

**A most convenient and patient compliance dosage form- Tablet****Rajiv Kumar¹, Kiranjeet Kaur Batth², Jaspreet Kaur³, Jaspreet Kaur^{4*}, Parminder Nain⁵, R.K. Dhawan⁶**^{1,2,3,6}Khalsa College of Pharmacy, Amritsar, Punjab, India^{4,5}Maharishi Markandeshwar University, Mullana, Ambala, Harayana, India**Article Info:** Received 05 November 2020; Accepted 10 December. 2020**DOI:** <https://doi.org/10.32553/jbpr.v9i6.815>**Corresponding author:** Jaspreet Kaur**Conflict of interest statement:** No conflict of interest**Abstract:**

Tablet is defined as solid pharmaceutical dosage form containing drug substance generally with suitable diluents and prepared by either compression which is given as a single unit and are known as solid unit dosage form. Tablets remain popular as a dosage form because of the advantages afforded, both to the manufacturer (e.g. simplicity and economy of the preparation, stability, and convenience in packing, shipping and dispensing) and the patient. The excipients include diluents, Binders and adhesives, disintegrates, etc. Tablets vary in shape and differ greatly in size and weight depending on the amount of the medicinal substance. The ingredients must be granulated prior to compression to assure an even distribution of the active compound in the final tablet. There are two basic techniques which can be used to granulate powders for compressions into a tablet are wet granulation and dry granulation. In this review article tablet manufacturing and evaluation have been discussed.

Keywords- Tablet, Granulation, Picking and sticking, Dissolution test, weight variation**Introduction:**

Tablets are defined as a compressed solid dosage form containing medicaments with or without excipients. According to the Indian Pharmacopoeia Pharmaceutical tablets are solid, flat or biconvex unit dosage form, prepared by compressing a medicament or a blend of medicament, with or without various types of excipients. They vary in shape and differ greatly in size and weight, depending on dose of medicaments and the intended mode of administration. It is the most popular dosage form and 70% of the total medicines are formulated in the form of tablet. Tablets are prepared primarily by compression of granules or powder blends, with a limited number prepared by moulding technique. Most tablets are used in the oral administration of drugs. Many of these are prepared with colourants and coatings of various types. Other tablets, such as sublingual, buccal, or vaginal tablets, are prepared to have features most applicable to their particular route of administration^{1,2}.

General properties of tablets:

- A tablet must be strong and hard to withstand mechanical shock during manufacturing, packing, shipping, dispensing and use.
- The drug content of the tablet must be bioavailable i.e; the tablet must be able to release its content in a predictable and reproducible manner.
- The tablet must be chemically and physically stable to maintain its chemical and physical attributes during manufacture, storage, and use.
- The tablet should have elegant product identity which is free from any tablet defect.

- Tablets must be uniform in weight and in drug content^{3,4}.

Advantages of tablets:

1. They are unit dosage form and offer the greatest capabilities of all oral dosage form for the greatest dose precision and the least content variability.
2. Cost is lowest of all oral dosage form.
3. Lighter and compact.
4. Easiest and cheapest to package and strip.
5. Easy to swallowing with least tendency for hang-up.
6. Sustained release product is possible by enteric coating.
7. Objectionable odour and bitter taste can be masked by coating technique.
8. They are better suited to large-scale production than other unit oral forms.
9. They have the best-combined properties of chemicals, mechanical and microbiologic stability of all the oral forms.
10. Product identification is easy and rapid requiring no additional steps when employing an embossed and/or monogrammed punch face.

Disadvantages of tablet

1. Difficult to swallow in case of children and unconscious patients.
2. Some drugs resist compression into dense compacts, owing to amorphous nature, low density character.
3. Drugs with poor wetting, slow dissolution properties, optimum absorption high in GIT may be

difficult to formulate or manufacture as a tablet that will still provide adequate or full drug bioavailability.

