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FAST DISINTEGRATION DRUG DELIVERY SYSTEM: A REVIEW

Ashwin Shinde*, Vishal Yadav, Vinay Gaikwad and Shree Dange

Department of Pharmaceutics, Arvind Gavali College of M. Pharmacy, Satara, Maharashtra, India

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Correspondence to Author:

Ashwin Shinde

Research Scholar, Department of Pharmaceutics, Arvind Gavali College of M. Pharmacy, Satara, Maharashtra, India

E-mail: ashwinashinde@gmail.com

ABSTRACT: In recent decades, a variety of pharmaceutical research has been conducted to develop new dosage forms. Fast dissolving tablets are one of the fruitful results of these researches. Fast dissolving tablets disintegrate and/or dissolve rapidly in the saliva without chewing and additional water. Mouth dissolving tablets have been formulated for pediatric, geriatric, and bedridden patients and for active patients who are busy and travelling and may not have access to water. This review includes advantages, disadvantages, desired characteristics and various methods used for formulation of fast dissolving tablets.

INTRODUCTION: Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self- medication, pain avoidance and most importantly the patient compliance [1]. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients, is the difficulty to swallow. Drinking water plays an important role in the swallowing of oral dosage forms [2]. Often times people experience inconvenience in swallowing of the conventional dosage forms such as tablet when water is not available, in the case of the motion sickness and sudden episodes of coughing during the common cold, allergic condition and bronchitis [3, 4].

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Orodispersible tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people [5].

Mouth Dissolving Tablet: It is a tablet that disintegrates and dissolves rapidly in the saliva, within a few seconds without the need of drinking water or chewing. A mouth dissolving tablet usually dissolves in the oral cavity within 15 second to 3 minutes. Most of the MDTs include certain super disintegrants and taste masking agents [6].

The European Pharmacopoeia defines Orodisperse as a tablet that can be placed in the mouth where it disperses rapidly before swallowing. Researchers have formulated ODT for various categories of drugs, which are used for therapy in which rapid peak plasma concentration is required to achieve desired pharmacological response. These include neuroleptics, cardiovascular agents, analgesics, anti-allergic and drugs for erectile dysfunction.

Biopharmaceutical consideration: When new drug delivery system put on, it is a must to consider Biopharmaceutical factor like metabolism and excretion [7].

Pharmacokinetics: In this consideration, study has done on absorption, distribution, metabolism and excretion. After absorption, drug attains therapeutic level and therefore elicits pharmacological effect, so both rate and extend of absorption is important. In conventional dosage form there is delay in disintegration and therefore dissolution while FDT is rapidly disintegrates in oral cavity and dissolution is fast. Due to disintegration of FDT in mouth absorption is started from mouth, pharynx and esophagus. Some factors like age, GI pH and blood flow through GI are taken into consideration, because elders may be considered as separate unique Medicare population. Drug distribution depends on many factors like tissue permeability, perfusion rate, binding of drug to tissue, disease state, drug interaction etc.

In geriatric patients, decrease in body mass and total body water result in decreased volume of distribution of water- soluble drugs and increased volume of distribution (Vd) of lipid soluble drugs. Duration and intensity of action depends upon rate of drug removal from the body or site of action i.e. biotransformation. Decrease in liver volume, regional blood flow to liver reduces the biotransformation of drug through oxidation, reduction and hydrolysis. Excretion by renal clearance is slowed, thus half-life of renal excreted drugs increase.

Pharmacodynamic: Drug receptor interaction impaired in elderly as well as in young adult due to undue development of organ. Decreased ability of the body to respond baro-reflexive stimuli, cardiac output, and orthostatic hypotension may see in taking antihypertensive like prazosin.

- Decreased sensitivity of the CVS to β – adrenergic agonist and antagonist.
- Immunity is less and taken into consideration while ad ministered antibiotics.
- Altered response to drug therapy-elderly show diminished bronchodilator effect of theophylline shows increased sensitivity to barbiturates.
- Concomitant illnesses are often present in elderly, which is also taken into consideration, while multiple drug therapy prescribed.
- Research workers have clinically evaluated drug combination for various classes' cardiovascular agents, diuretics, anti-hypertensive in geriatrics. The combination choice depends on disease state of the patient.

Requirements of Mouth Dissolving Tablet [8, 9, 10]:

- Require no water for oral administration, yet dissolve/disperse/disintegrate in mouth within seconds.
- Give good mouth feel.
- Have a satisfactory taste masking property.
- Be harder and less friable.
- Leave minimal or no residue in mouth after administration.

Advantages of Fast Dissolving Tablets [11, 12, 13, 14]:

- Ease of Administration to the patient who cannot swallow, such as the elderly, stroke victims, bedridden patients, patient affected by renal failure and patient who refuse to swallow such as pediatric, geriatric & psychiatric patients.
- No need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
- Rapid dissolution and absorption of the drug, which will produce fast onset of action.
- Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases bioavailability of drug is highly increased.
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patient.
- The risk of chocking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety.

Disadvantages:

- Fast dissolving tablet is hygroscopic in nature so must be keep in dry place.
- Some time it possesses mouth feeling.
- MDT requires special packaging for properly stabilization & safety of stable product.

Limitations to Fast Dissolving Tablets [15, 16]:

- Drugs with relatively larger doses are difficult to formulate into FDT e.g. antibiotics like ciprofloxacin with adult dose tablet containing about 500 mg of the drug.
- Patients who concurrently take anticholinergic medications may not be the best candidates for FDT. Similarly patients with Jorgen's syndrome or dryness of the mouth due to decreased saliva production may not be good candidates for these tablet formulations.
- The tablets usually have insufficient mechanical strength; hence, careful handling is required.
- The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.

Superdisintegrants [17, 18]: Disintegrating agents are substances routinely included in the tablet formulations to aid in the breakup of the compacted mass when it is put into a fluid environment. They promote moisture penetration and dispersion of the tablet matrix. In recent years, several newer agents have been developed known as "Superdisintegrants". These newer substances are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. On contact with water the superdisintegrants swell, hydrate, change volume or form and produce a disruptive change in the tablet. Effective superdisintegrants provide improved compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing high-dose drugs (**table 1**).

