

FAST DISSOLVING TABLETS: A NOVEL DRUG DELIVERY SYSTEM

Shehla Khan*, Sadhana Shahi, Santosh Borde and Saliya Shaikh

Department of Pharmaceutics, Government College of Pharmacy, Aurangabad - 431005, Maharashtra, India.

***Corresponding Author: Shehla Khan**

Department of Pharmaceutics, Government College of Pharmacy, Aurangabad - 431005, Maharashtra, India.

Article Received on 30/09/2017

Article Revised on 20/10/2017

Article Accepted on 10/11/2017

ABSTRACT

In today's era, many novel drug delivery approaches have been developed which are aimed at both to increase the performance of the dosage form as well as patient compliance. A fast dissolving tablet is one such novel drug delivery system. FDT dissolves or disintegrates in the oral cavity within seconds without intake of water, has drawn a great attention. Fast dissolving tablet is the safest, most convenient and economical having highest patient compliance especially for geriatric, pediatric, bedridden patients, patients who have swallowing difficulties (dysphagia) and for patients who are busy, travelling or have no access to water. The main advantage of FDT is its quick disintegration in the oral cavity without the aid of water or chewing. It has provided new area of research and development for both industries and academics. This article reviews the importance and unique concept of the fast dissolving tablets with an overview of oral mucosa for drug delivery through it. It also reviews the diverse superdisintegrants used along with different technologies (patented and non patented) employed for the fabrication of fast dissolving tablets, their pros and cons, and characteristics.

KEYWORDS: Fast Dissolving Tablet, Mouth Dissolving Tablet, Fast Disintegrating Tablet, Techniques.

INTRODUCTION

Among the total dosage forms available, the conventional dosage forms i.e., tablet / capsules is still the most popular, with wide acceptance up to 50-60%. It is however allied with few drawbacks such as delayed onset of action, low bioavailability or difficulty in swallowing (dysphagia) which is common among all age groups and specific with pediatric and geriatric patients. This resulted higher patient noncompliance and ineffective therapy. Such limitations compelled scientist to develop rapid - dissolving oral formulations. Today, Fast Dissolving Tablets, commonly known as the Oral Dispersible Tablet are widely accepted formulations. The other names for fast dissolving tablets (FDT) are mouth-dissolving tablets, melt-in mouth tablets, orodispersible

tablets, rapimelts, rapid dissolving tablet, porous tablets and quick dissolving tablets. According to European pharmacopoeia "ODT (Oral Dispersible Tablet) should disperse or disintegrate in less than 3 minute when placed on tongue"^[1,2,3]

The Center for Drug Evaluation and Research (CDER), US FDA defined Oral Disintegrating Tablets (ODT) as "A solid dosage form containing medicinal substances or active ingredient which disintegrates rapidly, usually within a matter of seconds, when placed on the tongue."^[2] Advantages, limitations, challenge and requirement for drug of FDT has been shown below in table 1.^[2,4,5,6]

Table 1: Advantages, limitations, challenges and requirement for drug of FDT.

Advantages of FDT	Challenges and limitations of FDT	Requirements for the drug and the delivery system
Avoidance of presystemic metabolism in the liver and gut wall.	Small surface area for absorption (~100 cm ²).	Sufficient solubility in saliva.
Rapid onset of action.	Low permeability compared to intestinal absorption.	Sufficient dissolution rate in saliva.
Avoidance of gastric conditions (enzymatic degradation, low pH).	Considerable differences in permeability between different regions of the oral cavity.	Sufficient permeability through oral mucosa.
Low enzymatic activity	Small volume of saliva.	Sufficient potency and low dose.
Robust mucosa that recovers fast from damage and stress.	Involuntary swallowing of saliva.	Acceptable taste and texture.
Good patient acceptability.	Short residence time in the oral.	No adverse effect on teeth or oral microflora.

Easy and painless administration.	Short residence time in the oral cavity (with the exception of mucoadhesive formulations.	No irritancy and allergenicity.
Suitable for patients suffering from nausea, vomiting or swallowing difficulties.	Limited dose of drug.	Be harder and less friable.
Water not needed for administration.	Hygroscopic in nature so required to be kept in dry place.	Exhibit low sensitivity to environmental conditions (temperature and humidity).
Pregastric absorption can resulting in improved bioavailability and improved clinical performance.	FDT required careful handling due to insufficient mechanical strength.	Be compatible with taste masking and other excipients.
New business opportunities such as product differentiation and patent-life extension etc.	FDT not suitable for patients with Sjogren's syndrome or dryness of the mouth due to decreased saliva production.	Leave minimal or no residue in the mouth after oral administration.

Overview of oral mucosa

1. Anatomy and histology of the oral cavity

The oral cavity is the first part of the gastrointestinal tract. The main anatomical parts of the oral cavity are the lips, cheeks, tongue, teeth, gums, hard and soft palate and the floor of the mouth. The oral mucosa consists of a stratified squamous epithelium, a basement membrane and a connective tissue that contains the supportive collagen fibres, blood vessels and nerves (Figure1). The oral mucosa can be functionally classified into three types:

1. Masticatory mucosa (25%),
2. Lining mucosa (60%) and
3. Specialized mucosa (15%)

The oral epithelium undergoes a continuous process of renewal, where cells are shed from the epithelial surface and replaced from below. Structure of keratinized (left) and non-keratinized (right) oral mucosa has been shown below in figure 1.^[4]

