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REVIEW ARTICLE

A Review of Formulation Techniques and Evaluation Parameters of Fast Dissolving Tablets

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Abstract: Fast dissolving tablets (FDTs) have gained significant popularity as a convenient and patient-friendly dosage form, particularly beneficial for pediatric, geriatric, and patients with swallowing difficulties. These tablets are formulated to disintegrate or dissolve rapidly in the oral cavity, eliminating the need for water and enhancing patient compliance. This review article provides a comprehensive overview of FDTs, covering various aspects such as their definition, ideal characteristics, advantages, and formulation techniques. The manufacturing methods employed in the development of FDTs are discussed in detail, including direct compression, lyophilization, tablet molding, mass extrusion, spray drying, nanotization, sublimation, and the cotton candy process. Special emphasis is placed on the critical role of superdisintegrants, such as croscarmellose sodium, crospovidone, and sodium starch glycolate, in achieving rapid disintegration of the tablets. The review also highlights the essential pre-compression and post-compression evaluation parameters for FDTs, ensuring their quality and performance. These parameters include angle of repose, bulk density, tapped density, compressibility index, Hausner's ratio, tablet hardness, thickness, friability, drug content uniformity, weight variation, wetting time, water absorption ratio, in-vitro disintegration time, and in-vitro dissolution studies. The advantages of FDTs include patient compliance, rapid onset of action, increased bioavailability, and improved stability.

Keywords: Fast dissolving tablets; Super-disintegrants; Patient compliance; Formulation; Evaluation

1. Introduction

Fast dissolving tablets (FDTs) have gained significant attention in the pharmaceutical industry due to their unique properties and advantages over conventional oral dosage forms [1]. The United States Food and Drug Administration (USFDA) defines FDTs as solid dosage forms containing medicinal substances that disintegrate rapidly, usually within a matter of seconds, when placed upon the tongue [2]. The European Pharmacopoeia describes orally disintegrating tablets as uncoated tablets that disperse rapidly in the mouth before being swallowed, typically within 3 minutes [3].

FDTs offer several advantages, including ease of administration, precise dosing, rapid dissolution and absorption, and increased bioavailability [4]. They are particularly beneficial for patients who have difficulty swallowing tablets, such as pediatric, geriatric, and psychiatric individuals [5]. Moreover, FDTs are highly convenient for travelers as they eliminate the need for water during administration [6]. The key approaches in the development of FDTs involve optimizing the porous structure of the tablet matrix, incorporating appropriate disintegrating agents, and using highly water-soluble excipients [7]. The manufacturing techniques employed in FDT formulation include direct compression, lyophilization, tablet molding, mass extrusion, spray drying, nanotization, sublimation, and the cotton candy process [8].

1.1. Ideal Characteristics of Fast Disintegratig Tablets

An ideal FDT should possess the following characteristics [9]:

1. Convenient and easy to administer, requiring no water for oral administration
2. Disintegrates and dissolves in the mouth within a few seconds
3. Possesses sufficient mechanical strength to withstand the manufacturing process and handling
4. Allows high drug loading
5. Provides enhanced flavor with no lingering residue after disintegration
6. Unaffected by environmental factors such as humidity and temperature
7. Compatible with taste masking
8. Has a pleasant mouth feel

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2. Manufacturing Techniques

Various manufacturing techniques have been employed in the development of FDTs, each with its own advantages and limitations [10].

2.1. Direct Compression

Direct compression is the simplest and most cost-effective method for manufacturing FDTs. It involves the compression of a powder blend containing the active ingredient, superdisintegrants, and other excipients into tablets using conventional tableting equipment [11]. The success of this method relies on the proper selection of excipients and optimization of the compression process.

2.2. Lyophilization (Freeze-Drying)

Lyophilization is a process that involves the removal of water from a frozen suspension or solution of the drug and excipients, resulting in a highly porous and lightweight tablet matrix [12]. The tablets prepared by this method exhibit rapid disintegration due to their porous structure, which allows quick penetration of saliva. However, the lyophilization process is relatively expensive and time-consuming.

2.3. Tablet Molding

Tablet molding involves the preparation of a molded matrix by using water-soluble ingredients, which are then dried to form a porous and highly soluble matrix [13]. The molded tablets disintegrate rapidly when placed in the mouth. This technique is suitable for heat-sensitive drugs but requires specialized equipment and may have limited mechanical strength.

2.4. Mass Extrusion

In the mass extrusion method, a blend of the drug and excipients is softened using a solvent mixture of water-soluble polyethylene glycol and methanol [14]. The softened mass is then extruded through a syringe to form cylindrical extrudates, which are subsequently cut into uniform tablets. This technique produces tablets with good mechanical strength and rapid disintegration.

