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An Overview on Formulation and Evaluation Aspects of Tablets

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Abstract

Nothing in this world is stable and ever accepted. Change is the requirement of nature for the sake of adaptability. However, the pharmaceutical world is also not far off from this change. Technical advancement in pharma world also leads to the development of new dosages forms. This leads to the replacement of the older dosages forms with the newer once. But for the tablet dosages forms this replacement is substituted with modifications. On the top of it the availability of numerous evaluation parameters provides these new modifications in tablets a clear cut demonstration idea. Tablets are defined as solid unit dosage form of medicaments intended for oral use. They became most popular as they were easy in preparation compared to any other type of dosage forms. But the major drawback exists in its manufacturing. If any minor problem occurs during their manufacturing then the whole batch of the unit should be discarded. It is necessary to avoid any sort of errors during its manufacturing and as a result evaluation of tablets is very important before dispatching of a batch. In the present study, we discussed about the manufacturing techniques and evaluation tests for tablets.

Keywords: Tablets, Solid unit dosage, Compression method, Indian pharmacopoeia, Manufacturing, Evaluations

Introduction

Oral solid dosage forms are administered for attaining a local therapeutic effect in the mouth, throat and digestive tract or for a systemic effect in the body after oral or gastrointestinal absorption. For preparing oral solid dosage forms, active ingredients and suitable excipients can be milled, dried, encapsulated, blended, granulated or tableted. Various oral solid dosage forms such as tablets, capsules, lozenges, powders and granules etc. have been widely used for delivering active pharmaceutical ingredients (API) due to their convenience and consequent patient compliance[1]. Tablet is the most widely used dosage form among the total available dosage forms because it is simple for administration, lower price of production and elegance[2]. Tablets are a solid dosage form of medicaments with or without excipients which are prepared by compression method. According to the Indian Pharmacopoeia tablets are solid, flat or biconvex unit dosage form of a medicament alone or medicament along with excipients prepared by compressing technique. They may vary in its size shape and weight depending on the medicament and its mode of administration. Tablets are said to be most widely used conventional dosage forms due to its variety of advantages and 70% of the medicaments were dispensed in tablet forms. Most of the medicaments can be processed into tablets but there are some exceptions like medicaments with low density characters, hygroscopic and the medicaments which were not possible to administer[3-7]. Tablet formulations which provide a unit dose which is either immediate drug release or modified release or is taste masked are some of the most popular and extensively explored aspects of oral solid dosage form development. Tablet manufacturing (apart from the direct compression method) is a multistep process and hence is a complex process with many potential variables. The processes and parameters associated with tablet manufacture are still not fully understood. Extensive research is ongoing to develop understanding in all areas of the tablet manufacturing process. Numerous advances have been introduced to improve material attributes, engineering of manufacturing equipment and development of efficient analytical techniques. Qualities by design-based formulation development approaches have been applied to reduce the variability in the processes to develop robust tablet dosage forms. In addition, new raw materials have been deployed to improve manufacturability and functionality of tablet formulations. These include the modification of existing excipients with enhanced purity or physical properties (e.g. particle size) and co processing with other materials to improve their performance in manufacturing processes. Moreover, development and use of multi-functional materials provide lean manufacturing opportunities with significant economic impact. The last few years have seen the development of novel tableting technologies which improve machine performance. These advances in machine design aim to overcome limitations associated with conventional manufacturing approaches such as the denaturation of thermolabile active ingredients, material wastage, multiple processing steps and elevated costs due to protracted processing time, labour and maintenance of

equipment. In addition, lean and continuous manufacturing concepts have been employed to ensure rapid, safe and efficient manufacturing operations. Developments relating to engineering and machine design have also been implemented in the pharmaceutical industry. The concept of quality by design has been applied to enhance productivity by the application of novel process analytical technologies that track quality attributes of formulations. These also can document data as a function of input variables (materials and process) in a real time manner[1]. This manuscript aims to provide a comprehensive summary of numerous manufacturing technologies and evaluation parameters plays a major role to release any dosage form into the market.