TABLE 1: SUPERDISINTEGRANTS EMPLOYED IN FDT

Super Disintegrants	Nature	Mechanism	Brand Names
Crosscarmellose	Modified Cellulose	Wicking Due To Fibrous Structure Swelling With Minimal Gelling	Ac-Di-SolNymce 25X
Crosspovidone	Cross Linked PVP	Water Wicking, Swelling And Possibly Some Deformation Recovery	Kollidon, Polyplasdone
Aliginic Acid Nf	Cross Linked Aliginic Acid	Wicking Action	Satialgine
Soy Polysaccharides	Natural Disintegrants	-	Emcosoy
Calcium Silicate	_	Wicking Action	-
Sodium Starch Glycolate	Modified Starch	Rapid And Extensive Swelling With Minimal Gelling	Explotab, Primogel
Ion Exchange Resin	Resins	-	Amberlite
L-HPC	Low Hydroxyl Propyl Cellulose	Both Swelling And Wicking	-
Acrylic Acid	Poly (Acrylic Acid) Superporous	Wicking Action	-

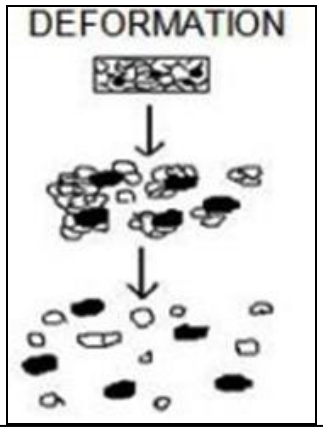
Mechanism of Superdisintegrants: There are four major mechanisms for tablets disintegration as follows**:**

1. **Swelling:** Perhaps the most widely accepted general mechanism of action for tablet disintegration is swelling. Tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.
2. **Porosity and Capillary action (Wicking):** Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles.

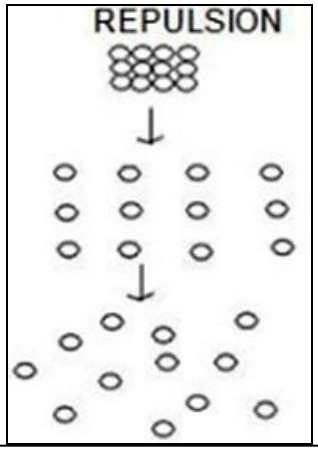
Water uptake by tablet depends upon hydrophilicity of the drug /excipient and on tableting conditions For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles Water is pulled by Particles swell and breakup disintegrant and the matrix form physical bonding force.

3. **Due to disintegrating particle/particle repulsive forces:** Another mechanism of disintegration attempts to explain the swelling of tablet made with 'non-swellable' disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that non-swelling 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.

4. **Due to Deformation:** During tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a breakup of the tablet. This may be a mechanism of starch and has only recently begun to be studied (**figure 1**).



Particles swell to precompression size and break up the matrix



Water is drawn into the pores and particles repel each other because of the resulting electrical forces

FIG. 1: DISINTEGRATION BY DEFORMATION AND REPULSION

Approaches for Taste masking of Mouth Dissolving Tablets [19, 20]**:** Mouth dissolving tablet, which disintegrate or dissolve in the saliva produce a positive or negative taste sensation. Most of the drugs have unpalatable taste in which taste masking plays critical role in formulating OFDT. The negative taste sensation of drugs can be reduced or eliminated by various approaches which include:

1. Taste masking using flavors and sweeteners
2. Taste masking using Lipophilic Vehicles
3. Taste masking by Coating with Hydrophilic Vehicles
4. Taste masking by Ion-Exchange Resins

1. **Taste masking using Flavors and Sweeteners:** Maximum patient acceptability with FDT is seen if they provide pleasant taste and mouth feel. To provide this property in tablets various sweeteners and flavors are employed. Usually sugar-based excipients are used as they are highly water soluble and dissolve quickly in saliva and provide pleasant taste and mouth feel to the final product (**table 2**).

2. **Taste masking using Lipophilic Vehicles:** It is the property of oils, surfactants, poly alcohols and lipids to increase the viscosity in the mouth and to coat the taste buds and therefore they are potential taste masking agents (**table 3**).

TABLE 2: LIST OF DRUGS USING FLAVOURS AND SWEETENER

Sr. no.	Drug	Taste masking agent(s)
1	Aspirin	Sodium phenolate
2	Chlorpheniramine, Phenyl propanolamine	Sod. bicarbonate, citric acid, orange/cream flavor
3	Famotidine	Sod. bicarbonate, citric acid, lemon flavor
4	Ibuprofen	Sod. Citrate, dehydrate, sod. saccharin, refined sugar
5	Theophylline	D-sorbitol, sodium saccharin, sodium glutamate, and vanilla Essence
6	Acetaminophen	Sod. bicarbonate, citric acid, cherry flavor
7	Caffeine	Starch, lactose, and mannitol

TABLE 3: LIST OF DRUGS AND LIPOPHILIC VEHICLES

Sr. no.	Drug	Taste masking agent(s)
1	Isoprothiolane	Hydrogenated oil and HPMC
2	Acetaminophen	Molten stearyl stearate
3	Talampicillin HCl	Magnesium aluminum silicate & soyabean, Lecithin
4	Clarithromycin	Glycerylmonostearate and AMCE
5	Indeloxazine HCl	Hydrogenated oil and surfactants

3. **Taste masking by Coating with Hydrophilic Vehicles:** Carbohydrates can be used as a coating material to mask the taste of orally administered drugs. Various forms of proteins have been used extensively for taste masking (**table 4**).

