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Mini Review

Tablets: A Brief Overview

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Abstract

Solid dosage forms, such as tablets, are widespread in practice. This is due to the ease of administration and capability of mass production by the pharmaceutical industry. Tablet formulation consists of the active ingredient along with fillers that serve various functions in the product. Tablets are prepared on machines known as presses. Material to be compacted is ready by either dry or wet methods. The United States Pharmacopeia lists tests to be performed on the finished products. A description of tablets, their characteristics, preparation, and quality control tests applied to them is the subject of this brief review.

Introduction

As a solid dosage form, tablets are prepared from dry powders containing pharmacologically active and inert ingredients. Most drug products available on the market are found in the form of tablets. Tablets are found on the market in different shapes, weight, colors, disintegration time, dissolution time, and for various routes of administration [1]. The oral tablets are usually easily swallowed and provide either an immediate drug action or a sustaining effect. In addition to the Active Pharmaceutical Ingredient (API), a tablet formulation may contain one or more of the following essential parts: Diluents, binders, lubricants, glidants, anti-adherents, disintegrating substances, coloring agents, flavoring and sweetening agents, and absorbents [2]. The instrument that forms powders into tablets is known as a tablet press. Tablets may be prepared either using dry methods or by wet granulation [3]. In this paper, the basic ingredients that are commonly found in tablets are briefly reviewed along with quality control tests performed on the finished product. The objective of this paper is to present the reader who is not familiar with tablet formulations the basic information available on this dosage form.

Ingredients

Table 1 summarizes and provides examples of ingredients that are commonly found in tablet formulations [4,5].

The bulk of the tablet formulation is made of diluents, also known as bulking agents. Microcrystalline cellulose (Avicel®) is commonly found in formulations as well as lactose. Starch from corn, rice, or wheat is also a possible bulking material for tablets. A couple of sugars, sorbitol, and mannitol may be found in tablets formulation serving as diluents. Avicel® is useful in tablets that are formulated by direct compression because it possesses binding and disintegrating properties. Other directly compressible vehicles

are calcium phosphate, spray-dried lactose, and anhydrous lactose. There also exist pre-blended vehicles where the API is added directly to the dry powder vehicle and compressed as is. Sta-Rx 1500 is an example of such as a vehicle with self-binding and disintegrating properties. An interesting diluent for tablets is Emdex® which is hydrolyzed starch. Emdex® may be used whenever greater strength in tablets is desirable [4].

Tablet Ingredients	Examples
Diluent	Calcium Phosphate; Carboxymethylcellulose Calcium; Cellulose; Dextrin; Lactose; Microcrystalline Cellulose; Pregelatinized Starch; Sorbitol; Starch
Binders	Acacia; Alginic Acid; Carboxymethylcellulose; Cellulose; Dextrin; Gelatin; Liquid Glucose; Magnesium Aluminum Silicate; Maltodextrin; Methylcellulose; Povidone; Sodium Alginate; Starch; Zein
Lubricants	Calcium Stearate; Glyceryl Palmitostearate; Magnesium Oxide; Poloxamer; Polyvinyl Alcohol; Sodium Benzoate; Sodium Lauryl Sulfate; Sodium Stearyl Sulfate; Stearic Acid; Talc; Zinc Stearate
Glidants	Magnesium Trisilicate; Cellulose; Starch; Talc; Tribasic Calcium Phosphate
Anti-adherents	Corn Starch; Metallic Stearate; Talc
Disintegrants	Alginic Acid; Carboxymethylcellulose; Cellulose; Colloidal Silicon Dioxide; Croscarmellose Sodium; Crospovidone; Potassium Polacrilin; Povidone
Coloring Agents	FD&C or D&C Dyes or Lake Pigments
Flavoring Agents	Ethyl Maltol; Ethyl Vanillin; Menthol; Vanillin
Absorbents	Kaolin; Magnesium Aluminum Silicate; Tricalcium Phosphate

Table 1: Commonly added ingredients in tablet formulations.

