

# **Pharmacophore**

(An International Research Journal)

Available online at <http://www.pharmacophorejournal.com/>

## **Review Article**

### **FAST DISINTEGRATING TABLET AS A NEW DRUG DELIVERY SYSTEM:**

#### **A REVIEW**

**Agrawal V.A.\***, Rajurkar R.M Thonte S.S, Ingale R.G

Channabasweshwar College of Pharmacy (Degree),

Kava Road, Latur-412513

Maharashtra, India

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#### **ABSTRACT**

The demand for FDT (Fast Disintegrating Tablet) has been increasing from the last decade particularly in geriatric, pediatric and patient with some sort of disabilities in swallowing. FDTs are those tablets which when placed in mouth get dissolved rapidly in saliva without the need of liquid and can be swallowed. European pharmacopoeia adopted the term Orodispersible tablet for FDTs. Fast disintegrating tablets are also known as Fast melting tablets, Orodispersible tablets, fast dissolving/dispersing tablets or melt in mouth tablets. This article reviews the potential benefits offered by FDTs as an oral drug delivery system for various kinds of patients suffering from different diseases and disabilities. Desired characteristics and challenges for developing fast disintegrating drug delivery systems, quality control tests, various techniques used in the preparation of fast disintegrating drug delivery systems like lyophilization technologies, tablet molding method, sublimation techniques, spray drying techniques, mass extrusion technology, direct compression method and use of superdisintegrants. It also reviews the patented technologies for fast dissolving tablets, advantages and disadvantages of different technologies for preparing fast disintegrating dosage form, future prospective for FDTs. The growing importance for FDTs is due to the potential advantages offered by this technology. FDT is a New Drug Delivery system with least disintegration time and ease of self administration.

**Keywords:** FDT, Orodispersible tablets, Fast dissolving/dispersing tablets, Melt in mouth tablets, Mass extrusion, Superdisintegrants.

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#### **INTRODUCTION**

The most important drug delivery route is no doubt the oral route. It has advantages like convenience of administration and less manufacturing cost. Drugs administered by oral route are, solid oral dosage forms particularly

tablets, the preferred class of product. Today drug delivery companies are focusing on solid oral drug delivery systems that offer increased patient compliance and effect. Melt in mouth tablet (MMT) or fast disintegrating/dissolving or orodispersible tablet, which is known to be one of the most innovative methods in oral drug

delivery. This kind of melt in mouth tablet is good for those patients who have difficulty to swallow oral dosage forms, especially geriatric, pediatric patients. These dosage forms are also suitable for the mentally ill, bedridden, developmentally disabled patients and in patients with underlying diseases which disrupts swallowing ability (e.g. *Migraine, Parkinsonism, Throat cancer, Mouth ulcers, and Throat infections*), the patients with persistent nausea and vomiting, who are in traveling, and who do not have easy access to water.<sup>1</sup>

Fast Melting tablets (FMT) or fast disintegrating/dissolving tablets (FDT) are single unit solid unit dosage forms that disintegrate or dissolve rapidly (in few seconds) in mouth without the need of water or chewing. These dosage forms show good stability, ease of manufacturing and ease of handling by patient. The drug is immediately released from dosage form and is readily available for absorption, improving its onset of action and its bioavailability in some cases (soluble drugs), to some extent it is also possible to achieve absorption of some drugs across the oral mucosa directly into the systemic circulation, avoiding first pass metabolism & its subsequent side effects. The product can be taken any way and any time. It does not require liquid to swallow. It is ready for use in emergency situations.<sup>2</sup>

Upon ingestion, the saliva serves to rapidly dissolve the dosage form. The saliva containing the dissolved or dispersed medicament is then swallowed and the drug absorbed in the GIT. Drug is absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In these cases bioavailability of drugs is greater than those observed from standard dosage forms.<sup>3</sup>

The main criteria for fast disintegrating (dissolving) tablet is to disintegrate or dissolve rapidly in oral cavity with saliva in 15 to 60 seconds, without need of water and should have pleasant mouth feel.<sup>4</sup>

The novel technology of oral fast-dispersing dosage forms is known as fast dissolve, rapid dissolve, rapid melt and quick disintegrating tablets. However, the function and concept of all these dosage forms are similar.<sup>5</sup>