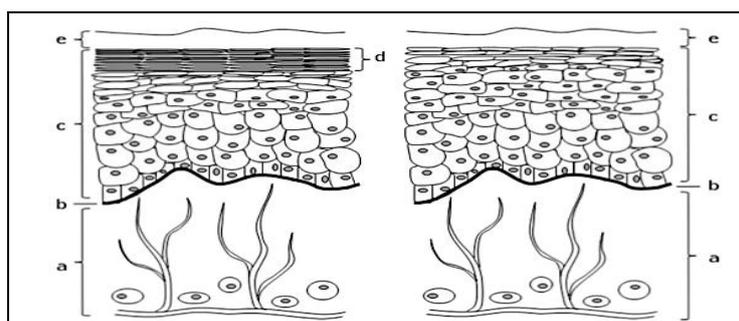


Fig. 1: General structure of keratinized (left) and non-keratinized (right) oral mucosa: connective tissue (a), basement membrane (b) and stratified squamous epithelium (c). In the upper cell layers of keratinized epithelium, the cells contain keratin and the extracellular spaces are filled with lipid sheets (d). The epithelium is covered by a salivary layer (e).

2. Physiological environment of the oral cavity

The most important factor controlling the oral environment is the continuous secretion of saliva. Saliva is an aqueous fluid secreted by the three major salivary glands and several minor salivary glands located beneath the oral mucosa. The properties of saliva are as depicted

in table 2. Another physiological characteristic affecting the intraoral delivery of drugs is the vasculature of the oral cavity. Drugs absorbed through the oral mucosa enter directly into the systemic circulation via the three main veins that drain in the internal jugular vein.^[4]

Table 2: Properties of saliva

Composition	Saliva is mainly composed of water but it does contain approximately 1% of inorganic and organic substances, such as electrolytes, proteins and mucins.
pH	5.8 to 7.4 (weak buffer)
Average volume of saliva:	0.9 ml
Men	0.8 ml
Women	0.8 ml
Five-year-old children	0.4 ml
Functions	<ol style="list-style-type: none"> 1. To protect and lubricate the oral tissues. 2. To maintain an appropriate oral pH and enzymatic activity. 3. In intraoral drug delivery, the continuous production of saliva provides a solvent for drug dissolution.

3. Absorption of drugs through the oral mucosa

The absorption of a drug through the oral mucosa involves several steps as depicted in Figure 2. Any of these steps can be rate-controlling, depending on the physicochemical properties of the drug. Before absorption through the oral epithelium can take place, the drug needs to be released from the formulation and to dissolve in saliva. The dissolved drug then has to diffuse

through the unstirred salivary layer and the underlying epithelium. Most drugs move through the oral epithelium by passive diffusion via either the transcellular or the paracellular pathways. Both hydrophilic and lipophilic drugs can use either of the two routes or both routes simultaneously, but the route with the least penetration resistance is preferred.^[4]

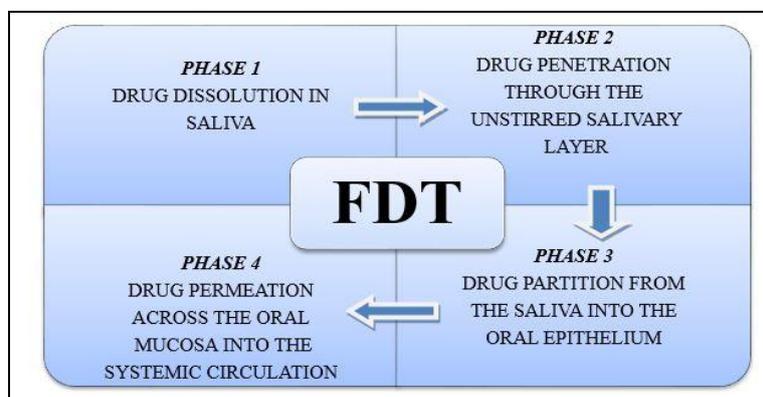


Fig. 2: Phases of drug dissolution and absorption through the oral mucosa in Fast Dissolving Tablet (FDT).

Factors affecting drug dissolution and absorption through the oral mucosa in fast dissolving tablet (FDT)

Factors affecting drug dissolution and absorption through the oral mucosa in fast dissolving tablet (FDT) have been depicted in table 3 below.^[4]

Table 3: Factors affecting drug dissolution and absorption through the oral mucosa in fast dissolving tablet (FDT).

Phases	Factors
Drug dissolution in saliva	<ul style="list-style-type: none"> • Aqueous solubility of the drug • Release rate of the drug from the formulation • Volume and pH of the saliva • Residence time in the oral cavity before swallowing
Drug penetration through the unstirred salivary layer	<ul style="list-style-type: none"> • Drug interaction with salivary mucins • Thickness of the salivary layer
Drug partition from the saliva into the oral epithelium	<ul style="list-style-type: none"> • Partition coefficient between epithelium and saliva(log p or log d of the drug)
Drug permeation across the oral mucosa into the systemic circulation	<ul style="list-style-type: none"> • Molecular size and weight of the drug • Permeability coefficient of the drug • Presence of the absorption enhancers

Requirement for FDT preparation

1. Drug / API

Some of the examples of drug types that can be incorporated in FDT are Analgesics and Anti-inflammatory Agents, Anthelmintics, Anti-Arrhythmic Agents, Anti-bacterial Agents, Anti-coagulants, Anti-Epileptics, Anti-Gout Agents, Anti-Hypertensive Agents, Anti-Malarials, Anti-Migraine Agents, Anti-Muscarinic Agents, Anti-Neoplastic Agents and Immunosuppressants, Anti Protozoal Agents, Anti-Thyroid Agents, Anxiolytic, Sedatives, Hypnotics and Neuroleptics, Cardiac-Inotropic Agents, Corticosteroids, Anti-Parkinsonian Agents, Gastro-Intestinal Agents, Nutritional Agents etc.^[2]

2. Excipients

For the preparation of fast dissolving tablet the excipients commonly in use are at least one disintegrant (superdisintegrant), a lubricant, a diluent and optionally a swelling agent, a permeabilising agent, sweeteners and flavouring agents.

