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Overview of Fast Dissolving Tablets

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ABSTRACT

Oral drug delivery is the most convenient route when compared to other routes. Solid oral dosage forms like conventional tablets are having the problem of swallowing, chocking especially in children and old patients. FDTs are the first doctor or patient choice as it is easy to administer for all age group patients. As there is no requirement of water there is no risk of chocking and swallowing. Due to its advantages over conventional tablets and having more stability than liquid dosage forms these are preferred . Currently many researches are going on . FDTs are easily manufactured at low cost with enhanced dissolution are the new promising approach.

Keywords: Super disintegrants, Oral dissolving tablets, Direct compression.

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INTRODUCTION[1,2,3]

Patients compliance is one of the major factors that attract the scientists towards the development of new drug delivery systems. Among all the different routes oral route has his own stature and it is most appealing route of drug delivery. Tablets are the most preferred form of dosage forms because of their stability when compared with the liquids and more tamper proof then capsule. But many patients express difficulty while swallowing the tablets this leads to ineffective therapy. Recent advancements in novel drug delivery system has enhanced the safety and efficacy of the drug molecule by formulating a convenient dosage forms for administration and to increase patient compliance . Among various dosage forms which help to improve ease of administration, FDTs are prior importance.

Definition[1] United States food and drug administration(FDA) defined FDT as " a solid dosage form containing medical substances or active ingredients which disintegrate rapidly usually within a matter of seconds when placed on the tongue". FDTs are also known by several other names such as oral fast disintegrating tablets, rapid melt tablets and quick disintegrating tablets .

UNIQUE PROPERTIES OF FDTs[4,5]

FDTs should have the following properties :

- Easily dissolve or disintegrate in salivary fluid with no time.
- No water is required.
- Low sensitivity towards environmental conditions like temperature, humidity etc.
- Tablet should be hard and friable.
- Have a gratifying taste.
- Should leave no residue in the mouth.
- Production should be of cost efficient.
- Packing should be done in conventional tablet packing materials only.

ADVANTAGES[6-8]

- Zero requirement of water.
- Highly helpful in the cases of motion sickness, sudden episodes of attack of coughing, where an ultra rapid onset of action is required .
- No chewing is required.
- Leave minimum residue.
- Improved drug stability.
- Better taste.
- Rapid drug therapeutic interaction.
- Allow high drug loading.
- Cost efficient.

LIMITATIONS OF FDTs[2]

- It is a huge challenge to mask the taste of bitter tasting drugs selected for FDTs.
- The sufficient strength to withstand the rigors of manufacturing process and handling is difficult to be achieved.

FORMULATION OF FDTs[11-13]

The ideal drug characteristics for FDTs are as follows :

- The therapeutic dose must not exceed more than 20mg .
- The drug should be partially unionized at oral PH .
- Drug should penetrate the oral mucosal tissue.
- Free from bitter taste .
- Small to moderate molecular weight.

EXCIPIENTS USED[4,12]

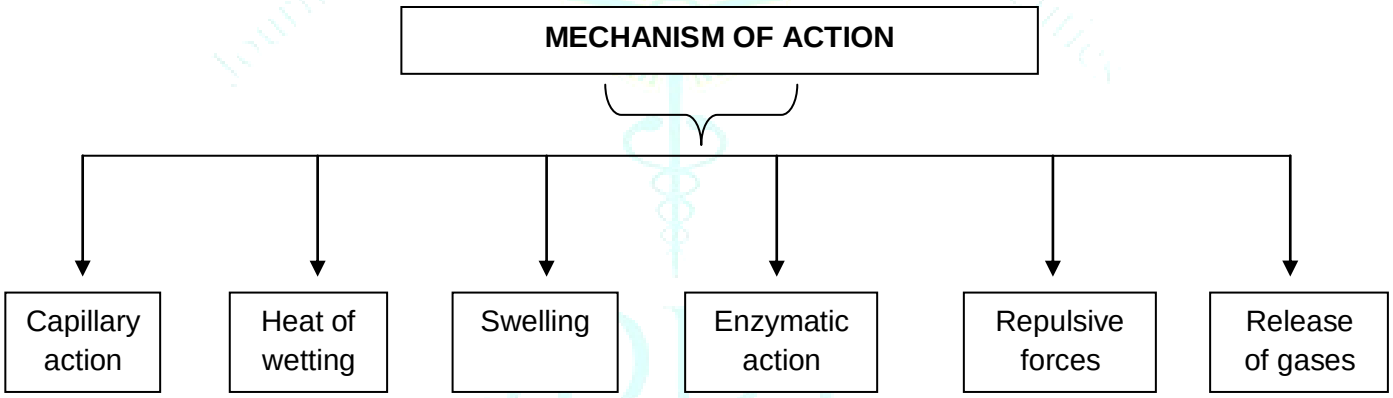
The main excipients used are Disintegrents, a diluent , lubricant, swelling agent, a permeabilizing agent, sweeteners and flavoring agents .

