

Fast-disintegrating tablets: a novel approach in pharmaceutical preparation

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ABSTRACT

Fast Disintegrating Tablets (FDTs) have emerged as a promising pharmaceutical dosage form that addresses the challenges of patient compliance and convenience. These tablets are designed to disintegrate rapidly in the mouth without the need for water, offering several advantages such as ease of administration, improved medication adherence, and enhanced bioavailability. Fast Disintegrating Tablets have overcome the main drawbacks of conventional oral pharmaceutical dosage forms, such as the difficulty of swallowing especially for pediatric and geriatric populations, the lack of patient compliance, and the erratic pattern in bioavailability due to exposure to the first-pass metabolism. Fast Disintegrating Tablets can rapidly disintegrate in the oral cavity, depending on saliva. The disintegration occurs within a few seconds, less than one minute. There are several techniques for preparing the orodispersible tablets such as Direct

Compression, Freeze-drying (Lyophilization), Spray Drying, Sublimation, Molding, Effervescent Technology, Orodispersible Films (ODFs), and Cotton candy process. This review has introduced a brief introduction to the advantages, disadvantages, mechanisms of action, criteria for excipients used in FDTs, excipients used in FDTs, techniques for preparation, and the evaluation of FDTs depending on pharmacopeia.

Keywords: Fast disintegrating tablet; formulation techniques; super-disintegrants; excipients; bioavailability.

1. Introduction

Despite several drug administration routes; oral drug administration is the most appropriate. The oral route has many advantages and benefits over other routes of administration, like the ease of oral drug administration, cost-effectiveness, patient preference, painless way for treatment, non-invasiveness, and simplicity of producing oral dosage forms on a wide scale of the manufacturing process (1). According to current evaluations, approximately 90% of the global market share of drugs intended for human consumption is held by oral formulations (2).

Despite these benefits, producing oral formulations is difficult due to the large variation in physical and chemical characteristics of medications, like as their poor water solubility and membrane permeability. Drugs' limited stability in terms of both chemicals and biology in addition to physiological barriers related to humans, including pH variation along the gastrointestinal tract (GIT), efflux transporters such as the P-glycoprotein efflux pump, and metabolic enzymes, can also limit absorption. Also, some medications can make you feel nauseous and irritated locally (3).

1.1 Physiological Barriers:

- The intestinal epithelial cell is one of the main obstacles to the gastrointestinal tract's ability to absorb drugs (1).
- pH, which varies along the gastrointestinal tract and differs according to the fasting state and the fed state (4).
- efflux transporters such as P-glycoprotein efflux pumps remove the drug back to the extracellular medium before reaching the cell cytoplasm (5).
- Metabolism occurs due to digestive enzymes concentrated in the microvilli of the small intestine (6).

1.2 Physical and chemical Barriers (physicochemical properties):

- The water solubility of the drug is a critical step, as the drug must be in soluble form in GIT fluid to be absorbed.
- Membrane permeability of the intestinal epithelial membrane varies according to the BCS of drugs (7).

The tablet is one of the most widely used traditional solid unit forms of administration. It is simple to swallow, ideal for sustained, controlled, prolonged, extended, and fast-release formulation, and it includes an active pharmaceutical ingredient and excipients that are made by compressing powdered medication into a solid, smooth pill. Another name for these is pills. It can be divided into four categories: molded tablets, controlled-release tablets, sustained-release tablets, and fast-dissolving tablets (8). FDTs are one of the newest oral delivery drug technologies that have attracted attention lately. FDTs are solid oral dose forms that, when inserted into the mouth, quickly dissolve in just a few seconds (9). Because super-disintegrants such as croscarmellose sodium, sodium starch glycolate, and crospovidone are key components of the formulation, FDTs, as their name suggests, exhibit rapid disintegration and subsequent

dissolution in the mouth. Fast disintegration technology (FDT) enhances absorption and the start of therapeutic activities, making it a better dose form than traditional tablets (10). The FDTs are intended for patients who have trouble swallowing tablets, including young children, the elderly, bedridden individuals, and others. Together with these benefits, FDTs can also be used to treat a variety of acute diseases that call for immediate medical attention, such as motion sickness, nausea, vomiting, sudden episodes of coughing, psychosis, stroke, and recurrent emesis (11).

This review article investigates the description of fast disintegrating tablets, their advantages, disadvantages, method of preparation, and examples of prepared FDTs.

