PROCESSING TECHNOLOGIES FOR PHARMACEUTICAL TABLETS: A REVIEW

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ABSTRACT
Pharmaceutical oral solid dosage forms have been used widely for decades mainly due to their convenience of administration and their suitability for delivery for delivery of drugs for systemic effects. The most commonly used pharmaceutical solid dosage forms today include granules, pellets, tablets and capsules. The tablets and capsules can be made directly from powders or from granules pellets, or from film-coated multiple units. Tablets are now the most popular dosage form, accounting for some 70% of all ethical pharmaceutical preparations produced. Tablets may be classified as directly compressible tablets, chewable tablets and tablet triturates. Compressed tablets can be further classified as directly compressible tablets, chewable tablets and tablet triturates.

KEYWORDS: Systemic, pellets, granules, film-coated multiple units, diluents, compression, molding, tablet triturates.

INTRODUCTION
A tablet is a compressed solid unit dosage form containing medicaments with or without excipients. According to the Indian Pharmacopoeia, pharmaceutical tablets are solid flat or biconvex dishes prepared by compressing a drug or a mixture of drugs, with or without diluents.1 They vary in shape and differ greatly in size and weight, depending on the amount of medicinal substances and the intended mode of administration. It is the most popular dosage form and 70% of the total medicines are dispensed in the form of tablets. Tablets offer advantages over both patients and manufacturers. Tablets are the most popular dosage form due to their simplicity and economy of manufacture, relative stability and convenience in packaging, shipping and storage. For the patients, the ease of manufacturing, convenience in administration, accurate dosing and stability compared to oral liquids, tamper-proofness compared to capsules, safe compared to parental dosage forms makes it a popular and versatile dosage form.2 Properties of Tablets3

- Should be elegant product having its own identity while being free of defects such as chips, cracks, discoloration and contamination.
- Should have strength to withstand the rigors of shocks encountered in its production, packaging, shipping and dispensing.
- Should have the physical stability to maintain its physical attributes over time.
- Must be able to release the medicament agent(s) in the body in a predictable and reproducible manner.
- Must have a suitable chemical stability over time so as not to alter the medicinal agent(s).

Manufacturing of tablets requires number of unit operations like product includes weighing, milling, granulation, drying, blending, lubrication, compression and coating.

Advantages of Tablets4

- 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.
- Cost is lowest of all oral dosage form.
- Lighter and compact.
- Easiest and cheapest to package and strip.
- Easy to swallow with least tendency for hang-up.
- Sustained release product is possible by enteric coating.
- Objectionable odour and bitter taste can be masked by coating technique.
- Suitable for large scale production.
- Greatest chemical and microbial stability over all oral dosage form.
- Product identification is easy and rapid requiring no additional steps when employing an embossed and/or monogrammed punch face.

Disadvantages of Tablets5

- Difficult to swallow in case of children and unconscious patients.
- Some drugs resist compression into dense compacts, owing to amorphous nature, low density character.
- 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.
- Irritant effects on the GI mucosa by some solids (e.g., aspirin).
- Possibility of bioavailability problems resulting from slow disintegration and dissolution.

TYPES OF TABLETS
Tablets can be prepared either by compression or molding. Various types of tablets are as follows:

> Molded tablets
> Compressed tablets

MOLDED TABLETS
While most commercially available tablets are primarily prepared by compression, tablets can also be prepared by molding. Molded tablets are prepared by tablet machinery or manually by forcing dampened tablet material into a mold of any shape.5 The formed tablet is then ejected from the mold and allowed to dry. The molds are shown in fig 1. Molding is generally reserved for laboratory and small-scale production. Molded tablets are shown in fig 2. The commercial preparation of tablets by molding has been replaced by the tablet compression process.6
COMPRESSED TABLETS
They are the most widely used solid dosage form so they must satisfy a number of physical requirements in terms of hardness, thickness, friability and weight uniformity. The compressed tablets are shown in fig 3. To provide these tablet characteristics in accordance with the chosen ingredients, manufacturers can use three different processing technologies:

- direct compression,
- dry granulation and
- wet granulation

DIRECTLY COMPRESSED TABLETS
Direct compression consists of compressing tablets directly from powdered materials without modifying physical nature of materials. This method is applicable for crystalline chemicals having good compressible characteristic and flow properties such as: Potassium salt (chlorate, chloride, bromide), Sodium chloride, Ammonium chloride, Methenamine etc.

Compressed tablets are prepared by single compression using tablet machines. After a quantity of powdered or granulated tabletting material flow into a die, the upper and lower punches of the tablet machine compress the material under a high pressure (~tons/in2).

Direct compression is a popular choice because it provides the shortest, most effective and least complex way to produce tablets. The manufacturer can blend an API with the excipient and the lubricant, followed by compression, which makes the product easy to process. No additional processing steps are required.

Moisture or heat sensitive ingredients, which would be contraindicated in wet granulation, can also be used in this type of process. However, it does require a very critical selection of excipients in comparison to granulation processes because the raw materials must demonstrate good flowability and compressibility for successful operation. The processing steps involved in direct compression are shown in flowchart 1

CHARACTERISTICS OF COMPRESSED TABLETS
When compressed tablets are prepared, various physical specifications are examined for quality control. They should be controlled to assure not only the outward appearance of the product but also its therapeutic efficacy. The shapes of the compressed tablets differ widely. It can be round, oblong, or triangular. Tablets may be flat or have varying degree of convexity depending on the contours of the punches, such as flat face, shallow cup, deep cup or modified ball.