Table 1 : Various ingredients of FDTs[14]

S.N.	Types of ingredients	Percentage in formulation
1.	Active pharmaceutical agent	1-25%
2.	Water soluble film forming polymer	40-50%
3.	Plasticizer	0-20%
4.	Sweetening agent	3-6%
5.	Saliva stimulating agent	2-6%
6.	Colors and Flavors	0-10%

1. Super-disintegrants[3] : FDTs are meant to disintegrate within seconds for which superdisintegrants play a major role, the rapid high dissolution and disintegration are possible only if they are choosed in a best concentration possible. Commonly used Superdisintegrants iare sodium starch glycolate, croscarmellose sodum (Vivasol, Ac-Di-Sol), crospovidone (Polyplasdone), carmellose (NS-300), carmellose calcium (ECG-505), sodium starch glycolate (SSG) etc.

MECHANISM OF ACTION OF DISINTEGRANTS[15,16]



a. **By capillary action*: The*** air adsorbed on the particles is replaced by the medium when the tablet is placed in a suitable medium by penetration and thus they weakens the intermolecular spaces and bonds and then breaks the tablet into final particles.

b. **Because of the heat of wetting:** When exothermic disintegrants gets wet, due to capillary air expansion localized stress is developed, which helps in disintegration of the tablet.

c. **By swelling: This** is the most widely accepted theory. Porosity plays an important role ,high porosity show disintegration due to lack of adequate swelling ,on the other hand sufficient swelling force is accepted in the tablet with low porosity.

d. **By enzymatic reaction:** The binding action of the binders is inhibited by the homogenous enzymes in the body.

e. **Due to repulsive forces:**Non swelling particles also cause disintegration of tablets as proposed by GUYOT-HERMANN in particle expulsion theory the electric repulsive forces between the particles are the mechanism of disintegration and water is required for it.

f. **Due to release of gases:**Bicarbonate and carbonate of citric acid or tartaric acid gets interacted due to the wetting of tablets and they release CO2 and it causes the disintegration of the tablet

2. Binders :

During the compression stage the composition of the tablet has to be kept together for which binders are useful cellulose polymers, povidones, polyvinyl alcohols and acrylic polymers are commonly used binders. Ethyl cellulose or HydroxyPropylMethylCellulose(HPMC) and Hydroxypropyl Cellulose (HPC) can be either used alone or as admixtures .The stability and integrity of the tablet will

be a result of right selection of a binder or combination of binders.

3. **Diluents:**

The materials function as bulking agents, fillers and cost reducer. They are used to improve the bulk characteristics and also help to limit the active compound concentration.The most recommended once are of sugar bases like mannitol ,polydextrose, lactitol, DCL (Direct Compressible Lactose) , starch hydrolysate. These bulking agents add from 10 to 90% of the final weight .

4. **Emulsifying Agents**[6,21]

They are helpful in rapid disintegration and drug release without chewing swallowing or with water. They are also helpful in enhancing bioavailability. Alkyl sulphate , propylene glycol esters, and other can be used as emulsifying agents. They constitute at about 0.05% to 15% by weight of the final composite.

5.**Flavours And Sweeteners**

The bitter taste of the tablets can be masked by using flavours and sweeteners which make the tablets more palatable. Sugar, dextrose and fructose, as well as non nutritive sweeteners such as aspartamine , Sodium saccharin and sucralose are used.

