INDUSTRIAL PHARMACY-I
UNIT III

EVALUATION OF CAPSULES

MRS. SHILPA RAUT

K. K. WAGH COLLEGE OF PHARMACY, NASHIK

1.Disintegration test for capsules

- The capsules are placed in the basket rack assembly, which is immersed 30 times per minute into a thermostatically controlled fluid at 37°C and observed over the time described in the individual monograph.

- To satisfy the test, the capsules disintegrate completely into a soft mass having no palpably firm core and only some fragments of the gelatin shell.

Disintegration test for capsules

- Unless otherwise specified in the individual monograph, use water as the immersion fluid at a temperature of 37 ± 2 °C. Place one capsule in each of the six tubes and, if prescribed, add a disc to each tube.
- Operate the apparatus for the specified period of time, withdraw the assembly, and examine the state of the capsules. All six capsules should disintegrate to pass the test

Disintegration testing condition and interpretation (IP)

Sr. No	Type of capsule	Medium	Temperature	Limit
1	Hard gelatin	Water/buffer	37 °± 2 °C	30 min or as per individual monograph
2	Soft gelatin	Water	37 °±2 °C	60 min or as per individual monograph

Disintegration testing condition and interpretation (BP)

Sr. No	Type of capsule	Medium	Temperature	Limit
1	Hard gelatin	Water/0.1 M HCl/ Artificial gastric juice R	37 °± 2 °C	30 min or as per individual monograph
2	Soft gelatin	Water/0.1 M HCl/ Artificial gastric juice R	37 °±2 °C	60 min or as per individual monograph

2. Dissolution test for capsules

- However, if the capsule shells interfere with the analysis, the contents of a specified number of capsules can be removed and the empty capsule shells dissolved in the dissolution medium before proceeding with the sampling and chemical analysis.
  - Dissolution test is an official method to determine the dissolution rate of a solid dosage form.

    Dissolution rate is defined as the rate at which the drug is released into the systemic circulation from the dosage form.
  - Dissolution test apparatus:-

a) **Apparatus-I (rotating basket dissolution apparatus):**

Small wire mesh size basket – 22

- Temperature - 37±5ºc Rotated speed – 25-150 rpm
- Dissolution medium height from the bottom of the vessel – 23-27mm.

a) **Apparatus-2 (rotating paddle dissolution apparatus):**

Small wire mesh size: 22

- Dissolution medium height from the bottom of the vessel – 23-27mm
- Temperature - 37±5ºc Rotated speed – 25-150 rpm

Dissolution testing interpretation IP Standard

Stage.	Quantity Stage/level	Number of Capsules tested	Acceptance criteria
1	S1	6	Each unit is not less than D* + 5 percent**
2	S2	6	Average of 12 units (S1 +S2) is equal to or greater than (>)D, and unit is less than D - 15 percent**
3	S3	12	Average of 24 units (S1+S2+S3) is equal to or greater than (>)D, not more than 2 units are less than D-15 percent** and no unit is less than D- 25 percent**

*D is the amount of dissolved active ingredient specified in the individual monograph

Dissolution testing interpretation BP/USP Standard

Stage.	Quantity Stage/level	Number of Capsules tested	Acceptance criteria
1	S1	6	Each unit is not less than Q + 5 percent**
2	S2	6	Average of 12 units (S1 +S2) is equal to or greater than (>)Q, and no unit is less than Q - 15 percent**
3	S3	12	Average of 24 units (S1+S2+S3) is equal to or greater than (>)Q, not more than 2 units are less than Q-15 percent** and no unit is less than Q- 25 percent**

*The quantity Q, is the specified amount of dissolved active substance.

Comparison Of Specifications & Parameters

Tests	IP	BP	USP
Drug Content Uniformity	85 – 115%	85-115%	90-110%
Content uniformity	85 - 115%	85 - 115%	85 - 15 %
Weight uniformity	<300mg=10% >300mg=7.5%	<300mg=10% >300mg=7.5%	NS
Disintegration test		**Disintegration time**	
Hard Gelatin Soft Gelatin Enteric coated	<30 min <60 min 2hr in HCl 60min. In Buffer	<30 min <60 min 2hr in HCl 60min. In Buffer	<30 min <60 min NS
Gastro Resistent	60	60	60
Dissolution test	>70%	>70%	> 70%

3. Weight variation

The uniformity of dosage units may be demonstrated by determining weight variation. The weight variation method is as follows.

- 20 capsules are selected and weighed individually, take average and compare each capsule weight with average.
- Then test passes if none of the individual weights are less than 90% and more than 110% of average.
- If test requirements are not met we have to remove the powder, net content of powder can be weighed individually. They have to be averaged.
- Test requirements are met if not more than 2 of the individuals difference is not greater than 10% of average. In any case difference should not be more than or equal to 25%
- If more than 2 and less than 6 net weights determined, they deviates 10%. Then we go for additional 40 capsules.
- The average of 60 capsules is determined by weighing capsules individually and compared with average.
- Test requirements are met if the difference does not exceed more than 6 of the 60 capsules.
- Deviation should not be more than 25% in any case.
- Then particular batch passes weight variation test

Weight variation test of Soft Capsules

- The gross weight of 10 intact capsules is determined individually. Then each capsule is cut open and the contents are removed by washing with a suitable solvent.
- The solvent is allowed to evaporate at room temperature over about 30 minutes, with precautions to avoid uptake or loss of moisture.
- The individual shells are weighed and the net contents calculated.
- From the results of the assay directed in the individual monograph, the content of the active ingredient in each of the capsules is determined.