Advantages

- Unit dosage forms with dose precision,
- Least content variability,
- Administration of accurate amounts of minute doses of a drug is possible,
- Economical of all oral dosage forms as its production doesn't requires additional processing steps,
- Easy transportation,
- Sustain release of a drug can be achieved through enteric coating,
- Medicaments with bitter taste can be masked with coating technique (Sugar coating),
- Tablet dosage form is stable when compared to all oral dosage forms.

Disadvantages

- Administration of drugs is not easy in case of children,
- Drugs with slow dissolution is not acceptable for tableting with good bioavailability,
- Medicaments with low density characters and amorphous in nature are difficult to compress,
- Hygroscopic nature of drugs is not acceptable for tablet compression.

Tablet manufacturing techniques[8-12]

Direct compression

The direct compression method is by far the most effective technique of tablet manufacturing. This technique is least tedious and hence is preferred over the other techniques. Direct compression is the simplest and most economical method for the manufacturing of tablets because it requires less processing steps than other techniques such as wet granulation and roller compaction. However, most pharmaceutical active ingredients cannot be compressed directly into tablets due to lack of flow, cohesion properties and lubrication. Therefore they must be blended with other directly compressible ingredients to manufacture satisfactory tablets.

Wet granulation

Wet granulation is a process of using a liquid binder to lightly agglomerate the powder mixture. The amount of liquid required to be properly adjusted, as over-wetting will cause the granules to be too hard and under-wetting will cause them to be too soft and friable. Aqueous solutions have the advantage of being safer to deal with solvent-based systems but may not be suitable for drugs which are degraded by hydrolysis.

Dry granulation

Dry granulation requires drugs or excipients with cohesive properties. Dry granulation is simpler than wet granulation, therefore the cost is reduced. This process is often used when the product to be granulated is sensitive to moisture and heat. Dry granulation can be conducted on a tablet press using slugging tooling or on a roll press called a roller compactor. Dry granulation often produces a higher percentage of fine granules, which can compromise the quality or create yield problems for the tablet. Steps-by-step tablet manufacturing processes which are being utilized by various manufacturers are enlisted in Table 1. Evaluations of these tablets are being carried out by using various response variables. Both preformulation and post formulation parameters are being evaluated to cement the effectiveness of formulated preparations.

Table 1: Steps of tablet manufacturing processes

Wet granulation	Milling and mixing of drugs and excipients. Preparation of binder solution. Wet massing by addition of binder solution or granulating solvent. Screening of wet mass followed by drying of the wet granules. Screening of dry granules. Blending with lubricant and disintegrant to produce running powder, Compression of tablet
Dry granulation	Milling and mixing of drugs and excipients, Compression into slugs or roll compaction, Milling and screening of slugs and compacted powder, Mixing with lubricant and disintegrant, Compression of tablet
Direct compression	Milling and mixing of drugs and excipients, Compression of tablet
Nanonization	Involves size reduction of drug to nanosize by milling the drug using a proprietary wet-milling technique. The nanocrystals of the drug are stabilized against agglomeration by surface adsorption on selected stabilizers, which are then incorporated
Cotton candy process	Involves the formation of matrix of polysaccharides by simultaneous action of flash melting and spinning. This candy floss matrix is then milled and blended with active ingredients and excipients after re-crystallization and subsequently compressed to FDT.
Mass extrusion	Involves softening the active blend using the solvent mixture of water soluble polyethylene glycol, methanol and expulsion of softened mass through the extruder or syringe to get a cylindrical shape of the product into even segments using heated blade to form tablets.
Sublimation	Inert solid ingredients that volatilize rapidly like urea, camphor ammonium carbonate, ammonium bicarbonate, and hexamethylenetetramine were added to the other tablet ingredients and the mixture is compressed into tablets. The volatile materials were then removed via sublimation, which generates

	porous structure.
Moulding	Water-soluble ingredients with a hydro alcoholic solvent is used and is molded into tablets under pressure lower than that used in conventional tablet compression.
Freeze drying/ Lyophilization	The drug is dissolved or dispersed in an aqueous solution of a carrier. The mixture is poured into the wells of the preformed blister packs. The trays holding the blister packs are passed through liquid nitrogen freezing tunnel to freeze the drug solution. Then the frozen blister packs are placed in refrigerated cabinets to continue the freeze drying. Finally the blisters are packaged and shipped.
Disintegrant addition	Involves the addition of superdisintegrants in optimum concentration to the formulation to achieve rapid disintegration/dissolution

