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Review Article

In process quality control tests of solid dosage forms: a comprehensive review

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Abstract: Among all the dosage forms available solid dosageforms widely accepted among the patients of different age groups. Drugs with poor aqueous solubility and those which undergo degradation in aqueous medium can preferentially formulated as solid dosageforms which include tablets,capsules, powders etc. These provide improved patient compliance and enhanced pharmacokinetics and improved bioavalilabity compared to other dosageforms. The test which are performed during the manufacturing of product which include thickness, hardness, friability, dissolution time, disintegration time. Inprocess quality control test is necessary to insure the safety of finished pharmaceutical product. In the present study we analysted the quality control tests for tablets and capsules.
Keywords: tablets, capsules, pharmacokinetics, bioavalilabity.

INTRODUCTION

Tablets

Tablets are unit solid dosage forms in which one usual dose of the drug has been accurately placed.

Advantages

- Tablets are unit dosage forms and they offer the greatest capabilities of the all oral dosage forms for the greatest dose precision and the least content variability.
- Their cost is lowest of all oral dosage forms.
- They are the lightest and most compact of all oral dosage forms.
- They are in general easiest and cheapest to package and ship of all oral dosage forms.
- They are better suited to large scale production than other unit oral dosage forms.
- They may provide the greatest ease of swallowing with the least tendency for hang up above the stomach, especially when coated.

Disadvantages

- Some drugs resist compression into dense compacts
- Drugs with poor wetting, slow dissolution, intermediate to large dosages may be difficult or impossible to formulate and manufacture as a tablet that provide adequate or full drug bioavailability.
- Bitter taste drugs, drugs with an objectionable odor, or sensitive to oxygen or moisture may require encapsulation or entrapment prior to compression or the tablets may require coating.

Essential properties of tablets

- Accurate dosage of medicament, uniform in weight, appearance and diameter.
- Have the strength to withstand the rigors of mechanical shocks encountered in its production, packaging, shipping and dispensing
- Release the medicinal agents in the body in a predictable and reproducible manner
- Elegant product, acceptable size and shape ,Chemical and physical stabilities

TYPES OF TABLETS

Ingested orally:-Used in oral cavity

Compressed tablet
Buccal tablet
Multiple compressed tablet
Sublingual tablets
Modified release tablets
Lozenges
Enteric coated tablets
Dental cone
Sugar coated tablet
Film coated tablet
Chewable tablet
Targeted tablets

Used to prepare solution:-Administered by other route

Effervescent tablet
Implants
Dispensing tablet
Vaginal tablet
Hypodermic tablet

Multiple compressed tablets

Reasons

- To separate physically or chemically incompatible ingredients &
- To produce repeat action/ prolonged action tablet.

The tablet manufacturing machine is generally operated at relative lower speed than for standard compression tablet.

There are three categories under this class:

- **Layered tablets** – two to three component systems.
- **Compression coated tablets** – tablet within a tablet.
- **Inlay tablet** – coat partially surrounding the core.

The layered tablet is preferred over compression coated tablet as the surface contact is less and the production is simple and more rapid.

Multilayered tablets

Reason

When two or more active pharmaceutical ingredients are needed to be administered simultaneously and they are incompatible, the best option for the formulation pharmacist would be to formulate multilayered tablet.

- It consists of several different granulations that are compressed to form a single tablet composed of two or more layers and usually each layer is of different color to produce a distinctive looking tablet.
- Each layer is fed from separate feed frame with individual weight control. Dust extraction is essential during compression to avoid contamination. Therefore, each layer undergoes light compression as each component is laid down. This avoids granules intermixing if the machine vibrates [1].

For example

- Admixture containing Phenylephedrin HCL and Ascorbic Acid with Paracetamol.
- Paracetamol + phenylephedrine Hydrochloride → one layer
- Paracetamol + ascorbic acid → another layer.

Compression coated tablets

These tablets contain two parts, internal core and surrounding coat. Core is small porous tablet and prepared on one turret. For preparing final tablet, a bigger die cavity in another turret is used in which first the coat material is filled to half and then core tablet is mechanically transferred, again the remaining is filled with coat material and finally compression force is applied.

