are prepared by a special process designed to modify the rate, the place or the time at which the active substance(s) are released.

Modified release capsules include prolonged-release capsules and delayed-release capsules.

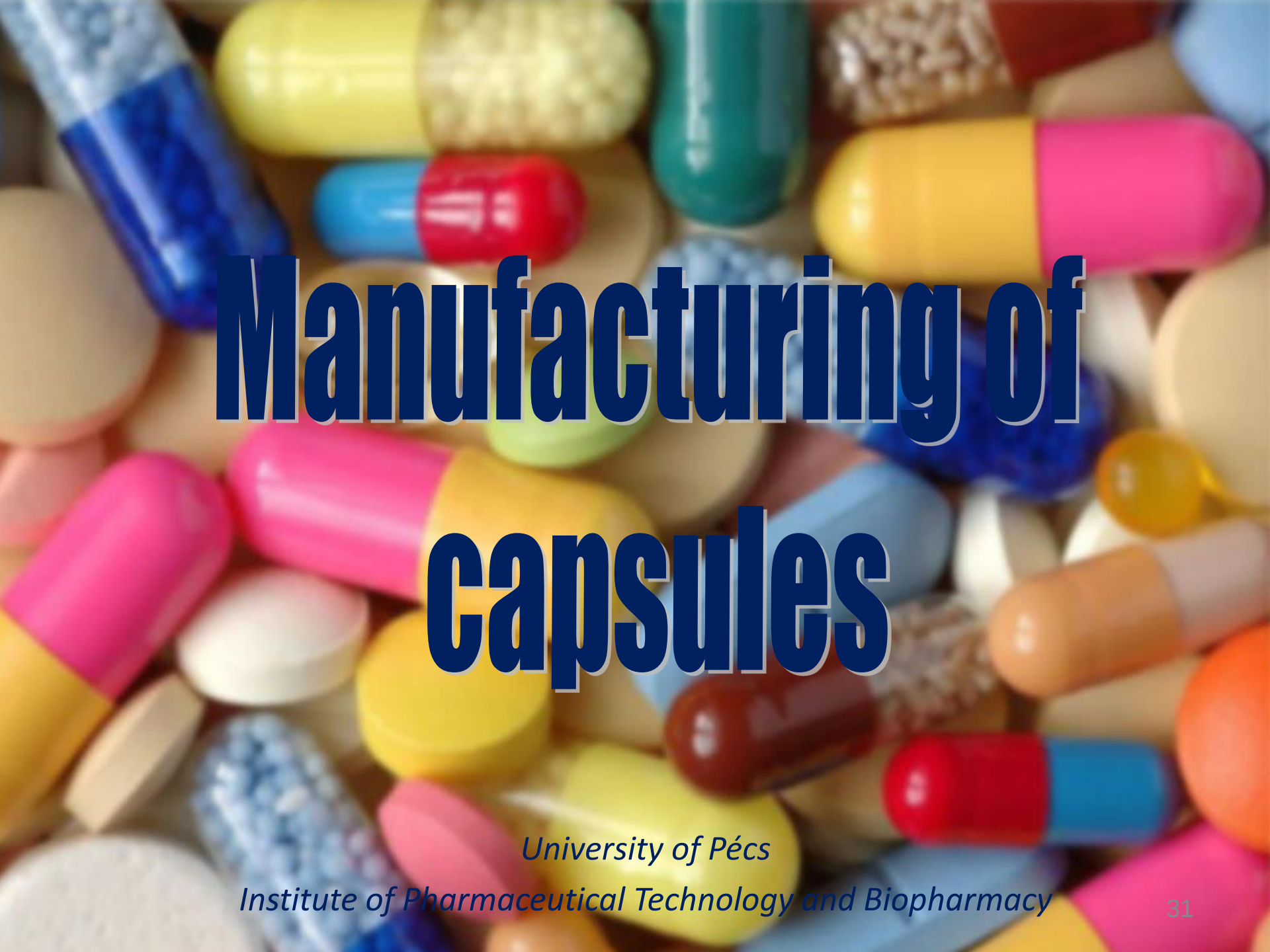
Biopharmaceutical aspects

Gastro-resistant capsules



Gastro-resistant capsules are delayed-release capsules that are intended to resist the gastric fluid and to release their active substance or substances in the intestinal fluid.
Usually they are prepared by filling capsules with granules or with particles covered with a gastro-resistant coating or in certain cases, by providing hard or soft capsules with a gastro-resistant shell (enteric capsules).

For capsules filled with granules or filled with particles covered with a gastro-resistant coating, a suitable test is carried out to demonstrate the appropriate release of the active substance(s)