Many patients have difficulty swallowing tablets and hard gelatin capsules and consequently do not take medications as prescribed by the physician. It is estimated that 50% of the population is affected by this problem, which results in a high incidence of noncompliance and ineffective drug therapy.<sup>6</sup>

Recent advances in Novel Drug Delivery System (NDDS) aims to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance. One such approach is "Fast Dissolving Tablet".<sup>6, 7, 8</sup>

Despite of tremendous advancements in drug delivery, the oral route remains the perfect route for the administration of therapeutic agents because of the low cost of therapy and ease of administration lead to increased patient compliance. Patient convenience and compliance oriented research has resulted in bringing out safer and newer drug delivery systems. Recently Fast disintegrating drug delivery systems have started gaining popularity and acceptance as one such example with increased consumer choice, for the reason of rapid disintegration or dissolution, self-administration even without water or chewing.

In order to allow fast dissolving tablets to dissolve in the mouth, these are made of either very porous or soft- moulded matrices or compressed into tablets with very low compression force, which makes the tablets friable and/or brittle, which are difficult to handle, often requiring specialized peel-off blister packaging. To overcome this problem, some companies introduced more robust forms of fast dissolving tablets such as Zydis (R.P. Scherer, Inc.), WOVOTAB (Yamanouchi Pharma

Technologies, Inc.) and OraSolv and DuraSolv (Cima Labs, Inc.), FlashDose (Fuisz Technologies, Ltd.), Flashtab (Prographarm Group), and OraQuick (KV Pharmaceutical Co., Inc.), Quick-Dis (Lavipharm Laboratories Inc.), NanoCrystal (Elan Corp.) Recent developments in technology have presented viable dosage alternatives for patients who may have difficulty swallowing tablets or liquids. Traditional tablets and capsules administered with a glass of water which may be inconvenient or impractical for some patients. However, some patients, particularly pediatric and geriatric patients, have difficulty swallowing or chewing solid dosage forms. Many pediatric and geriatric patients are unwilling to take these solid preparations due to fear of choking. For example, a very elderly patient may not be able to swallow a daily dose of antidepressant. An eight-year-old with allergies could use a more convenient dosage form than antihistamine syrup. A schizophrenic patient in the institutional setting can hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic. A middle-aged woman undergoing radiation therapy for breast cancer may be too nauseous to swallow H<sub>2</sub>-blockers. Fast-dissolving/disintegrating tablets (FDDTs) are a perfect fit for all of these patients. FDDTs disintegrate and/or dissolve rapidly in the saliva without the need for water. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. Others contain agents to enhance the rate of tablet disintegration in the oral cavity, and are more appropriately termed fast-disintegrating tablets, as they may take up to a minute to completely disintegrate.<sup>9</sup> The advantages of fast dissolving dosage forms are increasingly being recognized in both industry and academia. Their growing importance was underlined recently when European Pharmacopoeia adopted the term "Orodispersible Tablet" as a tablet that is to be placed in oral

cavity where it dissolves rapidly before swallowing.

### **Salient features/advantages of fast dissolving/disintegrating drug delivery system<sup>10-13</sup>**

- FDT passes all the advantages of solid dosage forms like good stability, easy manufacturing, unite and accurate dosing, easy handling etc.
- Provides rapid drug therapy intervention.
- There is no risk of physical obstruction due to dosage form.
- The possibility of an improved bioavailability due to rapid absorption and faster onset of action.
- FDTs provide new life for drugs which are at the end of their patent life period.
- Ease of administration to patients who are unable or refuses to swallow a tablet, such as pediatric, geriatric and psychiatric and disabled patients.
- Does not require water while administration good disintegration and dissolution of the dosage form in oral cavity.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Can be designed to leave minimal or no residue in the mouth after administration and also to provide a pleasant mouth feel.
- Allows high capacity of drug loading.
- FDTs helps avoids hepatic metabolism by allowing pregastric drug absorption thus reducing the dose of drug required.
- Adaptable to existing processing and packaging machinery.
- Cost- effective.

- Mark Potential faster onset of action than conventional oral dosage forms.
- Broad applicability to several drugs and diseases.

### **Desired characteristics and challenges for developing fast disintegrating drug delivery systems<sup>12</sup>**

#### *Time required for disintegration*

FDTs should disintegrate/dissolve/disperse or melt in mouth without the need of water in very short duration of time, possibly within 60 seconds.