- This tablet readily lend itself in to a repeat action tablet as the outer layerprovides the initial dose while the inner core release the drug later on. But, when the core quickly releases the drug, entirely different blood level is achieved with the risk of over dose toxicity.
- To avoid immediate release of both the layers, the core tablet is coated with enteric polymer so that it will not release the drug in stomach while, the first dose is added in outer sugar coating [2].

Inlay tablets

A type of layered tablet in which instead the core tablets being completely surrounded by coating, top surface is completely exposed. While preparation, only the bottom of the die cavity is filled with coating material and core is placed upon it.

- When compression force is applied, some coating material is displaced to form the sides and compress the whole tablet.
- It has some advantages over compression coated tablets:
- Less coating material is required.
- Core is visible, so coreless tablets can be easily detected.
- Reduction in coating forms a thinner tablet and thus freedom from capping of top coating.

Modified release tablet

- Modified-released tablet is either uncoated or coated.
- This contains special additives or prepared by special procedure which, separately or together, is intended to modify the rate of release of the drug into the gastrointestinal tract.
- It prolongs the effect of drug and also reduces the frequency of administration of drug.
- Several drugs are available in modified release tablet like indomethacin.
- There is another term popularly known as pill.
- Once the people's idea was to use of pill in every ill. Now days the term has been only used in contraceptive preparations such as combination pill, mini pill, and morning after pill.

Enteric coated tablet

- Some drugs are destroyed by gastric juice or causes irritation to stomach. These two factors can be overcome by coating the table with cellulose acetate phthalate.
- This polymer is insoluble in gastric contents but readily dissolves in intestinal contents.
- So there is delay in the disintegration of dosage form until it reaches the small intestine.
- Like coated tablet, enteric coated tablet should be administered in whole form Broken or crushed form of the enteric coated tablet causes destruction of the drug by gastric juice or irritation to the stomach.
- Enteric coated tablet is comparatively expensive.

Sugar coated tablet

- The tablet that contains active ingredient(s) of unpleasant taste may be covered with sugar to make it more palatable.
- This type of tablet should be administered in whole form; otherwise the patient will experience the unpleasant taste of the active ingredient.

Film coated tablet

- The tablet that is covered with a thin layer or film of polymeric substance which protects the drug from atmospheric conditions and mask the objectionable taste and the odor of drug.

Chewable tablet

- The tablet which is intended to be broken and chewed in between the teeth before ingestion.
- Antacid and vitamin tablets are usually prepared as chewable tablets. It is given to the children who have difficulty in swallowing and to the adults who dislike swallowing [3].

Targeted tablets

- When we need to release the API at a specific site in the elementary tract, targeted drug delivery is a preferred option.
- Depending upon the composition and release mechanism of a tablet, the drug is delivered to a particular region.

Two types of tablet

- Gastro retentive Tablet
- Colonic tablets

Gastro retentive Tablet

- This type of dosage form is to be opted when API release is desired in stomach (Antacids, APIs used against H.pylori infection) or site of absorption is either stomach or upper part of small intestine.

To retain the drug for longer time period in stomach, following approaches can be used:

- Low density tablet (effervescent or non effervescent)
- Tablets that can expand in gastric environment (swelling or by unfolding) and thus increasing the size so that it cannot cross the pyloric sphincter.
- Using mucoadhesivepolymers that stick to mucosa of stomach and provide slow drug release.
- Drugs like Diazepam, Levodopa and Ciprofloxacin are successfully marketed in this formulation.

Colonic tablets

- When the aim is to deliver the drug into colon without dilution in other regions of gastrointestinal tract or the drug has poor absorption in stomach or small intestine, colonic drug delivery is preferred.
- The pH in this region varies from 6.4 - 7 and presence of microbial flora plays as important role in drug release especially in this region.
- Various mechanisms are adopted for drug release in this area are coating with pH sensitive polymer e.g., Eudragit®S100, Eudragit® L100, biodegradable polymer like polymers which are sensitive to colonic bacteria, bioadhesive polymers which selectively sticks to colonic mucosa.
  e.g., polycarbophils or polyethans, redox sensitive polymers that respond to redox potential in colon which expresses total metabolic & bacterial action [4].

TABLETS USED IN ORAL CAVITY

Buccal tablets

These are usually small and some what flat and are intended to be held between the cheek and teeth or in the cheek pouch. To provide effective absorption over a period of 15-30mins.