Manufacturing of capsules

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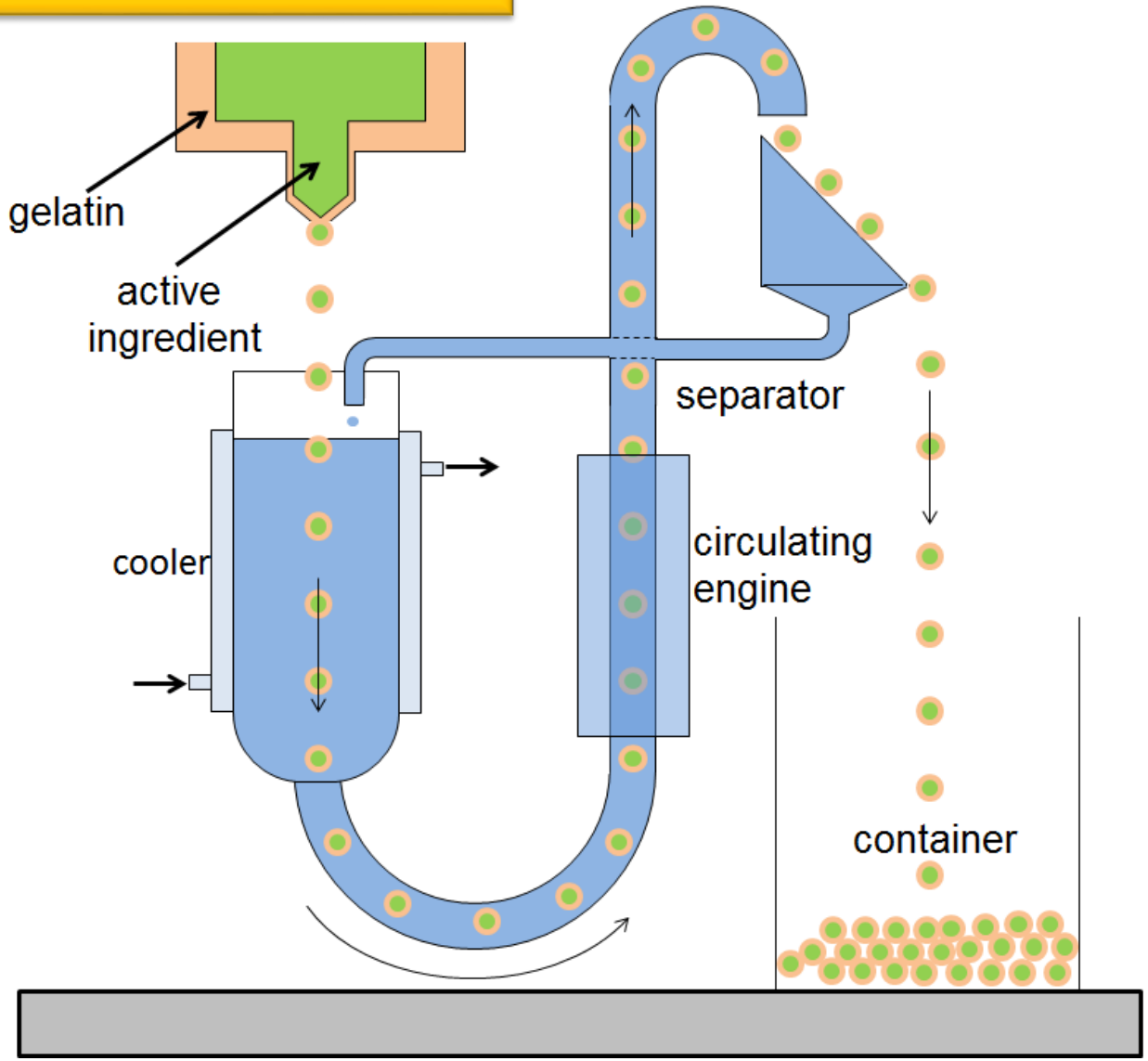
Manufacturing of capsules