Advances in tablet manufacturing processes

Tablet manufacturing routines involving advanced granulation approaches, hot melt extrusion, extrusion/spheronization, injection molding, spray drying, spray congealing, coprecipitation and nanotechnology-based approaches have been developed over a number of years to produce robust tablet formulations with improved performance characteristics.

Evaluation of tablets

- Appearance,
- Size and Shape,
- Organoleptic properties,
- Uniformity of thickness,
- Hardness,
- Friability,
- Drug Content Uniformity,
- Weight Variation Test,
- Wetting time,
- Water Absorption Ratio,
- *In vitro* Dispersion Time,
- *In vitro* Disintegration Test,
- *In vitro* Dissolution Studies,
- Two set of apparatus,
- Apparatus-1,
- Apparatus-2.

Appearance

Appearance is the first most required quality for the acceptance of tablet. General elegance and its identity play a major role for the consumer acceptance. Acceptance of the appearance of batches of the tablet has been done based on the measurement of the following factors like size, color, shape, presence or absence of odor, taste etc[13-18].

Size and shape

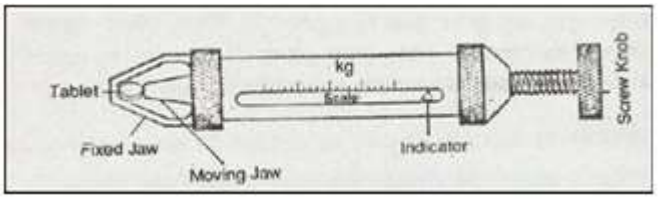
Size and shape of a tablet has been determined by its thickness. Size and shape of table plays an important role in its patient compliance as the size of the tablet increases it is not much easier for its administration. Micrometer is the devise which is used to determine the thickness of a tablet. It can be acceptable if the batch falls within the • ±5% of standard deviation.

Organoleptic properties

Color should be distributed uniformly without appearance of any signs of mottling. Colour of the tablet should be compared with the standard colour for comparison.

Uniformity of thickness

To determine the uniformity of thickness random selection of tablets has to be done from each and every batch and need to measure its thickness independently. If the thickness of any single tablet varies then the batch containing that batch will not be dispatched into market (Figure 1).



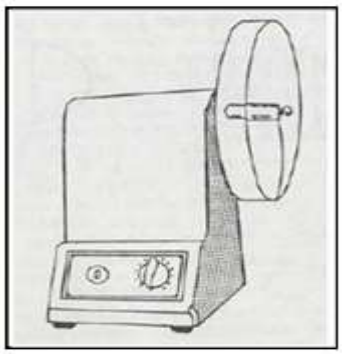
Hardness

The ability of a tablet to withstand for mechanical shocks is known as hardness. Pfizer hardness tester is the instrument which is used to determine the hardness of tablet. It is expressed in kg/cm2. Take three tablets from each batch and hardness should be determined and the selection of tabled should be done randomly. Then the mean and standard deviation values should be determined.