TABLE 4: LIST OF DRUGS AND HYDROPHILIC VEHICLE

Sr. no.	Drug	Polymer(s) used
1	Pinaverium bromide	Cellulose or shellac
2	Ibuprofen	Methacrylic acid copolymer (Eudragit)
3	Sparfloxacin	L-HPC, EC, HMC/EC, HPMC, TiO_2, sucrose, fatty acid ester mixture
4	Amoxycillintrihydrate	MCC, L-HPC
5	Clarithromycin	Carbopol, PVP
6	Roxithromycin	PEG, Eudragit L 100–55
7	Cefuroxime axetil	Eudragit L-55 and RL
8	Pirenzepine& Oxybutynin	Eudragit E-100, MCC, HPC
9	Levofloxacin	Eudragit E100, cellulose acetate

4. **Taste masking by Ion-Exchange Resins:** To stabilize the sensitive components, to sustain the drug release, to disintegrate tablets and to mask taste, ion-exchange resins are used in formulations (**table 5**).

TABLE 5: LIST OF DRUGS AND TASTE MASKING ION EXCHANGE RESINS

Sr. no.	Drug	Resin/complexing
1	Carbetapentane citrate	Cyclodextrin
2	Ibuprofen	Hydroxypropyl b-cyclodextrin
3	Diphenhydramine HCl	Indion CRP 244, indion, CRP 254
4	Buflomedil	Amberlite IRP 69
5	Orbifloxacin	Amberlite IRP 69

5. **MDTs with Patented Taste Masking Technology: (table 6)**

TABLE 6: PATENTED TECHNOLOGY

Sr. no.	Technology	Mechanism of Action
1	CIMA Labs	Coating of drug with dissolution retarding excipient
2	Microcaps	Microencapsulation by coacervation-phase separation technique
3	Solutab	Coating of drug with sustained release agent followed by coating enteric polymer and finally with mannitol
4	OraQuick	Produces microspheres known as MicroMask
5	AdvaTab	Combination of Microcaps technology for taste masking and Diffuscap controlled release technology

Approaches for preparation of FDT [21, 22, 23, 24]:

1. Freeze-drying or lyophilization
2. Sublimation
3. Spray drying
4. Molding
5. Mass extrusion
6. Direct compression
7. Cotton-candy process
8. Nanonization.
9. Fast dissolving films.
10. Melt granulation

1. **Freeze-drying or lyophilization:** Freeze drying or lyophilization is a process in which solvent is removed from a frozen drug solution or a suspension containing structure forming excipients. Tablets prepared by freeze drying or lyophilization are very porous in nature, disintegrate and dissolve rapidly when come in contact with saliva. Initially the material is frozen to bring it below its eutectic point. Primary drying is carried out to reduce the moisture to around 4% w/w of drug product. Then, secondary drying is done to reduce the bound moisture to the required volume. Due to lyophilization, bulking agent and sometimes drug acquire glossy amorphous structure and thus dissolution is enhanced. One of the main advantages of this method is, when stored in a dried state, the freeze-dried dosage form has relatively less stability problems during its shelf life. This technique is mainly useful for heat sensitive drugs i.e. thermo labile substances.

2. **Sublimation:** This process involves addition of some inert volatile substances like urea, urethane, naphthalene, camphor, etc. to other excipients and the compression of blend into tablet. Removal of volatile material by sublimation creates pores in tablet structure, due to which tablet dissolves when comes in contact with saliva. Additionally several solvents like cyclohexane, benzene etc. can also be used as pore forming agent.

3. **Spray drying:** In this technique, gelatin can be used as supporting agent and as a matrix, mannitol as a bulking agent and sodium starch glycolate or crosscarmellose or crosspovidone are used as superdisintegrants. Tablets manufactured from the spray-dried powder have been reported to disintegrate in less than 20 seconds in aqueous medium. The formulation contained bulking agent like mannitol and lactose, a superdisintegrant like sodium starch glycolate and crosscarmellose sodium and acidic ingredient (citric acid) and/or alkaline ingredients (e.g. sodium bicarbonate). This spray-dried powder, which compressed into tablets showed rapid disintegration and enhanced dissolution.

4. **Molding:** In this method, molded tablets are prepared by using water-soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydro-alcoholic solvent and is molded into tablets

under pressure lower than that used in conventional tablet compression. The solvent is then removed by air-drying. Molded tablets are very less compact than compressed tablets. These possess porous structure that increase dissolution

5. **Mass extrusion:** This technology involves softening of the active blend using the solvent mixture of water-soluble polyethylene glycol and methanol and subsequent expulsion of softened the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets.

6. **Direct compression:** This technique is easy way to formulate MDTs since limited number of processing steps, low manufacturing cost. The disintegration and dissolution of directly compressed tablets depends on single or combined effect of disintegrant, water soluble excipients and effervescing agents. Tablet size and hardness strongly affect the disintegrant efficacy. Hard and large tablets have more disintegration time than normally required. Very soft and small tablets have low mechanical strength. So, an optimum kind and concentration of disintegrant should be chosen to achieve quick disintegration and high dissolution rates.

7. **Cotton-candy process:** This process is so named as it utilizes a unique spinning mechanism to produce floss-like crystalline structure, which mimic cotton candy. Cotton candy process involves formation of matrix of polysaccharides or saccharides (foss)- sucrose, dextrose, lactose and fructose at temperatures ranging between 180–266°F by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have improved flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to MDTs

8. **Nanonization:** A recently developed Nanomelt technology involves reduction in the particle size of drug to nano size by wet-milling technique. Surface adsorption of the nano crystals of the drug is done on selected stabilizers for stabilizing them against agglomeration, which are then incorporated into MDTs. This technique is mainly advantageous for poor water soluble drugs and also for a wide range of doses (up to 200 mg of drug per unit).