ADVANTAGES

- The gastric environment, where decomposition may be extensive. Eg: steroids and hormones.
- A more rapid onset of drug action occurs than for tablets that are swallowed. Eg: vasodilators.

Dental cones

Dental cones are a relatively minor tablet form that is designed to be placed in the empty socket remaining following a tooth extraction.

- There usual purpose is to prevent multiplication of bacteria in the socket.
- To reduce bleeding by containing as a astringent or coagulant.
- The usual vehicle of these tablets is sodium bicarbonate, sodium chloride, amino acid.

- To provide effective absorption over a period of 20-40mins [5].

Sublingual tablet

The drug which is destroyed or inactivated within the gastrointestinal tract but can be absorbed through the mucosal tissue of the oral cavity is usually given in this formulation. The tablet is required to be placed below the tongue for then slow release of drug. But for immediate effect some medicaments are formulated in such a way to dissolve within 1 to 2 minutes. Nitroglycerin is prepared in this formulation.

Lozenge tablet

The tablet that is intended to produce continuous effect on the mucous membrane of the throat. There is no disintegrating agent. The quality of the binding agent is increased so as to produces low dissolution. Suitable sweetening (sugar), coloring and flavoring agent must be including in this formulation. Gum is used to give strength and cohesiveness to the lozenge and facilitating slow release of the active ingredient.

Soluble tablet

The tablet that dissolves completely in liquid to produce solution of definite concentration. Mouth wash, gargle, skin lotion, douche; antibiotic, certain vitamins, and aspirin are given along with this formulation.

TABLETS USED TO PREPARE SOLUTION

Effervescent tablets

- The tablet that contains acid substances and carbonate or hydrogen carbonate that react rapidly in the presence of water to release carbon dioxide.
- Sodium bicarbonate, citric acid and tartaric acid are added to the active ingredients to make the tablet effervescent. This preparation makes the tablet palatable.

Dispensing tablets

These are intended to be added to a given volume of water by the pharmacist or consumer to produce a solution of a given drug concentration.

- Materials that have a incorporated in dispensing tablets include mild silver proteinate, bichloride of mercury.
- Great care must be taken in the packaging and labelling of such tablets to attempt to prevent their oral consumption.
- In the past, bichloride of mercury was usually prepared in cotton shaped tablets with an embossed skull and cross bones to emphasize its toxicity [6].

Hypodermic tablets

These are composed of one or more drugs with other readily water soluble ingredients and are intended to be added to sterile water.

- These are little used today because their use increases the likely hood of administering a non sterile solution.
- The advantage of portability of tablets for injection is for outweighed by hazards.

TABLETS ADMINISTERED BY OTHER ROUTES

Implant

- A small tablet that is prepared for insertion under the skin by giving a small surgical cut into the skin which is stitched after the insertion of the tablet.
- This tablet must be sterile.
- The drug used in this preparation is usually water insoluble and the tablet provides a slow and continuous release of drug over prolonged period of time ranging from 3 to 6 months or even more.
- Contraceptive tablet is formulated as implant.

Vaginal tablet

- These are designed to undergo slow dissolution and release in the vaginal cavity.

  Ex: Clotrimazole tablets.

Evaluation of tablets

General Appearance

The general appearance of a tablet, its identity and general elegance is essential for consumer acceptance, for control of lot-to-lot uniformity and tablet-to-tablet uniformity. The control of general appearance involves the measurement of size, shape, color, presence or absence of odor, taste etc [7].

Size& Shape

The shape and dimensions of compressed tablets are determined by the type of tooling during the compression process. At a constant compressive load, tablets thickness varies with particle size distribution and packing of the powder mix being compressed and with tablet weight. Tablet thickness is consistent from batch to batch or within a batch only if the tablet granulation or powder blends is adequately consistent in particle size and particle size distribution, if the punch tooling is of consistent length, and if the tablet press is clean and in good working condition. It can be dimensionally described & controlled. The thickness of a tablet is only variables. Tablet thickness can be measured by micrometer or by other device. Tablet thickness should be controlled within a ± 5% variation of standard value.

Unique identification markings

These marking utilize some form of embossing, engraving or printing. These markings include company name or symbol, product code, product name etc.