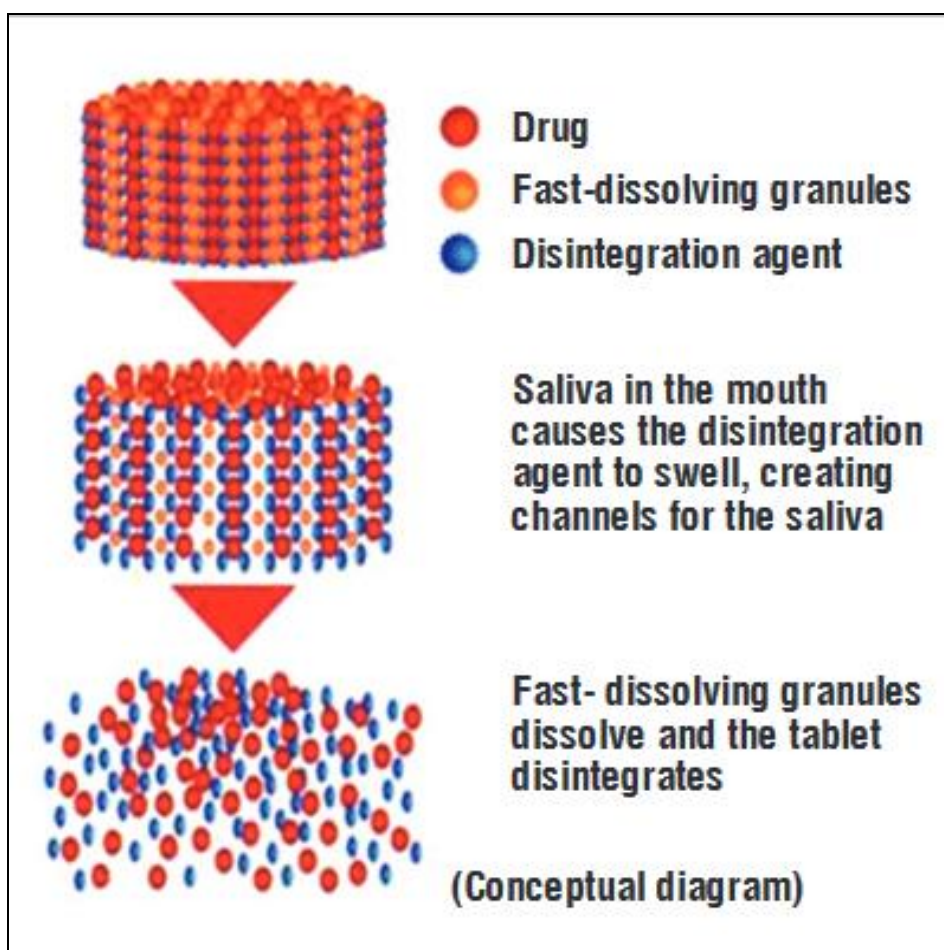


Figure 1: Disintegration of fast disintegrating tablet (12).

2. Advantages and Disadvantages of FDTs:

2.1 Advantages of FDTs:

FDTs are especially useful for patients who don't have access to water, as they dissolve in the buccal cavity in a matter of seconds and improve patient compliance. Because pharmaceutical compounds are absorbed through the mouth, throat, and esophagus and do not undergo first-pass metabolism, FDTs improve the bioavailability of medications. FDTs also have the advantage of being easy to carry, having good physical and chemical stability, without any mistakes in dosage, and being the preferred solution for elderly and pediatric patients. Because FDTs dissolve and absorb quickly in the mouth, they provide rapid action in emergencies and virtually no asphyxia. FDTs may be packaged using blister packaging, which enables economical production, and no specific tools or procedures are needed (13-15).

2.2 Disadvantages of FDTs:

The main disadvantages of FDTs are extremely porous, tablets can be brittle, and also friable. Because FDTs are hygroscopic, they are unable to retain their physical and structural integrity. Individuals who have dry mouths due to insufficient saliva production should not take FDTs (16).