4. Bitter tasting drugs, drugs with an objectionable odor or drugs that are sensitive to oxygen may require encapsulation or coating. In such cases, capsule may offer the best and lowest cost^{5, 6}.

Type of tablets

1. Compression tablet- Compressed tablets are formed by compression of powdered, crystalline, or granular materials into the required geometry by the application of high pressures, utilizing punching machine. In addition to the Active Pharmaceutical Ingredient(s) (APIs), compressed tablets usually contain a number of pharmaceutical excipients e.g., bulking agents, disintegrants, binders, lubricants, controlled-release polymers and other miscellaneous adjuncts such as colourants and flavourants which serve different and specialized purpose during tablet manufacture, storage, and use.

2. Sugar Coating tablets- These are compressed tablets that have been coated with concentrated sugar solution to improve patient's compliance, increase aesthetic appeal, mask objectionable tastes or odours, increase stability and/or modify the release of therapeutic agent(s). Sugarcoating was once quite common but lost commercial appeal due to the time and expertise required in the coating process, the increase in size and weight of coated tablets, high cost of process validation and shipping.

3. Film-coated tablets- Film-coated tablets are conventional tablets coated with a thin layer of polymer (e.g., hydroxypropyl methylcellulose, hydroxypropyl cellulose) or a mixture of polymers (e.g., Eudragit E100) capable of forming a skin-like film. The film is usually coloured and also impacts the same general characteristics as sugar coating with the added advantage of being more durable, less bulky, and less time-consuming to apply. By its composition, the coating is designed to break and expose the core tablet at the desired location in the gastrointestinal tract.

4. Effervescent tablets- Effervescent tablets are uncoated tablets that generally contain organic acids (such as tartaric or citric acid) and sodium bicarbonate in addition to the medicinal substance or API. They react rapidly in the presence of water by releasing carbon dioxide which acts as a disintegrator to produce either a drug suspension or an aqueous solution. These tablets are prepared by compressing granular effervescent salts (organic acid and bicarbonate) with the medicinal substances.

5. Enteric-coated tablets- Enteric-coated tablets are compressed tablets that have delayed-release properties. They are coated with polymeric substances (such as cellulose acetate phthalate/cellulose acetate butyrate; hydroxypropylmethylcellulose succinate; and methacrylic acid copolymers) that resist solution in

gastric fluid but disintegrate and allow drug dissolution and absorption in the intestine. Enteric coatings are primarily employed when the drug substance is inactivated or destroyed by gastric acid (e.g., erythromycin) or are particularly irritating to the gastric mucosa (e.g., non-steroidal anti-inflammatory drugs) or when bypass of the stomach substantially enhances drug absorption.

6. Chewable tablets- Chewable tablets are big sized tablets which are difficult to swallow and thus, are chewed within the buccal cavity prior to swallowing. They are especially useful for administration of large tablets to children and adults who have difficulty swallowing conventional tablets or antacid formulations in which the size of the tablet is normally large and the neutralization efficacy of the tablet is related to particle size within the stomach.

7. Buccal and sublingual tablets- Buccal and sublingual tablets are small, flat, oval tablets that are intended to be dissolved in the buccal pouch (buccal tablets) or beneath the tongue (sublingual tablets) for absorption through the oral mucosa to produce a systemic effect. These tablets are employed to achieve either rapid absorption into the systemic circulation or, alternatively, to enable oral absorption of drugs that are destroyed by the gastric juice and/or are poorly absorbed from the gastrointestinal tract.

8. Lozenges- These are disc-shaped solid preparations containing medicinal agents and generally a flavouring substance in a hard candy or sugar base. They are intended to be slowly dissolved in the oral cavity, usually for local effects.

9. Tablet triturates- Tablet triturates are small, usually cylindrical, moulded, or compressed tablets containing small amounts of usually potent drugs mixed with a combination of sucrose and lactose or any suitable diluent. They are prepared from moist material, using a triturate mould that gives them the shape of cut sections of a cylinder. Since tablet triturates must completely and rapidly dissolve in water, only a minimal amount of pressure is applied during their manufacture.