Soft gelatine capsules

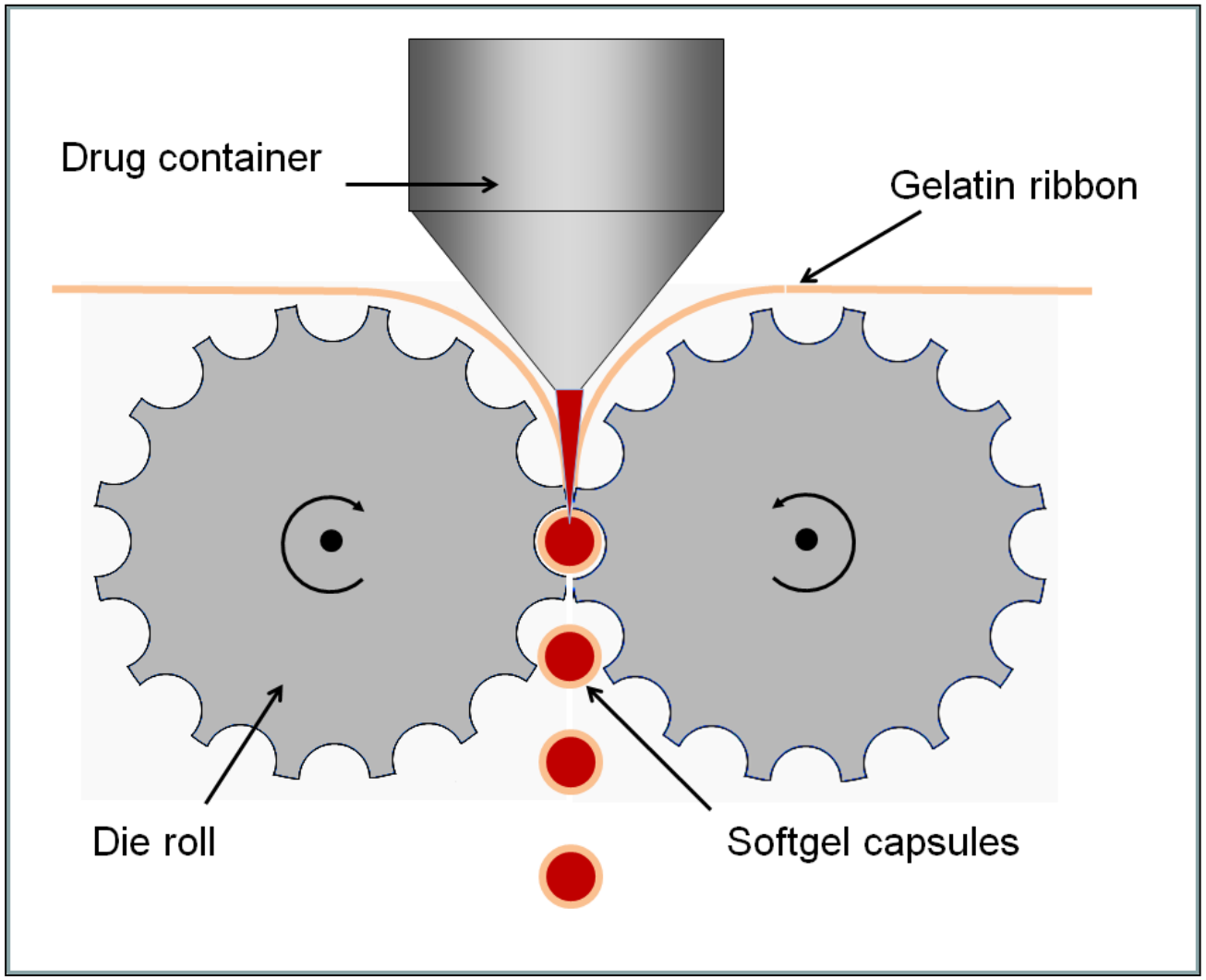
Soft gelatine capsules

Dropping method



Soft gelatine capsules

Rotary dye method



Soft gelatine capsules

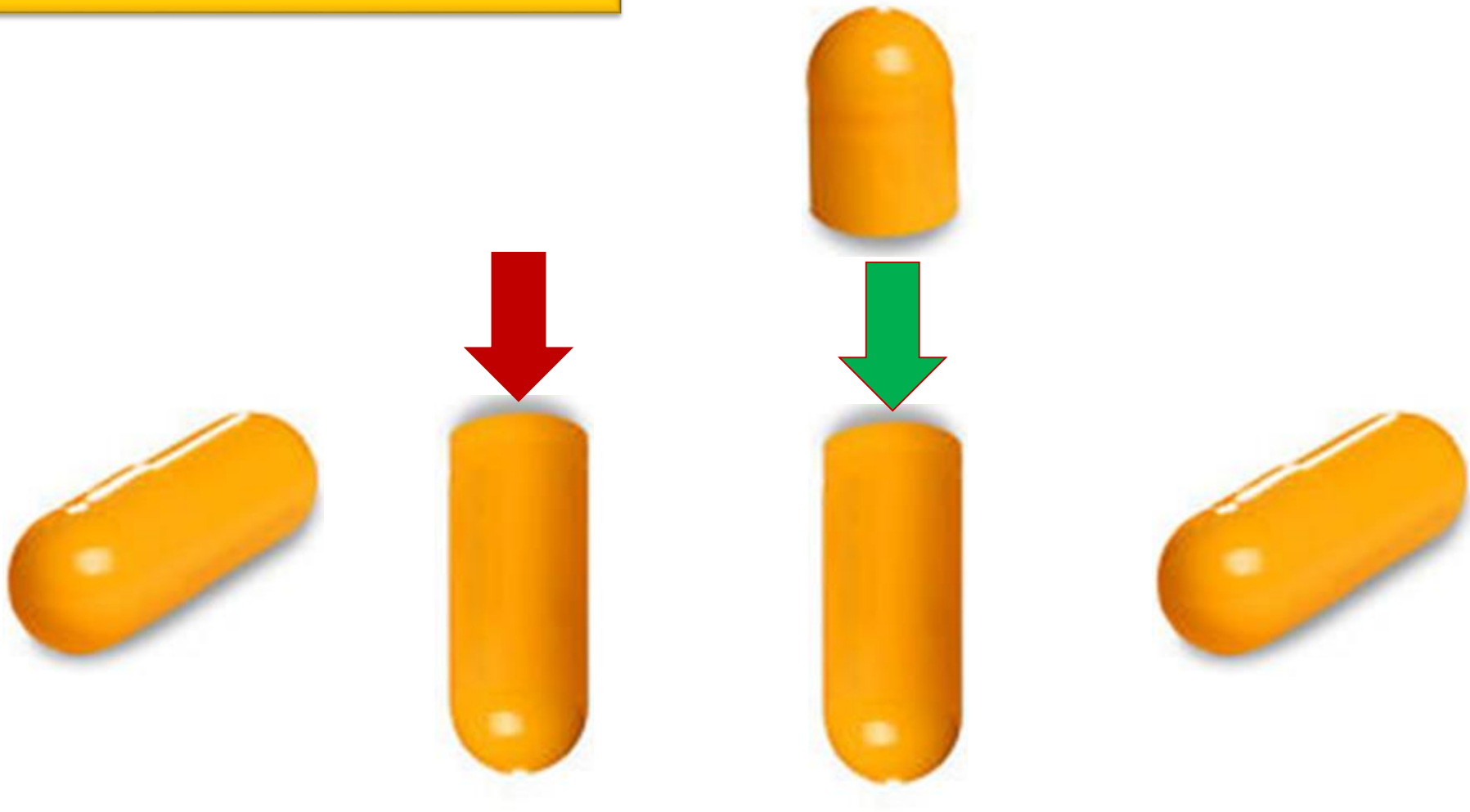
Rotary dye method

Manufacturing of capsules

Hard gelatine capsules

Hard gelatine capsules

Manual capsule filling



Hard gelatine capsules

Manual capsule filling

opening

filling