3- Mechanisms of Super-disintegrants:

Super-disintegrants are substances used in pharmaceutical formulations to enhance the dissolution and disintegration of solid dosage forms, such as tablets and capsules. They facilitate the rapid breakup of the dosage form into smaller particles, thereby increasing the surface area available for drug release and absorption. This improved disintegration and dissolution properties of the dosage form can lead to enhanced drug bioavailability and faster onset of action. The mechanisms of action of super-disintegrants can vary depending on the specific type of super-

disintegrant used (more details in **Table 1**). Here are some of the commonly recognized mechanisms:

3.1 Swelling: Some super disintegrants, such as cross-linked polymers (e.g., sodium starch glycolate, croscarmellose sodium), can rapidly absorb water and swell. This swelling process generates a significant increase in volume, exerting pressure on the surrounding matrix and promoting its disintegration (17).

3.2 Capillary Action/Wicking: Superdisintegrants like crospovidone and croscarmellose sodium are known for their capillary action mechanism. They can rapidly absorb liquid from the surrounding environment, creating capillary channels within the dosage form matrix. This action facilitates the penetration of dissolution fluid into the tablet, accelerating disintegration (18).

3.3 Porosity/Channeling: Certain super disintegrants can create pores or channels within the tablet matrix. As the dissolution fluid penetrates these channels, it causes the matrix to break apart, leading to rapid disintegration. Examples of superdisintegrants that employ this mechanism include modified cellulose (e.g., sodium carboxymethylcellulose) and certain calcium salts (19).

3.4 Effervescence: Effervescent superdisintegrants, such as sodium bicarbonate and citric acid, generate carbon dioxide gas when they come into contact with water or saliva. The gas formation creates internal pressure within the dosage form, leading to disintegration (20).

3.5 Cation Exchange: Certain super disintegrants, such as ion exchange resins (e.g., Indion 414), can undergo cation exchange with the ions present in saliva or dissolution fluid. This exchange process leads to swelling and subsequent disintegration of the dosage form (21).

It's important to note that different super disintegrants can employ multiple mechanisms simultaneously or rely primarily on one specific mechanism. The selection of a super disintegrant depends on various factors, including the formulation characteristics, drug properties, and desired

performance attributes. Pharmaceutical formulators consider these factors to choose the most suitable super disintegrant and optimize the disintegration and dissolution properties of solid dosage forms (22).

Table 1 Example of super disintegrants and their mechanism of action.

Super disintegrant	Mechanism of action	Properties
Gollan Gum	Excellent swell characteristics once interacting with water.	Super-disintegrant polysaccharide with anionic properties.
Xanthan Gum	Great Property Swelling	increased hydrophilic properties, solubility in water, and extremely low gelling tendencies.
Cross-linked alginic acid	A colloidal hydrophilic material.	Wicking and swell movement.
Soy Polysaccharide	Quick disintegration	Because these items don't include sugar or starch, they are utilized by diabetics.
Sodium-Starch Glycolate	Excellent Swelling Asset.	Water that is absorbed quickly creates 6% swelling, and high concentration results in gelling.
Cross-povidone	Wicking Action that Swells.	1-3% is the efficacy concentration. It comes in rapid dispersion, micronized grades, and water-swelling varieties.

4. Challenges to develop FDTs:

The development of Fast-Dissolving Tablets (FDTs) presents several challenges that need to be addressed during the formulation and manufacturing processes. Some of the key challenges include:

4.1 Drug Compatibility: Ensuring the compatibility of the active pharmaceutical ingredient (API) with the excipients used in the formulation is crucial. Some drugs may undergo degradation or chemical reactions under the conditions required for FDT preparation, such as high temperatures or exposure to moisture. Compatibility studies are necessary to mitigate any potential issues (23).

4.2 Taste Masking: FDTs are designed to dissolve rapidly in the oral cavity, which exposes the taste buds to the drug. Many drugs have unpleasant tastes, and masking or improving the palatability of the formulation is essential for patient acceptance. Various taste-masking techniques, such as the use of sweeteners, flavors, or encapsulation, may be employed to overcome this challenge (24).

4.3 Mechanical Strength: FDTs should be able to withstand handling during manufacturing, packaging, and transportation without excessive friability or breakage. Achieving the right balance between rapid disintegration and mechanical strength is crucial to ensure the tablet remains intact until administration (25).

4.4 Formulation Stability: FDTs often contain moisture-sensitive or unstable drugs, and maintaining their stability over the shelf life of the product can be challenging. Moisture absorption, drug degradation, and physical changes in the formulation can occur, leading to reduced efficacy or altered drug release profiles. Careful selection of excipients, packaging materials, and appropriate storage conditions is necessary to ensure long-term stability (26).

