Fast Dissolving Tablets: A Review

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ABSTRACT

Tables are the commonly used dosage forms because of its safety, easy administration and low cost, but still have low bioavailability and swallowing problems. To troubleshoot the problems, fast dissolving tablets (FDTs) provide a better alternative to conventional tablets. FDTs are solid dosage form which dissolves/disintegrates rapidly in saliva without chewing and additional water. The onset of action is remarkably quick for the fast dissolving tablets which provide immediate pharmacological effect. Bioavailability is the major problem for many drugs administered through oral route. Fast dissolving concept provides a good opening for improving bioavailability of many drugs. This review focuses on the importance of fast dissolving tablets, manufacturing methods and marketed products.

Key words: Fast dissolving tablets, orodispersible tablets, superdisintegrants, disintegration time

1. INTRODUCTION

In recent decades, there is a continuous advancement in the pharmaceutical technology which leads to development of novel drug delivery systems. Tablets and capsules are commonly used solid dosage forms. The major drawback of the tablets and capsules is the difficulty in swallowing particularly for the pediatric and geriatric patients. To meet the requirements for these patients, a new concept fast dissolving drug delivery emerged.

FDTs are tablets that dissolves/disintegrates rapidly in the oral cavity without need of water or chewing. FDTs are also called as mouth dissolving tablets, orodispersible, melt in mouth, porous tablets, quick dissolving or rapid disintegrating tablets or rapimelts. [1]

FDT can be used easily for the patients with diseases like stroke, parkinsonism and other neurological disorders like cerebral palsy. FDT dissolves rapidly in saliva within few seconds. As per the European Pharmacopoeia, the FDT should disperse in less than 3 minutes. [2, 3]

1.1. Ideal characteristics of FDT [1-8]

- It should require no water for administration
- It should dissolve/disperse in mouth within few seconds
- It should have pleasant mouth feel
- Ability to permeate to mucosal layer
- Compatibility of drug with taste masking agent
- It should leave minimum or no residue after oral administration
- Manufacturing should involve easy conventional techniques

1.2. Advantages of FDT [6, 7, 9]

- FDT can be easily administered to pediatric and geriatric patients
- Safest route of administration
- Rapid onset of action
- Enhancement in bioavailability
- High drug loading can be achieved
- Economic drug delivery system

1.3. Disadvantages of FDT [6, 7]

- FDTs usually possess insufficient mechanical strength
- In some cases taste masking agents make FDTs as expensive

1.4. Drugs suitable for FDT [8, 9]

- Drugs which are having less dose
- Stable in water and saliva
- Bitter drugs are not suitable for FDT. But by using taste masking agents bitter drugs can be formulated as FDT
- Drugs which require minimum or no residue
- Drugs which partially non-ionized at pH of oral cavity

2. FORMULATION EXCIPIENTS USED IN FDTs

All the excipients used for FDTs should be soluble in water. The excipients normally used for preparation of conventional tablets are used. Apart from that the excipients which are used in FDTs are given below

2.1. Superdisintegrants: [18]

These are the agents which are added to the tablet formulation to enhance the breakup of the compacted mass when it is put into aqueous environment. Examples: Crosspovidone, crosscarmellose, sodium starch glycolate, gellan gum, xanthan gum, calcium silicate

2.2. Taste masking agents [15, 12, 13, 14, 15]

These are the agents which are used to mask the bitter taste of the drugs. Examples: Hydroxy propyl methyl cellulose, magnesium aluminium silicate, glycercyl monostearate, eudragit, microcrystalline cellulose, cyclodextrin, amiblerite. Other than these flavoring and sweetening agents are also used as taste masking agents.

2.3. Flavouring agents: [15]

Flavoring agents are the substances which makes the product more palatable and pleasing feel for patients. These agents help in reducing the bitterness and obnoxious odour of drug substances. Examples: vanilla, citrus oils, fruit essences

2.4. Sweetening agents: [16]

Sweetening agents are the substances which make the product more palatable by making sweetening sensation to the taste buds. Examples: Maltose, dextrose, fructose, mannitol, aspartame, saccharin sodium, sucrose, xylitol

3. VARIOUS APPROACHES FOR FORMULATING FAST DISSOLVING TABLETS

Some of the approaches which are employed for the formulation of FDTs are

- Disintegrant addition method
- Freeze drying/Lyophilization
- Direct compression
- Sublimation
- Spray drying
- Tablet molding
- Mass extrusion
- Melt granulation
- Cotton candy process

3.1. Disintegrant addition method [17]

Disintegrant addition method is one of the commonly used methods for the formulation of FDTs. This method is simple and cost effective. This method involves addition of required concentration of superdisintegrants to the drug and other additives and then it is compressed into tablets. Examples of commonly used superdisintegrants are crosspovidone, crosscarmellose, sodium starch glycolate, gellan gum, xanthan gum, calcium silicate. Oxybutynin FDTs are prepared by this method.

