RECENT TRENDS IN FAST DISSOLVING DRUG DELIVERY SYSTEM - A NEW FORMULATION TECHNOLOGY

ABSTRACT

The Fast Dissolving Drug Delivery Systems sets a new benchmark was an expansion that came into existence in the early 1980's and combat over the use of the different dosage form like tablets, suspension, syrups, capsules which are the other oral drug delivery systems. Fast Dissolving Drug Delivery System has a major advantage over the conventional dosage forms since the drug gets rapidly disintegrated & dissolves in the saliva without the use of water .In spite of the downside lack of immediate onset of action; these oral dosage forms have valuable purposes such as self medication, increased patient compliance, ease of manufacturing and lack of pain. Hence Fast Disintegrating Tablet (FDT) technology has been gaining importance now-a-days with wide variety of drugs serving many purposes. Fast Disintegrating Tablets (FDT) has ever increased their demand in the last decade since they disintegrate in saliva in less than a minute that improved compliance in pediatrics and geriatric patients, who have difficulty in swallowing tablets or liquids. As fast dissolving tablet provide instantaneous disintegration after putting it on tongue, thereby rapid drug absorption and instantaneous bioavailability, whereas FDOFs are used as practical alternative to FDTs. These films have a potential to deliver the drug systemically through intragastric, sublingual or buccal route of administration and also has been used for local action

KEYWORDS

Fast Dissolving Drug delivery systems, patent, Fast disintegrating tablet, CDER, Pediatric, Geriatric, Bioavailability.

INTRODUCTION

The concept of FDTs came into trending with an objective of increased patient compliance because of its unique advantages. As the cost for developing a generic molecule is too expensive, the research is being done on the new dosage forms for having better patient compliance as compared to the different dosage forms of which the oral route serves to make a provenance. Some patients, particularly pediatric and geriatric patients, have difficulty swallowing or chewing solid dosage forms. Fast-dissolving tablets (FDTs) / orally disintegrating tablets (ODTs) are a perfect fit for all of these patients. Fast-dissolving drug delivery systems have rapidly gained acceptance as an important new way of administering drugs.

The Center for Drug Evaluation and Research (CDER), US FDA defined Oral Disintegrating Tablets (ODT) as a solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue. FDTs disintegrate and/or dissolve instantaneously in the saliva without the use of water. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets.

Others contain agents to enhance the rate of tablet disintegration in the oral cavity, and are more appropriately termed fast-disintegrating tablets, as they may take up to a minute to completely disintegrate. When placed on tongue, this tablet disintegrates rapidly, releasing the drug, which dissolves or disperses in the saliva. Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach.[1, 2, 3]

Ideal Properties of Fast Dissolving Tablets:

1. No need water for oral administration.
2. Should be harder and less friable.
3. Have an acceptable taste masking property.
4. Leave minimal or no residue in mouth after administration
5. Exhibit low sensitivity to environmental conditions (temperature and humidity).
6. Cost-effective production techniques

Advantages of Fast Dissolving Tablets:

1. Ease of administration to patients who cannot swallow like the bed-ridden, stroke victims and patients who refuse to swallow like geriatrics, pediatrics and psychiatrics.
2. Better taste
3. Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing,

Limitations of Mouth Dissolving Tablets

1. The tablets usually have insufficient mechanical strength. Hence, careful handling is required.
2. FDT requires special packaging for properly stabilization and safety of stable product.

Fast dissolving oral films

Fast dissolving oral films (FDOFs) are the most highly developed form of oral solid dosage form due to more flexibility and comfort. It improves the efficacy of drugs by dissolving within 60 seconds in oral cavity after the contact with saliva without chewing and no need of water for administration. It gives rapid absorption and instant bioavailability of drugs due to high blood flow and permeability. FDOFs are useful in patients such as pediatric, geriatrics, bedridden, emetic patients, diarrhea, sudden episode of allergic attacks, or coughing for those who have an active life style. Fast dissolving oral films are based on the technology of the transdermal patch. Sometimes taste masking agents are also added to mask the taste of the active ingredient. Fast dissolving oral films have advantages like:

- ✓ more stable
- ✓ durable and quicker than other conventional dosage forms
- ✓ avoid first pass metabolism
- ✓ pleasant mouth feel
- ✓ accurate dosing
- ✓ Rapid onset of action and no need of water with patient compliance
- ✓ Ease of handling and transportability.[1, 2]