➤ Superdisintegrants

Fast dissolving tablets /fast disintegrating tablets, the term itself emphasizes on disintegration of the tablet. Hence, disintegrants play a vital role in disintegration, dissolution and absorption of drug from FDT. Thus, choosing a most favorable superdisintegrant, in an optimum concentration is important to make sure quick disintegration and dissolution of FDT.^[7,8]

1. Natural superdisintegrant

Natural superdisintegrant are most commonly chosen disintegrants. These types of superdisintegrants are natural in source.

FDA –approved natural superdisintegrants

The table 4 below shows natural superdisintegrants approved by FDA.^[9-24]

Table 4: FDA –approved natural superdisintegrants.

Sr. no	Natural Superdisintegrant	Marketed Drug	Disintegration Time	Concentration Used	Technique
1	Chitin and chitosan	Cinnarizine	60 sec	3% w/w	Wet granulation
2	Guar gum	Glipizide	30 sec	1% w/w	Direct compression
3	Gum karaya	Amlodipine, granisetron hydrochloride	17.10 sec	4% w/w	Direct compression
4	Agar and treated agar	Theophylline, flurbiprofen	20 sec	1-2% w/w	Direct compression
5	Fenugreek seed mucilage	Metformin hydrochloride	15.6 sec	4% w/w	Direct compression
6	Soy polysaccharide	Lornoxicam, Simvastatin	12 sec	8% w/w	Direct compression
7	Gellan gum	Metronidazole	155 sec	4% w/w	Wet granulation
8	Mango peel pectin	Aceclofenac, Diclofenac sodium	11.59 sec	0.1–4% w/w	Wet granulation
9	Lepidium sativum mucilage	Nimesulide, Domeperidone	17 sec	5–15% w/w	Direct compression
10	Plantago ovata seed mucilage	Granisetron HCl	17.10 sec	5% w/w	Direct compression
11	Aegle marmelos gum	Aceclofenac	8–18 min	6% w/w	Direct compression
12	Locust bean gum	Nimesulide	13 sec	10% w/w	Direct compression
13	Lepidium sativum	Nimesulide	17 sec	10% w/w	Direct compression
14	Mangifera indica gum	Metformin HCL, paracetamol	3–8 min	6% w/w	Direct compression
15	Hibiscus rosa-sinensis mucilage	Aceclofenac, Amlodipine besylate	20 sec	6% w/w	Direct compression
16	Dehydrated banana powder	Ondansetron HCl/propranolol, gabapentin	15–36 sec	6% w/w	Wet granulation

2. Synthetic superdisintegrant

The commonly used synthetic superdesintegrants are Sodium starch glycolate, Crosspovidone and Crosscarmellose sodium.

Advantages

- Shows effect in lower concentrations than starch
- Minimum effect on compressibility and flowability
- More efficient intragranularly^[25]

➤ Binders

In the fast dissolving tablet, the choice of the binder is critical for achieving the desired sensory and melting

characteristics, and for faster release of the active ingredient.

Examples of binders

1. Cellulosic polymer [ethyl cellulose, hydroxypropylcellulose (HPC), HPMC].
2. Polyvinyl alcohols (polyethylene glycol)
3. Acrylic polymers [ammonia-methacrylate copolymer (Eudragit RL and RS), polyacrylate (Eudragit NE), polymethacrylate (Eudragit E)].^[7]

➤ Antistatic agents, lubricants and diluents

Some examples of antistatic agents, lubricants and diluents have been given below in table 5.^[7]

Table 5: Examples of antistatic agent, lubricant and diluents.

Antistatic agent	Lubricant	Diluents
<ul style="list-style-type: none"> • Colloidal silica (Aerosil) • Precipitated silica (Sylod FP244) • Micronized or non micronized talc 	<ul style="list-style-type: none"> • Magnesium stearate • Stearic acid • Sodium stearyl fumarate • Micronized polyoxyethylene glycol (micronized Macrogl 6000) 	<ul style="list-style-type: none"> • Microcrystalline cellulose • Starches • Lactose • Polyols

➤ Colours

Colouring agents may be defined as substances employed in pharmacy for imparting colour which gives a pleasing appearance and as "sensory adjuvants" to the

flavours which gives product distinctiveness. Some of the provisionally listed colourants have been given in the table 6.^[26]

Table 6: Some of the provisionally listed colourants.

Colour	Common Name	Colour Index Number
FD&C blue #1 lake	D&C orange #11 lake	42090
FD&C blue #2 lake	Indigotine	73015
FD&C green #3 lake	Fast green FCF	42053
D&C green #5 lake	Alizarine cyanide green F	61575
D&C orange #4 lake	Orange II	15510:2
D&C orange #5 lake	Dibromoflourescein	45370:2
D&C orange #11 lake	Erythrosine	14700

Mechanism of disintegrations by superdisintegrants

1. Swelling

The most widely accepted common mechanism of disintegration is via swelling. E.g., starch, agar, bentonite, sodium starch glycolate etc. When

disintegrants comes in contact with water, they swell and the adhesiveness of other ingredients in a tablet is lost causing the tablet to disintegrate. Swelling mechanism has been shown in figure 3 below.