3.2. Freeze drying/Lyophilization [18, 19, 20]

This technique has unique advantage that it can be used for heat sensitive materials. The FDTs prepared by this technique are very porous, and dissolves
rapidly in saliva. This technique involves freezing of drug with additives. Then it is dried. This technique is expensive and time consuming. This method can be done by using lyophilizer. Tablets prepared by this method possess low mechanical strength. Ketoprofen FDTs are prepared by using glycine, gelatin and sorbitol.

3.3. Direction compression: [21]
This technique is familiar because of simplicity, cost effective, time consuming and suitability for heat sensitive materials. In this method, tablets are prepared directly by compression of the mixture of drug and excipients without granulation. The method has limitations that it can be utilized for freely flowing drugs.

3.4. Sublimation: [21, 22]
The basis of this technique is to use highly volatile ingredients like camphor, menthol, ammonium bicarbonate, ammonium carbonate, benzoic acid that volatilize readily. In this method these highly volatile ingredients are added to other tablet excipients and the mixture is then compressed into tablets. This volatile material is then removed by sublimation leaving behind a highly porous matrix. These compressed tablets which have high porosity rapidly dissolved within 15 sec in saliva. Solvents like cyclohexane, benzene can also be used as pore forming agents.

3.5. Mass extrusion: [23]
In this technique solvent mixture of water soluble polyethylene glycol and methanol is used for softening the active blend. The cylindrical shaped extrude was formed by expulsion of softened mass through the extruder or syringe. These extrudes are finally cut into even segments using heated blade to form tablets. Taste of bitter drugs can be masked by coating the granules.

Spray drying can produce highly porous powders that dissolve rapidly. Allen et al. used spray-drying process for the production of FDTs. This technique is based on particulate support matrix. Maximum drug release and minimum disintegration time were observed with Kollidon CL excipients base as compared to tablets prepared by direct compression.

3.7. Tablet molding: [25]
Molding method is of two types. One is solvent method and the other is heat method. In the solvent method the powder mixture is moistened with hydro alcoholic solvent followed by compression at low pressure in molded plates. The solvent is then removed by air-drying. The tablets prepared by this way are less compact and possess a porous structure that enhances dissolution. The heat molding process involves preparation of suspension with drug and other additives like agar, mannotil or lactose. Then the suspension is poured in the blister packaging wells for solidifying and then it is dried. The disadvantage of this method is that the prepared tablets have low mechanical strength, which results in erosion and breakage during handling and storage.

3.8. Cotton candy process: [26]
Cotton candy process involves formation of matrix called as floss. Thermolabile drugs can be incorporated into floss. The matrix formed is partially recrystallized to improve the flow property. This candy floss matrix is then size reduced and mixed with active ingredients and additives and then compressed to tablets. The tablets prepared by this process are highly porous and possess sufficient mechanical strength. These FDTs produce pleasant mouth feel due to rapid disintegration of sugars in mouth. The major disadvantage of this process is it requires high temperature.

3.9. Melt granulation: [27, 28]
This technique can be utilized without water or organic solvents as there is no drying step. The process is less time consuming and uses less energy than wet granulation. Abdelbery et al described a preparation of FDTs with sufficient mechanical strength by using waxy binder by melt granulation or wet granulation. Report revealed that the melt granulation FDTs had better hardness than the wet granulation FDTs. But the disintegration time of melt granulation FDTs was more than one minute.

4. EVALUATION TEST FOR FDTs: [19, 30, 31, 32, 33]
The evaluation tests for FDTs are given below

4.1. General Appearance
The general appearance of a tablet includes size, shape, colour, odour and surface texture.

4.2. Thickness
Thickness of the tablets is measured by using vernier caliper.

4.3. Uniformity of weight
Twenty tablets should be weighed collectively and then individually by using weighing balance. The average weight of one tablet is determined from the 20 tablets weight. From this percentage deviation is calculated.

<table>
<thead>
<tr>
<th>S.No</th>
<th>Average weight of Tablet(s)</th>
<th>Maximum percentage difference allowed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>130 ± 10</td>
<td>± 10%</td>
</tr>
<tr>
<td>2</td>
<td>130-324</td>
<td>± 7.5%</td>
</tr>
<tr>
<td>3</td>
<td>More than 324</td>
<td>± 5%</td>
</tr>
</tbody>
</table>

4.4. Hardness
Hardness is one of the important tests for FDTs. Hardness is directly proportional to the disintegration time. Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. Hardness can be determined by using Monsanto or Pfizer hardness tester.

