WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 11, 956-970. Review Article ISSN 2277–7105

A COMPREHENSIVE REVIEW ON: PREPARATION OF FAST DISSOLVING TABLETS, CHARACTERIZATION, OPTIMIZATION AND EVALUATION

Ganesh Lal[1*], Satyanand Mourya[2], Roshan Kumar Dubey[3] and Dr. Abhishek Kumar[4]

[1]Assistant Professor, Department of Pharmaceutics, Saraswati Higher Education & Technical College of Pharmacy Gahani Varansi – 221202.

[2]M. Pharma, Saraswati Higher Education & Technical College of Pharmacy Gahani Varansi – 221202.

[3]Assistant Professor, Department of Pharmaceutics, Northern Institute of Pharmacy and Research, Alwar Rajasthan – 301028.

[4]Associate Professor, Department of Pharmacognosy, Saraswati Higher Education & Technical College of Pharmacy Gahani Varansi – 221202.

Article Received on
09 July 2021,

Revised on 30 July 2021,
Accepted on 20 August 2021

DOI: 10.20959/wjpr202111-21508

***Corresponding Author**
Ganesh Lal
Assistant Professor, Department of Pharmaceutics, Saraswati Higher Education & Technical College of Pharmacy Gahani Varansi – 221202.

ABSTRACT

The mouth is the most used route for administration of medication because of it's very cost-effective, safest and most convenient advantages. Previously Schere RP, developed the first lyophilized fast-dissolving technology Zydis in 1986, & since then, there has been a steady increase in patented technique, technique, names, & by other businesses like oraquick technology and Wowtab technique. Super disintegrants such as Croscarmellose Sodium, Crospovidone (CP), PVP and Sodium Sarch Glycolate (SSG), as binders are among the excipients used in the composition. The Fast Dissolving Tablet (FDT) was recently created by researchers to enhance sufferer convenience and compliance. FDTs are solids that melts quickly in mouth with no need of chewing or extra H2O. FDTs address the drawbacks of traditional dose forms, particularly dysphagia in juvenile & elderly people. There are many quick-dispersing Rx & OTC medicines on the market today, the majority of which were introduced in the last three to four years. The number of novel chemical compounds under research utilizing a quick- dissolving medicine delivery method has also increased significantly. As a result, it is anticipated that in the not-too-distant future,

this distribution method will be as important as traditional delivery methods. This study covers ideal formulation, difficulties, features, characteristics, drug candidate eligibility, patented techniques, different FDT techniques, assessment techniques, patented techniques and numerous commercial products.

KEYWORDS: Drug delivery system, Fast dissolving tablets, Super disintegrants, fast disintegrating, fast melting.

INTRODUCTION

Traditional dosage forms (tablet and pill) are widely accepted, accounting for 50-60percent of total dosage. Tablets are still the most common traditional dosage forms being used nowadays due to their ease of manufacturing, compact size, simplicity of use and ability to give precise doses. One significant disadvantage of solid dose forms is that certain individuals, especially juvenile and elderly sufferers, have trouble swallowing (dysphagia) or chewing them. Swallowing difficulties are prevalent in elderly sufferers because of choking fear, dysphasia, hand tremors & in youngsters because of undeveloped neurological and muscular system, and also in schizophrenics, resulting in poor patient compliance.[1] Swallowing issues with tablets & capsules may also happen when H_2O is unavailable, in bronchitis, coughing, common cold, diarrhoea and allergic conditions.[2] Swallowing problems affect around 1/3rd of the community (mostly children & the elderly), leading to poor adherence to oral tablet medication treatment & decreased overall therapeutic efficacy. As a result, tablets that disperse quickly in the oral cavity have received a lot of attention. Fast dissolving tablet (FDT) is described by the US Food and Drug Administration (FDA) as "a solid dosage form containing medicinal material or active component that disintegrates quickly, typically within a couple of seconds, once put onto the tongue."