9. **Fast dissolving films:** In this technique, a non-aqueous solution is prepared containing water soluble film forming polymer (pullulan, carboxymethylcellulose, hydroxypropylmethyl cellulose, hydroxyl propylcellulose, polyvinyl pyrrolidone, polyvinyl alcohol or sodium alginate, etc.), drug and other taste masking ingredients, which is allowed to form a film after evaporation of solvent. In case of a bitter drug, resin adsorbate or coated microparticles of the drug can be incorporated into the film. This film, when placed in mouth, melts or dissolves rapidly, releasing the drug in solution or suspension form. The features of this system include paper thin films of size less than 2X2 inches, dissolution in 5 sec, instant drug delivery and flavored after taste.

10. **Melt granulation:** Super polystate was incorporated in the formulation of ODT by melt granulation technique where granules formed by the molten form of this material. Crystallized paracetamol was used as model drug and in addition the formulation included mannitol as a water-soluble excipient and crosscarmellose sodium as disintegrating agent.

Patented technologies for preparation of MDT [25, 26, 27, 28]:

DURASOLV Technology: Durasolv technology was developed by Ciba to provide stronger tablets for packaging in blisters or bottles. The key ingredients in this formulation are filler and lubricant. The particle size of the filler is preferably between about 20 and 65 µm. Fillers, such as dextrose, mannitol, sorbitol, lactose, and sucrose, have the advantage of quick dissolution and avoid some of the grittiness. The tablets have low friability, which is about 2%.

The disintegration time is less than 60 seconds. The lubricant blending times can also be increased to 10-25 minutes or longer. This method can produce tablets by using the direct compression method, conventional tableting methodologies and conventional package equipment. Thus, the production cost is significantly reduced.

ZYDIS Technology: It is the first marketed new tablet technology. In this the drug is produced by freeze drying or lyophilizing the drug in gelatin matrix. The product thus produced is very light weight and packed in blister packs. It also utilizes microencapsulation using specialized polymers and resins hence mask the bitter taste of drug. This technology claims for increased bioavailability as compared to other conventional tablets. The main advantage of this technology is convenience and disadvantage is that the freeze drying process is quite expensive manufacturing process. Zydis formulation should be used within six month from opening.

OROSOLV Technology: This technology is being patented by CIMA Labs. This includes the use of effervescent disintegrating agents which is compressed with low pressure to produce the fast dissolving tablets. The evolution of carbon dioxide from the tablet produces a fizzing sensation, which is a positive organoleptic property. The concentration of effervescent mixture usually employed is 20-25% of tablet weight.

FLASH DOSE Technology: The Flash Dose technology uses a unique spinning mechanism so as to produce a floss-like crystalline structure, much like cotton candy. This crystalline sugar can be then incorporate the drug and compressed into a tablet. This procedure had been patented by Fuisz and is known as Shear form. The final product which is being produced has a very high surface area for dissolution. It disperses and dissolves quickly once placed on the tongue. The Flash dose tablets consist of self–binding shear form matrix termed as

FLASH TAB Technology: The Flashtab technology is yet another fast dissolving/disintegrating tablet formulation. Prographarm laboratories have patented the Flashtab technology. It utilizes most of the same excipients as in conventional compressed tablets. A disintegrating agent and a swelling agent are used in combination with coated drug particles in this formulation to produce a tablet that disintegrates in the mouth in less than one minute.

WOWTAB Technology: WOWTAB technology employs a combination of low- and high-moldability saccharides in order to produce fast-dissolving tablets using conventional granulation and tableting techniques. The typical low-moldability saccharides include lactose, mannitol, glucose, sucrose, and xylitol and high-moldability saccharimaltose, sorbitol, and oligosaccharides. When tablets are made by compressing a saccharide having low and high mold ability alone, the desired properties form and hence results in denser tablets with disintegration rates that are comparable with the loosely compressed fast melt formulations of adequate hardness and are disintegration in the mouth cannot be achieved simultaneously. Moreover, if saccharides having low mold ability and high mold ability are mixed (physical mixture) before tableting, quick disintegration and dissolution in the mouth cannot be obtained. For this reason, a saccharide having low mold ability was granulated with a saccharide having high mold ability as a binder.

QUICKSOLV Technology: In the Quicksolv formulation, the matrix compositions are dissolved in the solvent (usually water), and then this solution is frozen. At the temperature the first solvent will remain in the solid form, and then the frozen solution contacts the second solvent which is usually, ethanol, menthol, or acetone. Thus, the first solvent is removed after a few hours of contacting the second solvent to result in a usable matrix. The final product disintegrates almost instantly. This method is claimed to prevent or to reduce the incidence of cracking during the final preparation, having uniform porosity and also the adequate strength for handling.

LYCO: Lyoc utilizes a freeze drying process but it differs from Zydis in that the product is frozen on the freeze dryer shelves. In order to prevent homogeneity by sedimentation during this process, these formulations also require a large proportion of undissolved inert filler such as mannitol, to increase the viscosity of the process suspension. The high proportion of filler used reduces the potential porosity of the dried dosage form and hence results in denser tablets with disintegration rates that are comparable with the loosely compressed fast melt formulations.

PHARMABRUST Technology: Pharmaburst technology is being patented by SPI pharma. The tablet manufactured by this process involves a dry blend of a drug, flavors, and lubricant then followed by compression into tablets which then dissolve within 30-40 seconds. Tablets manufactured by this methodology have sufficient strength can be packed in blister packs and bottles.

Nanocrystal Technology: Nanocrystal technology includes lyophilization of colloidal dispersions of drug substance and water- soluble ingredients filled in to blister pockets. This method avoids manufacturing process such as granulation, blending, and tableting, which is more advantageous for highly potent and hazardous drugs. As manufacturing losses are negligible, this process is useful for small quantities of drug.

FROSTA Technology: Akina patents this technology. It utilizes the concept of formulating plastic granules and compressing at low pressure to produce strong tablets with high porosity. Plastic granules composed of:

i. Porous and plastic material,

ii. Water penetration enhancer, and

iii. Binder.

The process involves usually mixing the porous plastic material with water penetration enhancer and followed by granulating with binder. The tablets obtained have excellent hardness and rapid disintegration time ranging from 15 to 30 seconds depending on the size of tablet.