closing

Hard gelatine capsules

Small scale capsule filler

opening

filling

closing

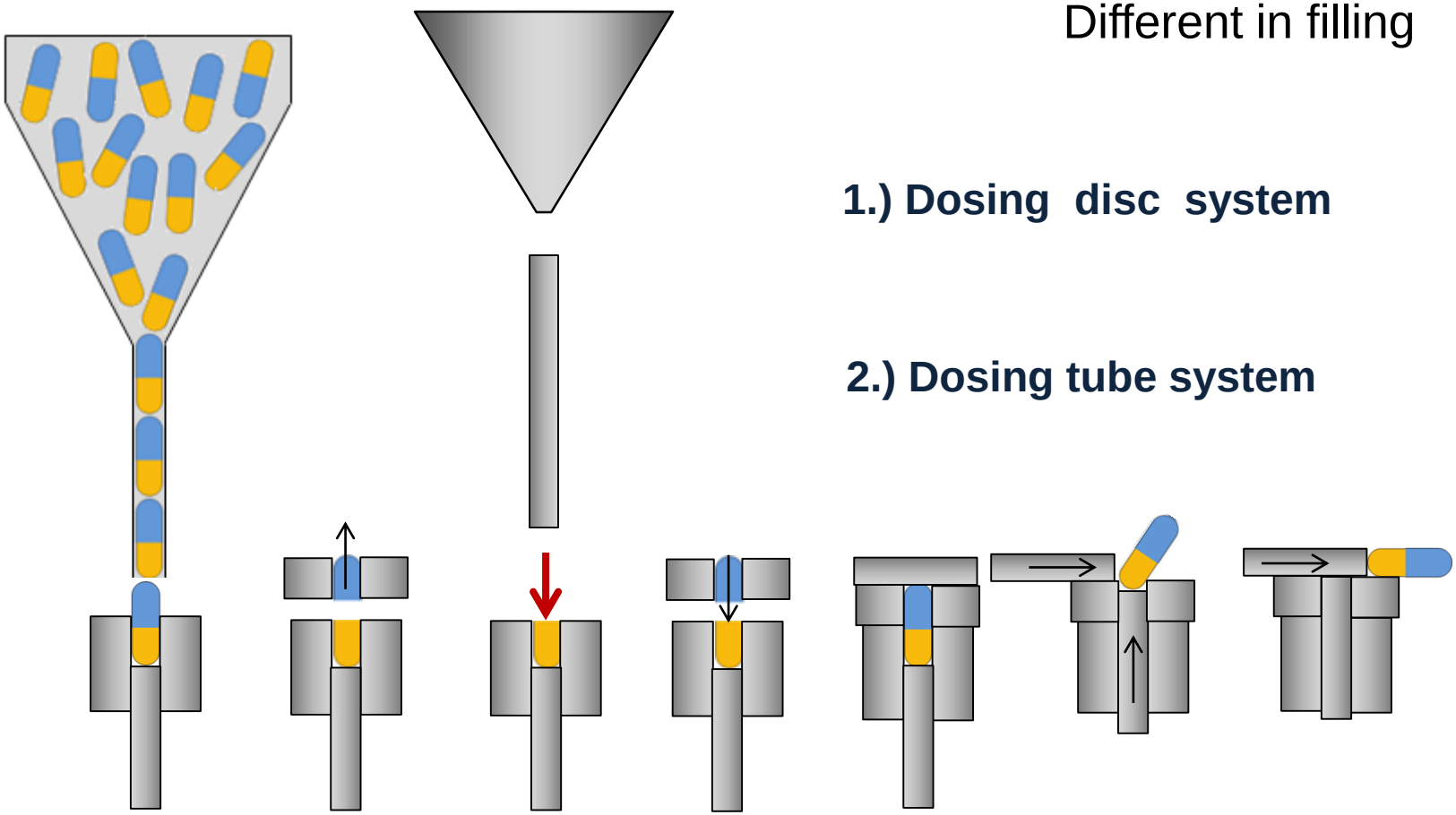
Hard gelatine capsules

Main steps of industrial encapsulation

Different in filling

1.) Dosing disc system

2.) Dosing tube system



Capsule feeding and direction adjusting

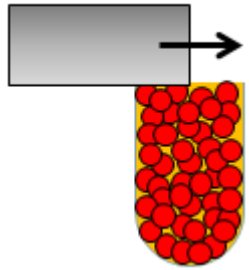
Opening and separating

Filling with powders, granules..