4.5. Friability
Friability of the FDTs can be determined by friability. Preweighed tablets are placed in plastic chamber of friabilator and allowed at 25 rpm for 4 minutes. Again it is weighed and the friability is calculated by the formula. Percentage Friability = (Loss in weight / Initial weight) x 100

4.6. Disintegration Test
Disintegration is the most important test for FDTs. Fast dissolving property of FDTs can be measured by disintegration test. In vitro disintegration time is measured by dropping a tablet in a beaker containing buffer pH 6.8. Time required for complete disintegration is measured.

4.7. Wetting time and water absorption ratio
Lower wetting time implies a quicker disintegration of the tablet. A piece of tissue paper folded twice is placed in a small Petri dish containing water. A weighed tablet is placed on the paper and the time required for wetting is measured which is known as wetting time. The wetted tablet is reweighed. Water absorption ratio is determined by the following equation

\[ \text{Water absorption ratio} = \frac{W_a - W_b}{W_b} \times 100 \]

Where, \( W_a \) is weight of tablet before water absorption & \( W_b \) is weight of tablet after water absorption.

4.8. Dissolution Test
Dissolution test was performed by using USP Type II Apparatus (Paddle type) at 50 rpm. Phosphate buffer pH 6.8 was used as dissolution medium. Temperature should be maintained at 37±0.5°C. Samples are collected at regular intervals for analysis of the release of the drug from tablet.

5. MARKETED PRODUCTS: [34]
Some examples of the marketed product of FDTs are given below.

<table>
<thead>
<tr>
<th>S.No</th>
<th>Category</th>
<th>Drug</th>
<th>Brand</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Anti-inflammation agents</td>
<td>Rofecoxib</td>
<td>Rofady MT</td>
<td>Warner Lambert</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diflunisal</td>
<td>Advil Fast melt</td>
<td>Reckitt Benckiser</td>
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<tr>
<td></td>
<td></td>
<td>Ibuprofen</td>
<td>Nurofen meltlets</td>
<td>Eli Lilly</td>
</tr>
<tr>
<td>2</td>
<td>CNS drugs</td>
<td>Citracet</td>
<td>Zypraxa</td>
<td>Teva Corp.</td>
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<tr>
<td></td>
<td></td>
<td>Risperidone</td>
<td>Risperdal</td>
<td>Janssen</td>
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<td>Selegiline</td>
<td>Zelprin</td>
<td>Otsuka</td>
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<td>Aprazepam</td>
<td>Ability Discmelt</td>
<td>Eisai Co</td>
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<td></td>
<td></td>
<td>Donepezil</td>
<td>Aricept ODT</td>
<td>Takeda Pharmaceuticals</td>
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<tr>
<td>3</td>
<td>Antidiarrhoeal</td>
<td>Loperamide HCl</td>
<td>Imodium instant melts</td>
<td>Janssen</td>
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<td></td>
<td>Domperidone</td>
<td>Domay MD</td>
<td>Ray Remedies</td>
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<td></td>
<td>Ondansetron</td>
<td>Ondanestron ODT</td>
<td>Teva Pharmaceuticals</td>
</tr>
<tr>
<td>4</td>
<td>Anti-arithmetic</td>
<td>Donepezil</td>
<td>Rostilast</td>
<td>Ranbaxy</td>
</tr>
<tr>
<td>5</td>
<td>Anti-ulcer</td>
<td>Famotidine</td>
<td>Pepcid ODT</td>
<td>Merck</td>
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<tr>
<td></td>
<td></td>
<td>Misopropil</td>
<td>Mood MT</td>
<td>Torrent</td>
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<tr>
<td></td>
<td></td>
<td>Lansoprazole</td>
<td>Prevacid Solu Tab</td>
<td>Takeda Pharmaceuticals</td>
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</tbody>
</table>

6. CONCLUSION:
Fast dissolving tablets are newer dosage forms which are formulated to dissolve/disintegrate rapidly in the saliva generally within few seconds. FDTs offer lot of advantages over conventional dosage forms such as improved efficacy, bioavailability, rapid onset of action, better patient compliance. Particularly FDTs provide more comfort to pediatric and geriatric patients. FDTs can be prepared by several methods based on the drug and additives used. Usually FDTs possess less mechanical strength. But by applying some new technologies and additives FDTs with sufficient mechanical strength can be prepared. Even bitter
drugs can be incorporated in FDTs by using taste masking agents. The research for FDTs is still going on. FDTs provide wide marketing also which makes the dosage form successful in the market. Many drugs will be formulated as FDTs in future for its market potential.

REFERENCES:

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