Several marketed products are available of FDOFs, as listed in Table 1

Table 1: Comparison between Fast Dissolving, Tablets and Films[2]

Fast Dissolving Tablets	**Fast Dissolving Films**
It is a tablet	It is a film
Lesser dissolution due to less surface area	Greater dissolution due to larger surface area
Less durable as compared with oral films	Better durable than oral disintegrating tablets
Less patient compliance than films	More patient compliance
High dose can be incorporated	Low dose can only be incorporated
It has a fear of chocking	No risk of chocking

Ideal Drug Candidates of Fast Dissolving Tablets

A drug candidate must be follow the following conditions

- ✓ The dose must be lower than 20 mg.
- ✓ The drug should be partially unionized at oral pH.
- ✓ Drug should permeate through the oral mucosal tissue.

Examples for Ideal drug candidate for FDDS are active Drugs like Ibuprofen, Indomethacin, Ketoprofen, Meclofenamic Acid, MefenamicAcid, Nabumetone, Carbamazepine, Clonazepam are the potential candidate for the FDDS.

MATERIALS AND METHODS

Selection of Excipients

Excipients maintain the properties of the active ingredients in fast-melting tablets. This demands a thorough understanding of the chemistry of these excipients to prevent interaction with the actives. These inactive food-grade ingredients, when incorporated in the formulation, impart the desired organoleptic properties and product efficacy like bulk agents, emulsifying agent, lubricant, sweeteners, flavor etc.

BulkAgents

Bulk agents are important in the formulation of fast-dissolving tablets. The material contributes functions of a diluent, filler and cost reducer. Bulk agents improve the appeal & enhance the disintegration in the mouth, besides adding bulk also reduces the concentration of the active in the composition. The recommended bulking agents for this delivery system should be more sugar-based such as mannitol, polydextrose, lactitol, DCL (direct compressible lactose) and starch hydrolystate for higher aqueous solubility and good sensory perception.

The sugar based excipients which are commonly used are especially bulking agents (like dextrose, fructose, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol) which display high aqueous solubility and sweetness, and hence impart taste masking property. Mizumito et.al, classified sugar-based excipients on the basis of molding and dissolution rate

Type 1

Saccharides like lactose and mannitol exhibit low mouldability but high dissolution rate.

Type 2

Saccharides like maltose and maltilol exhibit high mouldability but low dissolution rate.

Emulsifying agents

These are important excipients for formulating fast-melting tablets. They support in rapid disintegration and drug release without chewing, swallowing or drinking water. A wide range of emulsifiers is recommended for fast-dissolving tablet formulation, including alkyl sulfates, propylene glycol esters, lecithin, sucrose esters and others. These agents can be incorporated in the range of 0.05 percent to about 15 percent by weight of the final composition.

Lubricants

Lubricants, though not essential excipients, can further assist in making these tablets more palatable after they disintegrate in the mouth. Lubricants remove grittiness and assist in the drug transport mechanism from the mouth down into the stomach.

Flavors and Sweeteners

Flavors and taste-masking agents make the products more palatable and pleasing for patients. The addition of these ingredients aids in overcoming unpleasantness and distasteful of some active ingredients. Both natural and synthetic flavors can be used to improve the organoleptic characteristics of fast-melting tablets. Formulators can choose from a wide range of sweeteners including sugar, dextrose and fructose, as well as non-nutritive sweeteners such as aspartame, sodium saccharin, sugar alcohols and sucralose.

Superdisintegrants

Disintegrants are substances usually mixed in tablet formulations and in some hard shell capsule formulations to enhance moisture dispersion and dispersion of the matrix of dosage form in dissolution fluids. Superdisintegrants are generally used at a low concentration, typically 1-10% by weight relative to total weight of dosage unit.