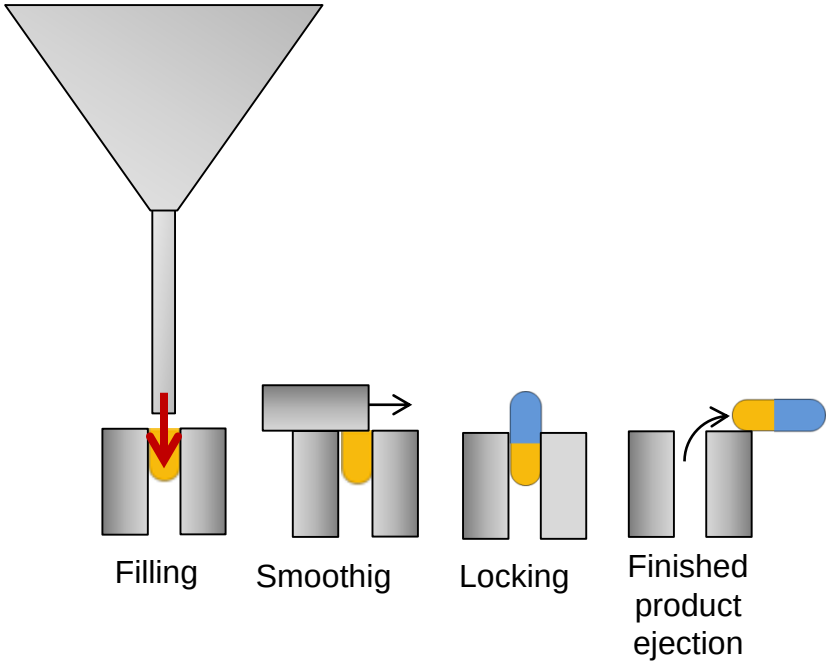
Locking

Finished product ejection

Hard gelatine capsules

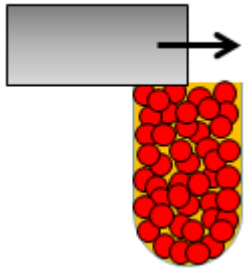


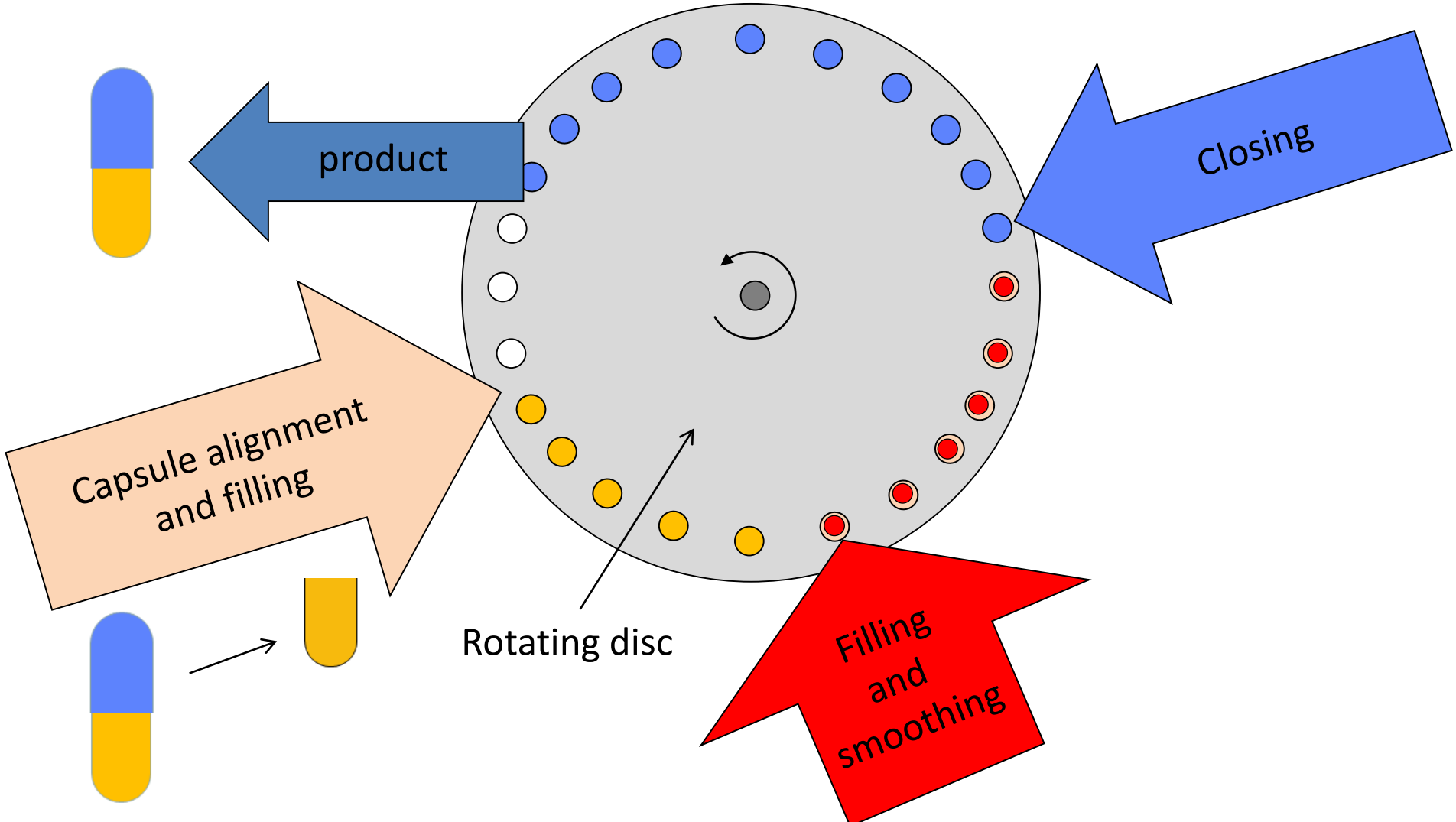
Dosing disc system



Hard gelatine capsules

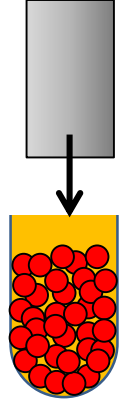
Dosing disc system

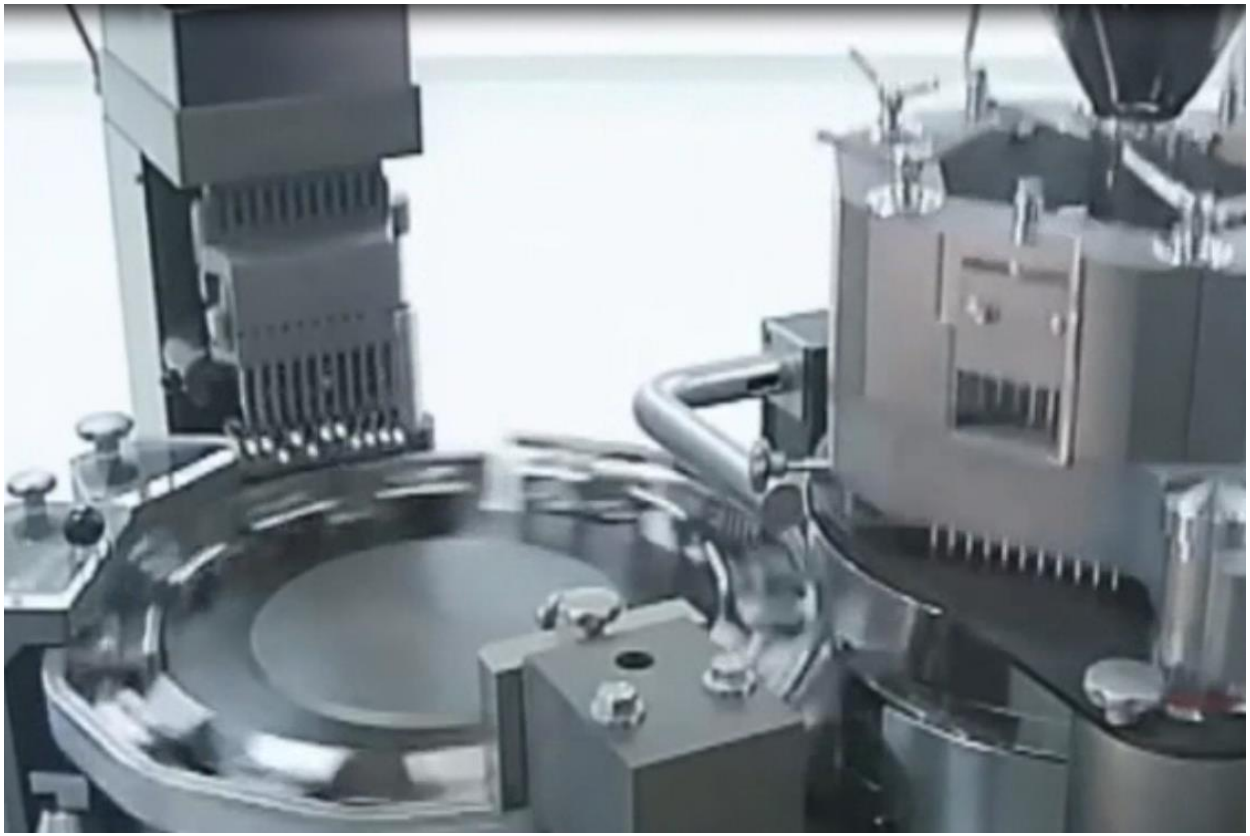




Hard gelatine capsules

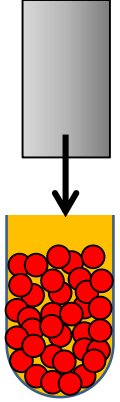
Dosing tube system

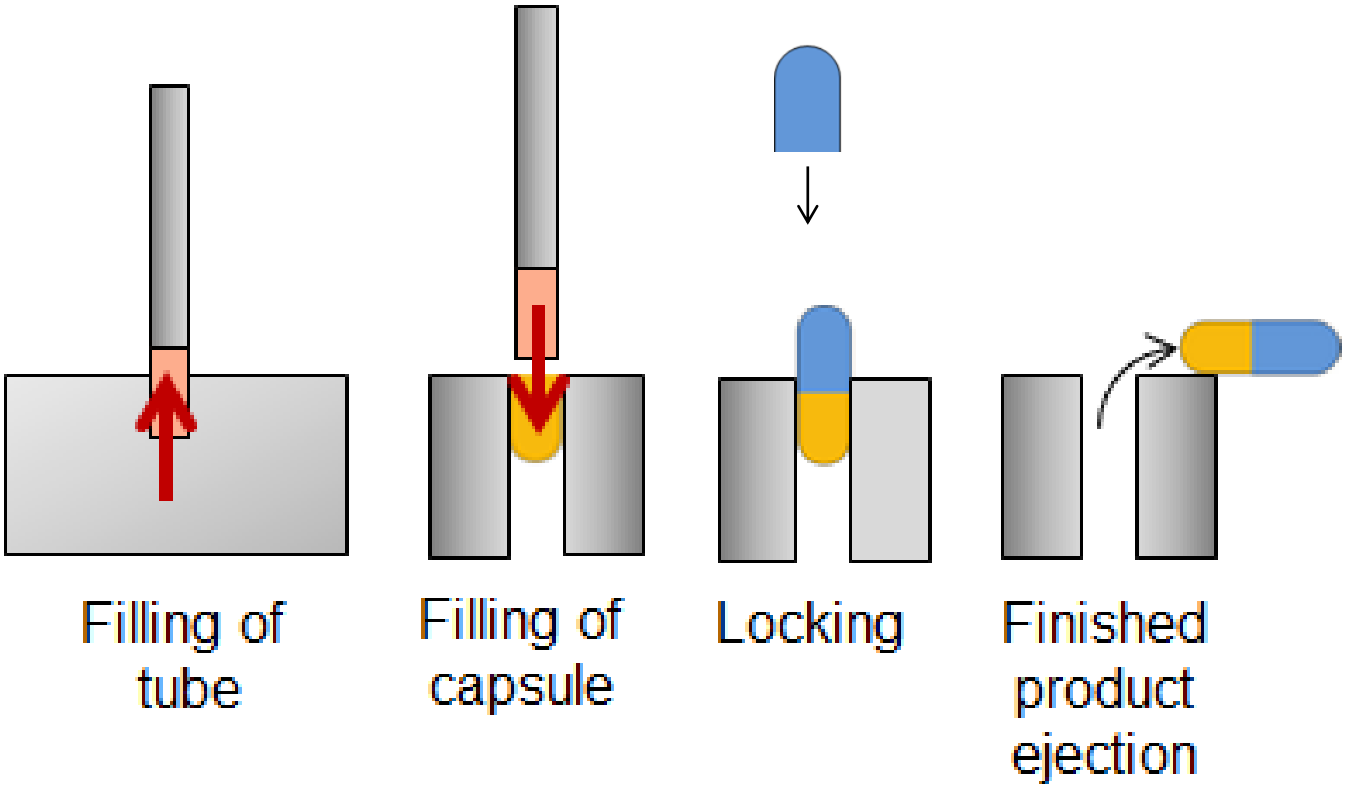




Hard gelatine capsules

Dosing tube system





Quality control of capsules

Examination of capsules

General tests

Uniformity of content

Unless otherwise prescribed or justified and authorised, capsules with a content of active substance less than 2 mg or less than 2 per cent of the total mass comply with test B for uniformity of content of single-dose preparations. If the preparation has more than one active substance, the requirement applies only to those ingredients which correspond to the above conditions.

Examination of capsules

General tests

Uniformity of mass