#### *Taste of the active ingredient*

As most drugs are unpalatable, fast disintegrating drug delivery systems usually contain the medicament in taste-masked form. Delivery systems dissolve or disintegrate in patient's mouth, thus releasing the active ingredients which come in contact with the taste buds and hence, taste masking of the drugs becomes critical to patient compliance.

#### *Ease of administration*

Fast disintegrating drug delivery Systems are easy to administer and handle hence, leads to better patient compliance. Usually, elderly people experience difficulty in swallowing the conventional dosage forms (tablets, capsules, solutions and suspensions) because of tremors of extremities and *dysphasia*. Fast Dissolving Delivery Systems may offer a solution for these problems.

#### *Tablet strength, Friability and porosity*

In order to allow fast disintegrating tablets to disintegrate in the mouth, they are made of either very porous or soft- moulded matrices or compressed into tablets with very low compression force, which makes the tablets friable and/or brittle, which are difficult to handle, often requiring specialized peel-off blister packaging.

#### *Hygroscopic nature*

Several fast disintegrating drug delivery dosage forms are hygroscopic and cannot maintain physical integrity under normal condition from humidity which calls for specialized product packaging.<sup>14</sup>

#### *Mouth feel<sup>15</sup>*

Mouth feel is critical, and patients should receive a product that feels pleasant. Any large particles from the disintegrating tablet that are insoluble or slowly soluble in saliva would lead to an unpleasant gritty feeling. This can be overcome by keeping the majority of the particles below the detectable size limit. In some cases, certain flavors can imbibe an improved mouth feel perception, resulting in a product that is perceived as being less gritty, even if the only change is the flavor. Effervescence can be added to aid disintegration and improve mouth feel by reducing the "dryness" of a product.

### **Quality control tests for fast disintegrating tablets**

- Appearance, size and shape
- Hardness and friability
- Wetting time
- Weight variation test
- Dissolution characteristics
- Water absorption ratio
- Disintegration time
- Content uniformity

### **Various techniques used in the preparation of fast disintegrating drug delivery systems<sup>10-12</sup>**

- Freeze-drying (Lyophilization technologies)
- Tablet molding method
- Sublimation techniques
- Spray drying techniques

- Mass extrusion technology
- Direct compression method
- Use of disintegrates

#### *Freeze drying or Lyophilization technology*

A process by which, water get sublimated from product after freezing. Lyophilization is a pharmaceutical technology which allows drying of heat sensitive drugs and biologicals at low temperature under conditions that allows removal of water by sublimation.<sup>16</sup>

Lyophilization results in preparations, which are highly porous, with a very high specific surface area, which dissolve rapidly and show improved absorption and bioavailability.<sup>17</sup> R.P. Scherer patented Zydis technology by employing freeze drying process for the preparation of mouth dissolving tablet. On the basis of patent issued to Gregory *et al.*<sup>18</sup> Seager discussed formation, process technology & bioavailability of fast dissolving tablets prepared by using Zydis technology.<sup>19</sup>

#### *Molding method*

Moulded tablets are prepared by using water-soluble ingredients so that the tablet dissolve or disintegrate rapidly and completely.<sup>20</sup> Powder is moistened with the help of hydro alcoholic solvent and then moulded into tablets under pressure less than the conventional dosage form. The solvents are removed by air-drying. The tablet Possesses porous structure, which facilitates easy dissolution. Adding sucrose, acacia or PVP k30 may increase the mechanical strength of the tablet.

#### *Sublimation method*<sup>21-24</sup>

The basic principle involved in preparing fast dissolving tablets by sublimation technique is addition of a volatile salt to the tableting components, mixing the components to obtain a substantially homogeneous mixture & volatilizing a volatile salt. The removal of volatile salts creates pores in the tablet, which help in achieving rapid disintegration when the tablet

comes in contact with saliva. Camphor, Naphthalene, Urea, ammonium bicarbonate, etc, can be used to prepare porous tablets of good mechanical strength. Koizumi *et al.* used mannitol as diluent and camphor as a volatile material to prepare porous compressed tablets. The tablets were subjected to vacuum at 80°C for 30 min to eliminate the camphor and thus form the pores in the tablet. Makino *et.al* utilized water as a pore forming material in order to prepare porous tablets with excellent mechanical strength and dissolution character.

