TABLET MANUFACTURING PROCESSS AND DEFECTS OF TABLETS

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ABSTRACT

Tablet is defined as solid pharmaceutical dosage form containing drug substance generally with suitable diluents and prepared by either compression or molding methods. 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. Because of their composition, method of manufacture or intended use, tablets present a variety of characteristics and consequently there are several categories of tablets. Tablet formulation and design may be described as the process where by the formulator ensures that the correct amount of the drug in the right form is delivered at or over the proper time at the proper rate and in the desired location, while having its chemical integrity protected to that point. Latest concepts and regulations focus on bioavailability, bioequivalence and validation etc. impact formulation designing and manufacture.

Introduction The oral route of drug administration is the most important method of drug administration for systemic effects. The Parenteral route of administration is important in treating the medical emergencies in which subject is comatose or can not swallow and in providing various types of maintenance therapy. Nevertheless, about 90% of all the drugs used to produce systemic effects

are administered by the oral route. Among the drugs that are administered orally, solid dosage form represents the preferred class of product. Solid dosage form provides best protection to the drug against temperature, humidity, oxygen, light and stress during transportation and also ensures accuracy of dosage, compactness, portability, blandness of taste, and ease of administration. Although the basic medicinal approach for their manufacture has remained the same, tablet technology has undergone great improvement. Efforts are being made continually to understand more clearly the physical characteristics of powder compaction and the factors affecting the availability of the drug substance from the dosage form after oral administration. Tabletting equipment continues to improve in both production speed and the uniformity of the tablets compressed. Although tablets frequently are discoid in shape, they also exist in several shapes such as round, oval oblong, cylindrical or triangular etc. They may differ greatly in size and weight depending on the amount of the dug substance present and the intended method of administration. They are divided in to two general classes by whether they are made by compression or molding. Compressed tablets usually are prepared by largescale production methods, while molded tablets generally involve small-scale operations.

Types of tablets Compressed Tablets

The tablets are formed by compression of powdered, crystalline, or granular active materials (API), alone or in combination with certain expients as required, such as binders, disintegrants, sustained release polymers, lubricants, diluents, flavors and colorants.

A) Sugar coated tablets (sct)

B) Film coated tablets (fct)

C) Enteric-coated tablets (ect)

D) Multi compessed tablets (mct): these are compressed Tablets made by more than one compression cycle.

I) Layered tablets ii) Press coated tablets

E) Sustained release tablets

F) Tablets for solution

G) Effervescent tablets

H) Compressed suppositories or inserts

I) Buccal and sublingual tablets

Molded tablets or tablet triturates (tt)

Tablet triturates usually are made from moist material, using a mold that gives them the shape of cut sections of cylinder. Such tablets must be completely and rapidly soluble. Suitable water-soluble lubricant is many times a constraint.

Dispensing Tablets (Dt)

These tablets provide a convenient quality of potent drug that can be incorporated readily in to powders and liquids, thus circumventing the necessity to weigh small quantities. These tablets are supplied primarily as a convenience for extemporaneous compounding and never dispensed as a dosage form.

Hypodermic Tablets (Ht)

Hypodermic tablets are soft, readily soluble tablets. Though these tablets are now made for oral administration they are not yet recognized by the official compendia. Advantages of the tablets The additional advantages of tablet dosages forms are as follows:

• Their cost is lowest of all the dosage forms.

• They are in general the easiest and cheapest to package and ship of all oral dosage forms.

• They may provide the greatest ease of swallowing with the least tendency for “hang-up” above the stomach, especially when coated, provided that tablet disintegration is not excessively rapid.

• They lend themselves to certain special release profile products, such as enteric or delayed release products.

• They are better suited to large-scale production than the other unit oral forms.

• They have the best-combined properties of chemical, mechanical and microbiological stability of all the oral forms. Disadvantages of the tablets For very

few disadvantages, these dosage forms are most suitable and widely accepted:

• Some drugs resist compression in to dense particles, owing to their amorphous nature or flocculent, low density character.

• Drugs with poor wetting, slow dissolution properties, intermediate to large dosages, optimum absorption high in the GIT or any combination of these features are very challenging for the formulators.

Tablet Processing

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 intractions and stability.

Direct compression: The tablets are made by directly compressing the powdered materials without modifying the physical nature of the materials itself. Direct compression is generally done for the crystalline materials having good physical properties such as flow property, compressibility etc. Main advantages of direct compression are time saving, safety of operations and low cost.

Wet granulation: 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. 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 consuming.

Dry granulation: 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 moister 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 then 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 method.The manufacture of oral solid dosage forms such as tablets is a complex multi-stage process under which the startingmaterials change their physical characteristics a number of times before the final dosage form is produced. Traditionally, tablets have been made by granulation, a process that imparts two primary requisites to formulate: compactibility and fluidity. Both wet granulation and dry granulation (slugging and roll compaction) are used. Regardless of weather tablets are made by direct compression or granulation, the first step, milling and mixing, is the same; subsequent step differ. Numerous unit processes are involved in making tablets, including particle size reduction and sizing, blending, granulation, drying, compaction, and (frequently) coating. Various factors associated with these processes can seriously affect content uniformity, bioavailability, or stability.