Generally employed superdisintegrants are like croscarmellose sodium (Ac-Di-Sol), Crosspovidone (CP), sodium starch glycolate (SSG). The properties of super disintegrants are listed in table 2.[1, 4, 5]

Table2: Properties of Modified Starches/Celluloses Used in FDTs[1]

S.No.	Superdisintegrant	Properties
1	Croscarmellose	High swelling capacity, effective at low concentration
	sodium	(0.5-2.0%); can be used up to 5%.
2	Crospovidone	Completely insoluble in water. Rapidly disperses and
		swells in water, but does not gel even after prolonged
		exposure. Greatest rate of swelling compared to other
		disintegrants. Greater surface area to volume ratio
		than other disintegrants. Effective concentration (1-
		3%). Available in micronized grades if needed for
		improving state of dispersion in the powder blend.
3	Sodiumstarch	Absorbs water rapidly, resulting in swelling up to 6%.
	glycolate	High concentration causes gelling and loss of
		disintegration

Formulation Methodology Employed For Fast Dissolving Tablets

Various methods are employed for the formulation of fast dissolving tablets is like

1. Lyophilization or freeze drying
2. Tablet Moulding
3. Spray drying
4. Sublimation
5. Mass extrusion
6. Direct compression
7. Melt granulation
8. Cotton candy process

1. **Lyophilization or freeze drying**

The tablets prepared by freeze-drying or lyophilization are very porous in nature and disintegrate or dissolve quickly when come in contact with saliva. In this process, water is sublimated from the product after freezing. The active drug is dissolved or dispersed in an aqueous solution of a carrier/polymer. The mixture is done by weight and poured in the walls of the preformed blister packs. The trays holding the blister packs are passed through liquid nitrogen freezing tunnel to freeze the drug solution or dispersion. First of all, the material is frozen to bring it below its

eutectic point. Then primary drying is done to decrease the moisture to about 4% w/w of dry product. Lastly, secondary drying is made to reduce the bound moisture to the required volume. However the use of freeze-drying is restricted due to high cost of equipment and processing.

Limitation

A major limitation of the final dosage form comprises lack of physical resistance in standard blister packs.

2. **Tablet Moulding**

Moulding process is of two type's i.e. solvent method and heat method.

Solvent method

It Involves damping the powder blend using an alcoholic solvent and later on compressing at low pressure in molded plates to form a wet mass (compression moulding).The solvent is then removed by air-drying. The tablets prepared by this technique are less compact than compressed tablets and posses a porous structure that accelerates the dissolution.

The heat moulding process

It 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 30ºC under vacuum. The mechanical strength of molded tablets is to be notified and hence binding agents are mixed to give strength. Taste masking is an additional trouble in this technology. The taste masked drug particles were prepared by spray congealing a molten mixture of hydrogenated cottonseed oil, sodium carbonate, lecithin, polyethylene glycol and an active ingredient into a lactose based tablet triturate form.

3. **Spray Drying:**

Spray drying can produce highly porous and fine powders that dissolve rapidly. The formulations are incorporated by hydrolyzed and non hydrolyzed gelatins as supporting agents, mannitol as bulking agent, sodium starch glycolate or croscarmellose sodium as disintegrating and an acidic material (e.g. citric acid) and/ or alkali material (e.g. sodium bicarbonate) to enhance disintegration and dissolution. Tablet compressed from the spray dried powder disintegrated within 20 seconds when immersed in an aqueous medium shown in figure 1.

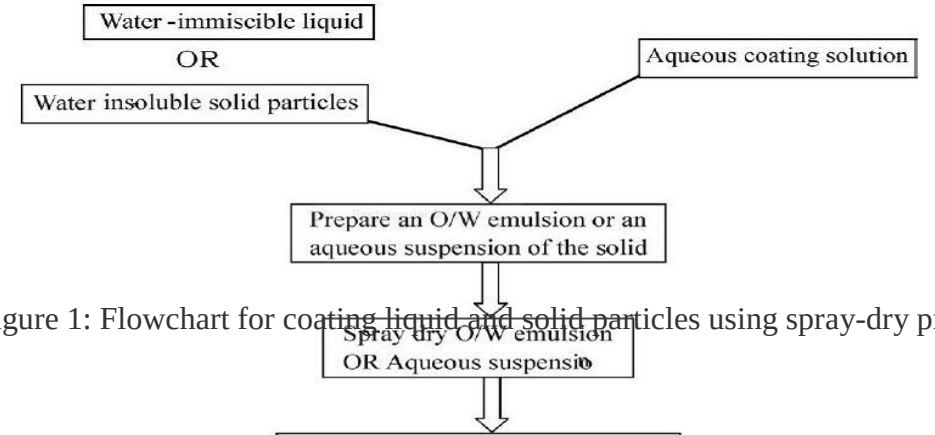

Figure 1: Flowchart for coating liquid and solid particles using spray-dry process[8]