#### *Spray drying method*

Spray drying is a process by which highly porous, fine powders can be produced. Spray-dryers are invariably used in the pharmaceutical industry to produce highly porous powders. Allen *et al.* have reported applying this process to the production of fast dissolving tablets.<sup>25-28</sup> Spray Drying can be used to prepare rapidly dissolving tablet. This technique is based upon a particulate support matrix that is prepared by spray drying and aqueous composition containing support matrix and other components to form a highly porous & fine powder. This is then mixed with active ingredient & compressed into tablet. The fast dissolving tablet prepared from spray drying technique disintegrated within 20 seconds.<sup>29, 30</sup>

#### *Mass-Extrusion technology*<sup>31</sup>

This technology involves softening the active blend using the solvent mixture of water soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby masking their bitter taste.

#### *Direct compression*<sup>9, 32</sup>

It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing

steps are involved in direct compression. Also high doses can be accommodated and final weight of tablet can easily exceed that of other production methods. This technique can now be applied to fast dissolving tablets because of the availability of improved tablet excipients, especially tablet disintegrants and sugar-based excipients.

#### *Use of disintegrates*

Use of various disintegrants in fast dissolving tablets, leads to quick disintegration of tablets and hence improves dissolution. In many fast dissolving tablet technologies based on direct compression, the disintegrants principally affect the rate of disintegration and hence the dissolution. The introduction so-called superdisintegrants and better understanding of their properties has increased the popularity of this technology. Tablet disintegration time can be optimized by concentrating the disintegrants. Below critical concentration, tablet disintegration time is inversely proportional to disintegrants concentration. Above the critical

concentration level, however, disintegration time remains approximately constant or even increases.<sup>33</sup>

#### **Patented technologies for fast dissolving tablets**

There are some patented technologies are described in (Table 1). Each technology has a different mechanism, and each fast-dissolving/disintegrating dosage form varies regarding the following.<sup>35</sup>

- Rate of absorption from the saliva
- Mechanical strength and porosity of final product
- Drug and dosage form stability
- Taste and Mouth feel
- Ability to Swallow after disintegration in saliva
- Overall bioavailability
- Rate of dissolution of drug formulation in saliva

**Table 1:** Some patented technologies for fast dissolving tablets

<b>Technology</b>	<b>Company's name</b>	<b>Technology base</b>
Durasolv, Orasolv	CIMA Labs Inc.	Molding
Flash Tab	Ethypharm	Molding
Wow Tab	Yamanouchi pharma	Molding
Flash dose	Fuisz Technology Ltd	Cotton candy process
Ziplets	Eurand	Molding
Fast Melt	Elan Corp.	Molding

**Table 2:** Summary of advantages and disadvantages of different technologies for preparing fast disintegrating dosage form

Technology	Advantages	Disadvantages
Freeze-drying	Immediate dissolution (<5 sec.)	Very poor physical resistance, High cost of production, Low dose of water soluble drugs
Moulding	Very rapid disintegration (5-15 sec)	Very rapid disintegration (5-15 sec), High dose, High cost of production, Weak mechanical strength, Possible limitation in stability
Tabletting (Standard)	Low cost of production	Use of standard equipment/materials, High dose, Good physical resistance, Disintegration capacity markedly limited by the size and hardness of the tablet
Tabletting (Effervescent)	High dose, Good physical resistance, Pleasant effervescent mouth feel	Operating in controlled low humidity, Need specialized packaging i.e. Totally impermeable blister

### Future Prospective for FDTs

Now there are various products available commercially in market which is produced by fast dissolving tablet technologies. Still there is wide area for research on this technology. Some of the challenges like formulating a drug of bitter taste and moisture absorbing nature create problems for formulation scientist. When the dose of drug is large it causes problem of increased disintegration time. The two points to be considered in case of FDTs are shortening the disintegration time at the same time keeping other parameters like friability, taste, and mouth feel and tablet strength within the accepted range. Using taste masking agents and super-

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disintegrating without significant increase in the weight and volume of final dosage forms. Also there is a scope to develop better packaging system to make FDTs more stable during handling.

### CONCLUSION

Fast disintegrating tablets technology gained more popularity in last decade. It emerged as a New Drug Delivery system for treating various patients and diseases. FDT offers advantages of both solid and liquid oral dosage forms. This system allows easy self administration without the need of water to swallow. It has provided new area for research and development both for industries and academics.

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