Dispersible Tablet Technology: Lek in Yugoslavia was issued patents for dispersible tablets of dihydroergotoxine and cimetidine, which were claimed to disintegrate in less than 1 minute when in contact with water at room temperature. Dihydroergotoxine is poorly soluble in water in the free base form. An improved dissolution rate of dihydroergotoxinemethanesulphonate was observed with dispersible tablets containing 0.8–10%, preferably about 4% by weight, of an organic acids. One of the essential excipients in the cimetidine formulation was a disintegrating agent. The disintegrating agents include starch or modified starches, microcrystalline cellulose, alginic acid, cross-linked sodium carboxymethyl cellulose, and cyclodextrin polymers.

Sheaform Technology: This technology make Sheaform matrix consisting of floss preparation. Floss is produced by subjecting to a feed shock containing a sugar to flash heat processing.

Ceform Technology: In this technology microspheres containing active ingredients are prepared. Basic requirement of this technology is placing dry powder containing either pure drug or special blend of drug and excipients. The microspheres then mixed and compressed into previously selected oral dosage form.

Marketed products [29]:

TABLE 7: THE COMMERCIALIZED PRODUCTS OF FDTS WHICH ARE AVAILABLE IN MARKET.

Trade Name	Active Drug	Manufacturer
Felden fast melt	Piroxicam	Pfiser Inc., NY, USA
Claritin redi Tab	Loratidine	Schering plough Corp., USA
Maxalt MLT	Rizatriptan	Merck and Co., NJ, USA
Zyprexia	Olanzapine	Eli lilly, Indianapolis, USA
Pepcid RPD	Famotidine	Merck and Co., NJ, USA
Zofran ODT	Ondansetron	GlaxoWellcome, Middlesex, UK
Zoming-ZMT	Zolmitriptan	AstraZeneca, Wilmington, USA
Zeplar TM	Selegilline	Amarin Corp., London, UK
TempraQuiclets	Acetaminophen	Bristol myers Squibb, NY, USA
Febrectol	Paracetamol	Prographarm, Chateauneuf, France
Nimulid MDT	Nimesulide	Panacea Biotech, New delhi , India
Torrox MT	Rofecoxib	Torrent pharmaceuticals , India
Olanexinstab	Olanzapine	Ranbaxy lab. Ltd. New-delhi, India
Romilast	Montelukast	Ranbaxy lab. Ltd. New-delhi, India
Benadryl Fastmelt	Diphenhydramine and pseudoephedrine	Warner Lambert, NY, USA

Promising Drugs to be incorporated in Fast Dissolving Tablets [30, 31]: There are no particular limitations as long as it is a substance which is used as a pharmaceutical active ingredient.

1. **Analgesics and Anti-inflammatory Agents:** Aloxiprin, Auranofin, Azapropazone, Benorylate, Diflunisal , Etodolac, Fenbufen, FenoprofenCalcim, Flurbiprofen, Ibuprofen, Indomethacin, Ketoprofen, Meclofenamic Acid, Mefenamic Acid, Nabumetone, Naproxen, Oxaprozin, Oxyphenbutazone, Phenylbutazone, Piroxicam, Sulindac.

2. **Anthelmintics:** Albendazole, Bephenium Hydroxy naphthoate, Cambendazole, Dichlorophen, Iverrnectin, Mebendazole, Oxarnniquine, Oxfendazole, Oxantel Embonate, Praziquantel, PyrantelEmbonate, Thiabendazole.

3. **Anti-Arrhythmic Agents:** Amiodarone, Disopyramide, Flecainide Acetate, QuinidineSulphate,

4. **Anti-bacterial Agents:** Benethamine Penicillin, Cinoxacin, Ciprofloxacin, Clarithromycin, Clofazimine, Cloxacillin, Demeclocycline, Doxycycline, Erythromycin, Ethionamide, Imipenem, NalidixicAcid, Nitrofurantoin, Rifampicin, Spiramycin, Sulphabenzamide, Sulphadoxine, Sulpha merazine, Sulphacetamide, Sulphadiazine, Sulphafurazole, Sulphamethoxazole, Sulpha pyridine, Tetracycline, Trimethoprim.

5. **Anti-coagulants:** Dicoumarol, Dipyridamole, Nicoumalone, Phenindione.

6. **Anti-Depressants:** Amoxapine, Ciclazindol, Maprotiline, Mianserin, Nortriptyline, Trazodone, Trimipramine Maleate, Acetohexamide, Chlorpropamide, Gliben-clamide, Gliclazide, Glipizide, Tolazamide,

7. **Anti-Epileptics:** Beclamide, Carbamazepine, Clonazepam, Ethotoin, Methoin, Methsuximide, Methylphenobarbitone, Oxcarbazepine, Paramethadione, Phenacemide, Phenobarbitone, Phenytoin, Valproic Acid.

8. **Anti-Fungal Agents:** Amphotericin, Butoconazole Nitrate, Clotrimazole, EconazoleNitrate, Fluconazole, Fiucytosine, Griseofulvin, Itraconazole, Ketoconazole, Miconazole, Natamycin, Nystatin, Sulconazole Nitrate, Terbinafine, Terconazole, Tioconazole, Undecenoic Acid.

9. **Anti-Gout Agents:** Allopurinol, Probenecid, Sulphinpyrazone.

10. **Anti-Hypertensive Agents:** Amlodipine, Carvedilol, Benidipine, Darodipine, Dilitazem, Diazoxide, Felodipine, Guanabenz Acetate, Indoramin, Isradipine, Minoxidii, Nicardipine, Nifedipine, Nimodipine, Phenoxybenzamine, Prazosin, Reserpine, Terazosin.

11. **Anti-Malarials:** Amodiaquine, Chloroquine, Chlorproguanil, Halofantrine, Mefloquine, Proguanil, Pyrimethamine, Quinine Sulphate.