4. **Sublimation**

Inert solid ingredients (ex. urea, urethane, ammonium carbonate, camphor, naphthalene) were added to other tablet excipients and the blend was compressed into tablet. Removal of volatile material by sublimation generated a porous structure. The tablets dissolve in less than 20 seconds and exhibit sufficient mechanical strength. The key to rapid disintegration for mouth dissolving tablets is the presence of a porous structure in the tablet matrix. Conventional compressed tablets that contain highly water-soluble ingredients often fall to dissolve rapidly because of low porosity of the matrix shown in figure 2.[1, 7]

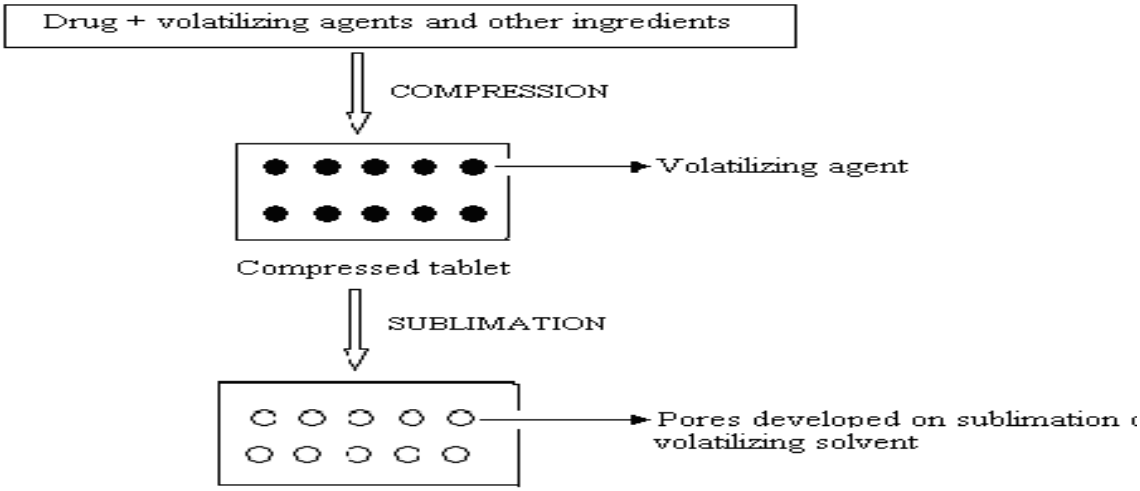

Figure 2: Schematic Diagram of Sublimation Technique for Preparation of FDT [9]

5. **Direct Compression**

The disintegration and solubilization of directly compressed tablets depends on single or combined action of disintegrants, water soluble excipients and effervescent agents used. Breakage of tablet edges during handling and tablet crack during the opening of blister alveolus, all result from insufficient physical resistance. To ensure a high disintegration rate, choice of suitable type and an optimal amount of disintegrant is important. Other formulation components such as water soluble excipients or effervescent agents can promote improved dissolution or disintegration properties. But the main problem of using effervescent excipients is that they are highly hygroscopic in nature.

6. **Melt Granulation**

Melt granulation technique is a process by which the pharmaceutical powders are capably agglomerated by a meltable binder. The benefit of this technique compared to a conventional granulation is that no water or organic solvents is required. Since there is no drying step, the process is less time consuming and requires less energy than wet granulation. It is a technique useful to enhance the dissolution rate of poorly water-soluble drugs, such as griseofulvin.

7. **Mass extrusion**

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

8. **Cotton candy process**

This process is so called as it makes use of a unique spinning mechanism to produce floss-like crystalline structure, which mimic cotton candy. Cotton candy process involves the formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have better flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to ODT. This process can accommodate larger drug doses and offers improved mechanical strength. However, high-process temperature limits the use of this process.[8, 10]

Patented Technologies

i. Zydis (R.P. Scherer, Inc.)
I. Wowtab (Yamanouchi Pharma Technologies,Inc.)
II. OraSolv (Cima Labs, Inc.)
III. DuraSolv (Cima Labs, Inc.)
IV. FlashDose (Fuisz Technologies, Ltd.)
V. Flashtab (Prographarm Group)
VI. OraQuick (KV Pharmaceutical Co., Inc.)
VII. Quick –Dis Technology (Lavipharm Laboratories Inc.)
VIII. Ziplets/Advatab, (Passano con Barnago, Italy)
IX. Lyoc technology (PHARMALYCO)
X. Pharmaburst technology (SPI Pharma, New Castle)
XI. Frosta technology (Akina)
XII. Nanocrystal Technology (Elan, King of Prussia)
XIII. Quick solv (Janssen Pharmaceuticals). [1, 12, 19]

Formulation Methodology Employed For Fast Dissolving Oral Films

Solvent casting method

In solvent casting method water soluble polymers are dissolved in water and the drug along with other excipients is dissolved in suitable solvent then both the solutions are mixed and stirred and finally casted in to the Petri plate dried and cut in to uniform dimensions.