Capsules comply with the test for uniformity of mass of single-dose preparations. If the test for uniformity of content is prescribed for all the active substances, the test for uniformity of mass is not required.

Examination of capsules

General tests

Dissolution

A suitable test may be carried out to demonstrate the appropriate release of the active substance(s), for example one of the tests described in

Dissolution test for solid dosage forms(2.9.3). Where a dissolution test is prescribed, a disintegration test may not be required.

Examination of capsules

Hard capsules

Disintegration

Hard capsules comply with the test for disintegration of tablets and capsules (2.9.1). Use water R as the liquid medium. When justified and authorised,0.1 M hydrochloric acid or artificial gastric juice R may be used as the liquid medium. If the capsules float on the surface of the water, a disc maybe added.

Operate the apparatus for 30 min, unless otherwise justified and authorised and examine the state of the capsules. The capsules comply with the test if all 6 have disintegrated.

Examination of capsules

Soft capsules

Disintegration

Soft capsules comply with the test for disintegration of tablets and capsules (2.9.1). Use water R as the liquid medium. When justified and authorised,0.1 M hydrochloric acid or artificial gastric juice R may be used as the liquid medium. Add a disc to each tube. Liquid active substances dispensed in soft capsules may attack the disc; in such circumstances and where authorised, the disc may be omitted. Operate the apparatus for 30 min, unless otherwise justified and authorised and examine the state of the capsules. If the capsules fail to comply because of adherence to the discs, repeat the test on a further 6 capsules omitting the discs. The capsules comply with the test if all 6 have disintegrated.

Examination of capsules

Modified-release capsules

Dissolution

A suitable test is carried out to demonstrate the appropriate release of the active substance(s)

Examination of capsules

Gastro-resistant capsules

Dissolution

For capsules prepared from granules or particles already covered with a gastro-resistant coating, a suitable test is carried out to demonstrate the appropriate release of the active substance(s), for example the test described in Dissolution test for solid dosage forms(2.9.3)