Mouth-dissolving tablets, Rapimelts, Orodispersible pills, melt-in-mouth tablets & porous tablets, are all terms used to describe FDTs. Without the use of liquid, quickly disintegrating pills melts in the buccal cavity. The bitter taste of the active component must be disguised in most quick dissolving pills. The disguised active component, together with the soluble and insoluble excipients, is subsequently ingested by the sufferer's saliva.[3,4] The quicker the breakdown, the quicker the absorption (just the unionised form of medication) and the start of action. As saliva travels down in the stomach, certain medicines are absorbed from the mouth cavity, throat, and oesophagus. As a result, the drug's bioavailability is considerably higher than that found with traditional tablet dose form.[5] Fast dissolving pills are usually thought to

disintegrate in less than a min.[6-9]

The quickly disintegrating pill types dissolve rapidly into a soft paste or liquid for comfortable swallowing, eliminating the danger of choking.[11,12] A number of enhanced drug delivery systems have developed in recent times with the goal of increasing patient compliance, bioavailability, convenience. Some tablets, known as genuine quick-dissolving tablets, are intended to disintegrate in saliva in a couple of seconds. The benefits of rapid dissolving technique are as follows.[13-17]

- No water needed.
- Improved added convenience /compliance.
- No chewing needed.
- Improved stability.
- Allows high drug loading.
- Better taste.
- Suitable for controlled as well as fast release actives.
- Capability to give advantages of fluid medication in the type of solids.
- Cost- effective.
- Amenable & flexible to existing processing and packing equipment.

Salient Features of FDTs[18]

- Have enough power to endure the rigors of the development & post development handling.
- Does not need H_2O for administration from mouth.
- Allow high drug loading.
- Insensible to conditions of environmental such as temperature & humidity have a pleasant mouth feel.
- Cost effective.

The Need for Development of FDTs

Patient factors[19, 20]

People (especially geriatric and pediatric patients) which are unable to swallow traditional capsules & pills with an 8-oz glass of H_2O should use rapidly dissolving dose forms. The following are some of them:

- Patient's incompliance due to fear of choking

- Patients who have trouble swallowing or digesting solid dose forms may benefit from this medication.
- Patients suffering from depression who are very old and may not be able to take the solid dose forms.
- A middle-aged woman receiving radiation treatment for breast cancer may be unable to swallow her H_2-blocker because she is feeling sick.
- In order to make allergy medication more convenient for an eight-year-old child, an antihistamine syrup is being considered.
- A sufferer with continuous nausea, who may travel, & has little access to H_2O.
- A sufferer of schizophrenia who can try to hide a conventional pill under his or her tongue to avoid their daily dose

Effectiveness factor

Pre-gastric absorption of the medication occurs when it is dispersed in saliva in the mouth cavity. Many medicines are absorbed in the stomach, oral & pharyngeal portions. Any pre-gastric absorption avoids hepatic metabolism in the 1st pass, thus increases bioavailability. Moreover, safety profiles for medicines that generate large quantities of hazardous metabolites through 1st-pass gastric and hepatic metabolism, and also pharmaceuticals with a significant percentage of absorption in the oral cavity and pre-gastric regions of the GIT, might be improved.

Manufacturing and marketing factors

Pharmaceutical companies often produce a particular drug entity in a better & new dosage type when a drug's sufferer life approaches its conclusion. A novel form enables a company to prolong patent protection, value-added product line extension, market exclusivity and distinctive product differentiation, all while providing a much accessible dosage form to its patient audience. This increases income while simultaneously focusing on underrepresented & undertreated sufferer groups. For e.g., in reaction to a generic competition filed in the United States by Eisai Inc., Ranbaxy introduced Aricept FDT, a line extension of donepezil for Alzheimer's, in Japan in 2004 & in the United States in 2005. In reply to 17 generic registrations of simvastatin filed for in Japan in 2004, Merck's Japanese unit developed Lipola M (simvastatin ODT), a line extension of their blockbuster, Zocor®, a cholesterol-lowering medication. Marketers help to create a better brand, which helps to enhance a company's image.