4.5 Manufacturing Technology: Developing robust and scalable manufacturing processes for FDTs can be complex. The selection of suitable equipment and techniques, such as direct compression, freeze-drying, or spray-drying, requires careful consideration. Ensuring uniform drug distribution, homogeneity of the formulation, and consistent tablet properties across production batches are critical for quality control (24).

4.6 Regulatory Considerations: FDTs may have specific regulatory requirements, depending on the region or country where they will be marketed. Compliance with regulations related to drug development, safety, efficacy, and labeling is essential. Additionally, demonstrating the bioequivalence of FDTs to conventional oral dosage forms may be necessary in some cases.

Overcoming these challenges requires a systematic approach involving formulation optimization, excipient selection, process development, and comprehensive testing. Collaboration between formulation scientists, pharmacists, and manufacturing experts can help address these challenges and develop FDTs that meet the desired quality, efficacy, and patient acceptability standards.

5. Criteria for excipient used in FDTs:

When selecting excipients for Fast-Dissolving Tablets (FDTs), several criteria need to be considered to ensure their suitability for the formulation. Here are some key criteria for excipient selection in FDTs:

5.1 Disintegration and Dissolution Enhancement: Excipients should possess disintegrating properties to facilitate rapid tablet disintegration and dissolution. Super disintegrants, such as croscarmellose sodium, sodium starch glycolate, crospovidone, or modified cellulose, are commonly used in FDT formulations due to their ability to promote rapid disintegration and dissolution (27).

5.2 Taste-Masking and Flavoring: FDTs often need to mask the unpleasant taste of drugs to enhance patient acceptability. Sweeteners, flavors, and taste-masking agents can be incorporated into the formulation to improve the taste of the tablet. Examples include mannitol, aspartame, sucralose, and various natural and artificial flavors (28).

5.3 Mouthfeel and Texture: Excipients that contribute to the desirable mouthfeel and texture of the FDTs can enhance the overall user experience. They should provide a smooth and pleasant sensation in the mouth, without any grittiness or chalkiness. Examples of such excipients include microcrystalline cellulose, lactose, and pregelatinized starch (29).

5.4 Mechanical Strength and Integrity: Excipients should provide sufficient mechanical strength to the tablet, ensuring it remains intact during handling, packaging, and transportation. The tablet should not be too brittle or friable. Diluents or binders, such as mannitol, sorbitol, or low-substituted hydroxypropyl cellulose (L-HPC), can contribute to tablet hardness and structural integrity (29).

5.5 Compatibility with Active Pharmaceutical Ingredient (API): Excipients should be compatible with the API to maintain drug stability and prevent any chemical interactions that may affect efficacy or safety. Compatibility studies between the API and excipients should be conducted to ensure there are no adverse effects on drug stability or release (29).

5.6 Regulatory Considerations: Excipients used in FDTs should comply with relevant regulatory requirements and be approved for use in pharmaceutical formulations. They should have a well-established safety profile and be listed in regulatory compendia, such as the United States Pharmacopeia (USP) or European Pharmacopoeia (Ph. Eur.).

5.7 Manufacturing Compatibility: Excipients should be compatible with the chosen manufacturing process, whether it is direct compression, freeze-drying, or other techniques. They

should exhibit good flow properties, compressibility, and compatibility with the equipment used for tablet manufacturing (30).

5.8 Cost and Availability: Excipients should be cost-effective and readily available from reputable suppliers to ensure commercial viability and scalability of FDT production (31).

It's important to note that the specific excipients and their concentrations in FDT formulations will vary depending on the drug characteristics, desired tablet properties, and the intended route of administration. Excipient selection should be based on a thorough understanding of the formulation requirements and compatibility with the overall product design.

6. Excipients that are used for the production of the FDTs:

Several excipients are commonly used in the production of Fast-Dissolving Tablets (FDTs) to achieve the desired characteristics and performance of the dosage form. Here are some examples of excipients commonly used in FDT formulations:

6.1 Superdisintegrants: Superdisintegrants promote rapid tablet disintegration and dissolution. Examples include Croscarmellose sodium, Sodium starch glycolate, Crospovidone, and Modified cellulose (e.g., sodium carboxymethylcellulose) (31). More details about super disintegrants are explained in **Table 1**.