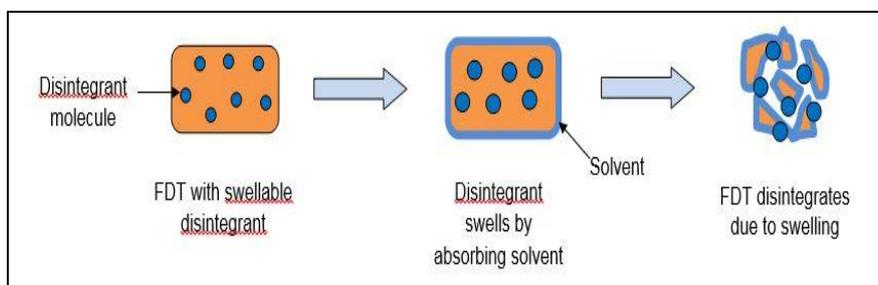


Fig. 3: Mechanism of disintegration via swelling.

2. Porosity and Capillary Action (Wicking)

Tablet porosity and capillary action provide pathways for the penetration of aqueous medium into tablets. When we put the tablet into suitable aqueous medium, the medium is drawn up or "wicked" into these pathways

through capillary action and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Mechanism of disintegration via Porosity and Capillary Action (Wicking) has been shown in figure 4 below.

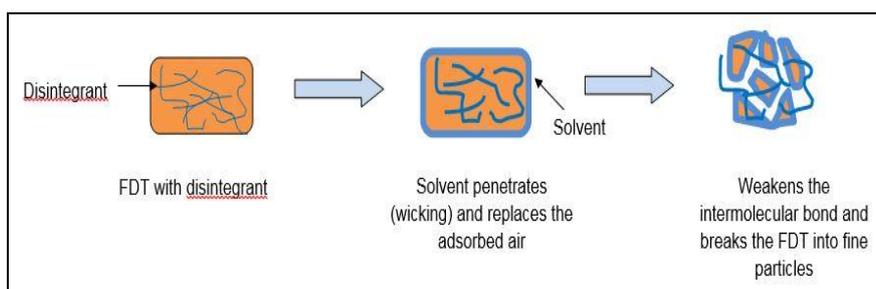


Fig. 4: Mechanism of disintegration via wicking.

3. Deformation

Figure 5 below shows mechanism of disintegration via deformation. Hess as proved that during tablet compression under high pressure disintegrant particles get deformed and these deformed particles get into their normal structure when they come in contact with

aqueous media or water and hence the tablet disintegrates. Seldom, the swelling capacity of starch was improved when granules were extensively deformed during compression. This causes increase in tablet disintegration.

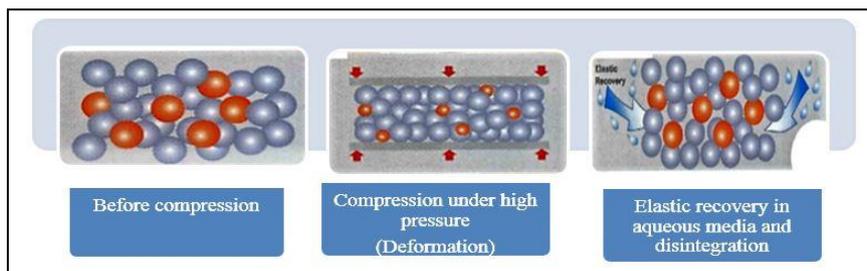


Fig. 5: Mechanism of disintegration via deformation.

4. Due to disintegrating particle/particle repulsive forces

Another mechanism of disintegration attempts to explain the swelling of tablet made with „nonswellable“ disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that nonswelling particle also cause disintegration of tablets.

The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking. Mechanism of disintegration via particle/particle repulsive forces is shown below in figure 6.

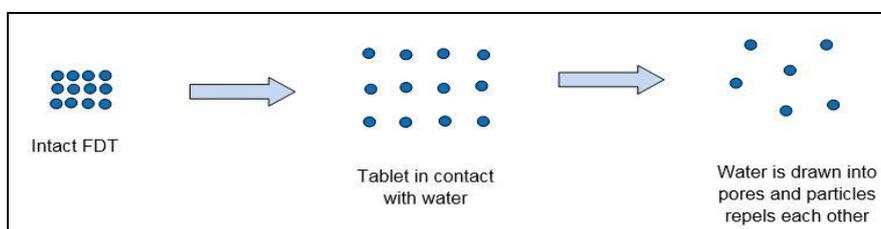


Fig. 6: Mechanism of disintegration via particle/particle repulsive forces.

5. Enzymatic reaction

Since, many enzymes are present in the body. They act as disintegrants and promote disintegration. These enzymes diminish the binding capacity of binder. Either due to swelling, pressure is exerted in the outer direction that causes the tablet to burst or enhanced absorption of

water leads to an enormous increase in the volume of granules to progress disintegration.^[2,7,25,27]

Technologies for fast dissolving tablets

- I. Non Patented technologies
- II. Patented technologies
- I. **Non Patented technologies**

1. Freeze drying or lyophilization technique

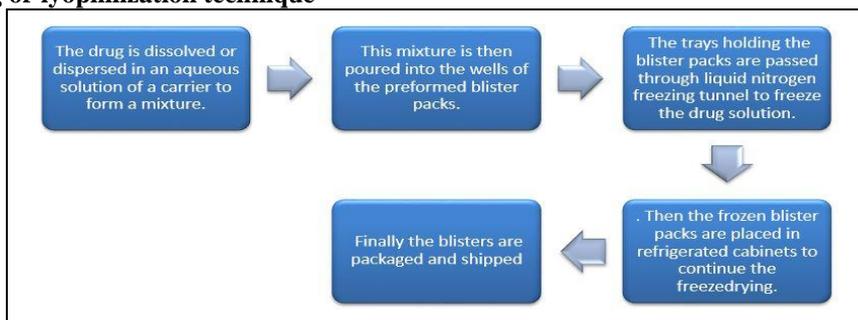


Fig. 7: Freeze drying method.