12. **Anti-Migraine Agents:** DihydroergotamineMesyiate, Ergotamine Tartrate, Methysergide Maleate, Pizotifen Maleate, Sumatriptan Succinate

13. **Anti-Muscarinic Agents:** Atropine, Benzhexol, Biperiden, Ethopropazine, Hyoscine Butyl Bromide, Hyoscyarnine, Mepenzolate Bromide, Orphenadrine, Oxyphencylcimine, Tropicamide.

14. **Anti-Neoplastic Agents And Immunosuppressants:** Aminoglutethimide, Amsacrine, Azathiopnne, Busulphan, Chlorambucil, Cyclosporin, Dacarbazine, Estramustine, Etoposide, Lomustine, Melphalan, Mercaptopurine, Methotrexate, Mitomycin, Mitotane, Mitozantrone, Procarbazine, Tamoxifen Citrate, Testolactone.

15. **Anti Protozoal Agents**: Benznidazole, Clioquinol, Decoquinate, Diiodohydroxy quinoline, Diloxanide Furoate, Dinitolmide, Furzolidone, Metronidazole, Nimorazole, Nitrofurazone, Omidazole, Tinidazole.

16. **Anti-Thyroid Agents:** Carbimazole, Propylthiouracil.

17. **Anxiolytic, Sedatives, Hypnotics And Neuroleptics:** Alprazolam, Amyiobarbitone, Barbitone, Bentazeparn, Bromazepam, Bromperidol, Brotizoiam, Butobarbitone,

Carbromal, Chlordiazepoxide, Chlormethiazole, Chlorpromazine, Clobazam, Clotiazepam, Clozapine, Diazepam, Droperidol, Ethinamate, Flunanisone, Flunitrazepam, Fluopromazine, Flupenuiixol Decanoate, Fluphenazine Decanoate, Flurazepam, Haloperidol, Lorazepam, Lormetazepam, Medazepam, Meprobamate, Methaqualone, Midazolam, Nitrazepam, Oxazepam, Pentobarbitone, Perphenazine Pimozide, Prochlorperazine, Suipiride, Temazepam, Thioridazine, Triazolam, Zopiclone.

18. **Cardiac Inotropic Agents:** Amrinone, Digitoxin, Digoxin, Enoximone, LanatosideC, Medigoxin.

19. **Corticosteroid:** Beclomethasone, Betamethasone, Budesonide, CortisoneAcetate, Desoxymethasone, Dexamethasone, Fludrocortisone acetate, Flunisolide, Flucortolone, Fluticasone Propionatu, Hydrocortisone, Methylprednisolone, Prednisolone, Prednisone, Triamcinolone.

20. **Diuretics:** Acetazolarnide, Amiloride, Bendrofluazide, Bumetanide, Chlorothiazide, Chlorthalidone, Ethacrynic Acid, Frusemide, Metolazone, Spironolactone, Triamterene.

21. **Enzymes:** All The Enzymes.

22. **Anti-Parkinsonian Agents:** BromocriptineMesylate, Lysuride Maleate.

23. **Gastro-Intestinal Agents:** Bisacodyi, Cimetidine, Cisapride, Diphenoxylate, Domperidone, Famotidine, Loperamide, Mesalazine, Nizatidine, Omeprazole, Ondansetron, Ranitidine, Sulphasaiazine.

24. **Histamine H, -Receptor Antagonists:** Acrivastine, Astemizole, Cinnarizine, Cyclizine, Cyproheptadine, Dimenhydrinate, Flunarizine, Loratadine, Meclozine, Oxatomide, Terfenadine, Triprolidine.

25. **Lipid Regulating Agents:** Bezafibrate, Clofibrate, Fenofibrate, Gemfibrozil, Probucol.

26. **Local Anaesthetics:** Lidocaine

27. **Neuro -Muscular Agents:** Pyridostigmine.

28. **Nitrates And Other Anti-Anginal Agents:** Amyl Nitrate, Glyceryl Trinitrate, Isosorbide Dinitrate, Isosorbide Mononitrate, Pentaerythritol Tetranitrate.

29. **Nutritional Agents:** Betacarotene, Vitamin A, Vitamin B 2 , Vitamin D, Vitamin E, VitaminK

30. **Opioid Analgesics:** Codeine, Dextropropyoxyphene, Diamorphine, Dihydrocodeine, Meptazinol, Methadone, Morphine, Nalbuphine, Pentazocine.

31. **Oral Vaccines:** Vaccines designed to prevent or reduce the symptoms of diseases of which the following is a representative Influenza, Tuberculosis, Meningitis, Hepatitis, Whooping Cough, Polio, Tetanus, Diphtheria, Malaria, Cholera, Herpes, Typhoid, Hiv, Aids, Measles, Lyme Disease, Travellers Hepatitis A, B And C, Otitis Media, Dengue Fever, Rabies, Para influenza, Rubella, Yellow Fever, Dysentery, Legionnaires Disease, Toxoplasmosis, Q-Fever, Hemorrhagic Fever, .

32. **Proteins, Peptides And Recombinant Drugs:** Insulin (Hexameric/Dimeric/Monomeric Forms), Glucagon, Growth Hormone (Somatotropin), Calcitonins and synthetic modifications thereof, Enkephalins, Interferons (Especially Alpha-2 Interferon for treatment of common colds).

33. **Sex Hormones:** Clomiphene Citrate Danazol, Medroxy progesterone Acetate, Mestranol, Ethinyloestradiol Methyltestosterone, Norethisterone, Conjugated Oestrogens, Progesterone, Testosterone, Tibolone. Norgestrel, Stanozolol, Oestradiol, Stiboestrol,

34. **Stimulants:** Amphetamine, dexamphetamine, dexfenfluramine, fenfluramine, pemoline.