Characteristics

As a new dosage type, FDDTs has many features that set them apart from more conventional type. Since it is believed that the dose type will not disintegrate till it passes through the oral cavity, conventional pill preparations do not really need flavor masking. To mask the nasty aftertaste of the medication, many chewable tablets, syrups, suspensions, simply include sugars, flavors, & other sweeteners.[21] Flavors & sweeteners for taste masking are included in rapid disintegrating/dissolving tablets, however many bitter drugs are not disguised by taste masking agents. Adsorption onto or complexation with spray coating and carriers of drug particles, are the most common techniques of flavor masking.

Limitations

- The pills can leave unlikable taste &/or grittiness in buccal cavity if not formulated properly.
- The tablets generally have inadequate mechanical strength. Hence, cautious handling is necessary throughout developing process.
- Drugs with larger doses are hard to prepare into FDT e.g. ethambutol (1000mg), rifampin (600 mg), etc.

Ingredient to be used for FDTs

This contains the vigorous component (drugs) as well as the excipients. Excipients in FDTs help balance the characteristics of the active ingredients. Excipients play a significant role in the formulation of fast-melting tablets. For quicker dissolving characteristics, the excipients should be kept at a temp. of 30–350°C. Table 1 lists the technology & ingredients needed to make FDT.

Table 1: Ingredients and Technologies Used for Formulating FDT.[19]

Drugs	Ingredients	Technology	Disintegration time (Sec)
Rizatriptan benzoate	Primogel, Ac-di-sol, Kollidone, Talc, Aerosil, Magnesium stearate, aspartame and sucralose	Direct compresion	85
Capecitable	Crosspovidone, HPMC, Mannitol and MCC	Direct compression	50
Granisetron HCl	Cyclodextrin, CCS, magnesium stearate, lactose and mannitol	Direct compression	17.1
Amlodipine Besilate	Avicel PH 101 or 301, mannitol and Eudragit EPO	Direct Compression (Sublimation)	15 – 37.8

Aceclofenac	SSG, Mannitol and MCC	Direct compression	12.2 – 27.5
Modafinil	CCS, MCC, Lactose, pregelatinized and starch	Wet granulation	-
Resperidone	Mannitol, Aspartame, PEG 400, & 4000, MCC Ph 200), Gelucire 44/14	Spry drying and compression	Below 30
Clarithromycin or Cefixime	Cariageenan NF, Tiicalcium phosphate, Avicel PH 105, LS HPC, Sucrose steaiate.	Extrusion splieronization	Less than 60
Famotidine	Mannitol, PVP K30, Dextran, Sucralose, Sugar, Lactose.	Freeze drying	2 - 6
Epinephrine bitartrate	Avicel PH- 301,C'rospovidone, Mannitol, LS HPC(LHII), Magnesium stearate	Direct compression	Less than 10
Diclofenac, Acetylsaalicylic acid	Mannitol, Sodium CMC, Citric acid in ethanol, EC and aspartame	Molding, Decompression	-
ADH	CCS, sodium bicarbonate, Lactose	granulation	-
Ibuprofen, Indomethacin, Napoxen Diclofenac	Crospovidone, SSG, Mannitol, MCC, Xanthum Gum, Silica, Magnesium Stearate, Sodium saccharine, talc	Direct Compression	10 – 15
Fexofenadine	Mannitol, crospovidone, precipitated silica, magnesium stearate, sucralose	Direct compression	15 - 20
Ascorbic acid, climetidine	Erythritol, D-mannitol, MCC, starch, pegelatinized starch	Molding, Direct compression	37 - 37
Topiramate	Mannitol, CCS, hydroxypropyl-β-cyclodextrine	Wet granulation	-
Sildenafil	Crosspovidone, Aspartame, Mannitol	Freeze drying	<30
Olanzapine Donepezil	MCC, Mannitol, Sodium stearyl fumerate, polacrilin potassium, aspartame, strawberry flavor	Direct compression	<30
Chlorpromazine HCl	Sodium starch glycolate, crospovidone, croscarmellose, pregelatinised starch	Direct compression	Less than 60

HPMC: Hydroxypropylmethylcellulose, **MCC:** Microcrystalline cellulose, **CCS:** Crosscarmelose ssodium, **SSG:** Sodium starch glycolate, **PEG:** Polyethylene glycol, **PVP:** Polyvinylpyrollidone, **EC:** Ethylcellulose.