Examination of capsules

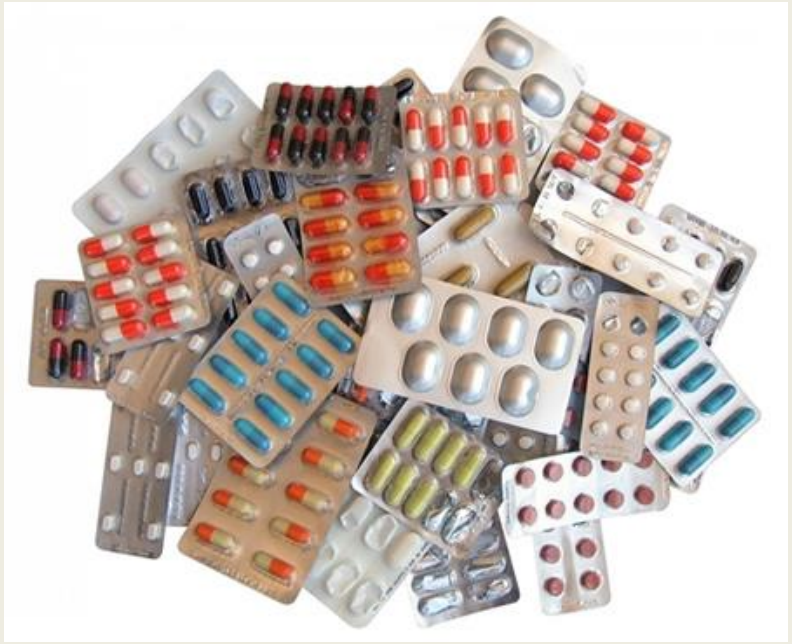
Gastro-resistant capsules

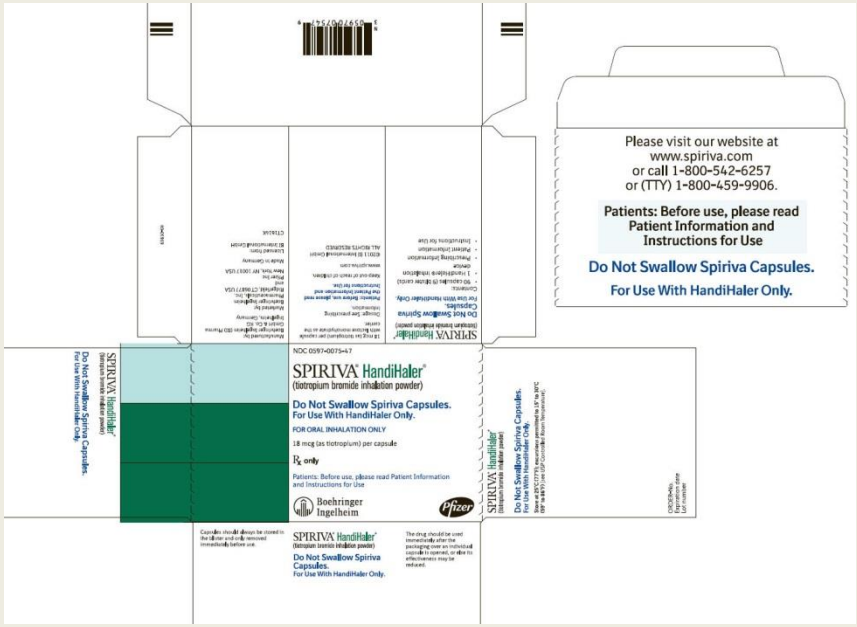
Disintegration

For capsules with a gastro-resistant shell carry out the test for disintegration (2.9.1) with the following modifications. Use 0.1 M hydrochloric acid as the liquid medium and operate the apparatus for 2 h, or other such time as may be authorised, without the discs. Examine the state of the capsules. The time of resistance to the acid medium varies according to the formulation of the capsules to be examined. It is typically 2 h to 3 h but even with authorised deviations it must not be less than 1 h. No capsule shows signs of disintegration or rupture permitting the escape of the contents. Replace the acid byphosphate buffer solution pH 6.8 R. When justified and authorised, a buffer solution of pH 6.8 with added pancreas powder (for example, 0.35 g ofpancreas powder Rper 100 ml of buffer solution) may be used.

Add a disc to each tube. Operate the apparatus for further 60 min and examine the state of the capsules. Ift he capsules fail to comply because of adherence to the discs, repeat the test on a further 6 capsules omitting the discs. The capsules comply with the test if all 6 have disintegrated.

Packaging of capsules





Packaging of capsules

Labelling

The label states the name of any added antimicrobial preservative.

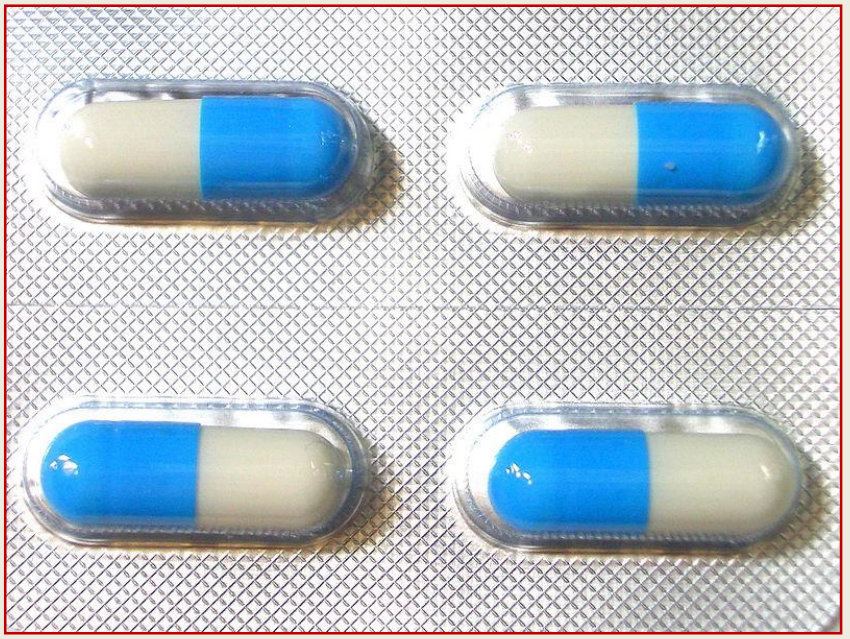
Packaging of capsules

Storage

Store at a temperature not exceding 30 °C.

Packaging of capsules

Blistering



Mechanical protection with packing

Thank you for your attention!