10. Hypodermic tablets- Hypodermic tablets are soft, readily soluble tablets that were originally used by physicians in extemporaneous preparation of parenteral solutions. These tablets are dissolved in a suitable vehicle (water for injections) and administered by parenteral route. Hypodermic tablets are no longer used in most countries due to the difficulty in achieving sterility. Also, the availability of stable parenteral solutions and prefabricated injectable products, some in disposable syringes have also discouraged their use in recent times

11. Gelatin-coated tablets- Gelatin-coated tablets are compressed tablets coated with either one or two-toned colour gelatin. The gelatin coating impacts the same general characteristics as sugar coating and film coating with the added advantage of improving the stability of photosensitive APIs. The gelatin coating also facilitates

swallowing, enables custom branding, and prevents counterfeit since they are more tamper-evident than unsealed capsules. Gelatin-coated tablets are also ideal for double-blind clinical studies, or for drug substances that can irritate the oesophageal mucosa when they are incorporated in an immediate-release tablet such as bisphosphonates.

12. Layered tablets- They are tablets composed of two or more layers of ingredients. Layered tablets are prepared by compressing additional tablet granulation on a previously compressed granulation to form two-layered or three-layered tablets, depending on the number of separate fills. Each layer may contain a different medicinal agent, separated for reasons of physical or chemical incompatibility, staged drug release, or simply the unique appearance of the layered tablet.

13. Immediate-Release tablets- Immediate-release tablets are tablets designed to disintegrate and release their medication with no special rate-controlling features, such as special coatings and other techniques. This is the most common type of tablet and examples include chewable, effervescent, sublingual and buccal tablets.

14. Rapid-release tablets- Rapid-release tablets, also called rapidly dissolving tablets, rapidly disintegrating tablets, orally-dispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast-dissolving tablets, rapid-dissolving tablets, or porous tablets are characterized by disintegrating or dissolving in the mouth within 1 minute, some within 10 seconds, leaving an easy-to-swallow residue.

15. Extended-release tablets- Extended-release tablets also called controlled-release tablets, prolonged-release, delayed release or sustained release tablets are tablets designed to release their medication in a predetermined manner over a prolonged period of time. These tablet types are categorized into

- Those that respond to some physiological condition to release the drug, such as enteric coatings;
- Those that release the drug in a relatively steady, controlled manner; and
- Those that combine combinations of mechanisms to release pulses of drug such as repeat action tablets.

16. Vaginal tablets- Vaginal tablets are uncoated, bullet-shaped, or ovoid tablets designed for vaginal administration. They are prepared by compression and are shaped to fit tightly on plastic inserter devices that accompany the product. Following insertion, retention and slow dissolution of the tablet occur, releasing the medicaments to provide the local pharmacological effect (e.g. for the treatment of bacterial or fungal infection). Vaginal tablets may also be used to provide systemic absorption of therapeutic agents⁵⁻⁸.

Formulation of tablet dosage form

In tablet formulation, many excipients are usually combined at various quantities to produce a tablet that is

of good standard. These excipients serve different and specialized functions in the tablet. The type and quantity of each raw material used is dependent on the intended tablet type and formulation technique.

1. Diluents': Diluents are fillers used to make required bulk of the tablet when the drug dosage itself is inadequate to produce the bulk. Secondary reason is to provide better tablet properties such as improve cohesion, to permit use of direct compression manufacturing or to promote flow. e.g., anhydrous lactose, spray dry lactose, microcrystalline cellulose, corn starch, dicalcium phosphate, calcium sulfate, lactose, cellulose, kaolin, mannitol, sodium chloride, etc.