Evaluation

Parameters of evaluation of pills stated in the Pharmacopoeias require to be assess.

Weight variation

To check for weight variance, 20 pills were randomly chosen from the batch and weighted separately. Table 2 shows the weight variation specification according to I.P.

Table 2: Accepted percent deviation and weight fluctuation.[26]

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

Hardness

To enable early breakdown in the oral cavity, the FDT's toughness limit is typically maintained at a low level. Traditional toughness testers may be used to decide the pill's rigidity (Monsanto pills rigidity tester). It is calculated in kilogrammes or pounds.[27]

Friability

A developer has a difficulty in achieving percent friability within limitations (0.1-0.9c/o) for an FDT since all techniques of FDT production are capable of raising percent friability values. Each batch's friability was tested in a "Electro lab friabilator." The following eq'n.[28] was used to determine the % of weight loss after 10 pre-weighed tablets were spun at twenty-five rpm for four minutes or Hundred revolutions. The pills then weighed & recorded & the % of lost weight was measured.

$$F = [W_{(initial)} - W_{(final)}] / W_{(initial)} * 100$$

Mechanical Strength

Pills must be mechanically strong enough to withstand stresses during production, packing, & delivery. Mechanical strength is determined by 2 key parameters: friability and crushing strength. Pill or Crushing Strength Strength in tensile: It is the force needed to shatter a pill in the radial direction by pressure; it is essential to remember that high strength of crushing, decreases time of disintegration. Pfizer hardness analyser were used to determine the pill's strength of crushing. An average of three observations is used to compute it. Equation T is used to determine the tensile strength for crushing (T).

$$T = 2F / \pi * d * t$$

Where, F is the crushing load, and d and t denote the diameter and thickness of the pill respectively.[29]

Measurement of Pill Porosity

The porosity of a pill may be measured with a hg penetrating porosimeter. The porosity of a pill (ε) may be determined by the following equation.

$\varepsilon = 1 - m / (\rho t V)$

Where ρt is the true density, and m and V are the weightand volume of the tablet, respectively.[30]

Mechanism of action of disintegrants[33, 34]

One or more of the processes mentioned below causes the tablet to break down into fundamental particles.

- By swelling
- By capillary action
- Because of heat of wetting
- By enzymatic action
- Due to release of gas
- Due to deformation
- Due to disintegrating particle/ particle repulsive force

Swelling

Swelling is the most generally recognised general process for pill breakdown. Leading to a shortage of sufficient swelling force, pills with a porous structure disintegrate poorly. But at the other side, the pill with limited porosity exerts adequate swelling force. It's important to note that even if the packing percentage is quite large, fluid cannot enter the pill and breakdown slows again.

Porosity and capillary action (Wicking)

The initial stage is usually dissolution through capillary forces. When we immerse the pill in an appropriate aqueous medium, the medium enters the tablet and replaces the air adsorbed on the particles, weakening the intermolecular link & causing the pill to shatter into tiny particles. Pill water absorption is influenced by the drug's or excipient's hydrophilicity as well as tableting circumstances. The preservation of a porous structure and low interfacial tension towards aqueous fluid is required for these kinds of disintegrants, which aids in dissolution by forming a hydrophilic network surrounding the drug particles.

Because of heat of wetting (air expansion)

When exothermic emulsions are saturated, localised tension is produced as a result of capillary air expansion, which aids in pill disintegration. However, this theory is restricted to a few kinds of disintegrants & does not well explain the behaviour among most current

disintegrating agents.

By enzymatic reaction

Body enzymes function as disintegrants in this case. These enzymes assist in dissolution by destroying the complex formation of the binders. Because of swelling, pressure applied in the radial or outer direction causes the pill to rupture or the faster absorption of H_2O, resulting in an immense rise in the volume of granules to promote dissolution.