6.2 Diluents/Fillers: Diluents or fillers are used to provide bulk to the tablet formulation and contribute to tablet hardness. Examples include Mannitol, Sorbitol, Lactose, and Microcrystalline cellulose (31).

6.3 Binders: Binders are used to promote tablet cohesion and ensure tablet integrity. Examples include Hydroxypropyl cellulose (HPC), Polyvinylpyrrolidone (PVP), and Starches (e.g., pregelatinized starch) (32).

6.4 Disintegrants: In addition to super disintegrants, other disintegrants may be used to further enhance tablet disintegration. Examples include Starches (e.g., pregelatinized starch), Sodium starch glycolate, and Cross-linked polyvinylpyrrolidone (crospovidone) (32).

6.5 Lubricants: Lubricants improve the flow properties of the tablet formulation and prevent sticking to the tablet punches during manufacturing. Examples include Magnesium stearate, Calcium stearate, and Stearic acid (33).

6.6 Sweeteners: Sweeteners are used to improve the taste of FDTs and enhance patient acceptability. Examples include Mannitol, Sorbitol, Aspartame, Sucralose (31).

6.7 Flavors: Flavors are added to FDTs to enhance palatability and mask the taste of drugs. Examples include various natural and artificial flavors (31).

6.8 Colors: Colors may be added to FDTs for aesthetic purposes and to aid in product identification. Examples include various colorants approved for pharmaceutical use (31).

6.9 pH Modifiers: pH modifiers may be used to adjust the pH of the formulation to optimize drug stability or enhance dissolution. Examples include citric acid, sodium bicarbonate, or tartaric acid (31).

It's important to note that the specific excipients used in FDT formulations may vary depending on factors such as the drug properties, desired tablet characteristics, and the chosen manufacturing process. The selection and concentration of excipients should be based on a comprehensive understanding of the formulation requirements and compatibility with the active pharmaceutical ingredient (API).

7. Techniques that used for preparing the FDTs:

Several techniques can be used for preparing Fast-Dissolving Tablets (FDTs), depending on the desired formulation characteristics and the properties of the active pharmaceutical ingredient (API) and excipients. Here are some commonly employed techniques:

7.1 Direct Compression: This is a simple and widely used technique where the API and excipients are blended, followed by compression into tablets using a tablet press. The excipients used should have good flow properties and compressibility. Direct compression is suitable for drugs that are stable and compatible with the compression process (34).

7.2 Freeze-drying (Lyophilization): This technique involves the preparation of a freeze-dried cake or powder, which is then compressed into tablets. It is particularly useful for heat-sensitive drugs or formulations containing volatile components. Freeze-drying helps preserve the stability of the drug and can enhance the disintegration and dissolution properties of the tablets (34).

7.3 Spray Drying: Spray drying involves atomizing a solution or suspension of the drug and excipients into a hot drying gas, resulting in the formation of dried particles. These particles can be directly compressed into tablets. Spray drying is often used for moisture-sensitive drugs or when rapid disintegration is desired (35).

7.4 Sublimation: This technique is used for volatile drugs that can undergo sublimation (conversion from solid to vapor state) under controlled conditions. The drug is combined with suitable excipients, and the mixture is compressed into tablets. During tablet compression, the volatile drug sublimes, leaving behind porous tablets that disintegrate rapidly upon contact with saliva or dissolution fluid (12).

7.5 Molding: Molding involves the use of a mold and pressure to shape the tablet formulation into the desired form. The formulation is typically a mixture of the API and excipients, including binders or polymers that provide cohesiveness. Heat or pressure is applied to facilitate the

molding process. Molding is particularly suitable for low-dose drugs or when taste masking is required (36).

7.6 Effervescent Technology: Effervescent tablets are prepared by combining the API, excipients, and effervescent components, such as citric acid and sodium bicarbonate. When the tablet comes into contact with saliva or dissolution fluid, the effervescent components react, generating carbon dioxide gas. The gas release aids in tablet disintegration and enhances patient acceptability due to effervescence (37).

7.7 Orodispersible Films (ODFs): ODFs are thin, flexible films that rapidly dissolve when placed on the tongue or in the oral cavity. The films are prepared by casting a solution or dispersion of the drug and excipients onto a suitable substrate. The solvent is then evaporated to form a solid film. ODFs offer a convenient and fast-dissolving dosage form for patients who have difficulty swallowing tablets (38).