TECHNOLOGIES USED TO MANUFACTURE MOUTH DISSOLVING TABLETS[1,18,19,20]

The technologies used to manufacture mouth dissolving tablets can be classified as:

1. Freeze Drying: In this process sublimation of water takes place from the product after the freezing. Water soluble water Matrix entraps the drug molecule, then it is freeze dried .

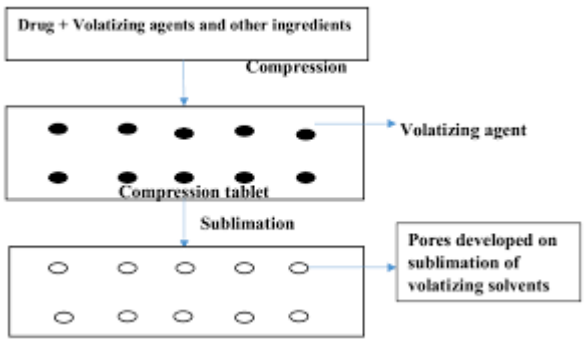
Advantages:

- Tablets produced by this technology have very low disintegration time.
- They also have great mouth feel.

Disadvantages:

- Time consuming manufacturing process and relatively expensive.

2. Sublimation: Inert Volatile substances like urea, naphthalene etc are added to other excipients and then compression of blend into tablets.



Later the volatile substances are removed which create pores in the tablet structure due to which tablet solubilizers when it comes in contact with saliva .Highly porous structure and good mechanical strength MDTs have been developed by this method.

3. **Spray Drying: A** highly porous and fine powder is prepared by spray Drying in an aqueous composition containing hydrolyzed and hydrolyzed gelatin as a supporting agent .Allen and Wong used this technique to prepare FDTs which disintegrate within 20 seconds.

4. **Molding: In** this, to make the tablet disintegrate and dissolve rapidly water-soluble ingredients are used . A hydro alcoholic solvent is used to damp the powder blend and then it is molded into tablet using compression pressure which must be lower than used in conventional tablets compression. The solvent is then removed by air-drying. Molded tablets have a porous structure that increases dissolution. Less mechanical strength and poor taste masking are the two major problems with molding.

5. **Direct Compression:** In this method, tablets are compressed directly from the mixture of the drug and excipients they do not require any preliminary treatment. The mixture to be compressed must have adequate flow properties and binds under pressure. Type of disintegrant and its proportion in formulation are of prime importance. The other factors which might be considered are particle size distribution, contact angle, pore size distribution, tablet hardness and water absorption capacity. This technology is cost effective and easy to implement at industrial level.

6. **Mass Extrusion :** It involves softening the active drug and other ingredients with a solvent mixture of water soluble polyethylene glycol, using mentnol then the softened masses extruded through the extruder to get cylndrical shaped products which is cut into small even fragments to form tablets.

7. **Nanonization :**This is a recently developed Nano melt Technology involves reduction in particle size of the drug by wet milling technique .The nanocrystals the drug are stabilized against agglomeration by surface adsorption on selected stabilizers which are incorporated into FDTs. Other advantage of this technology includes fast disintegration of nanoparticles leading to increased absorption and hence higher by bioavailability and reduction in dose.

8. **Cotton Candy Process:** Floss-like crystalline structure was formed by using a unique spinning mechanism so this process was named so. The floss-like crystalline structure resembles cotton candy. By the flash melting and by spinning of polysaccarides a matrix is formed. The compressability and the flow properties are improved by re-crystallization of the so formed matrix. Later these are blend with API and excipients, after milling and finally they are compressed.