2. Binders and Adhesives: These materials are added either dry or in wet- form to form granules or to form cohesive compacts for directly compressed tablet. e.g., include acacia gum, tragacanth, corn starch, methylcellulose, gelatin, ghatti gum, mucilage of isapol husks, carboxy methylcellulose, methylcellulose, polyvinyl pyrrolidone and sugars, such as sucrose, glucose, dextrose, molasses, and lactose etc.

3. Disintegrants: It facilitates tablet breaking or disintegration when it contact in water in the GIT. e.g., starch, clays, celluloses, algins, gums, and cross-linked polymers (croscarmellose, crospovidone, and sodium starch glycolate) etc.

4. Lubricants: Lubricants are intended to prevent adhesion of the tablet materials to the surface of dies and punches, reduce inter particle friction and improves the rate of flow of the tablet granulation. e.g., metallic stearate (0.1-0.2 % w/w) e.g., magnesium stearate, calcium stearate, stearic acid (0.25-1 %), hydrogenated vegetable oil, corn starch, boric acids, sodium chloride, sodium lauryl sulphate etc

5. Glidants: Glidants are intended to promote flow of granules or powder material by reducing the friction between the particles. e.g., colloidal silicon dioxide Cab-o-sil (Cabot), Talc (asbestos-free) etc.

6. Coloring agents: Colors and dyes are used in tablet for masking of off-color drugs, improves appearance of the product and product identification. e.g., FD&C Blue No. 1, FD&C Blue No. 2, FD&C Green No. 3, D&C Green No. 5, D&C Red No. 6, D&C Red No. 21. D&C Red No. 22, D&C Red No. 27 etc.

7. Flavoring agents: It imparts flavour to the tablet and used to mask unpleasant taste of the drug. e.g., Aspartame, vanilla, Mint, Cherry, etc.

8. Sweetening agents: They are added to make the ingredients more palatable, especially in chewable tablets such as antacid or liquids like cough syrup. Sugar can be used to mask unpleasant tastes or smells⁹⁻¹¹.

Manufacturing of tablets

The design and manufacture of pharmaceutical tablets is a complex multi-stage process whereby formulation scientists ensure that the correct amount of drug

substance in the right form is delivered at the appropriate time, at the proper rate and in the desired location with its chemical integrity protected to that point. Pharmaceutical products are processed all over the world using the direct compressing, wet granulation, or dry granulation methods. Method chosen depends on the ingredients' individual characteristics like flow property, compressibility etc. Right choice of method requires thorough investigation of each proposed ingredient in the formula for comprehensive approach for interactions and stability¹².

The primary goals include:

1. To formulate tablets that are strong and hard to withstand mechanical shock encountered during manufacturing, packing, shipping, dispensing and use.
2. To formulate tablets that is uniform in weight and in drug content.
3. To formulate tablets that is bioavailable according to indication requirements.
4. To formulate tablets that is chemically and physically stable over a long period of time.
5. To formulate tablets that have elegant product identity which is free from any tablet defects?

Direct compression method

The processing of drug with excipients can be achieved without any need of granulation and related unit operations. By simply mixing in a blender, formulation ingredients can be processed and compressed into tablets without any of the ingredients having to be changed. This procedure is called direct compression and it is used in the manufacture of tablets when formulation ingredients can flow uniformly into a die cavity.