2.5. Spray Drying

Spray drying involves the preparation of a liquid formulation containing the drug, polymer, and other excipients, which is then sprayed into a hot air stream to form fine droplets [15]. The droplets rapidly evaporate, leaving behind a highly porous powder that can be compressed into tablets. This method is suitable for heat-sensitive drugs and produces tablets with good disintegration properties.

2.6. Nanotization

Nanotization involves the reduction of drug particle size to the nanometer range, typically less than 1000 nm [16]. The nanoparticles are then incorporated into the tablet matrix along with other excipients. The increased surface area of the nanoparticles leads to enhanced dissolution and rapid disintegration of the tablets.

2.7. Sublimation

The sublimation method involves the incorporation of a volatile ingredient, such as camphor or ammonium bicarbonate, into the tablet matrix [17]. After compression, the tablets are subjected to a sublimation process, where the volatile ingredient is removed by applying heat or vacuum, resulting in a highly porous structure that facilitates rapid disintegration.

2.8. Cotton Candy Process

The cotton candy process utilizes a unique spinning mechanism to produce floss-like crystalline structure, which is then blended with the drug and other excipients and compressed into tablets [18]. The resulting tablets have a highly porous structure and exhibit rapid disintegration.

3. Superdisintegrants

Superdisintegrants are essential components in the formulation of fast dissolving tablets (FDTs), as they facilitate rapid disintegration of the tablet matrix [19]. These agents are more efficient than traditional disintegrants, requiring lower concentrations to achieve superior disintegration and mechanical strength. The incorporation of superdisintegrants in FDT formulations enhances the tablet's ability to break down quickly in the oral cavity, promoting faster drug release and improved patient compliance.

3.1. Types and Mechanisms of Superdisintegrants

Several superdisintegrants are commonly used in FDT formulations, including croscarmellose sodium, crospovidone, and sodium starch glycolate [20]. Each superdisintegrant exhibits unique mechanisms of action to promote rapid tablet disintegration [21]

3.1.1 Swelling: Croscarmellose sodium and sodium starch glycolate have a high capacity for water uptake, leading to rapid swelling and subsequent disintegration of the tablet matrix [22].

3.1.2 Wicking: Crospovidone possesses a fibrous and highly compressible structure, allowing for the quick wicking of water into the tablet matrix, thereby facilitating disintegration [23].

3.1.3 Deformation: Some superdisintegrants, such as crospovidone, can undergo deformation during compression, which contributes to the rapid disintegration of the tablet when in contact with water.

The choice of superdisintegrant depends on factors such as the desired disintegration time, drug properties, and compatibility with other formulation ingredients

Table 1. Commonly used Superdisintegrants

Superdisintegrant	Chemical Name	Mechanism of Action	Concentration Range
Croscarmellose Sodium	Crosslinked sodium carboxymethylcellulose	Swelling, wicking	0.5-5.0%
Crospovidone	Crosslinked polyvinylpyrrolidone	Wicking, deformation	2.0-5.0%
Sodium Starch Glycolate	Sodium carboxymethyl starch	Swelling	2.0-8.0%
Calcium Silicate	Calcium silicate	Wicking	0.5-5.0%
Kollidon CL-SF	Crosslinked polyvinylpyrrolidone	Wicking, deformation	0.5-3.0%

4. Evaluation Parameters for Fast Dissolving Tablets

The evaluation of FDTs involves both pre-compression and post-compression parameters to ensure the quality and performance of the final product [24].

4.1. Pre-compression parameters

4.1.1 Angle of Repose: The angle of repose measures the friction forces in a loose powder and indicates its flow properties [25]. It is determined by measuring the maximum angle between the surface of the powder pile and the horizontal plane.

4.1.2 Bulk Density: Bulk density is determined by pouring the powder blend into a graduated cylinder and measuring the volume and weight of the powder [26]. It provides information about the packing behavior of the powder.

4.1.3 Tapped Density: Tapped density is measured by subjecting the powder blend to a fixed number of taps in a graduated cylinder and determining the final volume and weight [27]. It indicates the ability of the powder to settle and compact.

4.1.4 Carr's Compressibility Index: Carr's index is a measure of the compressibility and flowability of the powder [28]. It is calculated based on the difference between the tapped density and bulk density of the powder.

4.1.5 Hausner's Ratio: Hausner's ratio is an indirect measure of the ease of powder flow [29]. It is calculated as the ratio of tapped density to bulk density. Lower values indicate better flow properties.