Although the diluent has its cohesiveness and perhaps can hold the powder particles together to form a tablet, binders are often used to ensure that tablets maintain their shape throughout their life cycle (i.e., from manufacturing to the use by patients). Binders act as a glue adding to the cohesiveness existing between solid particles. During formulations, binders are commonly added moist rather than in their dry form. The reason being is that the efficiency of binding the solid particles is enhanced in the presence of water. Exceptions to this do exist. For example, tragacanth gum is a better binder when added in its dry form than when it is moist. Acacia dispersion in water (10% w/w) is a suitable binder when mannitol is used as a diluent. A 10% solution of gelatin in water also serves as a binder, and so do syrups (50% to 65% w/w of sucrose in water). Although starch is considered a diluent when found in relatively large amount in the tablet formulation, it can also work as a binder after hydrating it with water (2% w/w). Colloidal guar gum dispersions in water may be used for binding solid particles as well [4-6].

Lubricants play an important role in tablet formulations as they reduce the friction between the tablet formulation and the tablet press walls, preventing ware and tare. Examples of lubricants are magnesium stearate and silicon dioxide. Lubricants are found in concentrations less than 1% w/w. Glidants on the other hand help improve the flow characteristics of the material being compressed. They achieve this by reducing inter particle friction. Corn starch in concentrations of 5-10% w/w can act as a glidant. Formulators add anti-adherents to the tablet formulations to prevent the material from sticking to the walls of the tablet press. Talcum powder is one of such agents and is used in concentrations of 5% w/w. Lubricants, glidants, and anti-adherents are added and mixed with the granulation just before compression [1-6].

Disintegrants are added to the formulation to allow the tablet to break apart upon contact with water. These agents tend to swell when they encounter water and thus break apart the tablet and cause it to disintegrate. Cellulosic materials and natural gums, as well as starch, may be used to function in this capacity. The typical concentration of disintegrants in formulations is between 0.5% to 5% [2,4,6].

The inclusion of absorbents in a tablet formulation is necessary if the product contains a substance with a high affinity to water. Hygroscopic materials, if present, render the blend wet and difficult to handle during manufacture. Silicon dioxide can absorb excess moisture and remain a dry powder. Examples of other absorbents are kaolin, bentonite, dry starch, tricalcium phosphate, Veegum® (colloidal magnesium aluminum silicate), magnesium oxide, and magnesium carbonate [4].

Coloring agents may be employed in tablet formulations to render the tablet aesthetically appealing and to perhaps distinguish one product from another by the color of the tablet. However, coloring agents may also serve to establish visual homogeneity of the blend once the color is uniformly distributed in the mixture. During wet granulation, the dye is dissolved or dispersed in the binder solution and added to the mix along with the binder. FD&C or D&C dyes or

Lake pigments may be used in the tablet formulation. Lake pigments, unlike dyes, are insoluble in water and they color by dispersion. Lake pigments are more suited to color solid dosage forms such as tablets [1,4].

Flavoring oils are needed for chewable tablets. The oil is generally added in a dry form such as spray-dried beadlets. An excess amount of the flavor oil can interfere with the flow ability of the granulation, and thus its concentration in the blend is kept at 0.5% or less [4,6].

Ingredients that may be included in a tablet formulation are often chosen by experimental and scientific knowledge in the field of manufacturing solid dosage forms as well by applying mathematical modeling such as the Design of Experiment (DoE). The utilization of DoE in finding the best composition of a tablet formulation may be achieved by choosing a proper design, defining a study domain, and by conducting experimentation. Among the useful designs in this respect are mixtures design and custom design (also known as D-optimal design). Whereas the latter allows more flexibility in choosing the appropriate amount of ingredients to be tested, the former is applied with the constraint that the sum of ingredients for a given formulation must be 100%. Statistical programs such as JMP Statistical Discovery Software (SAS Institute, Cary, NC) may be used to run the DoE planning and analysis. When applying the DoE on tablet formulation, the operator has to define at least one measurable outcome, define the ranges of the quantity of each ingredient to be tested within the formulation, and finally determine the number of runs (experiments) that should be performed. Each experiment in the DoE table then is executed by the operator and the value of the outcome is recorded. Once all the data are collected, the results are analyzed and the best composition for the tablet formulation is then obtained. As a proof of concept, this formulation is then prepared multiple times and subjected to further testing in order to define its suitability for manufacturing. The application of DoE in formulation is currently considered to be the state of art in preparing dosage forms.