Weighing of active and excipients



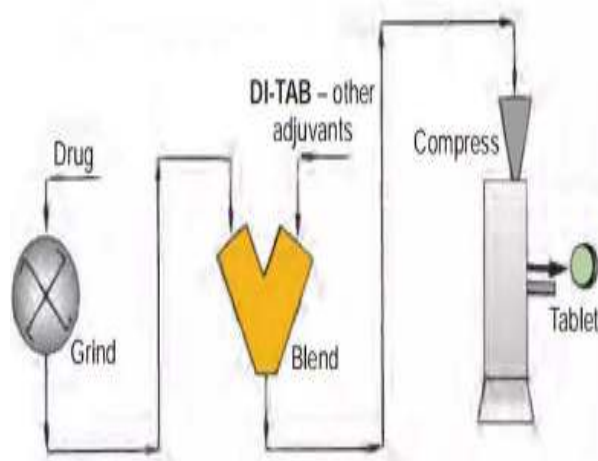
Mixing of all ingredients



Milling or Sieving



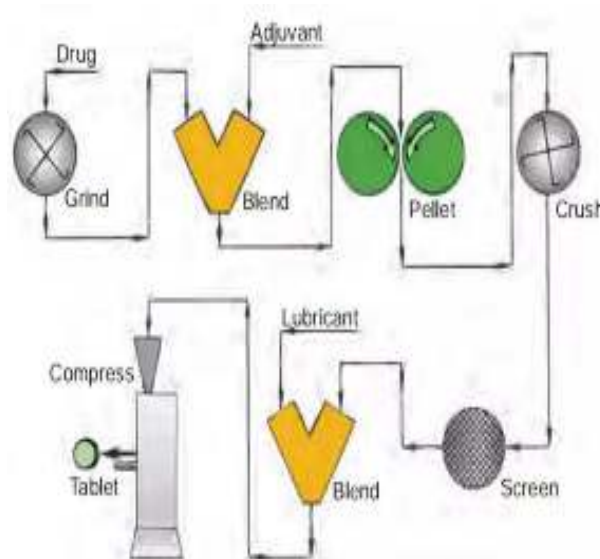
Discharge for compression



Main advantages of direct compression are time saving, safety of operations and low cost¹³⁻¹⁴.

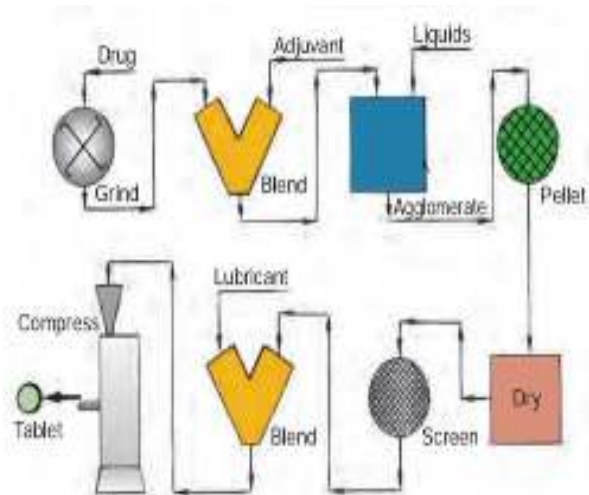
Dry Granulation method

The dry granulation process is used to form granules without using a liquid solution. This type of process is recommended for products, which are sensitive to moisture and heat. Forming granules without moisture requires compacting and densifying the powders. Dry granulation can be done on a tablet press using slugging tooling. On large-scale roller compactor commonly referred to as a chilsonator. The compacted mass is called slugs and the process is known as slugging. The slugs are then screened or milled to produce a granular form of tablet materials, which have the good flow properties than original powder mixture. The main advantage of dry granulation is it requires less equipment and eliminates the addition of moisture and the application of heat, as found in wet massing and drying steps of the wet granulation method¹⁴⁻¹⁵.



Wet granulation method

This is the most widely used method of tablet preparation. In this method the powders are bound by suitable binder by "adhesion". The binder is added by diluting with suitable solvent prior to addition to the blended powders to form wet granules which in turn are dried suitably to expel the solvent forming dried granules. After drying the granules, they are allowed to pass through the screen, usually 60-100 mesh nylon cloth is used. After dry granulation, lubricant is added as fine powder, which is required for proper filling of the die cavity. The surface tension forces and capillary pressure are primarily responsible for initial granules formation. The main advantage being it meets all the requirements for tablet formation though it is multistage, time consuming¹⁵⁻¹⁶.



Evaluation of tablet

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.