Some tablets are scored or grooved in halves, thirds, or quadrants. This allows fairly accurate breaking of the tablet for the administration of a partial amount. In general scored tablets are grooved on a single side. Tablet shapes and size are determined by the die and punches used for the compression of the tablet.

Tablets may be imprinted with a symbol of the manufacturer to denote the company, the product, or both. To make imprinted tablets punches having impressions are used. Punches with raised impressions will produce recessed (embossed) impressions on the tablets, and vice versa. By FDA regulation effective in 1995, all solid dosage forms for human consumption must be imprinted with product-specific identification codes. Code imprints, in conjunction with a product’s size, shape, and colour, permit the unique identification of a drug product and its manufacturer or distributor. Code imprints may contain any combination of letters and numbers, or the product’s National Drug Code number, and any marks, symbols, logos, or monograms assigned by the drug company to the product. Each product’s imprint must be registered with the FDA.

Tablets should be made sufficiently hard to resist breaking during packaging, shipment, and normal handling. At the time tablets should be soft enough to disintegrate and dissolve properly after administered. It is a common practice in hospitals and extended care facilities to crush tablets to mix with food or drink for easy swallowing. Some tablets, such as enteric coated tablets, controlled release tablets, and sublingual or buccal tablets should not be crushed, since the release characteristics of the drug from the dosage form and subsequently the drug absorption could adversely affect the patient’s welfare.

Advantages:
- Low labor input
- A dry process
- Fewest processing steps

Disadvantages:
- Stratification may occur due to differences in particle size and bulk density which results poor content uniformity.
- A large dose drug may cause problem in direct compression. It requires diluents. The tablet becomes large in size which is difficult to swallow and also costly.
- During handling of dry materials static charge may form which may present uniform distribution of drug.
- Direct compression diluent may interact with the drug. For example, amine drug with Lactose produce discoloration of tablet.

Challenges in Direct Compression Technology
Like any other process, direct compression has its own technical issues, among which the most important are:

- High weight and dose variation of the tablets.
- Low mechanical strength of the tablets
- Capping and lamination of the tablets
- Adhesion or sticking of powder material punch tips
- High friction during tablet ejection

Such problems are related to the properties of the powder intended to be formed tablets, and also to the design and conditions of the press. They should therefore be avoided by ensuring that the powder possesses adequate physical properties and also that a suitable, well conditioned tablet press is used, e.g. in terms of the use of forced-feed devices and polished and smooth dies and punches.

Important technical properties of a powder which must be controlled to ensure the success of a tabletting operation are:
- Homogeneity and segregation tendency
- Flowability
- Compression properties and compactability
- Friction and adhesion properties

Granulation
If a powder blend's properties do not suit direct compression tabletting, manufacturers will turn to granulation processes to create the desired flowability and low dustability. These characteristics are required to minimize tablet weight variations, and ensure high density for high tablet filling weight and high moldability for hard tablet manufacture. Granulation narrows the particle size distribution of a tablet formulation's bulk powder, eliminating segregation problems. This in turn ensures superior compressibility in the tabletting process, permitting higher quantities of API to be used and
ensuring good active distribution in the tablet. However, granulation is a more time-consuming technique compared with direct compression and there is also a risk of product cross-contamination and product loss during the different processing steps (granulation, drying, sieving). All of these factors can increase costs compared with direct compression.\(^{11}\)

**Dry granulation:**

It is defined as the formation of granules by slugging, if the tablet ingredients are sensitive to moisture and/or unable to withstand elevated temperature during drying.\(^{12}\)

The processing steps involved in dry granulation are shown in flowchart 2.

**Wet granulation:**

In wet granulation the active ingredient, diluents and disintegrants are mixed or blended well in a rapid mixer granulator (RMG). The RMG is a multi-purpose chopper which consists of an impeller and a chopper and is used for high speed dispersion of dry powders and aqueous or solvent granulations.\(^{13}\)

Moist materials from wet milling steps are placed on large trays and placed in drying chambers with a circulating air current and thermostable heat controller. Commonly used dryers are tray dryer, fluidized bed dryer. After drying, the granules are reduced in particle size by passing through smaller mesh screen. After this, the lubricant or glidant is added as fine powder to promote flow of granules. These granules are then compressed to get a tablet. The processing steps involved in wet granulation are shown in flowchart 3.

Dry granulation when compared with wet granulation has a shorter, more cost-effective manufacturing process. Because it does not entail heat or moisture, dry granulation is especially suitable for active ingredients that are sensitive to solvents, or labile to moisture and elevated temperatures.

**Effect of Granule Properties on Tablet**

The granule properties play a pivotal role in the final performance of a tablet; for example, granule size can affect the flowability and hence, the average tablet weight.\(^{14}\) Having consistent flow of a granulation provides the needed avenues to control weights. Consistent tablet weights will result in repeatable tablet hardness. Improved and homogeneous granulation will improve mixture, its flowability, compressibility and therefore, improved disintegration with acceptable dissolution rate.\(^{15}\)

**CONCLUSION**

From the above compiled data it was concluded that pharmaceutical tablets can produced by three methods viz. direct compression, dry granulation and wet granulation. Out of these three methods, direct compression is the most convenient and cheaper method. However, attributing to the few disadvantages of this method, wet and dry granulation methods are used nowadays so as to produce quality tablets.

**REFERENCES**

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Flowchart 1: Processing steps in Direct Compression

Flowchart 2: Processing steps in Dry Granulation

Flowchart 3: processing Steps in Wet Granulation