Semisolid casting

In semisolid casting method firstly a solution of water-soluble film forming polymer is prepared. The resulting solution is added to a solution of acid insoluble polymer (e.g. cellulose acetate phthalate, cellulose acetate butyrate), which was prepared in ammonium or sodium hydroxide. Then appropriate amount of plasticizer is added so that a gel mass is obtained. Finally the gel mass is casted in to the films or ribbons using heat controlled drums. The thickness of the film is about 0.015-0.05 inches. The ratio of the acid insoluble poly merto film forming polymer should be 1:4.

Hot melt extrusion

In hot melt extrusion method firstly the drug is mixed with carriers in solid form. Then the extruder having heaters melts the mixture. Finally the melt is shaped in to films by the dies. There are certain benefits of hot melt extrusion method:

- ✓ Fewer operation units

- ✓ Better content uniformity
- ✓ anhydrous process

Solid dispersion extrusion

In this method immiscible components are extrude with drug and then solid dispersions are prepared. Finally the solid dispersions are shaped in to films by means of dies

Rolling method

In rolling method a solution or suspension containing drug is rolled on a carrier. The solvent is mainly water and mixture of water and alcohol. The film is dried on the rollers and cut in to desired shapes and sizes.[13-16, 17]

Evaluation of Fast Dissolving Tablet

I. **Weight variation**

20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P. is shown in table 3.

Table 3: Limits for the weight variation of tablets

Average weight of tablet	% deviation
80mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250mg or more	±5

I. **Tensile Strength**

The tablet tensile strength is the force required to break a tablet by compressing it in the radial direction and is measured using a tablet hardness tester. For measuring the hardness of the tablets, the plunger of the hardness tester is driven down at a speed of 20 mm/min. Tensile strength for crushing (T) is calculated using equation given below

$$T = 2F / \pi dt$$

Wher

F is the crushing load, and d and t denote the diameter and thickness of the tablet, respectively .Though, this is a widely used and accepted method for hardness testing, it is not applicable to very delicate tablets prepared by lyophilization technique.

II. **Friability**

The pharmacopoeial limit of friability test for a tablet is not more than 1% using tablet friability apparatus, carried out at 25 rpm for 4 min (100 rotations). However, it becomes a great challenge for a formulator to achieve friability within this limit for FDT product keeping hardness at its lowest possible level in order to achieve a minimum possible disintegration time. This test is again not applicable for lyophilized and flash dose tablets, but is always recommended for tablets prepared by direct compression and moulding techniques to ensure that they have enough mechanical strength to withstand the abrasion during shipping and shelf life.

III. **Moisture Uptake Study**

MDTs usually contain high concentration of hydrophilic excipients with the minimum possible hardness which together contributes to their increased susceptibility to moisture uptake hence special attention is required during the storage and packaging of these dosage forms. Therefore, moisture uptake studies are strongly recommended for FDTs. The test can be carried out by keeping ten tablets along with calcium chloride in a desiccator maintained at 37 °C for 24 hrs to ensure complete drying of the tablets. The tablets are then weighed and exposed to 75% RH, at room temperature for 2 weeks. The required humidity can be achieved by keeping saturated sodium chloride solution in the dessicator for 24 hrs.The tablets are reweighed and the percentage increase in weight is recorded. The use of appropriate quantity of desiccant in HDPE bottle packs with minimum head space is highly recommended to ensure stability of the product during its shelf life.

IV. **Tablet Porosity**

The mercury penetration porosimeter can be used to measure the tablet porosity which is a relative assessment of the degree of water penetration in the formulation, responsible for its fast disintegration.