Table 2: Overview of Patented Technologies for Manufacture Of FDTs

S.No	Technology	Process involved	Patent owner	Drugs Used (Brand name)
1.	Zydis	Lyophilization	R.P.Scherer Inc.	Loratidine (Claritin Reditab and Dimetapp Quick Dissolve)
2.	Quicksolv	Lyophilization	Jansen Pharmaceutica	Cisapride monohydrate (PropulsidQuicksolv), Risperidone (Risperdal M-tab)
3.	Flashtab	Lyophilization	Ethypharm	Ibuprofen (Nurofen Flashtab)
4.	Lyoc	Multiparticulate Compressed tablets	Farmlyoc	Phloroglucinol Hydrate (SpasfonLyoc)
5.	Orasolv	Compressed tablets	Cima Labs Inc.	Paracetamol (TempraQuicklets), Zolmitriptan (ZolmigRepimelt
6.	Durasolv	Molding	Cima Labs Inc.	Hyoscyamine Sulfate (NuLev) Zolmitriptan (Zolmig ZMT)
7.	RapiTab	Compressed Tablets	Schwarz Pharma	---
8.	Wow tab	Compressed Molded Tablets	Yamanouchi Pharma Technologies, Inc.	Famotidine (Gaster D)
9.	Fast melt	Molding	Élan Corp.	---
10.	Ziplets	Molding	Eurand	Ibuprofen (Cibalgina Due Fast)
11.	Flashdose	Cotton-candy process	Fuisz Technology Ltd.	Tramadol HCl (Relivia Flash dose)
12.	Oraquick	Micromask taste Masking	KV Pharm. Co., Inc.	Hyoscyamine Sulfate ODT

EVALUATION OF FDTs[1,20,21]

1. **Weight Variation__** To check weight variation, select randomly 20 tablets from the batch and find weight of each tablet then find their average. Not more than two tables should deviate from the average . Weight variation specification as per I.P. is shown in table .

Average Weight of Tablet	% Deviation
80 mg or less	10.0
More than 80 mg but less than 250 mg	7.5
250 mg or more	5.0

Table No.3 Weight variation and % deviation

2. Angle of Repose_: Angle of repose of any powder material is the descent angle made with respect to the horizontal surface, where the powder stays there without slidingIt is calculated to determine the flow property by using following formula;

$$\theta = \tan^{-1}(h/r)$$

Where, θ -Angle of repose

h - Height of pile

r - Radius of the base of pile

3. **Tapped Density**: The material to be evaluated is taken in a measuring cylinder and was tapped for a fixed time. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (pt) was calculated using the following formula;

$$\text{Tapped density} = M/Vt$$

4. **Hausners ratio**:Hausner ratio is an ratio of tapped density to bulk density . It is calculated by the following formula

$$\text{Hausner ratio} = \rho t/\rho b$$

Where, ρt - tapped density, ρb - bulk density

5. **Wetting Time_**The tablet that has to be evaluated should be placed in a petri dish which contains soluble dye and time taken for complete wetting of the tablet is noted down and this time is known as wetting time.

6. **Water Absorption Ratio**: The tablet was weighed at the starting, and then it is placed on a tissue paper which was folded twice and placed in a petri dish containing water. The tablet was placed on this paper and is allowed to wet. The weight of the tablet is taken again. Water absorption ratio is given by

$$= \frac{(Wa - Wb) \times 100}{Wb}$$

Where, R is water absorption ratio, Wa and Wb are the weights of tablet before and after wetting respectively.

7. **Friability:** To check the friability of the tablets, randomly select 6 tablets from the batch. Weight of the each tablet was taken at the starting of the test. These tablets are kept in Roche Fribilator and this is run at a speed of 25 rpm for 4 minute. After finishing the tablets are weighed again. Formula for calculating the % weight loss is given below.

% FRIABILITY = weight of initial – weight of final / weight of initial * 100

8. **Thickness:** To measure the thickness of the tablets , randomly select 5 tablets fron the batch , and their thickness was measured by placing the tablet between the arms of the vernier calliper and later their average was calculated in mm

9. **Disintegration Test_**The time for disintegration of FDTs is generally less than 1 min and actual disintegration time that patient can experience ranges from 5 to 30s. The disintegration test for FDT should mimic disintegration in mouth within saliva .

CONCLUSION

FDTs have evoleved to be the novel route of drug delivery overcoming the disadvantages of the conventional tablets i.e., swallowing of tablets in pediatric and geriatric patients who accounts for more than 80% of world's population. The onset of action, dissolution rate , bioavailability of the drugs have been improved with the use of FDTs. Patient compliance in today's scenario of hectic life is very much important which is improved to a large extent by the use of FDTs , because of their advantages like the anywhere , anytime use, no water requirement etc. With all these advantages many pharmaceutical companies started to produce the FDTs and in future many more drugs will be available in the form of FDTs.

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