Organoleptic properties

Color is a vital means of identification for many pharmaceutical tablets and is also usually important for consumer acceptance. The color of the product must be uniform within a single tablet, from tablet to tablet and from lot to lot. Non uniformity of coloring not only lack esthetic appeal but could be associated by the consumer with non uniformity of content and general poor product quality. Non uniformity of coloring is usually referred to as mottling. Color distribution must be uniform with no mottling. For visual color comparison compare the color of sample against standard color [8].

Hardness

Hardness of Tablets Hardness may be defined as the resistance of tablets to capping, abrasion or breakage under conditions of storage, transportation and handling. Tablet hardness has been associated with other tablet properties such as density and porosity. Hardness generally increases with normal storage of tablets and depends on the shape, chemical properties, binding agent and pressure applied during compression. It is non-official quality control method. It is not prescribed by I.P. Hardness test: The small and portable hardness tester was manufactured and introduced by Monsanto in the Mid1930s. It is now designated as either the Monsanto or Stokes hardness tester. The instrument measures the force required to break the tablet when the force generated by a coil spring is applied diametrically to the tablet. Hardness generally measures the tablet crushing strength. Various devices used to test hardness are: Monsanto tester, Pfizer tester, Strong-cobb tester and schleuniger tester, erweka tester.

Fig-1: Monsanto Hardness tester

Pfizer tester

Fig-2: Pfizer tester

- It works on the mechanical principle as a pair of pliers.
- Tablet is compressed between holding anvil & a piston connected to the direct force reading guage.

Erweka tester

- Tablet is placed on the lower anvil & the anvil is adjusted so that the tablet just touches the upper test anvil

Fig-3: Erweka tester

Schleuniger tester

Fig-4: Schleuniger tester

- Operates in horizontal position
- An anvil is driven by an electric motor presses the tablet at a constant load rate against a stationary anvil until the tablet breaks

Friability

It is may be defined as the excessive breakness of tablets during mechanical shocks of handling in manufacture, packaging, and shipping. Friction and shock are the forces that most often cause tablets to chip, break. Why we test friability? Tablet hardness is not absolute indicator of strength since some formulations, when compressed into very hard tablets, tend to “cap” on attrition, losing there crown portions. Therefore another measure of tablets strength, its friability is often measured. They not only lack elegance and consumer acceptance but also spoil the areas of manufacturing such as coating and packaging. In friability test the tablets are prone to abrasion hence enabling us to check for the tablet strength under application of force in different manner. Friability is affected by various external and internal factorslike:1) Punches that are in poor condition or worn at their surface edges, resulting in ‘whiskering’ at the tablet edge and show higher than normal friability values. Friability of a tablet can determine in laboratory by

Roche friabilator. This consist of a plastic chamber that revolves at 25 rpm, dropping the tablets through a Distance of six inches in the friabilator, which is then operate for 100 revolutions. The tablets are reweighed. Compress tablet that lose less than 0.1 to 0.5 % of the Tablet weigh are consider acceptable [9].

Fig-5: Friability apparatus

Weight Variation test (U.S.P.)

Tablet weight is mainly affected by factors such as tooling of the compression machine, head pressure, machine speed and flow properties of the powder. Inconsistent powder or granulate density and particle size distribution are common sources of weight variation during compression. Variation between tablet with respect to dose and weight must be reduced to a minimum. Uniformity of weight is an in process test parameter which ensures consistency of dosage units during compression. Take 20 tablets and weighed individually. Calculate average weight and compare the individual tablet weight to the average. The tablet pass the U.S.P. test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit [10].

Table-1: I.p limits for weight variation of tablets

IP/BP	Limit	USP
80 mg or less	10%	130mg or less
More than 80mg or Less than 250mg	7.5%	130mg to 324mg
250mg or more	5%	More than 324mg

Content Uniformity Test

The content uniformity test is used to ensure that every tablet contains the amount of drug substance intended with little variation among tablets within a batch. Due to increase awareness of physiological availability, the content uniformity test has been included in the monographs of all coated and uncoated tablets and al capsules intended for oral administration.

Randomly select 30 tablets. 10 of these assayed individually. The Tablet pass the test if 9 of the 10 tablets must contain not less than 85% and not more than 115% of the labeled drug content and the 10th tablet may not contain less than 75% and more than 125% of the labeled content. If these conditions are not met, remaining 20 tablets assayed individually and none may fall outside of the 85 to 115% range.