Freeze drying or lyophilization technique is a process, in which water is sublimated from the product after freezing. The figure 7 below shows steps in freeze drying technique.

Characteristics

The prepared FDT by this technology were (1) highly porous, (2) have high specific surface area, (3) dissolve rapidly and ultimately show improved absorption and bioavailability.

Disadvantages

The major disadvantages of this technique are (1) expensive and time consuming; (2) fragility makes conventional packaging unsuitable for these products (3) poor stability under stressed conditions.^[1,3]

2. Molding technique

Molding technique is of following three types: (a) Solvent method, (b) Heat method and (c) Molding by vacuum evaporation without lyophilization. The

difference between solvent method and heat method is given below in table 7.^[6]

Advantages: (1) Soluble ingredient (saccharide) offers improved mouth feel and disintegration of tablets. (2) FDT is less compact than compressed tablets and posses a porous structure that hastens dissolution. (3) FDT

produced by the molding technique is easier to scale up for industrial manufacture as compared to lyophilization technique.

Disadvantage: (1) Low mechanical strength. (2) Taste masking is another problem to this technique.^[2]

Table 7: Solvent method v/s heat method.

Solvent method	Heat method.
<ul style="list-style-type: none"> ❖ The powder mixture previously wetted with the solvent is compressed into mold plates to form a wetted mass. ❖ Solvent method involves moistening the powder blend with a hydro alcoholic solvent followed by compression at low pressures in molded plates to form a wetted mass (compression molding). The solvent is then removed by air-drying. 	<ul style="list-style-type: none"> ❖ A molten matrix in which drug is dissolved or dispersed can be directly molded into FDT. ❖ The heat molding process involves preparation of a suspension that contains a drug, agar and sugar (e.g. mannitol or lactose) and pouring the suspension in the blister packaging wells, solidifying the agar at the room temperature to form a jelly and drying at 30 °C under vacuum.

c. Molding by vacuum evaporation without lyophilization

The method of preparation FDT by molding by vacuum evaporation without lyophilization is shown in figure 8 below:

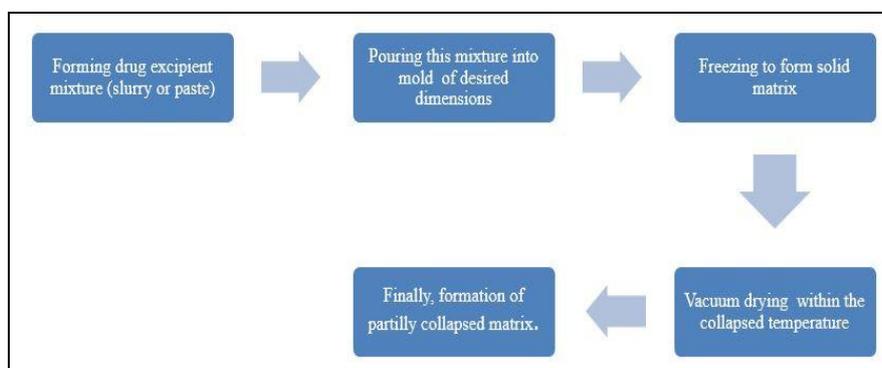


Fig. 8: Molding by vacuum evaporation without lyophilization.

3. Sublimation

The method of formulation for FDT by sublimation method is shown in figure 9.

Characteristic: (1) FDT prepared by this technology have shown disintegration time usually between 10-20 sec. (2) Tablets revealed sufficient mechanical strength.^[1,2,7]

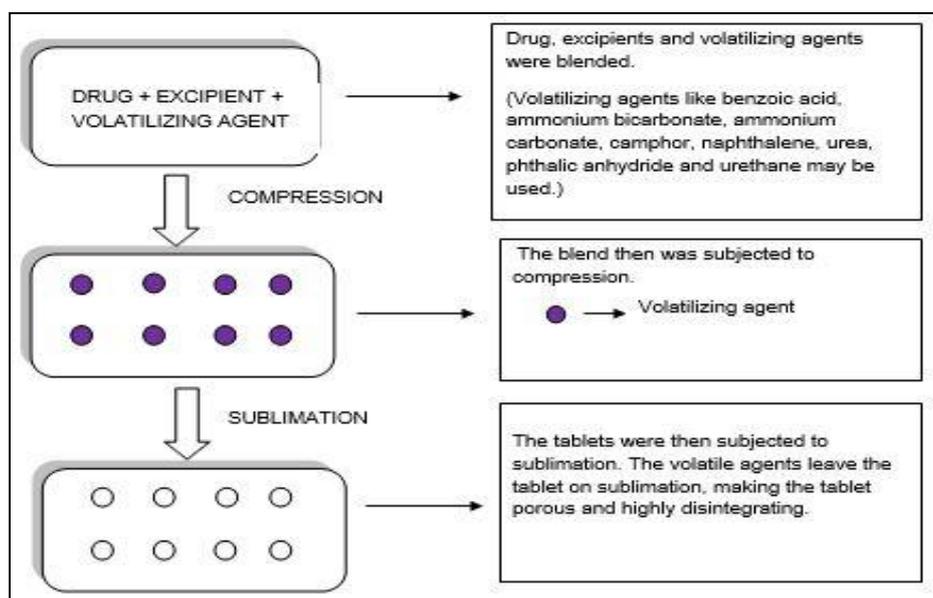


Fig. 6: Sublimation process.