Due to release of gases

When pills are moist, CO_2 is produced owing to the interactions of carbonate and bicarbonate with tartaric acid or citric acid. The tension inside the pill causes the pill to dissolve. This fizzy combination is used by pharmacists when they need to make extremely quickly dispersing pills. Because these disintegrants are extremely sensitive to minor variations in temperature and humidity, careful environmental control is needed during pill production. The fizz mix may be introduced either just before compaction or in 2 distinct fractions of the composition.

Due to deformation

Disintegrated particles are distorted during pill compression, and when they come into touch with liquid medium like H_2O, they revert to their original shape. When granules were substantially distorted upon pressure, starch's swelling intensity was sometimes enhanced. The pill breaks apart due to the increased size of the distorted particles.

Due to disintegrating particle/particle repulsive forces

Another disintegrant method that tries to explain pill swelling is the use of non-swellable disintegrants. Guyot-Hermann suggested a particle repulsion hypothesis based on the fact that non swelling particles also induce pill breakdown. The process of dissolution involves electric repelling interactions between water & particles are needed. Scientists discovered that wicking comes second to repulsion, Figure 1 & 2.

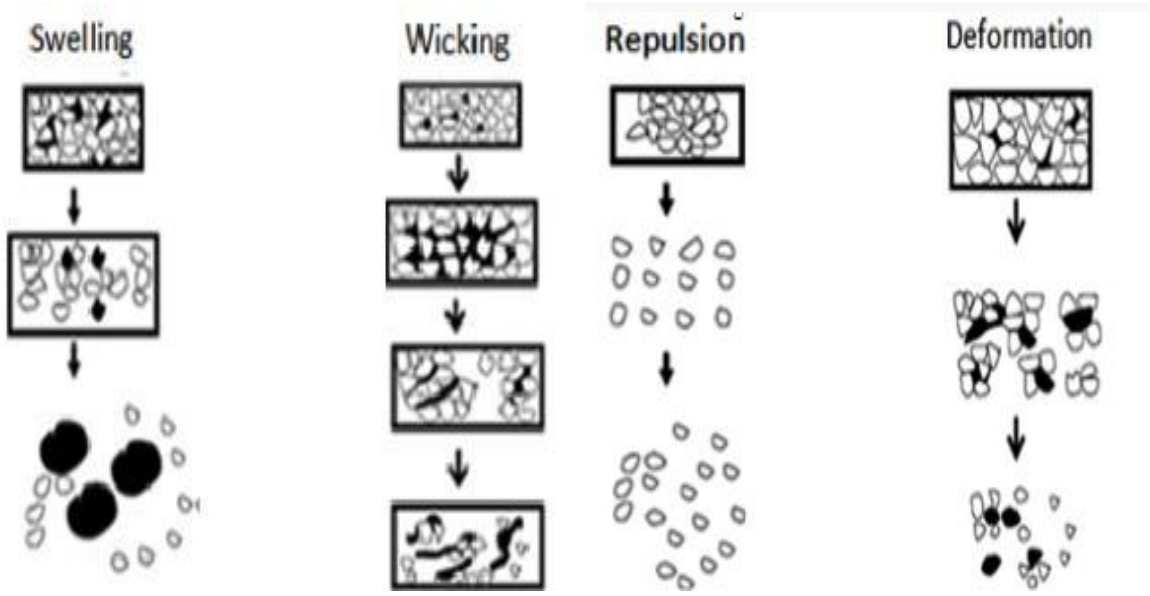

Figure 1: Dissolution of tablets via swelling and wicking mechanism[35]

Figure 2: Disintegration of Orodispersible tablets.[36]

Challenges In Formulating FDTs[37-41]

Palatability

The active components in most mouth dissolving medicine delivery systems crumble in the sufferer's buccal mucosa, bringing them into touch with the taste receptors; therefore, masking of taste of the medicines are essential to sufferers compliance.

Mechanical strength

FDTs are manufactured with a weak pressure force to enable them to dissolve in the oral, that makes pills brittle & friable, hard to tackle, & frequently necessitates specialist peel-off blister packaging, which can raise the amount. Just some techniques, like CIMA Labs Durasolv and Yamanouchi Shaklee's Wowtab, can create pills that are hard and robust enough for packed in multi dose bottle.