Disintegration Test (U.S.P.)

For a drug to be absorbed from a solid dosage form after oral administration, it must first be in solution, and the first important step toward this condition is usually the break-up of the tablet; a process known as disintegration. The time of disintegration is a measure of the quality. This is because, for example, if the disintegration time is too high; it means that the tablet is too highly compressed or the capsule shell gelatin is not of pharmacopoeial quality or it may imply several other reasons. And also if the disintegration time is not uniform in a set of samples being analysed [12], it indicates batch inconsistency and lack of batch uniformity. The U.S.P. device to test disintegration uses 6 glass tubes that are 3" long; open at the top and 10 mesh screens at the bottom end. To test for disintegration time, one tablet is placed in each tube and the basket rack is positioned in a 1-L beaker of water, simulated gastric fluid or simulated intestinal fluid at 37 ± 20 C such that the tablet remain 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement. Move the basket containing the tablets up and down through a distance of 5-6 cm at a frequency of 28 to 32 cycles per minute. Floating of the tablets can be prevented by placing perforated plastic discs on each tablet.According to the test the tablet must disintegrate and all particles must pass through the 10 mesh screen in the time specified. If any residue remains, it must have a soft mass [11].

Fig-6: Disintegration apparatus

Table-2: disintegration limits for tablets

Uncoated	15 minutes
Plain coated tablet	60 minutes
Enteric coated tablet	3 hours
Dispersible tablet	3minutes
Effervescent tablet	< 3 minutes
Sublingual tablet	4 hours
Buccal tablet	4 hours
Vaginal tablet	60minutes
chewable tablet	not required

Dissolution Test

Dissolution is the process by which a solid solute enters a solution. Dissolution is pharmaceutically defined as the rate of mass transfer from a drug substance into the dissolution medium or solvent under standardized conditions of liquid/solid interface, temperature and solvent composition. It is a dynamic property that changes with time and explains the process by which a homogenous mixture of a solid or a liquid can be obtained in a solvent. It happens to chemically occur by the crystal break down into individual ions, atoms or molecules and their transport into the solvent. Dissolution is considered one of the most important quality control tests performed on pharmaceutical dosage forms and is now developing into a tool for predicting bioavailability, and in some cases, replacing clinical studies to determine bioequivalence. Two types of apparatus are generally used to carry out dissolution [12].

Apparatus-1 (Basket Type)

A single tablet is placed in a small wire mesh basket attached to the bottom of the shaft connected to a variable speed motor. The basket is immersed in a dissolution medium (as specified in monograph) contained in a 1000 ml flask. The flask is cylindrical with a hemispherical bottom. The flask is maintained at 37±0.50C by a constant temperature bath. The motor is adjusted to turn at the specified speed and sample of the fluid are withdrawn at intervals to determine the amount of drug in solutions.

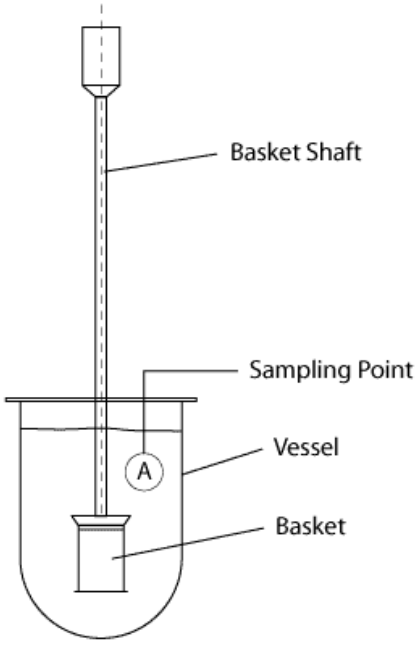

Fig-7: Basket type apparatus

Apparatus-2 (Paddle Type)

It is same as apparatus-1, except the basket is replaced by a paddle. The dosage form is allowed to sink to the bottom of the flask before stirring. For dissolution test U.S.P. specifies the dissolution test medium and volume, type of apparatus to be used, rpm of the shaft, and time limit of the test and assay procedure for.