4.2. Post-compression parameters

4.2.1 Tablet Hardness and Thickness: Tablet hardness is measured using a hardness tester and expressed in units of force, such as kilogram-force or Newton [30]. The thickness of the tablet is determined using a micrometer or vernier caliper. These parameters indicate the mechanical strength and uniformity of the tablets.

4.2.2 Friability: Friability testing evaluates the ability of the tablets to withstand abrasion and mechanical stress during handling and packaging [31]. It is determined by subjecting a sample of tablets to a specified number of rotations in a friabilator and measuring the percentage weight loss.

4.2.3 Drug Content Uniformity: Drug content uniformity is assessed by determining the amount of active ingredient present in a sample of tablets [32]. It ensures that each tablet contains the labeled amount of the drug within specified limits.

4.2.4 Weight Variation: Weight variation is determined by weighing a sample of tablets individually and calculating the average weight and percentage deviation from the average [33]. It ensures consistency in the weight of the tablets.

4.2.5 Wetting Time and Water Absorption Ratio: Wetting time is the time required for a tablet to become completely wet when placed on a moist surface [34]. Water absorption ratio is determined by comparing the weight of the tablet before and after water absorption. These parameters provide insights into the hydrophilicity and disintegration behavior of the tablets.

4.2.5 In-vitro Disintegration Time: In-vitro disintegration time is measured using a disintegration apparatus as specified in pharmacopeias [35]. It determines the time required for the tablets to disintegrate completely under simulated conditions.

4.2.6 In-vitro Dissolution Studies: In-vitro dissolution studies are conducted using a dissolution apparatus to assess the release profile of the drug from the FDTs [36]. Samples are withdrawn at specific time intervals, and the amount of drug released is determined using a suitable analytical method

5. Marketed formulations

The marketed formulations using superdisintegrants and their key features are listed out in Table 2.

Table 2. Marketed fast dissolving tablet products using superdisintegrants

Product	Active Ingredient	Superdisintegrant	Key Features
Zyprexa Zydis	Olanzapine	Crospovidone	- Rapid disintegration within seconds - Improved patient compliance in psychiatric patients
Claritin RediTabs	Loratadine	Crospovidone	- Quick relief from allergic symptoms - Convenient oral disintegrating form
Zofran ODT	Ondansetron	Croscarmellose Sodium	- Fast onset of action for preventing nausea and vomiting - Improved patient compliance during chemotherapy
Maxalt-MLT	Rizatriptan Benzoate	Crospovidone	- Rapid relief from migraine attacks - Disintegrates within seconds on the tongue
Pepcid RPD	Famotidine	Crospovidone	- Rapid relief from acid reflux and heartburn - Convenient oral disintegrating form
Zomig ZMT	Zolmitriptan	Crospovidone	- Fast onset of action for migraine treatment - Disintegrates rapidly in the mouth
Feldene Melt	Piroxicam	Croscarmellose Sodium	- Rapid pain relief for arthritis and other inflammatory conditions - Convenient oral disintegrating form for elderly patients
Zelapar	Selegiline	Crospovidone	- Rapid disintegration and absorption for Parkinson's disease treatment - Convenient oral disintegrating form for patients with swallowing difficulties
Risperdal M-Tab	Risperidone	Crospovidone	- Fast onset of action for treating schizophrenia and bipolar disorder - Improved patient compliance in psychiatric patients
Nulev	Hyoscyamine Sulfate	Crospovidone	- Rapid relief from abdominal pain and cramping - Convenient oral disintegrating form for on-the-go use

6. Conclusion

Fast dissolving tablets have emerged as a promising approach to enhance patient compliance and improve the therapeutic efficacy of drugs. The unique properties of FDTs, such as rapid disintegration, ease of administration, and improved bioavailability, make

them an attractive option for various patient populations, including pediatric, geriatric, and psychiatric patients. The development of FDTs involves the selection of suitable manufacturing techniques, such as direct compression, lyophilization, tablet molding, mass extrusion, spray drying, nanotization, sublimation, and the cotton candy process. The incorporation of superdisintegrants, such as croscarmellose sodium, crospovidone, and sodium starch glycolate, plays a pivotal role in achieving rapid disintegration of the tablet matrix. In conclusion, fast dissolving tablets offer a promising approach to improve patient compliance and enhance the therapeutic outcomes of drugs. With continued advancements in formulation techniques and evaluation methods, FDTs are poised to revolutionize the oral drug delivery landscape and provide a convenient and effective alternative to conventional tablets.

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