Hygroscopicity

Most are hygroscopic, meaning they lose their physical integrity when exposed to normal humidity & temperatures. As a consequence, they need humidity protection, which necessitates the use of specific product packaging. The drugdose has to be less than 60 mg for soluble medications in lyophilized dosage forms & less than 400 mg for insoluble medicines.

Patented Technologies[42]

The quick dissolution property of FDTs is due to the rapid entry of water into the pill matrix, leads to rapid breakdown. Various techniques were created & patented by pharmaceutical firms based on composition characteristics & various procedures. The following is Table 3 of patented technologies.

Table 3: Important patented technologies for preparation of FDTs.[43]

S. No.	Technique	Advantages	Disadvantages
1	Orasolv	Taste masking is two fold, quick dissolution	Low mechanical strength
2	Zydis	Quick dissolution, self preserving and increased bioavailability	Expension process, poor stability at higher temperature and humidity
3	Flashdose	High surface area for dissolution	High temperature required to melt the matrix can limit the use of heat sensitive drugs, sensitive to moisture and humidity
4	Durasolv	Higher mechanical strength than orasolv, good rigidity	Inappropriate with larger dose
5	Wow tab	Adequate dissolution rate and hardness	No significance change in bioavailability
6	Zipet	Good mechanical strength, satisfactory properties can be obtained at high dose (450mg) and high weight (850mg)	As soluble component dissolves, rate of water diffusion in to tablets is decreased because of formation of viscous concentrated solution

List of Patented technologies based branded Products

The list of patented technologies and their brand products are given in Table 4.

Table 4: For patented technology and their brand products.[43]

S. No.	Technology	Patent Owner	Process involved	Drugs used (Brand Name)
1	Quicksolv	Jansen Pharmaceutical	Lyophilization	Cisapride monohydrate (propulsid quicksolv), Risperidone (Risperdal m-tab)
2	Zydis	R.P. Scherer Inc	Lyophilization	Loratidine (Claritin Reditab and Dimetapp quick dissolve)
3	Lyoc	Farmlyoc	Multiparticulate compressed tablets	Phloroglucinol hydrate (Spasfon Lyoc)
4	Flashtab	Ethpharm	Lyophilization	Ibuprofen (Nurofen flashtab)
5	Durasolv	Cima labs Inc	molding	Hyoscyamine Sulfate (Nulev) Zolmitriptane (Zolming ZMT)
6	Orasolv	Cima Labs	Compressed tablets	Paracetamol, Zolmitriptane
7	Wow tabl	Yamanouchi Pharma Technologies, Inc.	Compressed molded tablets	Famotidine (Gaster D)
8	Rapi Tab	Schwarz Pharma	Compressed tablets	-
9	Fast melt	Elan corp	Molding	-
10	Oraquick	KV Pharm.co.Inc.	Micromask Taste masking	Hyoscyamine sulfate ODT
11	Flashdose	Fuisz technology Ltd.	Cotton candy process	Tramadol HCl (Relivia Flash dose)
12	Ziplets	Eurand	Molding	Ibuprofen (Cibalgina Due fast)
13	Advatab	Eurand International	Microcaps and Diffuscap CR Technology	Adva tab cetirizine, Advatab Paracetamol

CONCLUSION

The FDT concept was created to solve a few troubles which exist in conventional solid types, such as trouble in engulfing pills in children & the elderly, who make up a large portion of the earth's community. FDT may improve efficacy, bioavailability, quick onset of action, & sufferers' compliance because of rapid incorporation from buccal cavity to GI Tract when saliva pass. A quick disintegrating pills behaves as a solid when administered exterior of body & as a liquid when taken up within the body. Quick dissolving pills can become the extremely widely recognized & recommended type in the future because of its rapid impact. Their intrinsic benefits, like taking up without H2O, anyplace, at any time, lead to better suferrer compliance in now a days tough environment. Given lots of advantages of quick dissolving pills, most pharmaceutical companies offer a range of FDT formulations. As a consequence of rising sufferer demand, various dosage forms will definitely become more

common in the future.