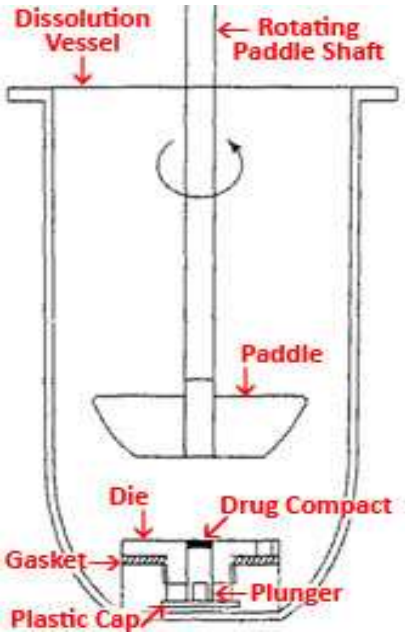

Fig-8: Paddle type apparatus

Fig-9: Dissolution apparatus paddle type

The test tolerance is expressed as a % of the labeled amount of drug dissolved in the time limit.

Dissolution testing can be continued in three stages if necessary.

- In stage 1(S1), six tablets are tested and are acceptable if all of the tablets are not less than the monograph tolerance limit (Q) plus 5%.
- If the tablets fail S1, an additional six tablets are tested (S2). The tablets are acceptable if the average is tested. The tablets are acceptable if the average of the twelve tablets is greater than

or equal to Q and no unit is less than Q minus 15%.

- If the tablets fail the test an additional 12 tablets are tested. The tablets are acceptable if the average of all 24 tablets is greater than or equal to Q and no unit if no more than 2 tablets are less than Q minus 15%.

TYPE III: RECIPROCATING CYLINDER DESIGN

- **Vessel-** cylindrical flat bottom glass vessel.
- **Agitation type-** reciprocating generally 5 to 35 RPM
- **Volume of dissolution fluids**-200 – 250 ml
- **water bath-** maintained at 37± 0.5 ˚c
- **Use-** extended release eg : chloramphenicol, chewable tablets eg : carbamazepine

Fig-10: RECIPROCATING CYLINDER

Type IV: FLOW THROUGH CELL
DESIGN
Reservoir- For dissolution medium
Pump: forces dissolution medium through cellholds the sample
Flow rate:10 – 100 ml / min
Laminar flow is maintained peristalic / centrifugal pumps are not recommended
Water bath 37± 0.5 ˚c

Fig-11: Flow through cell apparatus

TYPE V: PADDLE OVER DISC
DESIGN
Sample holder

Disc assembly that holds the product in such a way that release surface is parallel with paddle; Paddle is directly attached over disc assembly. Samples are drawn away between the surface of medium & top of the paddle blade

Volume: 900ml

Water bath: 32 ˚c

TYPE VI: ROTATING CYLINDER
DESIGN
Vessel:-In place of basket, cylinder is used

Cylinder:-Stainless steel 316

Sample:-Mounted to cuprophan(inner porous cellulosic material) an entire system is adhering to cylinder. Dosage unit is placed in cylinder & released from outside water bath maintained at 37± 0.5˚c

Use:-Transdermal patches

TYPE VII: RECIPROCATING DISC
Vessel:-Flat bottom cylindrical vessel, volume of dissolution medium 50 – 200ml. Sample is placed on disc shaped holders

Agitation:-Reciprocation
Reciprocating frequency 30 cycles / min

Water bath:-Maintained at 37± 0.5 ˚c

Use:-Transdermal patches

Introduction to capsules

These are unit solid dosage forms of medicament in which the medicament is enclosed in either soft or hard soluble shell of a suitable grade of gelatin.

Advantages

- Capsule dosage forms mask the taste or odour of objectionable substance.
- More attractive in appearance.
- They become slippery when moist. A properly stored capsule shell contains 12 to 15% of moisture.
- It provides flexibility to shell and more resistance to mechanical shocks.
- Less number of adjuvant is required. Processing problems are reduced.
- Shells are either opacified or colored ones which protect from light.
- If you encapsulate drugs in powdered form, bioavailability of drugs is more.

- The shells are made to very fine levels; capsules will not allow entry of air and moisture.
- Softening the Gastro intestinal tract, shells are inert, easily digested in GIT and physiologically inert.