4. Mass extrusion technique

This technology involves softening of the active blend using the solvent mixture of water soluble polyethylene glycol and methanol and expulsion of softened mass through the extruder or syringe to get a cylindrical

shaped extrude which are finally cut into even segments using heated blade to form tablets. This process can also be used to coat granules of bitter drugs to mask their taste.^[28]

5. Cotton candy technique

The manufacturing process of FDT is divided into following four steps as shown in figure 10.

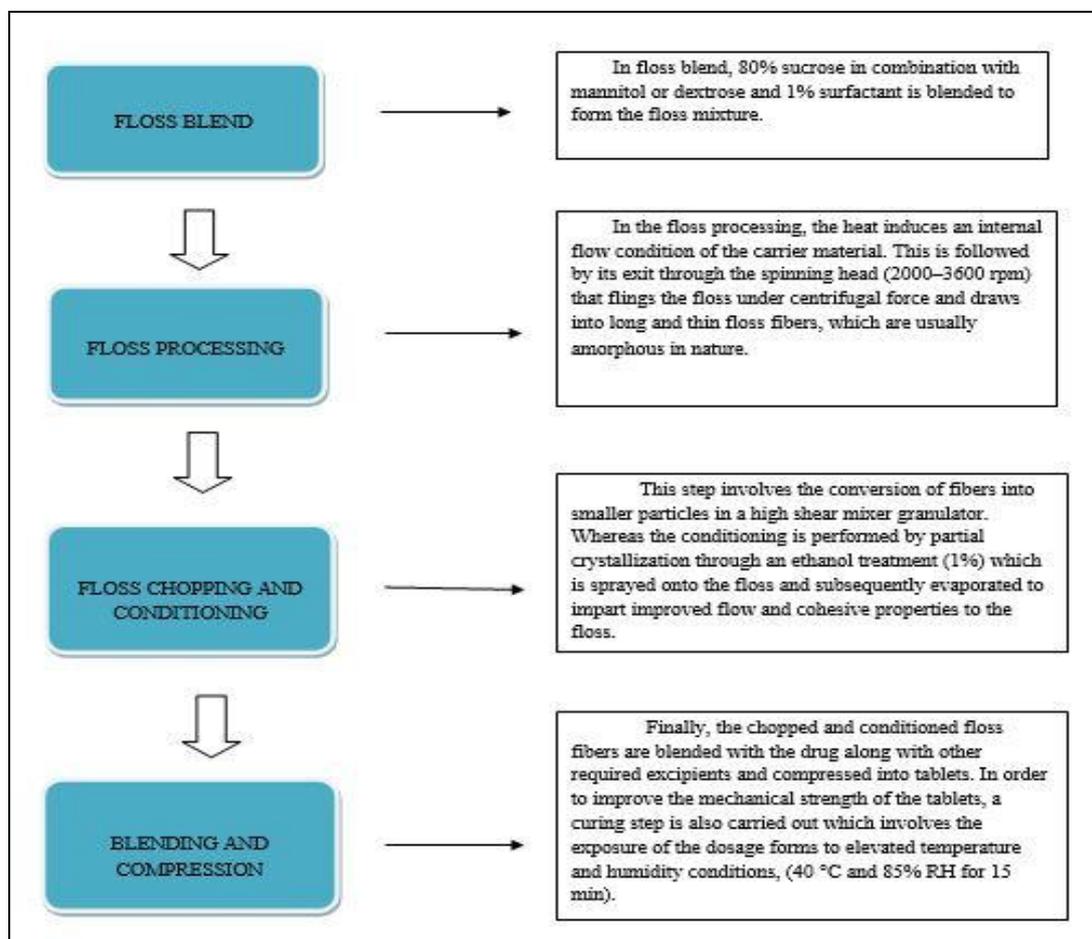


Fig. 7: Cotton candy technique.

Characteristics: (1) The FDT manufactured by this technique are highly porous in nature and offer very pleasant mouthfeel due to fast solubilization of sugars in presence of saliva. (2) It can accommodate high dosage drug. (3) Improved mechanical strength.^[6]

6. Spray drying

Spray drying techniques are used enormously in pharmaceutical and biochemical procedures. Through spray drying the solvents are rapidly and efficiently eliminated producing highly porous and fine powders. For this, an aqueous coating solution and water immiscible liquid/water insoluble particles are mixed to form O/W emulsion or an aqueous suspension of solid. Then this emulsion or suspension is spray dried producing free flowing highly porous dry powder of encapsulated liquid or coated solid. Finally this fine and

porous powders when compressed into tablets showed improved disintegration.

Characteristics: FDT manufactured by this technique showed disintegration time of less than 20 sec when immersed in an aqueous media.^[2,29]

7. Direct compression technique

Direct compression is the most simplest and easiest tablet manufacturing technique. This technique can also be used to manufacture FDT by selecting suitable combinations of excipients, which can afford fast disintegration. For the reason that improved excipients especially super-disintegrants and sugar based excipients are available FDT can be prepared using this technique. Mizumoto et al classified sugar-based excipients into two types on the basis of molding and dissolution rate as shown in figure 11.