REFERENCES

1. Habib W, Khankari R, Hontz J. Fast-dissolve drug delivery systems. Critical Reviews in Therapeutic Drug Carrier Systems, 2000; 17(1).
2. Seager H. Drug-delivery products and the Zydis fast-dissolving dosage form. Journal of pharmacy and pharmacology, 1998 Apr; 50(4): 375-82.
3. Kuchekar BS, Badhan AC, Mahajan HS. Mouth dissolving tablets: A novel drug delivery system. Pharma times, 2003 Jun; 35(1): 7-9.
4. Allen Jr LV, Wang B, inventors; University of Oklahoma, assignee. Particulate support matrix for making a rapidly dissolving tablet. United States patent US 5,595,761, 1997 Jan 21.
5. Pebley WS, Jager NE, Thompson SJ. Rapidly disintegrating tablet. US patent, 1994 Mar; 5(298): 261.
6. Liang AC, Chen LL. Fast-dissolving intraoral drug delivery systems. Expert opinion on therapeutic patents, 2001 Jun 1; 11(6): 981-6.
7. Morita Y, Tsushima Y, Yasui M, Termoz R, Ajioka J, Takayama K. Evaluation of the disintegration time of rapidly disintegrating tablets via a novel method utilizing a CCD camera. Chemical and pharmaceutical bulletin, 2002; 50(9): 1181-6.
8. Schiermeier S, Schmidt PC. Fast dispersible ibuprofen tablets. European journal of pharmaceutical sciences, 2002 Apr 1; 15(3): 295-305.
9. Siewert M, Dressman J, Brown CK, Shah VP, Aiache JM, Aoyagi N, Bashaw D, Brown C, Brown W, Burgess D, Crison J. FIP/AAPS guidelines to dissolution/in vitro release testing of novel/special dosage forms. Aaps Pharmscitech, 2003 Mar; 4(1): 43-52.
10. Fu Y, Yang S, Jeong SH, Kimura S, Park K. Orally fast disintegrating tablets: developments, technologies, taste-masking and clinical studies. Critical Reviews™ in Therapeutic Drug Carrier Systems, 2004; 21(6).
11. Bogner RH, Wilkosz MF. Fast Dissolving Tablets: New Dosage Convenience. US pharmacist, 2002; 27(3): 34-43.
12. Reddy LH, Ghose B and Rajneesh, Indian J. Pharm. Sci, 2002; 64(4): 331-336.
13. Kuchekar BS and Arumugam V, Indian J. Pharm. Edu, 2001; 35: 150.
14. Bhaskaran S, and Narmada GV, Indian Pharmacist, 2002; 1(2): 9-12.
15. Indurwade NH, Rajyaguru T H and Nakhat PD, Indian Drugs, 2002; 39(8): 405-09.
16. Devrajan, PV and Gore SP, Express Pharma Pulse, 2000, Nov. 23; 7(1): 16.