7.8 Cotton candy process: The reason for the process's name is that it uses a special spinning mechanism to create a crystalline structure that resembles floss and resembles cotton candy. During the cotton candy-making process, a matrix of saccharides or polysaccharides is formed by simultaneously spinning and flash melting. The resulting matrix is partially recrystallized for better compressibility and flow characteristics. After milling and blending this candy floss matrix with excipients and active substances, it is compressed to form FDTs (39).

The selection of the most appropriate technique depends on various factors, including drug properties, desired tablet characteristics, manufacturing scalability, and equipment availability. Each technique has its advantages and considerations, and formulation scientists choose the technique that best suits the specific requirements of the FDT formulation.

8. Evaluation of the fast-disintegrating tablets:

The evaluation of Fast-Dissolving Tablets (FDTs) involves assessing various characteristics and performance parameters to ensure their quality, effectiveness, and patient acceptability. Here are some key aspects to consider during the evaluation of FDTs:

8.1 Weight variation: Weight variation testing is performed to assess the uniformity of tablet weight within a batch. Tablets are randomly selected and weighed individually, and the results are compared against specified acceptance criteria. Minimal weight variation ensures consistent dosing (40,41).

8.2 Disintegration time: FDTs should disintegrate rapidly in the oral cavity to facilitate quick dissolution and drug release. Disintegration time is measured using standardized methods, such as the United States Pharmacopeia (USP) disintegration test. The tablets should disintegrate within a specified time limit, typically a few seconds to a minute (40,41).

8.3 Dissolution rate: The dissolution rate of the drug from FDTs is an important parameter to determine the drug release profile. Dissolution testing is conducted using suitable apparatus and media, following established guidelines and specifications. The drug should dissolve rapidly and completely within a specific time frame (40-42).

8.4 Mechanical strength: FDTs should possess sufficient mechanical strength to withstand handling, packaging, and transportation without excessive friability or breakage. The tablets undergo hardness testing using a tablet hardness tester, and the results are compared against predefined limits (40).

8.5 Content Uniformity: Content uniformity ensures that each tablet contains the appropriate amount of the active pharmaceutical ingredient (API) and excipients, providing consistent dosage and efficacy. Content uniformity testing involves analyzing multiple tablets from a batch to confirm that the drug content is within defined limits (40,43).

8.6 Friability: Friability testing measures the tendency of tablets to chip, crack, or break under mechanical stress. The tablets are rotated in a friability apparatus, and the weight loss resulting from the abrasion is measured. The tablets should exhibit low friability to maintain their structural integrity (40,41).

8.7 Taste Evaluation: FDTs should have an acceptable taste to ensure patient compliance and acceptability. Taste evaluation is conducted using sensory evaluation techniques, involving a panel of human volunteers who assess the taste attributes, such as sweetness, bitterness, or aftertaste of the tablets (34,40).

8.8 Packaging Compatibility: FDTs should be compatible with the chosen packaging materials to maintain their stability and protect them from environmental factors, such as moisture, light, or oxygen. Packaging compatibility studies evaluate the interaction between the tablets and packaging materials to ensure integrity and shelf-life (40).

8.9 Stability Testing: Stability testing is performed to assess the long-term stability and shelf-life of FDTs under various storage conditions. The tablets are stored at specified temperatures and humidity levels, and samples are periodically tested for physical, chemical, and microbiological stability (40-44).

8.10 In vitro/In vivo Performance: In addition to the above tests, in vitro and/or in vivo performance studies may be conducted to evaluate the drug release, absorption, and pharmacokinetics of the FDTs. These studies provide insights into the bioavailability and therapeutic effectiveness of the formulation (45).

It's important to note that the specific evaluation parameters and tests may vary depending on regulatory requirements, the nature of the drug, and the desired performance characteristics of

the FDTs. The evaluation process should be conducted in accordance with applicable guidelines and standards to ensure the quality and performance of the FDTs.

9. Conclusion

In recent years, oral fast-disintegrating tablets have become one of the most popular pharmaceutical preparations compared with conventional techniques. FDTs have many advantages, such as giving rapid onset of action, improving the bioavailability of the drugs, overcoming the problem of old dosage forms like difficulty swallowing, especially in geriatric and pediatric patients, and improving patient compliance. FDTs have many technologies for production, finally giving rapidly dissolving dosage forms with many advantages.

Conflict of Interest

The authors declare that they have no conflicts of interest to disclose.

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