Preformulation Studies [32, 33]:

1. **Bulk Density:** Apparent bulk density was determined by pouring the 5 gram of powder into a 100 ml granulated cylinder. The bulk volume (V) poured drug was determined. The bulk density was calculated using the formula.

$$\rho b = M / V$$

2. **Tapped Density:** Weight 5 g. of powder and placed in a measuring cylinder. Measuring cylinder containing known mass (5 gm) of powder was tapped for 100 times or fixed time. The minimum volume (Vt) occupied was measured. The tapped density was calculated using following formula.

$$\rho t = M / Vt$$

3. **Compressibility index:** The simplest way for measurement of free flow of powder is compressibility, a indication of the ease with which a material can be induced to flow is given by Compressibility Index. The value below 15% indicates a powder with give rise to good flow properties, whereas above 25% indicate poor flowability. Which is calculated follows.

$$\% \text{ C.I.} = \rho t - \rho b / \rho t \times 100$$

4. **Hausner's ratio:** Hausner's ratio is an indirect index of ease of powder flow. Hausner's ratio is the ratio of tapped density to bulk density. Lower the value of Hausner's ratio better is the flow property. Powder with Hausner's ratio less than 1.18, 1.19, 1.25, 1.3- 1.5 and greater the 1.5 indicate excellent, good, passable, and very poor, respectively. It is calculated by following formula

Hausner's ratio $= \rho t / \rho b$

5. **Porosity:** Percent relative porosity (ε) was obtained using the relationship between apparent density (ρapp) and true density (ρ true) which is calculated by following formula.

$$\varepsilon = (1 - \rho app / \rho true) \times 100$$

6. **Void Volume:** Void volume (V) was obtained by difference between bulk volume (Vb) and tapped volume (Vp). Void volume can be calculated by following formula.

$$V = Vb - Vp$$

7. **Angle of Repose:** The angle of repose was determined using funnel method. Funnel that can be fit vertically with stand at suitable height was used. The opening end of funnel is closed with thumb until drugs are poured. The 5 gm of powder was poured into funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and the angle of repose (Θ) was calculated using the formula**.**

$$\Theta = \text{Tan-1} (h / r)$$

Evaluation of Mouth dissolving Tablets:

1. **Thickness:** Tablet thickness can be measured using a simple procedure. 5tablets were taken and their thickness was measured using Varnier calipers.

2. **Hardness:** It is the force required to break a tablet by compression in the radial direction, it is an important parameter in formulation of mouth dissolve tablets because excessive crushing strength significantly reduces the disintegration time. In the present study the crushing strength of the tablet was measured using Pfizer hardness testers. An average of three observations is reported.

3. **Uniformity of weight:** I.P. procedure for uniformity of weight was followed, 20 tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity.

4. **Disintegration time:** The test was carried out on 6 tablets using the apparatus specified in I.P.-1996 distilled water at 37ºC ± 2ºC was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds.

5. ***In-vitro*** **Drug Release:** The development of dissolution methods for ODTs is comparable to the approach taken for conventional tablets, and is practically identical. Dissolution conditions for drugs listed in a pharmacopoeia monograph, is a good place to start with scouting runs for a bioequivalent ODT. Other media such as 0.1N HCl and buffers (pH - 4.5 and 6.8) should be

evaluated for ODT much in the same way as their ordinary tablet counter parts. The USP 2 Paddle apparatus is used for this purpose which isthe most suitable and common choice for orally-disintegrating tablets, with a paddle speed of 50 rpm commonly used. Typically the dissolution of ODT is very fast when using USP monograph conditions; hence slower paddle speeds may be utilized to obtain a profile. The USP 1 Basket apparatus may have certain applications but sometimes tablet fragments or disintegrated tablet masses may become trapped on the inside top of the basket at the spindle where little or no effective stirring occurs, yielding irreproducible dissolution profiles.

6. **Friability test:** Friability of the tablets was determined using Roche friability apparatus. This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6inches in each revolution. Pre weighed sample of tablets was placed in the friabilator and were subjected to 100revolutions. Tablets were de dusted using a soft muslin cloth and reweighed. The friability (f) is given by the formula.

$$f = (1- W0 / W) \times 100$$

7. ***In-vitro*** **Dispersion time test:** To determine dispersion time 10 ml measuring cylinder was taken in which 6 ml distilled water was added and tablet was dropped in it. Time required for complete dispersion was determined.

8. **Wetting time:** Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter. 10 mm of water-containing Eosin, a water-soluble dye, is added to petridish. A tablet is carefully 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.

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,

$$R = 10 (Wa /Wb)$$

CONCLUSION: FDTs offer numerous significant advantages over conventional dosage forms because of improved efficacy, bioavailability, and rapid onset of action, better patient compliance, and acceptance. Pharmacists are in the ideal position to become familiar with the different technologies and educate their patients to what to expect upon taking their first dose. The majorities of the patients receiving FDDTS preparations have little understanding of this new dosage form.

Paediatric and geriatric patients are primary concerns, as both the groups find these dosage forms convenient to administer as compared to the conventional dosage forms. FDTs can be prepared in several ways and product performance depends upon the drug suitability and excipients selection in the delivery system. Due to the availability of various formulation techniques, good patient compliance and huge potential, several products have already been commercialized.

Furthermore, market size and popularity of these dosage forms will surely expand in future. It is also emphasized that newer with continued development of new pharmaceutical scientific and technological innovations should be undertaken for the emergence of promising and versatile dosage form with novel performance and characteristics for FDTs in days to come.

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REFRENCES:

1. Konapure SA, Chaudhari PS, Oswal RJ, Kshirsagar SS, Antre RV, Chorage TV: Mouth Dissolving Tablets an Innovative Technology, International Journal Of Applied Biology And Pharmaceutical Technology 2011; 02(01):496-503.
2. Neeta, Dureja H, Bhagwan S, Seema, Dahiya J: Fast Dissolving Tablet: An Overview, Novel Science International Journal of Pharmaceutical Science 2012; 01(05):228-232.
3. Bangale SG, Shinde GV, Rathinaraj BS: New generation of orodispersible tablets: recent advances and future prospects, International Journal of Advances in Pharmaceutical Sciences 2011; 02(03):17-28.
4. Jesmeen T, Uddin R: Orodispersible Tablets: A Short Review, Stamford Journal of Pharmaceutical Sciences 2011; 04(01):96-99.