17. Kuchekar BS and Arumugam V, Indian J. Pharm. Edu, 2001; 35: 150.
18. Slowson M, Slowson S. What to do when patients cannot swallow their medications. Pharma Times, 1985; 51(1).
19. Chang RK, Guo X, Burnside BA, Couch RA. Fast-dissolving tablets. Pharmaceutical technology, 2000; 24(6): 52.
20. Bonger RH, Wilkosz MF, Fast dissolving Tablet. Accessed, 2008.
21. Anon, Flavors and Flavoring, Int J Pharm Compounding, 1997; 1: 90-92.
22. Fiese EF, Hagen TA, Lachman L, Lieberman HA, Kanig JL. The theory and practice of industrial pharmacy. Lachman, L., Lieberman, HA, Kanig, JL, Eds, 1987; 171.
23. Lindberg NO, Pålsson M, Pihl AC, Freeman R, Freeman T, Zetzener H, Enstad G. Flowability measurements of pharmaceutical powder mixtures with poor flow using five different techniques. Drug development and industrial pharmacy, 2004 Jan 1; 30(7): 785- 91.
24. Yadav G, Kapoor A, Bhargava S. Fast dissolving tablets recent advantages: A review. International journal of pharmaceutical sciences and research, 2012 Mar 1; 3(3): 728.
25. Pharmacopoeia I. Controller of publications. New Delhi, 1996; 2: 764.
26. Siddiqui MN, Garg G, Sharma PK. Fast dissolving tablets: preparation, characterization and evaluation: an overview. International Journal of Pharmaceutical Sciences Review and Research, 2010 Sep; 4(2): 87-96.
27. Liberman HA, Kanig JL. The theory and practice of industrial pharmacy.
28. Khan S, Kataria P, Nakhat P, Yeole P. Taste masking of ondansetron hydrochloride by polymer carrier system and formulation of rapid-disintegrating tablets. AAPS pharmscitech, 2007 Jun; 8(2): E127-33.
29. Bi YX, Sunada H, Yonezawa Y, Danjo K, Evaluation of rapidly disintegrating tablets prepared by a direct compression method, Drug Dev Ind Pharm, 1986; 25: x, 571-581.
30. Iles MC, Atherton AD, Copping NM, inventors; Catalent Pharma Solutions Inc, assignee. Freeze-dried dosage forms and methods for preparing the same. United States patent US 5,188,825. 1993 Feb 23.
31. Morita Y, Tsushima Y, Yasui M, Termoz R, Ajioka J, Takayama K. Evaluation of the disintegration time of rapidly disintegrating tablets via a novel method utilizing a CCD camera. Chemical and pharmaceutical bulletin, 2002; 50(9): 1181-6.
32. Shukla D, Chakraborty S, Singh S, Mishra B. Mouth dissolving tablets II: An overview of evaluation techniques. Scientia Pharmaceutica, 2009 Jun; 77(2): 327-42.
33. Fu Y, Yang S, Jeong SH, Kimura S, Park K. Orally fast disintegrating tablets:

developments, technologies, taste-masking and clinical studies. Critical Reviews™ in Therapeutic Drug Carrier Systems, 2004; 21(6).

34. Rish RK. A review on fast dissolving tablets techniques. The pharma review, 2004; 2(1): 32.
35. Pahadia A, Gawde R, Agrawal S, Manocha N. Utilization of Natural Superdisintegrants in Orodispersible Tablets: A Review. International Journal of Pharmacy Research & Technology, 2013; 3: 06-10.
36. www. Pharmatips-Article, Sustained -release multiple unit-dispersible tablets.
37. Goel H, Rai P, Rana V, Tiwary AK. Orally disintegrating systems: innovations in formulation and technology. Recent patents on drug delivery & formulation, 2008 Nov 1; 2(3): 258-74.
38. Brown D. Orally disintegrating tablets-taste over speed. Drug Delivery Technol, 2003; 3: 58-61.
39. Aurora J, Pathak V. Oral disintegrating technologies: Oral disintegrating dosage forms: An overview. Drug Deliv Technol, 2005; 5(3): 50-4.
40. Ghosh TK, Chatterjee DJ, Pfister WR, Jarugula VR, Fadiran EO, Hunt JP, Lesko LJ, Tammara VK, Hare DB. Quick-Dissolving Oral Dosage Forms: Scientific and Regulatory Considerations from a Clinical Pharmacology and Biopharmaceutics Perspective. DRUGS AND THE PHARMACEUTICAL SCIENCES, 2005 Feb 28; 145: 337.
41. Sugihara M, Hidaka M, Saitou A. Discriminatory features of dosage form and package. Jpn J Hosp Pharm, 1986; 12: 322-328.
42. Modi A, Tayade P. Enhancement of dissolution profile by solid dispersion (kneading) technique. AAPS pharmscitech, 2006 Sep; 7(3): E87-92.
43. Takagi H, Kajiyama A, Yanagisawa M, inventors; Yamanouchi Pharmaceutical Co Ltd, assignee. Rapidly disintegrable pharmaceutical composition. United States patent US 6,899,899. 2005 May 31.