Disadvantages

- Capsules are not usually administered for highly soluble drugs like Potassium bromide, Potassium chloride and Ammonium chloride.
- Capsules should not be used for efflorescent, deliquescent and hygroscopic materials.
- More complicated machinery is required for large scale.
- Cost is more.

Types of capsules

Based on type of Gelatin shell used capsules are of two types

- Hard Gelatin Capsules
- Soft Gelatin Capsules

Fig-13: Hard gelation capsules

Hard Gelatin Capsules

- Prepared from Gelatin blends, contains certified dyes, coloring agents, opasifying agents, plasticizers, preservatives.
- Also made from ethyl cellulose, polyvinyl alcohol, for solubulising and enteric release of drugs.
- Basic component is Gelatin derived by irreversible hydrolytic extraction of animal collagen.
- The chemical and physical properties of Gelatin depends upon
  Type of collagen used
  Source of collagen
  pH value, Chemical properties
  Method of extraction
  Thermal degradation
  Electrolyte concentration
- Common sources of collagen are pork skin and animal skin
- Two basic types Gelatin are available
  Type A
  Type B

Type A

- It is produced by acid hydrolysis and usually manufactured from pork skin. It produces clear and flexible film.
- This is having an isoelectric point at pH 9

T ype B

- It is produced by alkaline hydrolysis and manufactured from animal bone.
- It is having an isoelectric point at pH 4 to 7

Table-3: Different sizes of capsules

Size	Volume (ml)	Weight (gm)
000	1.37	1.096
00	0.95	0.760
0	0.68	0.544
1	0.5	0.400
2	0.37	0.296
3	0.3	0.24
4	0.21	0.168
5	0.13	0.104

Soft Gelatin Capsules

Advantages

- Used as oral dosage forms of medicament for human and veterinary use.
- As suppository dosage form of medicament for rectal/vaginal use. Available in different shapes.
- As special package in tube form used in humans and veterinary as single dose purpose for topical, ophthalmic, rectal ointments and oral administration.
- In cosmetic industry, they are used as special package for drug fresheners, perfumes, bath oils, suntan oils, and various skin creams.
- Some are filled with liquids are usually advantageous.
- Rapid release of content and so increased bio availability is seen with liquid capsules [11].

Disadvantages

- Requires special filling equipment and suitable experienced persons.
- Material is filled in capsules and outside shell packing is done simultaneously. This can be transformed to soft gelatin and return back to manufacturers after filling hence expensive.
- There will be close contact between shell and inner liquid so that, the inner ingredients sometimes migrate into shell and vice versa thus interactions develop. Drugs sometimes migrate from oily liquid into capsule shell, due to partition coefficient factor [12].

Soft Gelatin Capsules

Fig-14: Soft Gelatin capsules

It mainly composed of the following

Shapes and Sizes

- Round, oval, oblong, tube and other miscellaneous shapes.

Round – Available from 1 to 90 minims
Oval - Ranges from 1 to 110 minim
Oblong- 1 to 360 minims
Tube - 5 to 480 minims

- The maximum shape and size for human use is
  20 minims oblong
  16 minim oval
  9 minims round