Tablet Preparation

As mentioned above, tablets are made on machines known as presses. These can be single-punch or multi-stationary presses. The main components of a press are the hopper, guiding scrapers, dies, punches, and cams. The material to be tableted is placed in the hopper and with the help of the feeders is distributed into the die cavity. The upper punch descends with force guided by cams to compress the material into a tablet. The formed tablet is then released from the die cavity with the movement of the lower punch. The position of the lower punch inside the die determines the size of the die cavity. Thus, dies shape and control the size of the tablets. Punches also influence the shape of the tablets as well. Some tablets are shaped like capsules for easy swallowing the unit [4]. These are known as caplets.

Two methods of making tablets are recognized. These are the dry methods and wet methods. The dry methods are of two types, direct compression, and granulation by compression. The first method relies on the presence of a directly compressible vehicle. The API is added to the vehicle and compressed. Granulation by compression includes formation of a large, poorly formed tablets (known as slugs), followed by gridding the slugs into granules. The resulting granules are made into slugs and then one more time made into granules. These final granules are then compressed into tablets. Due to twice formation of granules and slugs, the cohesive forces in the mixture is strong enough, and thus binders are not needed in the formulation. Moreover, since no water is used during the preparation of slugs or granules, there is also no need for drying steps [1-3].

In wet granulation methods, the API is mixed homogeneously with other fillers that include half the quantity of disintegrants and then wetted with an aqueous dispersion of the binder containing the dye. Following proper mixing, the wet mass is then forced through sieve openings to form granules. The resulting granules are dried and passed again through sieve openings smaller than the ones used before. Lubricants, glidants, anti-adherents, and half the quantity of disintegrants are added to the granules and mixed. The resulting dry granulation mixture is finally compressed into tablets. As a rule, small tablets require small granules and large tablets need large granules [1-3].

Quality Control Tests

The United States Pharmacopeia (USP) lists several tests to be performed on the finished tablets to assure their suitability to be used in therapy [1,2]. These tests are also essential to ensure that various batches of the same products produce consistent results on these tests. For more details on these tests, the reader is referred to the USP 41/NF 36.

Tablet breaking force tests the hardness of the tablet. Too much binder in the formulation produces hard tablets. If the tablet is soft, it can be damaged easily by handling, packaging, or shipping. On the other hand, too hard tablets cannot disintegrate easily, and the bioavailability of the API from the tablets is significantly affected.

Friability test examines the amount of material lost from tablets

after subjecting them to fall from a 6-inch hight while they are rotated 100 times (25 rotations/minute for 4 minutes). Tablets (20) are weighed before the test and immediately following the rotation. For the batch of tablets to pass this test, the loss in their weight should be less than 1%. In the case of capping (loss of top or bottom of the tablet) during the friability test, the tablets fail this test regardless of the weight loss.

Disintegration test is required to assure that the tablets can break apart when they contact aqueous fluids. The test utilizes a basket made of a mesh screen at its bottom and six columns where the tablets are placed, one tablet per column. The basket is then immersed in 900 mL of water (37°C) and moved up and down with the help of a motor that controls a handler where the basket is attached to it. For most immediate release tablets, their disintegration time is within a few minutes.

Among the important tests to be performed on the finished tablets is the dissolution test. The test utilizes six round-bottom flasks that are placed in a water bath for temperature control (37°C). One tablet is placed in each flask containing the test medium (usually water, 900 mL). It is expected that at a minimum 70-75% of the API is dissolved in the test medium within 30-45 minutes. In practice, for most immediate release tablets, a minimum of 90% of API is dissolved within 30 minutes.

Weight variation test requires the selection of 10 tablets from the tablets batch and pulverizing them together in a mortar. A weight equivalent of a single tablet is then taken from the powder mixture and analyzed for its content of API. This amount is then compared with the labeled amount of the API in the product.

Content uniformity test is like the weight variation test. However, the API content in 10 different random tablets is determined individually.

Conclusion

As a solid dosage form, tablets are popular among patients and practitioners alike as they provide a means of self-administration. The formulation of a tablet contains, in addition to the API, various substances to assure proper delivery of the API to the patient. Quality control tests on the finished products are required and follow USP standards.

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