

Capsules

Capsules are solid dosage forms in which the drug or a mixture of drugs is enclosed in Hard Gelatin Capsule Shells, in soft, soluble shells of gelatin, or in hard or soft shells of any other suitable material, of various shapes and capacities. They usually contain a single dose of active ingredient(s) and are intended for oral administration. Capsules may also be used for other applications such as dry powder inhalers, suppositories etc. The consistency of soft shells may be adjusted by the addition of substances such as Glycerin and Sorbitol. Excipients such as opaque fillers, anti-microbial preservatives, sweetening agents, flavouring agents and one or more colouring agents permitted under the Drugs and Cosmetic Rules, 1945 may be added. Capsules may bear surface markings.

The contents of capsules may be of solid, liquid or paste-like consistency. They consist of the medicament(s) with or without excipients such as vehicles, solvents, diluents, lubricants, fillers, wetting agents and disintegrating agents. The contents should not cause deterioration of the shell, but the capsules are attacked by the digestive fluids thereby releasing the contents.

Production

During Manufacture, packaging, storage and distribution of capsules, suitable means shall be taken to ensure their microbial quality; acceptance criteria for microbial quality are given in chapter 2.2.9.

Tests

Content of active ingredients. Determine the amount of active ingredient(s) by the method described in the Assay and calculate the amount of active ingredient(s) in each capsule. The result lies within the range for the content of active ingredient(s) stated in the monograph. This range is based on the requirement that 20 capsules, or such other number as may be indicated in the monograph, are used in the Assay. Where 20 capsules cannot be obtained, a smaller number, which must not be less than 5, may be used, but to allow for sampling errors the tolerances are widened in accordance with Table 1. The requirements of Table 1 apply when the stated limits are between 90 and 110 per cent for limits other than 90 to 110 per cent, proportionately smaller or larger allowances should be made.

Table 1

Weight of Active ingredients in each Capsules	Subtract from the lower limit for samples of			Add to the upper limit for samples of		
	15	10	5	15	10	5
0.12 g or less	0.2	0.7	1.5	0.3	0.8	1.8
More than 0.12 g and less than 0.3 g	0.2	0.5	1.2	1.2	0.6	1.5
0.3 g or more	0.1	0.2	0.8	0.2	0.4	1.0

Uniformity of weight. This test is not applicable to capsules that are required to comply with the test for Uniformity of content for all active ingredients.

Weigh an intact capsule. Open the capsule without losing any part of the shell and remove the contents as completely as possible. To remove the contents of a soft capsule the shell may be washed with *ether* or other suitable solvent and the shell allowed to stand until the odour of the solvent is no longer detectable. Weigh the shell, the weight of the contents is the difference between the weighings. Repeat the procedure with a further 19 capsules. Determine the average weight of capsule contents. Not more than two of the individual weights deviate from the average weight by more than the percentage deviation shown in Table 2 and none deviates by more than twice that percentage.

Table 2

Average weight of capsule Contents	Percentage deviation
Less than 300 mg	10
300 mg or more	7.5

Uniformity of content. This test is applicable to capsules that contain less than 10 mg or less than 10 per cent w/w of active ingredient. For capsules containing more than one active ingredient carry out the test for each active ingredient that corresponds to the afore-mentioned conditions.

The test should be carried out only after the content of active ingredient(s) in a pooled sample of the capsules has been shown to be within accepted limits of the stated content.

NOTE — The test is not applicable for capsules containing multivitamins and trace elements.

Determine the content of active ingredient in each of 10 capsules taken at random using the method given in the monograph or by any other suitable analytical method of equivalent accuracy and precision. The capsules comply with the test if not more than one of the individual values thus obtained is outside the limits 85 to 115 per cent of the average value and none is outside the limits 75 to 125 per cent. If maximum of three individual values are outside the limits 85 to 115 per cent of the average value repeat the determination using another 20 capsules. The capsules comply with the test if in the total sample of 30 capsules not more than three individual values are outside the limits 85 to 115 per cent and none is outside the limits 75 to 125 per cent of the average value.

Disintegration. The disintegration test is not applicable to prolonged-release capsules. For Hard Gelatin Capsules, Soft Gelatin Capsules and Hard Cellulose capsules for which the dissolution test (2.5.2) is included in the individual monograph, the test for Disintegration is not required.

Hard Gelatin Capsules.

Hard gelatin capsules have shells consisting of two prefabricated, cylindrical sections, each of which has one rounded, closed end and one open end. Hard gelatin capsules contain the medicament(s) in the form of powders, pellets or granules, semisolids or liquids etc. Where two mutually incompatible drugs are present in the mixture, one of the drugs can be put as a tablet or pellet or in small capsule and then encapsulated with the other drug in a larger capsule.

Production.

Hard gelatin capsules shells are made by a process that involves dipping shaped pins into gelatin solutions, after which the gelatin films are dried, trimmed, and removed from the pins, and the body and cap pieces are joined.

Tests

Disintegration. Comply with the disintegration test (2.5.1). Unless otherwise directed in the individual monograph use *water* as the medium. If the capsules float on the surface of the medium, a disc may be added. If the capsules adhere to the disc, attach a removable piece of stainless steel woven gauze with mesh aperture of 2.00 mm to the upper plate of the basket rack assembly and carry out the test omitting the discs. Operate the apparatus for 30 minutes unless otherwise directed.