SHAPES OF SOFT GELATIN CAPSULES

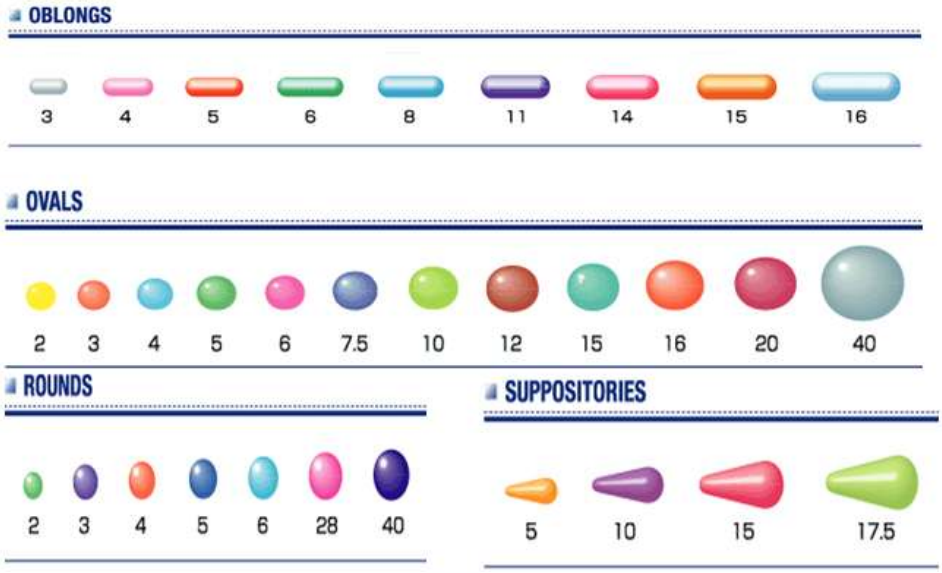

Fig-14: Different sizes of soft gelatin capsules

Evaluation of Capsules

Finished capsules are evaluated by following tests

1. Weight variation test
2. Content uniformity test
3. Dissolution test
4. Disintegration test

Weight variation test

- 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 individual's 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
- To weigh capsules we use Rotoweigh and Varicap 1200

Content Uniformity test

- 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 10^{th} 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 [13].

Disintegration Test

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 [14].

Fig-15: Disintegration tests for capsules

Dissolution Test

Procedure

Place the stated volume of the dissolution medium (± 1 per cent) in the vessel of the specified apparatus. Assemble the apparatus, equilibrate the dissolution medium to 37 ± 0.5 °C, and remove the thermometer. The test may also be carried out with thermometer in place, provided it is shown that results equivalent to those obtained without the thermometer are obtained.

Place 1 dosage unit in the apparatus, taking care to exclude air bubbles from the surface of the dosage unit. Operate the apparatus at the specified rate. Within the time interval specified, or at each of the times stated, withdraw a specimen from a zone midway between the surface of the dissolution medium and the top of the rotating basket or blade, not less than 1 cm from the vessel wall, where multiple sampling times are specified, replace the aliquots withdrawn for analysis with equal volumes of fresh dissolution medium at 37 °C or, where it can be shown that replacement of the medium is not necessary, correct for the volume change in the calculation. Keep the vessel covered for the duration of the test and verify the temperature of the medium at suitable times. Perform the analysis using a suitable assay method. Repeat the test with additional dosage units.

If automated equipment is used for sampling or the apparatus is otherwise modified, verification that the modified apparatus will produce results equivalent to those obtained with the apparatus described in this chapter, is necessary[15].

Dissolution medium

A suitable dissolution medium is used. The volume specified refers to measurements made between 20 °C and 25 °C. If the dissolution medium is a buffered solution, adjust the solution so that its pH is within 0.05 units of the specified pH. Dissolved gases can cause bubbles to form, which may change the results of the test. In such cases, dissolved gases must be removed prior to testing [4] .

Time

Where a single time specification is given, the test may be concluded in a shorter period if the requirement for minimum amount dissolved is met. Samples are to be withdrawn only at the stated times, within a tolerance of ± 2 percent

Fig-16: Dissolution test for capsules

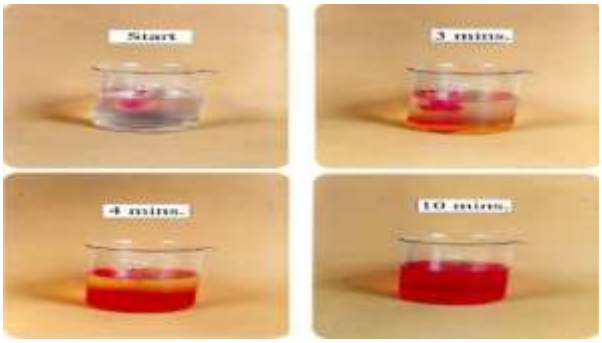

Fig-17: dissolution mechanism of capsules

CONCLUSION

The quality control testing is assigned to production or quality control depending on the company basis of large scale and small scale. The Quality executives evaluate the quality tests of the tablets to pass the products into markets. These are regularly checked by the RA and FDA bodies. The Quality tests are performed as discussed above, these tests brings out the errors, and misbranded and bad quality products. The standard of the products are based upon this analysis and results of the tests which achieve therapeutic and quality goals. It is the duty of the of the pharmaceutical companies to manufacture the dosage forms which can sustain rattling and handling to have more shelf life and demand in the pharmaceutical market

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