4.Content uniformity

- Unless otherwise stated in the USP monograph for an individual capsule, the amount of active ingredient, determined by assay, is within the range of 85% to 115% of the label claim for 9 of 10 dosage units assayed, with no unit outside the range of 70% to 125% of the label claim.
- If more than 1 but less than 3 capsules assayed should prove that not less than 27 of the 30 capsules are within the desired extremes i.e. between 85-115% and no capsule is beyond the stated potency range of 75-125%

Content uniformity

- This test is performed only when the content is specified in the individual monographs.
- If weight of capsules is completely filled no need of this test.
- If any weight difference is there this test is performed.
- In this 30 capsules are selected and 10 of them are for assay so that by proper analysis we can determine the amount of drug.
- If 9 of 10 is in the specified potency range of 85 to 115% and 10th is not outside 75 to 125%.
- If more than 1 but less than 3 deviate, we have to go for remaining 20 and assayed.
- Test requirements are met if none of capsules is outside 75-125% range and not less than 27 of 30 are within 85-115% range. Then particular batch passes this test

Content labeling requirement

- All official capsules must be labeled to express the quantity of each active ingredient in each dosage unit.

5.Stability testing

- The intrinsic stability of the active drug molecule and the influence of environmental factors such as temperature, humidity, light, formulative components, and the container and closure system.
- The battery of stress testing, long-term stability, and accelerated stability tests help determine the appropriate conditions for storage and the product's anticipated shelf life.
  - Stability tests for capsules are performed to know the integrity of gelatin capsule shell (but not to known the stability of therapeutically active agent) and for determining the shelf life of capsules.
  - The test helps in improving the quality of contents of capsule shell and for choosing the appropriate retail package.
  - Before actually performing the tests following fact:

The capsule shell are to be stabilized to know atmospheric condition with relative humidity about 20-30% and temperature about 21-24^{0}C.

a. Shell integrity test:

This test is performed to find out the integrity of capsule shell.

Relative Humidity	Temperature	Type of container
80%	Room Temp	Open
-	40 ^{0}C	Open
-	40 ^{0}C	Tightly Closed

- The capsule which are to be tested and the standard capsules are placed at one of the above conditions for two weeks with periodic examination. The gross and net changes occurring in them are as follows.
- The standard capsule shell kept at room temperature and 80% relative humidity became more soft, sticky and swollen.
- The test capsules kept under the same conditions undergo gross changes like discoloration, disintegration licking and turning brittle or soft. The net changes include loss of volatile gradient seems growing darker and wider and slide changes in colour of the shell.

b.Determination of shelf life:

- Shelf life or the expiry date of packed capsules is determined under normal storage conditions.
- Many a Time due to slow drying soft spots appear on those capsules which touch the container or other capsules. These spots are not of major concern as they form a letter by the action of capsule ingredients.
- In case they do not form then it indicates stability problems during shelf life.
- Such flaws therefore must be corrected as soon as possible by altering the ingredients of the shell or the field material.
- For increasing the shelf life of capsules they should be packed in a container designed to prevent their exposure to light humidity conditions and should be stored in cool and dry places at appropriate temperature.

6.Moisture permeation test

- The USP requires determination of the moisture permeation characteristics of single-unit and unit-dose containers to ensure their suitability for packaging capsules.
- The degree and rate of moisture penetration are determined by packaging the dosage unit together with a color-revealing desiccant pellet, exposing the packaged unit to known relative humidity over a specified time, observing the desiccant pellet for color change (indicating the absorption of moisture), and comparing the pretest and posttest weight of the packaged unit.
- The difference in the weights gives the amount of moisture absorbed. An alternative method for the determination of moisture content of soft gelatin capsules is by toluene distillation method.

Inspecting, counting, packaging, and storing capsules

- Capsules produced on a small or a large scale should be uniform in appearance. Visual or electronic inspection should be undertaken to detect any flaws in the integrity and appearance of the capsules.
- Defective capsules should be rejected. In commercial manufacture, Current Good Manufacturing Practice regulations require that if the number of production flaws is excessive, the cause must be investigated and documented and steps undertaken to correct the problem.

- In the pharmacy, capsules may be counted manually or by automated equipment.
- Computer-based automated dispensing systems are also available that will fill, label, and check the drug using bar code or video systems
- On the industrial scale, solid dosage forms are counted by large automated pieces of equipment that count and transfer the desired number of dosage units into bulk containers.
- The containers are then mechanically capped, inspected visually or electronically, labeled, and inspected once more.
- Some filled containers are then placed in outer packaging cartons.

- Capsules are packaged in glass or in plastic containers, some containing packets of a desiccant to prevent absorption of excessive moisture.
- Capsules should be stored in tightly capped containers in a cool, dry place.
- The unit-dose and strip packaging of solid dosage forms, particularly by pharmacies that service nursing homes and hospitals, provides sanitary handling of the medications, ease of identification, and security in accountability for medications.

THANK YOU