V. **Wetting Time and Water Absorption Ratio**

A study on wetting time and water absorption ratio reported the use of a piece of double folded tissue paper placed in a petridish containing 6 ml of water. One tablet was placed on this paper and the time for complete wetting of tablet was noted as wetting time. The wetted tablet was then weighed and the water absorption ratio, R, was determined according to equation

$$R = 100\ (Wa - Wb)/Wb$$

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

VI. **Invivo disintegration time**

The time for disintegration of ODTs is generally <1 minute and actual disintegration time that patient can experience ranges from 5 to 30 seconds. The standard procedure of performing disintegration test for these dosage forms has several limitations and they do not be sufficient the measurement of very short disintegration times. The disintegration test for ODT should mimic disintegration in mouth within salivary contents.

VII. **Dissolution Test**

The development of dissolution methods for ODTs and conventional tablet are same. 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 conventional tablets.USP dissolution apparatus 1 and 2 can be used. 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. USP 2 Paddle apparatus, which is the most suitable and common choice for ODTs, 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 2 Paddle apparatus at 50 to 100 rpm is suitable for dissolution testing of taste-masked drug as well.[1, 20]

List of commercially available Fast dissolving oral films and tablets

Table 3: Examples of commercially available Fast Dissolving Oral Films[1, 18]

Product	Active Drug	Dose Strength (mg)	Application	Company
Triaminic	Dextromethorphan HBr	5/7.5	Seasonal allergy	Novartis
Triaminic	Diphenhydramine HCl	12.5	Thin Strip for Long acting cough	Novartis
Theraflu	Dextromethorphan HBr	10 or 20	For Long acting cough	Novartis
Gas-X	Simethicone	62.5	Gas-X Thin Strip Anti Gas	Novartis
Sudafed PE	Phenylephrine HCl	10	Decongestant oral strips	Pfizer
Benadryl	Diphenhydramine HCl	12.5	Antihistaminic oral strips	Pfizer
Chloraseptic	Benzocaine: Menthol	3 mg	Chloraseptic Relief Strips	Prestige
Suppress	Dextromethorphan		Suppress Cough Strips	InnoZen
Suppress	Menthol	2.5	Suppress Herbal Cough relief strips	InnoZen

Table 4 : Commercially available Patented Fast dissolving Technologies[1, 18]

Patented Technology	**Patent Holder**	**Technology Basis**	**Active Ingredients**	**Available Products**
Zydus	R.P.Scherer,Inc [Cardinal Health]	Freeze-drying	Loratidine	Claritin®Reditab
			Fanotidine	Pepcid®ODT
			Ondansetron	Zofran®ODT
			Selegiline	ZelaparTM
			Rizatritpan benzoate	Maxalt-®MLT

Lyoc	Farmayoc	Freeze-drying	Phloroglucinol hydrate	Spasfon lyoc
QuickSolv	Janssen pharmaceutics	Freeze-drying	Cisapride monohydrate	Propulsid Quicksolv
Orasolv	Cima Labs Inc,	Direct compression	Mirtazapine	Remeron®SolTab
			Acetaminophen	Tempra Quicklets TempraFirs Tablet
Flash Dose	Biovail(Fuisz Technology, Ltd)	Cotton Candy Process	Tramadol HCl	Relivia Flashdose®
			Fluoxetine	FluoxetineODT
			Zolpidem Tertrate	Zolpidem ODT
Durasolv	Cima Labs Inc,	Direct compression	Zolmitriptane	Zolmig®ZMT
			Hyoscyamine Sulfate	Nulev®
			Baclofen	KemstroTM
Flashtab	Prographarm laboratories	Direct compression	Ibuprofen	Nurofen®Flash Tab
Wowtab	Yamanouchi Pharma Tech,Inc	Direct compression	Famotidine	Gaster D
			Ramosetoron HCl	Nasea OD
			Diphenhydramine Citrate	Benadryl®Fastmelt

CONCLUSION

Fast dissolving drug delivery system creates new plate form for better patient compliance, stabilizes drugs which facing difficulties in release pattern and may offer improved biopharmaceutical properties, improved efficacy and better safety compared with conventional oral dosage forms. FDT formulations obtained by some of these technologies have sufficient mechanical strength, quick disintegration/dissolution in the mouth. Many drugs can be incorporated in FDT especially unpalatable drugs. An extension of market exclusivity, which can be provided by a fast-dissolving/disintegrating dosage form, leads to increased revenue, while also targeting underserved and undertreated patient populations. However, geriatric and pediatric patients experience difficulty in swallowing conventional tablets, which leads to poor patient compliance. To overcome this weakness, scientists have developed innovative drug delivery systems known as fast dissolving tablets. Their characteristic advantages such as administration without water, anywhere, anytime lead to their suitability to geriatric and pediatric patients. Rapid onset, good stability and increased bioavailability lead to its current growth in the market. Now a day's new techniques are patented for the preparation of fast dissolving films and tablets day by day which is beneficiary for the pediatrics and geriatrics patient.