Friability

Roche friabilator is the equipment which is used for the determination of friability. It is expressed in percentage. Note down the initial weight of the tablets individually (W initial). Tablets are placed in a plastic chamber which revolves at 25 rpm and they are subjected to fall from a height of 6 inches in the friabilator for about 100 revolutions. Then measure the weight of the tablet (W final) and observe any weight difference before tablet and after the friabilator processing (Figure 2). Limits: loss in weight less than 0.5 to 1% of the initial weight of the tablet should be considered as acceptable limits. Percentage of friability is calculated as:

$$F=\{(W\ initial)-(W\ final)/(W\ initial)\}\times 100.$$



Drug content uniformity

Initially weigh the tablet and then powder it. Now the powdered tablet is transferred into a 100 ml volumetric flask and adds 0.1 N HCl up to mark. Now filter the solution and discard first few ml of filtrate. Take 10 ml of filtrate should be taken into a 50 ml volumetric flask and add 0.1 N HCl up to the mark and analysed spectrophotometrically at 274 nm and 234.5 nm. The concentration of the content of the drug (µg/ml) was calculated by using the standard calibration curve of the respective drug.

Drug content is calculated by using the below formula

Concentration of the drug in (µg/ml) × 100 × 50/10 × 1000

Weight variation test

Random selection of 20 tablets from each batch should be done and note down the weight of the tablet individually and check for any variation in its weight. According to US Pharmacopeias small variations in the weight is negligible and can be accepted. Below is the acceptable limit of percentage deviation in weight variation.

Wetting time

This method was performed to determine the wetting time of a tablet. A piece of tissue paper which is folded twice is kept in a Petri dish containing 6 ml of water and place the tablet on the tissue paper. Observe the time taken for complete wetting of the tablet. Following procedure should follow three times (three trial) for each batch and standard deviation is also calculated from the obtained results.

Water absorption ratio

A piece of tissue paper which is folded twice is kept in a Petri dish (i.d.=6.5 cm) containing 6 ml of water and place the tablet on the tissue paper. Observe the time taken for complete wetting of the tablet. Thus wetted tablet was weighed. Now the water absorption ratio R is calculated using the formula

$$R=100 \times Wa - Wb/Wb$$

Wb is the weight of the tablet before absorption, Wa is the weight of the tablet after absorption,

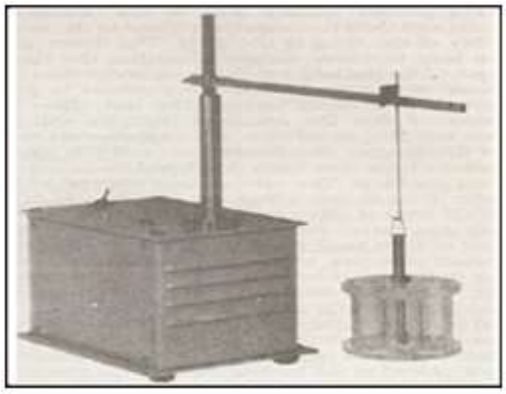
Following procedure should follow three times (three trial) for each batch and standard deviation is also calculated from the obtained results.

***In vitro* dispersion time**

Dispersion time of a tablet is determined by placing a tablet in 6 ml of 6.8 pH phosphate buffer and note down the time taken for complete dispersion of tablet. Following procedure should be done for three tablets from each batch and *in vitro* dispersion time is calculated. Standard deviation time is also determined from the obtained results. It is expressed in seconds.

***In vitro* disintegration test**

Disintegration is defined as the process of breakdown of tablet into small particles. Disintegration time of a tablet is determined by using disintegration test apparatus as per IP specifications. Place each tablet in each 6 tubes of the disintegration apparatus a then add a disc to each tube containing 6.8 pH phosphate buffer. The temperature of the buffer should maintain at 37±2°C and run the apparatus raised and lowered for 30 cycles per minute. Note down the time taken for the complete disintegration of the tablet without any remitants (Figure 3).



Conclusion

Tablet manufacturing and its evaluation has become the backbone of pharmaceutical research. From the various data sources it could be concluded that tablets have got uniqueness and power of adaptability. The tablets have shown vast changes in the last few decades or so both in manufacturing and evaluation. The advances in the evaluation techniques have proven to be both economical and time saving. From the number of manufacturing and evaluation parameters available the scope for the researchers also enhances and makes it possible for tablets to perfectly cement its place in this ever changing drug world.

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