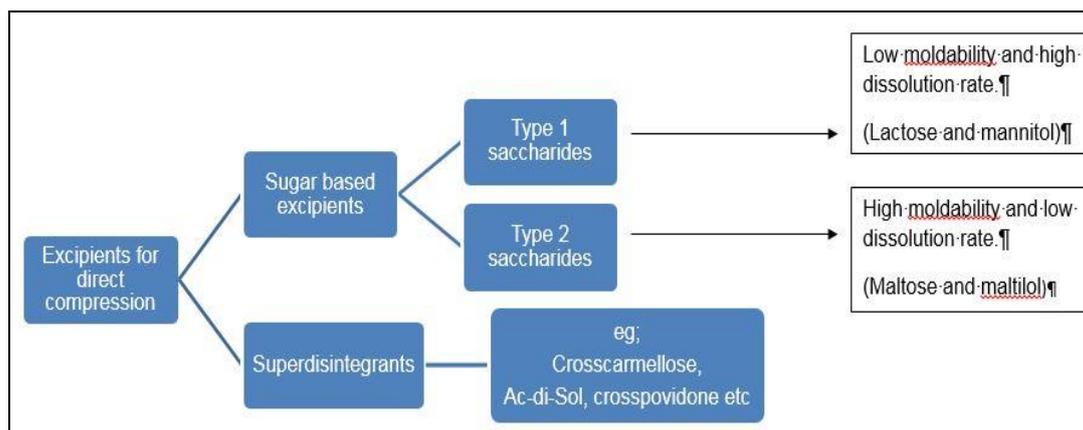


Fig. 8: Direct compression technique.

Characteristics: (1) Cost effective and simplest tablet manufacturing technique. (2) High doses can be accommodated. (3) Limited number of processing steps is involved in direct compression.^[30]

8. Melt granulation technique

Melt granulation is a technique in which pharmaceutical powdered drugs are efficiently agglomerated by a melt binder. The binders can be a molten liquid, a solid or a solid that melts during the processing of melt granulation like while mixing in a high shear mixer where the product temperature is raised higher than the melting point of binders either by a heating jacket or by the heat of friction generated by the impeller blades. The most commonly used binder is polyethylene glycol (e.g. Superpolystate®, PEG – 6 – stearate). The increased dissolution rate is due to:

- Hydrophilic nature of the system due to presence of water soluble carriers.
- The drug forms monotectic mixtures with PEG.

Advantages: (1) As compared to a conventional granulation, melt granulation do not require water or organic solvents. (2) This technique is less time consuming and uses less energy than wet granulation. (3)

This is a helpful technique to improve the dissolution rate of poorly water-soluble drugs, for e.g.; griesofulvin.

Characteristics: (1) The FDT manufactured by melt granulation showed sufficient mechanical integrity. (2) It melts in the mouth and solubilizes rapidly leaving no residue.^[7,31]

9. Nanoionisation

Nanoionisation technique involves reducing the drug particles to nanosize by milling the drug using proprietary wet-milling technique. The nanocrystals of the drug so formed are needed to be stabilized against agglomeration by surface adsorption on selected stabilizers, which are then compressed into FDT.

Characteristics: (1) This technique is used for poorly water soluble drugs. (2) It is a cost effective manufacturing process. (3) Conventional packaging due to exceptional durability and wide range of doses (up to 200 mg of drug per unit).^[5]

Patented technologies

Patented technologies for preparation of FDT are given in Table 8 below.^[3,30]

Table 8: Patented technologies and their products.

S.No	Technology	Process involved	Patent owner	Drug used	Drug release
1	Zydis	Lyophilization	R.P. Scherer Inc.	Loratidine (claritin rediva and Dimetapp quick dissolve)	Dissolves in 2 to 10 secs.
2	Quicksolv	Lyophilization	Jansen Pharmaceuticals	Cisapride monohydrate (Propulsid Quicksolv)	-----
3	Flashtab	Lyophilization	Ethypharm	Ibuprofen (Nurofen Flashtab)	Dissolves within 1 min.
4	Lyoc	Multiparticulate Compressed tablets	Farmlyoc	Phloroglucinol Hydrate (Spasfon Lyoc)	-----
5	Orasolv	Compressed tablets	Cima Labs Inc.	Paracetamol (Tempra Quicklets), Zolmitriptan (Zolmig Rapimelt)	Disintegrates in 5-45 sec.
6	Durasolv	Molding	Cima Labs Inc.	Hyoscyamine Sulphate (NuLev),	Disintegrates in 5-45 sec.
7	Rapitab	Compressed tablets	Schwarz Pharma	-----	-----

8	Wowtab	Multiparticulate Compressed	Yamanouchi PharmaTechnologies, Inc.	Famotidine (gaster D)	Disintegrates in 5-45 sec.
9	Fast Melt	Molding	Elan Corp.	-----	-----
10	Ziplets	Molding	Eurand	Ibuprofen (Cibalgina Due Fast)	-----
11	Flashdose	Cotton-candy process	Fuisz Technology Ltd	Tramadol Hcl (Relivia Flash dose)	Dissolves within 1 min
12	Oraquick	Micromask Taste masking	KV Pharm. Co, Inc.	Hyoscyamine sulphate ODT	-----
13	Advatab	Microcaps and diffuscaps CR Technology	Eurand International	Advatab Cetrizine, Advatab Paracetamol	Disintegrate in less than 30 sec.
14	Fuisz	Sugar based matrix known as floss	Fuisz pharmaceutical Ltd.	Diphenhydramine & Pseudoephedrine	-----
15	Advantol 200	Direct compression	SPI pharma	-----	Disintegrates in 30-40 secs.
16	NanoCrystal	Nanoionisation	Elan's proprietary NanoCrystal technology	-----	-----
17	Dispersible tablet technology	Incorporation of disintegrants	Lek, Yugoslavia	-----	Disintegrates in less than 60 secs.