Soft Gelatin Capsules.

Soft gelatin capsules made from gelatin (sometimes called softgels) or other suitable material require large-scale production methods. The soft gelatin shell is somewhat thicker than that of hard-shell capsules and may be

plasticized by the addition of a polyol such as sorbitol or glycerin. The ratio of dry plasticizer to dry gelatin determines the “hardness” of the shell and may be varied to accommodate environmental conditions as well as the nature of contents. Like hard shells, the shell composition may include approved dyes and pigments, opaquing agents such as titanium dioxide, and preservatives. Flavors may be added and up to 5 per cent sucrose may be included for its sweetness and to produce a chewable shell. Soft gelatin shells normally contain 6 per cent to 13 per cent of water.

Production.

Soft gelatin capsules shells are usually formed, filled with medicament and sealed in a combined operation on machines. In some cases, shells for extemporaneous use may be prefabricated. The shells which are thicker than those of hard capsules are formed to produce capsules which are spherical, oval or cylindrical with hemispherical ends.

Soft gelatin capsules also may be manufactured in a bubble process that forms seamless spherical capsules. The shells may sometimes contain a medicament. They may contain a preservative to prevent growth of fungi.

The contents of soft capsules usually consist of liquids or solids dissolved or dispersed in suitable excipients to give a paste-like consistency. With suitable equipment, powders, granules and other dry solids also may be filled into soft-shell capsule. There may be partial migration of the constituents from the capsule contents into the shell and vice versa because the nature of the materials and the surface in contact.

Tests

Disintegration. Comply with the disintegration test (2.5.1). Unless otherwise directed in the individual monograph use *water* as the medium. The disc may be omitted if the capsule adhere to the disc or if it is likely to be attacked by the contents of capsules. Operate the apparatus for 60 minutes unless otherwise directed.

If any of the capsules has not disintegrated, repeat the test on further 6 capsules. In the repeat test with additional capsules, if any of the capsules have not disintegrated, repeat the test on a further 6 capsules, replacing *water* in the vessel with *0.1 M hydrochloric acid or artificial gastric juice*. The capsule pass the test if all the six have disintegrated.

Prolonged-release Capsules.

Prolonged-release Capsules are hard or soft capsules in which the contents or the shell, or both, contain auxiliary substances or are prepared by a special process designed to modify the rate at which the active ingredients are released.

Tests

Dissolution (2.5.2). The test should be designed to demonstrate the appropriate release of the active substance(s). The manufacturer is expected to give specifications for drug release at 3 or more test-time points. The first point should be set after a testing period corresponding to a dissolved amount of typically 20 per cent to 30 per cent. The second point should define the dissolution pattern and should be set typically 45 per cent to 55 per cent release. The final point should ensure almost complete release that is generally understood as more than 80 per cent release.

NOTE — Above specification are non-mandatory.

Carry out the test as per the manufacturer’s specification for the indicated test-times.

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 substance in the intestinal fluid. Usually they are prepared by filling capsule with granules or with particles covered with a gastro-resistant coating or in certain cases, by providing hard or soft capsules with gastro-resistant shell.

Tests

Disintegration. Comply with the disintegration test (2.5.1). Use the apparatus as described under disintegration test, using one capsule in each tube. Operate the apparatus for 2 hours without the discs in *0.1 M hydrochloric acid*. No capsule shows sign of disintegration or of rupture permitting the escape of the contents. Replace the medium in the vessel with *mixed phosphate buffer pH 6.8*. When justified and authorized, a buffer solution of pH 6.8 with added pancreas powder (for example, 0.35 g of *pancreas powder* per 100 ml of buffer solution) may be used. Add a disc to each tube and operate the apparatus for a further 60 minutes

Hard Cellulose Capsules

Hard cellulose Capsule Shells are soluble containers for incorporation of drugs and food products, usually in the form of powders, pellets or granules, semisolids or liquids etc and are commonly intended for oral administration. The shells are acted upon by digestive fluids and the filled contents are released. They are composed of Hydroxy Propyl Methyl Cellulose or any other cellulose derivatives and water.

Hard cellulose capsules have shells consisting of two prefabricated, cylindrical sections, each of which has one rounded, closed end and one open end. . Hard Cellulose Capsule shells contain the medicament in the form of powders, pellets or granules, semisolids or liquids etc. Where two mutually incompatible drugs are present in the mixture, one of the drugs can be put as a tablet or pellet or in small capsule and then encapsulated with the other drug in a larger capsule.

Tests

Disintegration. Comply with the disintegration test (2.5.1). Unless otherwise directed in the individual monograph use water as the medium. If the capsules float on the surface of the medium, a disc may be added. If the capsules adhere to the disc, attach a removable piece of stainless steel woven gauze with mesh aperture of 2.00mm to the upper plate of the basket rack assembly and carry out the test omitting the discs. Operate the apparatus for 30 minutes unless otherwise directed.

Storage. Store at a temperature not exceeding 30°.

Labelling. The label states the name of any added antimicrobial preservative.