PHARMACEUTICAL DOSAGE FORMS

Tablets

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In Three Volumes
VOLUME 1

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Compressed Tablets by Wet Granulation

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Compressed tablets are the most widely used of all pharmaceutical dosage forms for a number of reasons. They are convenient, easy to use, portable, and less expensive than other oral dosage forms. They deliver a precise dose with a high degree of accuracy. Tablets can be made in a variety of shapes and sizes limited only by the ingenuity of the tool and die maker (i.e. round, oval, capsule-shaped, square, triangular, etc.).

Compressed tablets are defined as solid-unit dosage forms made by compaction of a formulation containing the drug and certain fillers or excipients selected to aid in the processing and properties of the drug product.

There are various types of tablets designed for specific uses or functions. These include tablets to be swallowed per se; chewable tablets formulated to be chewed rather than swallowed, such as some antacid and vitamin tablets; buccal tablets designed to dissolve slowly in the buccal pouch; and sublingual tablets for rapid dissolution under the tongue. Effervescent tablets are formulated to dissolve in water with effervescence caused by the reaction of citric acid with sodium bicarbonate or some other effervescent combination that produces effervescence in water. Suppositories can be made by compression of formulations using a specially designed die to produce the proper shape.

The function of tablets is determined by their design. Multilayer tablets are made by multiple compression. These are called layer tablets and usually consist of two and sometimes three layers. They serve several purposes: to separate incompatible ingredients by formulating them in separate layers, to make sustained or dual-release products, or merely for appearance where the layers are colored differently. Compression-coated tablets are made by compressing a tablet within a tablet so that the outer coat becomes the coating. As many as two coats can be compressed around a core tablet. As with layer tablets, this technique can also be used to separate incompatible ingredients and to make sustained or prolonged

release tablets. Sugar-coated tablets are compressed tablets with a sugar coating. The coating may vary in thickness and color by the addition of dyes to the sugar coating. Film-coated tablets are compressed tablets with a thin film of an inert polymer applied in a suitable solvent and dried. Film coating is today the preferred method of making coated tablets. It is the most economical and involves minimum time, labor, expense, and exposure of the tablet to heat and solvent. Enteric-coated tablets are compressed tablets coated with an inert substance which resists solution in gastric fluid, but disintegrates and releases the medication in the intestines. Sustained or prolonged release tablets are compressed tablets especially designed to release the drug over a period of time.

Most drugs cannot be compressed directly into tablets because they lack the bonding properties necessary to form a tablet. The powdered drugs, therefore, require additives and treatment to confer bonding and free-flowing properties on them to facilitate compression by a tablet press.

This chapter describes and illustrates how this is accomplished by the versatile wet granulation method.

I. PROPERTIES OF TABLETS

Whatever method of manufacture is used, the resulting tablets must meet a number of physical and biological standards. The attributes of an acceptable tablet are as follows:

1. The tablet must be sufficiently strong and resistant to shock and abrasion to withstand handling during manufacture, packaging, shipping, and use. This property is measured by two tests, the hardness and friability tests.
2. Tablets must be uniform in weight and in drug content of the individual tablet. This is measured by the weight variation test and the content uniformity test.
3. The drug content of the tablet must be bioavailable. This property is also measured by two tests, the disintegration test and the dissolution test. However, bioavailability of a drug from a tablet, or other dosage form, is a very complex problem and the results of these two tests do not of themselves provide an index of bioavailability. This must be done by blood levels of the drug.
4. Tablets must be elegant in appearance and must have the characteristic shape, color, and other markings necessary to identify the product. Markings are usually the monogram or logo of the manufacturer. Tablets often have the National Drug Code number printed or embossed on the face of the tablet corresponding to the official listing of the product in the National Drug Code Compendium of the Food and Drug Administration. Another marking that may appear on the tablet is a score or crease across the face, which is intended to permit breaking the tablet into equal parts for the administration of half a tablet. However, it has been shown that substantial variation in drug dose can occur in the manually broken tablets.
5. Tablets must retain all of their functional attributes, which include drug stability and efficacy.

II. FORMULATION OF TABLETS

The size and, to some extent, the shape of the tablet are determined by the active ingredient(s). Drugs having very small doses in the microgram range (e.g., folic acid, digitoxin, reserpine, dexamethasone, etc.) require the addition of fillers also called excipients to be added to produce a mass or or volume of material that can be made into tablets of a size that is convenient for patients. A common and convenient size for such low-dosage drugs is a 1/4-in. round tablet or equivalent in some other shape. It is difficult for some patients to count and handle tablets smaller than this. Tablets of this size ordinarily weigh 150 mg or more depending on the density of the excipients used to make up the tablet mass.

As the dose increases, so does the size of the tablet. Drugs with a dose of 100 to 200 mg may require tablet weights of 150 to 300 mg and round die diameters of 1/4 to 7/16 in. in diameter depending on the density and compressibility of the powders used. As the dose of the active ingredient(s) increases, the amount of the excipients and the size of the tablet may vary considerably depending on requirements of each to produce an acceptable tablet. While the diameter of the tablet may in some cases be fixed, the thickness is variable thus allowing the formulator considerable latitude and flexibility in adjusting formulations.

As the dose, and therefore the size, of the tablet increases, the formulator uses his expertise and knowledge of excipients to keep the size of the tablet as small as possible without sacrificing its necessary attributes. Formulation of a tablet, then, requires the following considerations:

1. Size of dose or quantity of active ingredients
2. Stability of active ingredient(s)
3. Solubility of active ingredient(s)
4. Density of active ingredient(s)
5. Compressibility of active ingredient(s)
6. Selection of excipients
7. Method of granulation (preparation for compression)
8. Character of granulation
9. Tablet press, type, size, capacity
10. Environmental conditions (ambient or humidity control)
11. Stability of the final product
12. Bioavailability of the active drug content of the tablet

The selection of excipients is critical in the formulation of tablets. Once the formulator has become familiar with the physical and chemical properties of the drug, the process of selecting excipients is begun. The stability of the drug should be determined with each proposed excipient. This can be accomplished as follows: In the laboratory, prepare an intimate mixture of the drug with an excess of each individual excipient and hold at 60°C for 72 hr in a glass container. At the end of this period, analyze for the drug using a stability-indicating assay. The methods of accelerated testing of pharmaceutical products have been extensively reviewed by Lachman et al in *The Theory and Practice of Industrial Pharmacy*, 3rd Ed., Lea and Febiger (1986).

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