Dispensing (weighing and measuring)

Dispensing is the first step in any pharmaceutical manufacturing process. Dispensing is one of the most critical steps in pharmaceutical manufacturing; as during this step, the weight of each ingredient in the mixture is determined according to dose. Dispensing may be done by purely manual by hand scooping from primary containers and weighing each ingredient by hand on a weigh scale, manual weighing with material lifting assistance like Vacuum transfer and Bag lifters, manual or assisted transfer with automated weighing on weigh table, manual or assisted filling of loss-in weight dispensing system, automated dispensaries with mechanical devices such as vacuum loading system and screw feed system. Issues like weighing accuracy, dust control laminar air flow booths, glove boxes), during manual handling, lot control of each ingredient, material movement into and out of dispensary should be considered during dispensing.

Sizing

The sizing (size reduction, milling, crushing, grinding, pulverization) is an impotent step (unit operation) involved in the tablet manufacturing. In manufacturing of compressed tablet, the mixing or blending of several solid ingredients of pharmaceuticals is easier and more uniform if the ingredients are approximately of same size. This provides a greater uniformity of dose. A fine particle size is essential in case of lubricant mixing with granules for its proper function. Advantages associated with size reduction in tablet manufacture are as follows:

1) It increases surface area, which may enhance an active ingredient's dissolution rate and hence bioavailability.

2) Improved the tablet-to-tablet content uniformity by virtue of the increased number of particles per unit weight.

3) Controlled particle size distribution of dry granulation or mix to promote better flow of xture in tablet machine.

4) Improved flow properties of raw materials.

5) Improved colour and/or active ingredient dispersion in tablet excipients.

6) Uniformly sized wet granulation to promote uniform drying. There are also certain disadvantages associated with this unit operation if not controlled properly. They are as follows:

7)A possible change in polymorphic form of the active ingredient, rendering it less or totally inactive, or unstable.

8) A decrease in bulk density of active compound and/or excipients, which may cause flow problem and segregation in the mix. iii)An increase in surface area from size reduction may promote the adsorption of air, which may inhibit wettability of the drug to the extent that it becomes the limiting factor in dissolution rate.

A number of different types of machine may be used for the dry sizing or milling process depending on whether gentle screening or particle milling is needed. The ranges of equipment employed for this process includes Fluid energy mill, Colloidal mill, Ball mill, Hammer mill, Cutting mill, Roller mill, Conical mill,

etc.

Powder blending

The successful mixing of powder is acknowledged to be more difficult unit operation because, unlike the situation with liquid, perfect homogeneity is practically unattainable. In practice, problems also arise because of the inherent cohesiveness and resistance to movement between the individual particles. The process is further complicated in many system, by the presence of substantial segregation influencing the powder mix. They arise because of difference in size, shape, and density of the component particles. The powder/granules blending are involved at stage of pre granulation and/or post granulation stage of tablet manufacturing. Each process of mixing has optimum mixing time and so prolonged mixing may result in an undesired product. So, the optimum mixing time and mixing speed are to be evaluated. Blending step prior to compression is normally achieved in a simple tumble blender. The Blender may be a fixed blender into which the powders are charged, blended and discharged. It is now common to use a bin blender which blends. In special cases of mixing a lubricant, over mixing should be particularly monitered. The various blenders used include “V” blender, Oblicone blender, Container blender, Tumbling blender, Agitated powder blender, etc. But now a day to optimize the manufacturing process particularly in wet granulation the various improved equipments which combines several of processing steps (mixing, granulation and/or drying) are used. They are “Mixer granulator” or“High shearmixing machine”.

Granulation

Following particle size reduction and blending, the formulation may be granulated, which provides homogeneity of drug distribution in blend.

Drying

Drying is a most important step in the formulation and development of pharmaceutical product. It is important to keep the residual moisture low enough to prevent product deterioration and ensure free flowing properties. The commonly used dryer includes Fluidized – bed dryer, Vacuum tray dryer, Microwave dryer,

Spray dryer, Freeze dryer, Turbo – tray dryer, Pan dryer, etc.

Tablet compression

After the preparation of granules (in case of wet granulation) or sized slugs (in case of dry granulation) or mixing of ingredients (in case of direct compression), they are compressed to get final product. The compression is done either by single punch machine (stamping press) or by multi station machine (rotary press). The tablet press is a high-speed mechanical device. It 'squeezes' the ingredients into the required tablet shape with extreme precision. It can make the tablet in many shapes, although they are usually round or oval. Also, it can press the name of the manufacturer or the product into the top of the tablet. Each tablet is made by pressing the granules inside a die, made up of hardened steel. The die is a disc shape with a hole cut through its centre. The powder is compressed in the centre of the die by two hardened steel punches that fit into the top and bottom of the die. The punches and dies are fixed to a turret that spins round. As it spins, the punches are driven together by two fixed cams - an upper cam and lower cam. The top of the upper punch (the punch head) sits on the upper cam edge .The bottom of the lower punch sits on the lower cam edge. The shapes of the two cams determine the sequence of movements of the two punches. This sequence is repeated over and over because the turret is spinning round. The force exerted on the ingredients in the dies is very carefully controlled. This ensures that each tablet is perfectly formed. Because of the high speeds, they need very sophisticated lubrication systems. The lubricating oil is recycled and filtered to ensure a continuous supply.

Conclusion

Among the different routes of drug administration, oral route is mostly preferred. About 90% of drugs are administered orally for systemic effect. Various kinds of solid dosage forms like tablet, capsules, pills, syrups etc are administered through oral route of drug administration. 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.

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