Evaluation parameters of FDT

1) Precompression characterization of FDT

The precompression characterization of FDT is given table 9.^[29,30]

Table 9: Precompression Characterization of FDT.^[30]

Parameter	Definition	Formula
Angle of repose (tan θ)	It is defined as the maximum angle possible between the surface of a pile of powder and the horizontal plane.	$\tan \theta = \frac{h}{r}$
Bulk density (D_b)	It is the ratio of total mass of powder to the bulk volume of powder.	$D_b = \frac{\text{weight of powder}}{\text{volume of packing}}$
Tapped density (D_t)	It is the ratio of total mass of the powder to the tapped volume of the powder.	$D_t = \frac{\text{weight of powder}}{\text{volume of tapped packing}}$
Hausner's ratio	Hausner's ratio is the ratio of tapped density to bulk density.	Hausner's ratio = $\frac{\text{tapped density}}{\text{bulk density}}$
Carr's index (% compressibility)	The percentage compressibility (Carr's index) was calculated as 100 times the ratio of the difference between tapped density and bulk density to the tapped density.	Carr's index = $\frac{(\text{tapped density} - \text{bulk density}) \times 100}{\text{tapped density}}$

2) Postcompression characterization of tablets

1. Weight variation test

According to I.P., twenty FDT are taken and their weight is determined individually as well as collectively on the weighing balance. From the collective weight the average weight of single tablet was determined. The weight variation test would be a satisfactory method of determining the drug content uniformity. Weight variation specification as per I.P. is shown in table 10 below.^[30]

Table 10: Weight variation specification as per I.P.

Average weight of Tablets (mg)	Maximum % deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

2. Thickness

Thickness of tablets is determined using Vernier caliper. The thickness in millimeters (mm) is measured individually for ten preweighed tablets using Vernier caliper. The average thickness and standard deviation is then compared. Tablet thickness should be controlled within a ± 5 % variation of a standard value.

3. Tablet hardness

Pfizer hardness tester or Monsanto tablet hardness tester can be used to determine the crushing strength. Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. The hardness is kept low in case of FDT so as to disintegrate rapidly in mouth.

4. Friability

Friability is measured of mechanical strength of tablets. The limit bound for friability is 0.1-0.9. Roche friabilator is used to determine the friability. A preweighed tablet is placed in the friabilator. The tablets are rotated in the friabilator at 25 rpm for 4 minutes for 100 revolutions. At the end of test, tablets are reweighed; the loss in the weight of tablet is the measure of friability and is expressed in percentage as;

$$\% \text{ Friability} = \frac{\text{Loss in weight} \times 100}{\text{Initial weight}}$$

5. Wetting time

For wetting time measurement five circular tissue papers of 10 cm diameter are placed in a Petri dish with a 10 cm diameter. In this petri dish ten mm of water-containing Eosin, a water soluble dye is added. A tablet is cautiously placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time. Lower wetting time implies a quicker disintegration of the tablet.

6. In-vitro dispersion time

Tablet was added to 10 ml of phosphate buffer solution, pH 6.8 at 37±0.5°C. Time required for complete dispersion of a tablet was measured.

7. Disintegration Time

The test is carried out using the disintegration apparatus. Phosphate buffer (pH 6.8) maintained at 37°C ± 2°C is used as a disintegration media and the time taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus is measured.

8. Dissolution test

In vitro Drug Release Studies have been done using USP dissolution apparatus II (paddle type) at 50 rpm in 900 ml of phosphate buffer (pH 6.8) at 37±0.5°C. At different time intervals, 10 ml of sample is withdrawn and filtered. An equal volume of the medium is introduced into the vessel after each withdrawal to maintain a constant volume. The absorbance of the samples is determined by UV Spectrophotometer at given max. The mean values of drug released are plotted as cumulative % drug release vs. time.

9. Water absorption Ratio

A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper & the time required for complete wetting was measured. The wetted tablet was then

weighed. Water absorption ratio, R, was determined using following equation,

$$R = 100 \times \left(\frac{W_b - W_a}{W_a} \right)$$

10. Stability study (Temperature dependent)

According to the ICH guidelines, for accelerated studies at following given conditions the fast dissolving tablets were stored: (i) 40 ± 1°C, (ii) 50 ± 1°C, (iii) 37 ± 1°C and RH 75% ± 5%. The tablets were then withdrawn after a period of 15 days and analyzed for physical characterization such as visual defects, Hardness, Friability, Disintegrations, and Dissolution etc. The data so obtained is then fitted into the first order equations to determine the kinetics of degradation.^[29]

CONCLUSION

Swallowing difficulties have been seen in approximately one third of the population especially in geriatric and pediatric population which resulted in the poor overall therapy effectiveness. Fast dissolving tablet have gained much importance in today's era as compared to other conventional oral dosage forms. This novel approach made easy self medication without the need of water to swallow. FDT has ensured high bioavailability through quick disintegration via pregastric absorption and avoiding first pass metabolism. This benefited researchers to develop FDT with incorporation of API which shows side effects with the first pass metabolites in case of conventional drug delivery. Many techniques have been evolved for manufacturing FDT which focuses to enhance the porous structure of the tablet matrix so as to increase tablet disintegration in the buccal cavity along with good taste-masking properties and satisfactory mechanical strength. Also FDT has ensured tremendous pharmaceutical marketing and extension of market exclusivity which lead to increased revenue. Thus, owing to the advancement in the scientific research and discovery of new excipients FDTs will have tremendous scope as a delivery system for most of the drugs in the near future.

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