5. Bhowmik D, Chiranjib, Jaiswal J, Dubey V, Chandira M: Fast Dissolving Tablet: A Review On Revolution Of Novel Drug Delivery System And New Market Opportunities, Scholars Research Library 2009; 01(02):262-270.
6. Kaur T, Gill B, Kumar S, Gupta GD: Mouth Dissolving Tablets: A Novel Approach To Drug Delivery, International Journal of Current Pharmaceutical Research 2011; 03(01):1-6.
7. Sharma D, Kumar D, Singh M, Singh G, Rathore MS: Fast Disintegrating Tablets: A New Era In Novel Drug Delivery System And New Market Opportunities, Journal of Drug Delivery & Therapeutics 2012; 02(03):74-86.
8. Kumar A, Bhushan V, Singh M and Chauhan A: A Review On Evaluation And Formulation Of Fast Dissolving Tablets, International Journal of Drug Research and Technology 2011; 01(01):8-16.
9. Agarwal VA, Rajurkar RM, Thonte SS, Ingale RG: Fast Disintegrating Tablet As a New drug Delivery System: A Review, Pharmacophore 2011, 02(01):1-8.
10. Saroha K, Mathur P, Verma S, Syan N and Kumar A: Mouth dissolving tablets: An overview on future compaction in oral formulation technologies, Pelagia Research Library 2010, 01(01):179-187.
11. Mangal M, Thakur N, Bansal R, Thakral S, Goswami M: Fast Dissolving Tablet: An Approach For Emergency Treatment, International Journal Of Research and Pharmaceutics 2012; 03(03):377-380.
12. Kumar VD, Sharma I, Sharma V: A Comprehensive Review on Fast Dissolving Tablet Technology, Journal of Applied Pharmaceutical Science 2011; 01(05):50-58.
13. Dutta S, De PK: Formulation Of Fast Disintegrating Tablets, International Journal Of Drug Formulation and Research 2011, 02(01):45-51.
14. Reddy RB, Chattu. VS, Kumar TS, Kumar KB, Reddy VY, Taraka LK Rapimelts: A Review, Journal Of Pharmaceutical And Biomedical Sciences 2011; 06(010): 1-8
15. Sharma R, Rajput M, Pawan P and Sharma S: Fast Dissolving Drug Delivery System - A Review, International Research Journal of Pharmacy 2012, 02(011):21-29.
16. Dixit S, Kaur R, Mishra V, Bhargava S: Fast Dissolving Tablet- A Promising Approach For Drug Delivery: A Review, Journal of Pharmacy Research; 05(03):1508-1513.
17. Deshmukh H, Chandrashekhara S, Nagesh C, Murade A, Usgaunkar S: Superdisintegrants: A Recent Investigation and Current Approach 2012; 02(01):19-25.
18. Shihora H, Panda S: Superdisintegrants, Utility in Dosage Forms: A Quick Review, Journal of Pharmaceutical Science and Bio Scientific Research 2011; 01(03):148-153.
19. Shekhar RS Vedavathi T: Recent Trends Of Oral Fast Disintegrating Tablets – An Overview Of Formulation And Taste Masking Technology, Research Journal Of Pharmaceuticals, Biological And Chemical Sciences 2012; 03(01):771-792.
20. Lewis S, Sharma S: Taste Masking Technologies: A Review, International Journal of Pharmacy and Pharmaceutical Science 2010; 02(02):6-12.
21. Gajare GG, Bakliwal SR, Rane B.R, Gujarathi NA, Pawar S.P, Mouth Dissolving Tablets: A Review, International Journal Of Pharmaceutical Research And Development 2011; 03(06):280-296.
22. Chawla G, Jain N: Mouth Dissolving Tablets: An Overview, International Journal Of Pharmaceutical Science And Research 2012; 03(09):2919-2925.
23. Bandari S, Mittapalli RK, Gannu R, Rao YM: Orodispersible tablets: An overview, Asiapharmaceutics 2010; 02(011):1-5.
24. Velmanickam MS, Manavalan R and Valliappan K: Mouth Dissolving Tablets: An Overview, International Journal Of Pharmaceutical Sciences And Research 2010; 01(012):43-55.
25. Yadav G. Kapoor A and Bhargava S: Fast Dissolving Tablets Recent Advantages: A Review, International Journal Pharmaceutical Sciences and Research 2012; 03(03):728-736.
26. Gauri S, Kumar G: Fast Dissolving Drug Delivery And Its Technologies, The Pharma Innovation 2012; 01(02):34-39.110.
27. Arunachalam A, Karthikeyan M, Kumar Sa, Konam K, Prasad Ph, Sethuraman S, Manidipa S: Fast Dissolving Drug Delivery System: A Review, Journal of Global Trend In Pharmaceutical Sciences 2010; 01(01):92-110.
28. Bhowmik D, Chiranjib B, Krishnakanth, Pankaj, Margret R, Chandira: Fast Dissolving Tablet: An Overview, Journal of Chemical and Pharmaceutical Research 2009; 01(01):163-177.
29. Parashar B, Yadav V, Maurya B, Sharma L: Fast Dissolving Tablet, International Journal of Applied Pharmaceutics 2012; 04(02):17-22.
30. Panigrahi R, A Review on Fast Dissolving Tablets, Webmed Central 2010; 01(09):1-15.
31. Pawar PB, Mansuk AG, Ramteke KH, Sharma YP, Patil SN: Mouth Dissolving Tablet: A Review, International Journal of Herbal Drug Research 2011; 01(01): 22-29.
32. Ashish P, Harsoliya MS, Pathan JK, Shruti S: A Review- Formulation of Mouth Dissolving tablet, International Journal of Pharmaceutical and Clinical Science 2011; 01(01):1-8.
33. Gupta AK, Mittal A and Jha KK: Fast Dissolving Tablet- A Review, The Pharma Innovation 2011; 01(01):1-8.

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