ACKNOWLEDGEMENT

Author express sincere thanks to Tarun Virmani sir, Assistant Professor MVN University for guiding and supporting me during my work.

CONFLICT OF INTEREST

"No conflict of interest associated with this work".

REFERENCE

1. Chawdory YK, Saumya M, MadhuBabu M et al. A review on fast dissolving drug delivery systems- A pioneering drug delivery technology. Bull. Env. Pharmacol. Life Scien. Volume 1 (12) November 2012: 08- 20.
2. Saini S, Nanda A, Hooda M, Komal. Fast dissolving films (fdf): innovative drug delivery system. Pharmacologyonline.2011; 2: 919-928.
3. US Food and Drug Administration, CDER Data Standards Manual. 2003. http://www.fda.gov/cder/dsm/DRG/drg00201.htm.
4. European Directorate for quality of Medicines. Pharmaeuropa. 1998; 10(4): 547. http://www.pheur.org.
5. Reddy LH, Ghosh B and Rajneesh. Fast dissolving drug delivery systems: A review of the literature, Indian J. Pharm. Sci., 2002, 64(4): 331-336.
6. Kuchekar BS, Badhan A, Mahajan C, H S. Mouth dissolving Tablets: A novel drug delivery system. Pharma Times, 35, 2003: 7-9.

7. Yadav G, Kapoor A and Bhargava S. Fast dissolving tablets recent advantages: A review. Int J Pharm Sci Research, Vol. 3(3): 728-738.
8. https://www.researchgate.net/figure/Flow-chart-for-coating-liquid-and-solid-particles-using-spray-drying-process-24_fig3_314145401
9. https://innovareacademics.in/journals/index.php/ijpps/article/viewFile/1745/850
10. Kumar S, Garg SK. Fast dissolving tablets (FDTs): Current status, new market oppurtunities, recent advances in manufacturing technologies and future prospects. Int. J. of Pharm and Pharmaceutical Sci. Vol. 6(7): 22- 35.
11. Gupta AK, Mittal A and Jha KK. Fast dissolving Tablet- A Review. The Pharma Innovation, Vol.1 (1).
12. Roser B.J, and Blair J. Rapidly Soluble Oral Dosage Forms, Method of making same and Compositions Thereof. US patent No., US 5762961, 1998.
13. Bhura N, Sanghvi K, Patel U, Parmar V and Patel D. A review on fast dissolving film. Int J of Pharm Research and biosci, vol.1 (3): 66-89.
14. Kumar SV, Gavaskar B, Sharan G and Rao YM. Overview on fast dissolving Films. Int J Pharmacy and Pharm Sci, Vol. 2, (3): 29-33.
15. Parmar D, Patel U, Bhimani B, Tripathi A, Daslaniya D and Patel G. Orally Fast dissolving films as dominant dosage form for quick release. Int J of Pharm Research and biosci, Vol. 1(3): 27- 41.
16. Sapkal NP, Kilor VA, Daud AS and Bonde MN. Development of fast dissolving oral thin films of ambroxol hydrochloride: Effect of formulation variables. J of Advanced Pharm Research, Vol. 2(2): 102-109.
17. Koizumi, IK. New method of preparing highly porous rapidly saliva soluble tablets by Sublimation technique. Int. J. Pharm, 1997, 152: 127-131.
18. Heer D, Aggarwal G, Harikumar SL. Recent trends in fast dissolving drug delivery system- An overview of formulation technology. Pharmacophore 2013, Vol. 4 (1): 1-9.
19. Prajapati BP and Ratnakar N. A Review on recent patents on fast dissolving drug delivery system. Int J of Pharm Tech Research, Vol. 1 (3): 790-798.
20. Patil SL, Madhvi, Shivnikar A. Formulation and technology of fast disintegration tablets: A review. J of Pharmaceutical & Bio med Sci. 9(11): 1- 7.