Size and shape

It can be dimensionally described and 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 $\pm 5\%$ variation of standard value.

Unique identification marking

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 distribution must be uniform with no mottling. For visual color comparison compare the color of sample against standard color.

Hardness

Tablet requires a certain amount of strength or hardness and resistance to friability to withstand mechanical shakes of handling in manufacture packaging and shipping. Hardness generally measures the tablet crushing strength



Monsanto Hardness tester

Friability

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 0.5 to 1.0 % of the Tablet weigh are consider acceptable.



Roche Friabilator

Weight Variation test (U.S.P.)

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.

Content Uniformity Test

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

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 remains 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.



Disintegration Apparatus

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.

Disintegration time: Uncoated tablet: 5-30 minutes,
Coated tablet: 1-2 hours.

Dissolution Test Apparatus-1

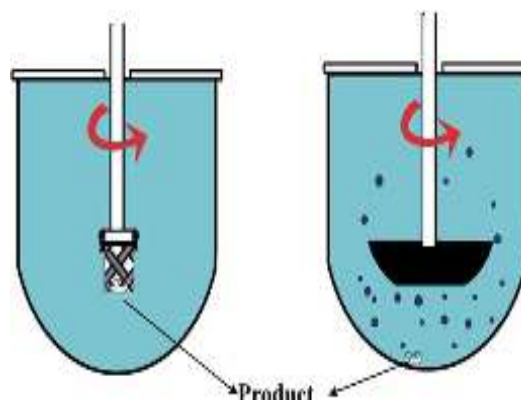
A single tablet is placed in a small wire mesh basket attached to the bottom of the shaft connected to a variable speed motor. The basket is immersed in a dissolution medium (as specified in monograph) contained in a 100 ml flask. The flask is cylindrical with a hemispherical bottom. The flask is maintained at $37 \pm 0.50^\circ\text{C}$ 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.



Dissolution apparatus

Apparatus-2

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, time limit of the test and assay procedure for. The test tolerance is expressed as a % of the labeled amount of drug dissolved in the time limit¹⁶⁻¹⁸.



Dissolution apparatus flasks

Defects in tablet dosage form:

Capping:

Capping continuously high speed of tablet machine and high degree of compression setting makes tablet to separate main surface into individual surface. Avoid defective punches and dies. High temperature adjustment also favors capping. Distance between upper and lower punches will entrap air is bone factor for capping. Fine particles were susceptible than coarse particles will affect ideality of tablets. Capping minimized by keeping the feed material with cohesive nature.

Lamination:

Lamination It is major problem among of all defects. Occur upon storage period, or soon after compression. Air entrapment between layers of tablet. Low levels of binding agent. It minimized by improving lubricant concentration. Change the method of granulation. By direct compression technique it is prevented to some extent. Use always dry material (feed).

Mottling

Unequal distribution of colour on the tablet surface with light and dark areas standing out in an otherwise uniform coloured surface.

Picking

Adherence of the tablet material from the surface of a tablet by a punch. Because of engraving or embossing or debossing on the punch tips like small enclosed areas in the letters like "A", "B", "D", "O", "Q" etc

Sticking

Sticking always occurs in low melting point substances, and moisture supports this defects, lower the speed up of upper and lower punch leads to weight variation of tablets. It produces rough and chipping surface tablets. It develops material on both punches. Lack of drying is basis of this one¹⁸⁻¹⁹.

Conclusion:

Among the different routes of drug administration, oral route is mostly preferred. About 90% of drugs are administered orally for systemic effect. In orally

administered dosage forms, tablet represents the preferred choice of class of product. The tablet is convenient, in terms of self medication, ease of administration, compactness, accurate dose, avoidance pain, versatility and most importantly patient compliance. Tablets can be produced by three methods viz. direct compression, dry granulation and wet granulation. During their manufacturing many inprocess problems and also after formulation also problems will arise. By using proper preventive methods we can reduce those problems or we can make them in standard limits.

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